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Preface

“Not what we have, but what we enjoy, constitutes our abundance.”
-J Petit-Senn

A second edition is both an opportunity and an enigma. It is an opportunity to improve on the original, to make it bigger, more insightful, clearer—simply better. Coming on the heels of a first edition that was very well received, it is a pleasure for us to aim higher. But if the original was a success, the revision is also an enigma, or even a hazard: how do we make a book that keeps the best of the old while adding the most of the new?

The *Clinical Veterinary Advisor: Dogs and Cats,* second edition, has aimed from the very beginning to find the best possible balance in this regard. The basic structure and content of the book should be recognizable to all readers of the first edition. Nevertheless, there are many innovations to be found here. There are all-encompassing changes within the repeating template structure of chapters, and there are also dozens of individual new chapters. Individual overview statements in 800 of the chapters now help guide the reader-practitioner toward implementing recommendations in a practical fashion. A great deal of new information for clients and for technicians is now available. Every chapter that was included in the first edition appears again in the second edition fully revised and updated; some have changed names to remain current (hemobartonellosis now appears as hemotropic mycoplasmosis, hepatocutaneous syndrome is now superficial necrolytic dermatitis, and so on), but users of the first edition can be assured that they will find up-to-date versions of all chapters in this edition. This has indeed been the greatest challenge: keeping the very best, trimming or condensing obsolete or duplicated facts, and introducing worthwhile new material. Doing so has required a herculean effort from authors and editors. George Bernard Shaw faced the same issue when he finished a letter of recommendation for a friend. In a note pinned to the letter, Shaw wrote, “Sorry the letter is so long. I didn't have time to write you a short one.” Similarly, the *Advisor's* authors and section editors had ample material at their disposal, but unlike Shaw, they seem to have spared no effort in distilling the most valuable essentials out of it. Their efforts translate into chapters that are focused, user-friendly, and up to date. Like the unreachable horizon, the permanent goal for which the *Advisor* will continue to strive is for its users to read each paragraph on every page and think “This is exactly what I wanted to know.”

A new edition is justified when there has been substantial change, and updates need to be introduced. These improvements should be evident to all readers through both changes in existing chapters, and the introduction of new chapters. **Over 60 new topics have been created and added to this new edition.** They are summaries of a wide range of disorders such as the MDR-1 (ABCB1) mutation, Xylitol toxicosis, Adulterated diets, Fear due to veterinary visits, Canine influenza, and dozens of others. The novelty of these topics is matched by their clinical relevance, and the appearance of these new chapters is a testament to their importance in veterinary practice. They are presented in the same chronological template format that reflects the way the patient is received and treated: Background information, then chief complaint and history, then physical exam, then analysis (etiology, pathophysiology, differential diagnosis), diagnosis, treatment, and outcome. Every topic has one or more current Suggested Reading sources for additional information, and these have, as much as possible, been drawn from easily accessible journals and textbooks. There are many, many new photographs and illustrations, to convey information graphically for those of us who are visual learners. The photographs in the printed version of the book are also available in color in the online edition of the book.

Over a dozen new Procedures and Techniques have been added, bringing the number of procedure descriptions to over 100. These additions range from the immediately practical (Porcupine quill removal, Breeding soundness exam, Nebulization/coupage/respiratory therapeutics) to the referral-level (Tracheal stent placement, Ethanol ablation of parathyroid nodules, Brain biopsy [stereotactic]). As before, these procedures are described in a step-wise, template-based format, and their inclusion is as much for clinicians involved in actually performing them as for attending veterinarians who plan to refer the patient and simply want to understand what is involved in the procedure.

An important set of specific improvements applied *en masse* to all Section I (Diseases & Disorders) chapters is the addition of clinical guidance statements. Chapters now have two new subsections within their Diagnosis and Treatment sections, called Diagnostic Overview and Treatment Overview, respectively. Briefly, the format of chapters in the first edition allowed for diagnostic tests to be presented in an orderly and clear manner. However, there was a risk of the “laundry list effect”: just because all relevant tests were stated

did not mean that the reader would know how to apply them, or which tests to use when. The information might be encyclopedic, but veterinary practice runs more along the lines of a narrative. In this new edition, authors covering every disease and disorder were tasked with adding a Diagnostic Overview statement to provide basic clinical guidance for achieving a reasonable diagnosis of the disorder in question. The result is a positive and deeply rewarding one. These overview statements now provide the insight of authors not only on what can be done but realistically what should be done to achieve a basic working diagnosis. A typical Diagnostic Overview statement for parvoviral enteritis of dogs, for example, states: “The diagnosis is suspected based on the presence of anorexia, vomiting, diarrhea, lethargy, or a combination of these, typically in a young and usually unvaccinated dog; confirmation requires fecal assay such as a parvovirus ELISA snap test.” It need not be complicated, and is not meant to address every conceivable variation of the disease. Rather, these overviews are a starting point for outlining a reasonable course of action. They offer a summary of expertise, “from the trenches,” of what should be considered when working up a typical patient suspected of having a particular disorder. Similarly, Treatment Overviews aim to address the unspoken questions that come up when looking at a list of possible medications or interventions: which treatments should be applied? In which cases? Overall, these changes are meant to improve what the book has to offer: not just facts, but insights into application of the information provided.

The “health care team” approach is far from an abstract concept. For many of us, our animal health technician colleagues spend as much time with our patients, if not more. To that end, **the *Advisor* now contains hundreds of Technician Tips** that were not available previously. The breadth of this information ranges from nursing care to client counseling, from technical skills required when caring for patients with a certain disorder, to common pitfalls to avoid. The overlap between what a veterinarian needs to know and what a technician needs to know is substantial, and this new chapter section recognizes this important interaction.

Perhaps one of the most innovative changes for this edition relates to client education sheets. These template-based, layperson's vocabulary-based summaries have been highly successful, with many, many positive comments and widespread use. While it was tempting to expand the collection by summarizing more diseases for clients to understand, it was apparent that there was an even greater need in client education: the importance of clients’ grasping not just disease processes, but the actual instructions we give them when they go home. These are the monitoring and treatment activities that we instruct owners to carry out as a follow-through on our care. Sources for information of this type are very few. Client education sheets from most veterinary textbooks are dedicated to informing, but not necessarily empowering, the client; they discuss the entire disease, from mechanism to outcome, rather than concentrating on what we expect the client to be actively doing. Public sources of information, such as dog care manuals or healthy cat books, are useful, but the extent of home medical care they describe is often very limited: how to trim the nails or how to give a tablet may be covered, but how to provide elevated feedings for a patient with esophageal disease usually is not. Niche sources such as websites or specialty books offer an individual approach for specific disorders but not a whole series of “How to” summaries for home care. This is what is missing: information that helps clients carry out the ancillary medical tasks we ask them to do at home after we discharge the patient.

To address this information gap, the *Advisor* now contains a compilation of 50 original medical “How-to” client education sheets. These new information documents cover a wide range of common home management situations, including how to perform range-of-motion exercises on a patient with orthopedic or neurologic disease, how to adapt the home environment for a pet that has become blind or deaf, how to deal with incessant coughing, how to manage a dog or cat that is having a seizure, and how to feed a dog or cat that has an indwelling (PEG or other) feeding tube. The range of topics reaches from the simple (how to remove the scent from a dog or cat that has been sprayed by a skunk) through the mid-range (how to check a bandage or cast for tightness) to the more complex (how to assist appropriately during caesarian section). In many cases, one How-to client education sheet can apply to several diseases and disorders; How to monitor respirations and How to construct and use an Elizabethan collar are such examples. The goal of all of these sheets is to provide a reference that owners can consult when we have asked them to do something specific to help their companion. Variations and modifications to suit individual patients are inevitable, and these information sheets are written to provide a general summary that practitioners can use as a base for this type of information.

Finally, one of the dominant features of the *Advisor* is the solid link between the print and electronic editions of the book. Since it is only possible to obtain both together (neither website access nor the print book is sold individually), the universal access of the web book and the hands-on gratification of opening the print book are literally bound together. This interchange has allowed for some of the less widely used material, or some chapters that overlap substantially with other chapters, to be updated and published only in the web

version of the book for this edition. As a result, the paper book remains portable, and the web book is comprehensive. Over time, the growth of information together with the limitations of a single volume book meant to be portable, means that we may rely on the web book as the vault of information and the paper book as the wallet. It is my hope that this approach will bring about the best of both worlds: new information is introduced without expanding the physical size of the paper book, and all the information can be found, whether one has the paper book handy or not, anywhere at any time online. Even those of us who consider ourselves bookworms will recognize the value of having online availability if we have worked relief shifts at other hospitals where the textbook selection is poor, or have found ourselves in an emergency setting searching for information on an uncommon topic in the middle of the night. Ultimately, this balanced approach is meant to be the answer to the riddle “How do we grow without getting bigger?”

As I noted in the first edition, it would be a pleasure to say that this edition of the *Advisor* will answer every question that comes up in small animal practice. We all know that an honest assessment of any book says otherwise. With the changes we have made, my hope is that past readers will be pleased to find that their early interest in the *Advisor* remains well founded, and that new readers will discover a source of information that speaks to their interests.

Acknowledgments

It has been the selection of information and the careful consideration of what to include that has required the most energy when creating this second edition. To you, the *Advisor's* incredibly dedicated section editors and authors, I offer my heartfelt thanks. From this vantage point I can see perhaps better than anyone the time you took and the effort you expended to create this book. You painstakingly identified relevant new information from the literature and then carefully crafted the material, both old and new, into these compact synopses. For an enthusiastic and learned author, it can be much harder to write less than to write more. All of us know that with writing comes sacrifice: we are busy with many obligations, and much of the work of good writing and editing simply comes when time is available, at night, on weekends, or instead of doing something else. We are willing to do it when there is a positive result: something that shows we made a difference for the better. Ultimately, this collective effort has produced a result of which we deserve to be proud, as I hope you will be. I expect your efforts will be noticed by a great many readers, as they were for the first edition. Many, many readers have commented so favorably on it and this positive feedback is as good a validation as any for showing the effect of your work. Students and veterinarians have told me repeatedly that the *Advisor* is their first "go-to" resource when they want to learn about something they are unfamiliar with; in many hospitals, the book is used so heavily that it has been reduced to tatters (see below) and has had to be re-bound; several board-certified specialists have told me they use the book routinely for information within and outside their specialty; and I have received many, many emails and letters praising your work, simply summarized as: "I think this book is terrific." These testimonials, as much as anything I can say, indicate the far reach of your work and the positive impact of your authorship.

Validation of our work: this is how a book ends up looking when it is used often.

Penny, you and your team deserve perhaps more credit and recognition than have ever been given to a publisher. Under your leadership, the group (Lauren Harms [Developmental Editor], Rachel McMullen [Senior Project Manager], Catherine Jackson [Publication Services Manager], Bruce Siebert [Senior Producer], and Lynn Hoops [Marketing Manager]) has exceeded my every expectation from the earliest planning stages onward. No one could hope for a kinder, more gratifying, and more effective approach for bringing the book together. It has been a pleasure, and my wish for other authors is that they be as fortunate as I have been to work with such a determined, proactive, and fun group.

With or without realizing it, many individuals made this book possible by helping me personally during its creation. My mentor, Steve Ettinger, was unfailing in his constructive criticisms and support. Unbeknownst to him, his candid observations led to many improvements in this edition, both large and small. His positive feedback and kindness during the creation of this book are irreplaceable. Thank you as always, Steve. Elizabeth Charuvastra RN, CEO of Targeted Medical Pharma LLC, stepped in and offered me an editor's dream (office space and support) while I was in California during the final stages of completion of the book. I could not have imagined a better-timed or more welcome gift, Liz. Many, many thanks. Similarly, my good friend and colleague Kirstie Barrett made it possible for me to have an immediately-usable work space during my West coast visit, and for this I am truly grateful. My friend David Edward gets a testimony of gratitude for providing an industrial quantity of PG Tips tea. Many thanks to Richard, Deirdre, and Evan Denis for hospitality during multiple layovers in Toronto. I also wish to thank all readers who sent me feedback aimed at making the second edition better. These messages from the front lines of practice helped reshape some of the content of this edition for the better, as readers will see for themselves.

I thank all members of the Atlantic Veterinary College who contributed directly or indirectly, especially my colleagues who provided feedback, the technical staff (notably Elaine Reveler) who made it possible to generate good images and graphics, and the administration and faculty association who provided the framework and support for my academic work and sabbatical leave to dedicate time to the *Advisor* specifically.

Last and most personally, I thank my family for their support and understanding. An endeavor such as this book is built on sacrifices, and their acceptance of my well-worn refrain, "I can't—I have a deadline," was the epitome of support. François, Diane, Antoine, and above all Jennifer: thank you.

5-Fluorouracil Toxicosis

BASIC INFORMATION

DEFINITION

Adverse effects caused by exposure to 5-fluorouracil (5-FU), a pyrimidine analog-type antineoplastic antimetabolite drug used for palliative management of certain carcinomas in humans and occasionally in dogs.

SYNONYMS

Common brand names: Efudex, Fluoroplex, and Carac. Generic: 2,4-dioxo-5-fluoropyrimidine; 5-fluoro-2,4(1H,3H); pyrimidinedione; 5-FU; NSC 19893; Ro2-9757; CAS 51-21-8.

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs and cats of any age, breed, and either sex. Dog cases are more common. Dogs are more likely to develop neurologic effects (seizures) compared to humans. Cats are more sensitive to toxic effects of 5-FU than dogs.

RISK FACTORS

- Preexisting liver or kidney dysfunction can increase risk of toxicity
- Presence of 5-FU in a pet's environment

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- History of exposure to product containing 5-FU
- Clinical signs begin within 30 minutes to 5 hours of exposure.
- Vomiting, hypersalivation, lethargy, vocalization, diarrhea, tremors, ataxia, seizures
- Some animals show vomiting progressing quickly to seizures; others may show tremors and seizures and no vomiting.

PHYSICAL EXAM FINDINGS

- Seizures (often status epilepticus)
- Vomiting (with or without blood)
- Diarrhea (with or without blood)
- Tremors
- Lethargy
- Ataxia
- Cardiac arrhythmias (all kinds)
- Respiratory depression

ETIOLOGY AND PATHOPHYSIOLOGY

Source

5-FU or similar agents are available for use as injection, topical creams (0.5%-5%) or lotions (1%-5%), and capecitabine (prodrug of fluorouracil) as tablets. Flucytosine is an antifungal agent that must be converted to 5-FU.

Toxicosis occurs after ingestion of products containing 5-FU and occasionally secondary to repeated use in dogs or cats.

Mechanism of Toxicosis

5-FU inhibits RNA processing and function and DNA synthesis and repair, inhibiting cell division. Actively dividing cell lines (bone marrow stem cells, intestinal crypt cells) are most affected.

The mechanism of neurotoxicity may be production of fluorocitrate, which limits cellular energy production by interfering with the Krebs cycle.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

History of exposure and presence of clinical signs consistent with exposure to 5-FU within 30 minutes to 5 hours after exposure

DIFFERENTIAL DIAGNOSIS

Diseases or intoxications that could cause vomiting (see p. 1173) and/or seizures (see pp. 1009 and 1425)

INITIAL DATABASE

- Serum biochemistry profile (elevated liver enzymes, azotemia possible in 24 hours)
- Electrolytes (hypokalemia possible due to severe vomiting, diarrhea)
- CBC with differential (baseline, monitor q 24-72 hours for 20 days); initial leukocytosis followed by evidence of myelosuppression, leukopenia, pancytopenia in 5-20 days. Hematocrit increased due to dehydration then decreased due to gastrointestinal (GI) bleeding.
- Blood gas analysis
- Urinalysis

ADVANCED OR CONFIRMATORY TESTING

- Analysis of 5-FU and its metabolites in plasma is possible but often difficult to obtain in timely fashion for acute toxicoses.
- Necropsy lesions: hemorrhagic colitis, GI mucosal ulceration (throughout), stomatitis, myocardial ischemia, pulmonary edema, hepatic and renal congestion

TREATMENT

TREATMENT OVERVIEW

Stabilize the patient first; control vomiting and seizures. Provide supportive care once the animal has been stabilized.

ACUTE GENERAL TREATMENT

- Decontamination of asymptomatic patient
  - Emesis using activated charcoal with a cathartic if patient is showing no clinical signs and the ingestion is recent (<1 hour)
  - Hemodialysis, peritoneal dialysis, or fluid diuresis may enhance elimination
- Manage vomiting
  - Maropitant, 1 mg/kg SQ q 24 h for up to 5 consecutive days
  - Do not use metoclopramide (contraindicated with GI hemorrhage and seizure disorder)
- GI protection
  - Sucralfate, 0.5 (small dog) to 1 gram (large dog) PO q 8 h
  - Famotidine, 0.5-1 mg/kg IV or PO q 12-24 h; or omeprazole, 0.5-1 mg/kg PO q 24 h
- Manage tremors and seizures (see p. 1009)
  - Seizures are rarely controlled with diazepam alone (dogs: 2-5 mg/kg IV; cats: 0.5-1 mg/kg IV). If seizures persist after diazepam therapy, give phenobarbital IV bolus, 2-5 mg/kg (can be repeated at 20-minute intervals up to two times). May then add phenobarbital IV infusion (2-10 mg/hour IV, titrated to effect) to diazepam; *or*
  - Pentobarbital, 3-15 mg/kg IV slowly to effect; *or*
  - Propofol, 4-6 mg/kg IV or as continuous IV infusion 0.6 mg/kg/min; *or*
  - Gas anesthesia
- Intravenous fluids
- Thermoregulation (correct hypothermia)
- Ventilatory support as needed
- Maintain normal acid-base status and electrolyte balance
- Manage pain
  - Butorphanol, 0.2-0.4 mg/kg q 2-5 h SQ, IM, or IV (dogs); 0.1-1 mg/kg IM, IV, or SQ q 1-3 h (cats); or tramadol, 1-4 mg/kg PO q 6-8 h; or buprenorphine, 0.005-0.05 mg/kg, IM, IV q 4-8 h; *or* fentanyl patch
- Consider giving broad-spectrum antibiotics to prevent secondary infection.
- For neutropenia: filgrastim (Neupogen), 4-6 mcg/kg SQ

CHRONIC TREATMENT

Intensive supportive care may be needed for days/weeks, especially if myelosuppression occurs.

NUTRITION/DIET

Tube feeding or bland diet if GI signs

DRUG INTERACTIONS

Metronidazole may increase toxicity of 5-FU by reducing clearance.

POSSIBLE COMPLICATIONS OF TREATMENT OR DISEASE PROCESS

- Severe brain damage from uncontrolled seizures
- Neutropenia, pancytopenia, myelosuppression (in 5-20 days)

RECOMMENDED MONITORING

- Heart rate, blood pressure
- Respiratory rate and character
- CBC (myelosuppression in 5-20 days), serum biochemistry profile (liver and kidney function)
- Blood gases

PROGNOSIS AND OUTCOME

Guarded to poor, once signs occur. Out of 72 cases of 5-FU toxicosis, 35 dogs died and 11 were euthanized.

PEARLS & CONSIDERATIONS

COMMENTS

- Severe signs or death can result from 5-FU toxicosis; early decontamination and immediate, intensive treatment are essential, and owners should be advised of the seriousness of exposure to 5-FU.
- Estimated toxic dose likely to cause clinical signs in dogs: 8.6 mg/kg PO. Minimum lethal dose in dogs: 20 mg/kg PO. If a 70-lb dog (32 kg) ingests 1 tablespoon (15 g) from a tube containing 5% 5-FU, the dose of 5-FU in this dog will be approximately 23 mg/kg, a potentially lethal dose.

PREVENTION

Keep medications out of pets' reach

TECHNICIAN TIPS

Estimating the ingested amount by obtaining a good history of exposure may predict the prognosis early on.

CLIENT EDUCATION

5-FU toxicosis in pets can be life threatening.

SUGGESTED READING

Albretson J: 5-Fluorouracil Toxicosis in dogs. Vet Med 96:270–274, 2001

AUTHOR: SHARON WELCH

EDITOR: SAFDAR KHAN

Abdominal Compartment Syndrome

BASIC INFORMATION

DEFINITION

Impaired organ function resulting from increased intraabdominal pressure (IAP >20 mm Hg). This syndrome is likely underrecognized in veterinary medicine and has a high prevalence in human ICU patients.

SYNONYMS

ACS, increased IAP, intraabdominal hypertension (IAH)

EPIDEMIOLOGY

SPECIES, AGE, SEX

No species, age, sex, genetic, or breed predisposition

RISK FACTORS

- Any patient with abdominal disease or accumulations of fluid, gas, or tissue in the abdominal cavity can develop elevated IAP.
- Specific risk factors include underlying diseases that lead to gas or fluid accumulation in the abdominal compartment (within organs, viscera or as free fluid) or interfere with the abdominal wall's ability to expand and compensate for increased abdominal contents.
    - Abdominal effusion
    - Abdominal neoplasia
    - Abdominal surgery or trauma (most common causes)
    - Abdominal wraps/bandages
    - Decreased abdominal wall compliance (edema, hematoma, muscle activity)
    - Hepatic abscess
    - High-volume fluid resuscitation
    - Ileus
    - Pancreatitis
    - Peritonitis
    - Sepsis

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Primary ACS: intraabdominal cause, most commonly postoperative or trauma patients
- Secondary ACS: extraabdominal cause, most commonly sepsis or burn patients that require aggressive fluid resuscitation
- Recurrent ACS: redevelopment of ACS after surgical or medical treatment for primary or secondary ACS

HISTORY, CHIEF COMPLAINT

- Frequent history of abdominal trauma or surgery
- Indications to check IAP are (usually in combination):
    - New or progressive organ failure
    - Particularly azotemia, reduced urine output
    - Elevated central venous, mean arterial, right and left atrial pressures
    - Rising intracranial pressure, altered mentation
    - New vomiting and diarrhea
    - Acidosis, rising blood lactate levels

PHYSICAL EXAM FINDINGS

- Physical examination and abdominal perimeter (girth) measurements are insensitive for detecting elevated IAP.
- Progressive abdominal distension or tympany, jugular vein distension, tachypnea, tachycardia are possible

ETIOLOGY AND PATHOPHYSIOLOGY

- IAP in healthy adults is subatmospheric − 0 mm Hg; IAP in critically ill adults is 5-7 mm Hg.
- IAH is defined as a sustained elevation in IAP = 12 mm Hg.
- ACS (sustained IAP > 20 mm Hg with new organ dysfunction/failure) develops if IAH is not recognized and treated.

- ACS is not a disease, but a distinct syndrome of clinical signs and abnormalities that can have multiple causes.
- At low intraabdominal volumes, the abdominal wall is very compliant. Large increases in abdominal volume result in minor increases in IAP. At higher abdominal volumes, abdominal wall compliance decreases, and even small increases in volume can cause major increases in IAP.
- Increased pressure in the abdomen leads to hypoperfusion and ischemia of abdominal organs and, when severe, direct compression of blood vessels. This leads to alterations in renal (most recognized), hepatic, and gastrointestinal functions. Anuria can occur with IAP > 30 mm Hg. Liver function, including cytochrome P450 function, is impaired. Intestinal edema can develop, as well as bacterial translocation through gastrointestinal walls.
- Reduced ability for the diaphragm to contract against the tense abdomen impairs tidal volume and compromises ventilation, resulting in hypoxia and hypercapnia. Mechanical/positive pressure ventilation is similarly affected.
- Increase in central venous pressure (CVP) and drop in cardiac output (increased systemic vascular resistance, decreased venous return to the heart, compression of vascular structures from increased intrathoracic pressure) result in altered cardiovascular function.
- Intracranial pressure elevations can occur because of elevated CVP.
- Hormonal changes occur in response to the altered cardiovascular state, including elevations in renin-angiotensin activity, antidiuretic hormone, and catecholamine levels.
- Ischemia-reperfusion injury occurs after shock resuscitation and can affect distant organ function.
- Abdominal wall complications can occur secondary to hypoperfusion, including delayed or impaired wound healing, dehiscence, and surgical site infection.
- Recognition of increasing IAP and prevention of ACS are crucial to reducing morbidity and mortality.
- There is no single threshold IAP that will result in organ dysfunction or failure in all patients and can be used for decision making. The critical IAP in most patients is between 10 and 15 mm Hg; at this pressure, initial organ dysfunction develops.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

IAP must be measured to confirm the diagnosis of abdominal compartment syndrome.

INITIAL DATABASE

Most common method of measuring IAP is the intravesicular or “bladder” technique, which is an indirect measurement.

- A water manometer is attached to a stopcock in the evacuation line from a standard urinary (urethral) catheter.
- The urinary bladder is emptied, and a few milliliters of isotonic sterile saline are placed in the bladder (3-10 mL, depending on patient size).
- After 30-60 seconds (to allow the saline to warm and the detrusor muscle to relax, avoiding a falsely elevated reading), the zero mark on the manometer is held at the level of the cardiac atria (level of the umbilicus in lateral recumbency).
- The manometer is filled with saline.
- The stopcock is then opened to the bladder.
- The reading (in mm Hg) is taken when the column of saline reaches a stable level.
- The measurement should be taken at end expiration.
- Abdominal muscle contractions can increase IAP readings. Obese patients may have a higher baseline IAP.
- Alternative measurement techniques include nasogastric balloon catheter (good for continuous measurement), direct intraabdominal catheter/abdominal drain, and venous catheter in the caudal vena cava. These techniques give similar information but can be more cumbersome to place and maintain.
- Trends in pressure parameters may be more important than any single number. It is important to use the same positioning each time a measurement is taken.
- The IAP measured at one point in the abdominal cavity can be assumed to be the pressure throughout the abdominal cavity.
- Imaging can be helpful for looking for underlying causes of IAH but is insensitive at detecting increased IAP.

ADVANCED OR CONFIRMATORY TESTING

- Repeated IAP measurements are essential for monitoring.
- Lactate levels, liver enzyme changes, urine output, blood urea nitrogen, and creatinine levels to identify abdominal organ dysfunction associated with ACS
- Measurements of cardiac output and other cardiovascular parameters and monitoring mentation and intracranial pressure give a more extensive assessment of cardiovascular function and perfusion.
- Abdominal perfusion pressure (APP; mean arterial pressure minus IAP) has been proposed as a more accurate predictor of visceral perfusion. It assesses the severity of IAP, as well as the adequacy of abdominal blood flow, and should be maintained at 50-60 mm Hg in patients with IAH/ACS.

TREATMENT

TREATMENT OVERVIEW

Medical management is crucial to prevention and treatment of IAH. Surgical decompression is the definitive treatment if medical management fails to prevent further increases in IAP and organ dysfunction and failure.

ACUTE, GENERAL TREATMENT

- IAP of 10-20 mm Hg is a mild elevation and should be monitored.
- IAP of 20-35 mm Hg is a moderate to severe elevation.
    - Consider active (centesis or surgical) decompression if pressure continues to rise or if other parameters continue to deteriorate.
- IAP > 35 mm Hg is a severe elevation.

    - ACS is extremely likely.
    - Abdominal decompression is required.
    - If a correctible source is not identified, surgical exploratory laparotomy is indicated.
- Medical Management
    - Sedation, analgesia, and/or neuromuscular blockade to reduce muscle tone secondary to pain, agitation, and ventilator dyssynchrony, which result in increased IAP
    - Not effective at treating severe IAH/ACS
    - Nasogastric or colonic decompression can reduce IAP and treat mild/moderate IAH.
    - Prokinetic motility agents useful in decreasing visceral volume
    - Aim for euvolemia.
    - Hypervolemia can lead to ACS development.
    - Hypertonic crystalloid and colloid resuscitation shown to reduce IAP and decrease risk of ACS
    - Diuretics to mobilize third space fluid accumulation
    - Percutaneous decompression to remove free abdominal fluid or air
    - If this fails to resolve IAH, patient must undergo surgical decompression.
- Surgical Management (VERY rare in companion animals, barring arterial hemorrhage)
    - Direct removal of the fluid or tissue causing the problem
    - Performed when organ dysfunction/failure and IAH are refractory to medical management
    - Open abdomen or temporary abdominal closure techniques often employed in human medicine

CHRONIC TREATMENT

- Placement of abdominal drains or repeated drainages/centeses in chronic conditions to maintain reduced pressure may be necessary. Treatment of the underlying disease is essential.

DRUG INTERACTIONS

Hepatic and renal elimination of drugs may be altered by ACS, requiring dosage adjustment or alternative drug choices.

RECOMMENDED MONITORING

IAP, CVP, blood pressure, blood chemistry, lactate, urine output, diagnostic imaging as indicated by underlying cause and progression of IAP over time

PROGNOSIS AND OUTCOME

Prognosis depends on underlying cause and associated abnormalities, organ dysfunction, and disease. In human medicine, ACS is a significant cause of morbidity and mortality (approaching 70%). Disregard for elevated IAP and delay of surgery are associated with further increases in patient mortality.

PEARLS & CONSIDERATIONS

COMMENTS

- Most critically ill patients should have urethral catheters in place to monitor urine output, which allows for IAP monitoring and early detection of ACS.
- IAH may falsely elevate indirect intracardiac pressure readings due to abdominothoracic transmission of pressure.
- Monitoring and management of patients this ill requires 24-hour care.

TECHNICIAN TIP

IAP is most easily measured in recumbent patients. If the patient is conscious and mobile, care must be taken to prevent the patient from chewing the catheter and retaining the proximal portion in the abdomen or bladder (Elizabethan collar essential).

PREVENTION

Avoid excessive fluid volume resuscitation. Careful monitoring essential, with early preventive action taken if IAP rises.

SUGGESTED READING

Cheatham ML: Abdominal compartment syndrome. Curr Opin Crit Care 15:154–162, 2009.

Drellich S: Intraabdominal pressure and abdominal compartment syndrome. Compend Contin Educ Prac Vet 22:764–769, 2000.

AUTHOR: CATHERINE SUMNER

EDITOR: ELIZABETH ROZANSKI

1ST EDITION AUTHOR: SHARON DRELLICH

Abdominal Distention

BASIC INFORMATION

DEFINITION

Enlargement of the abdominal cavity

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dependent on underlying cause

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

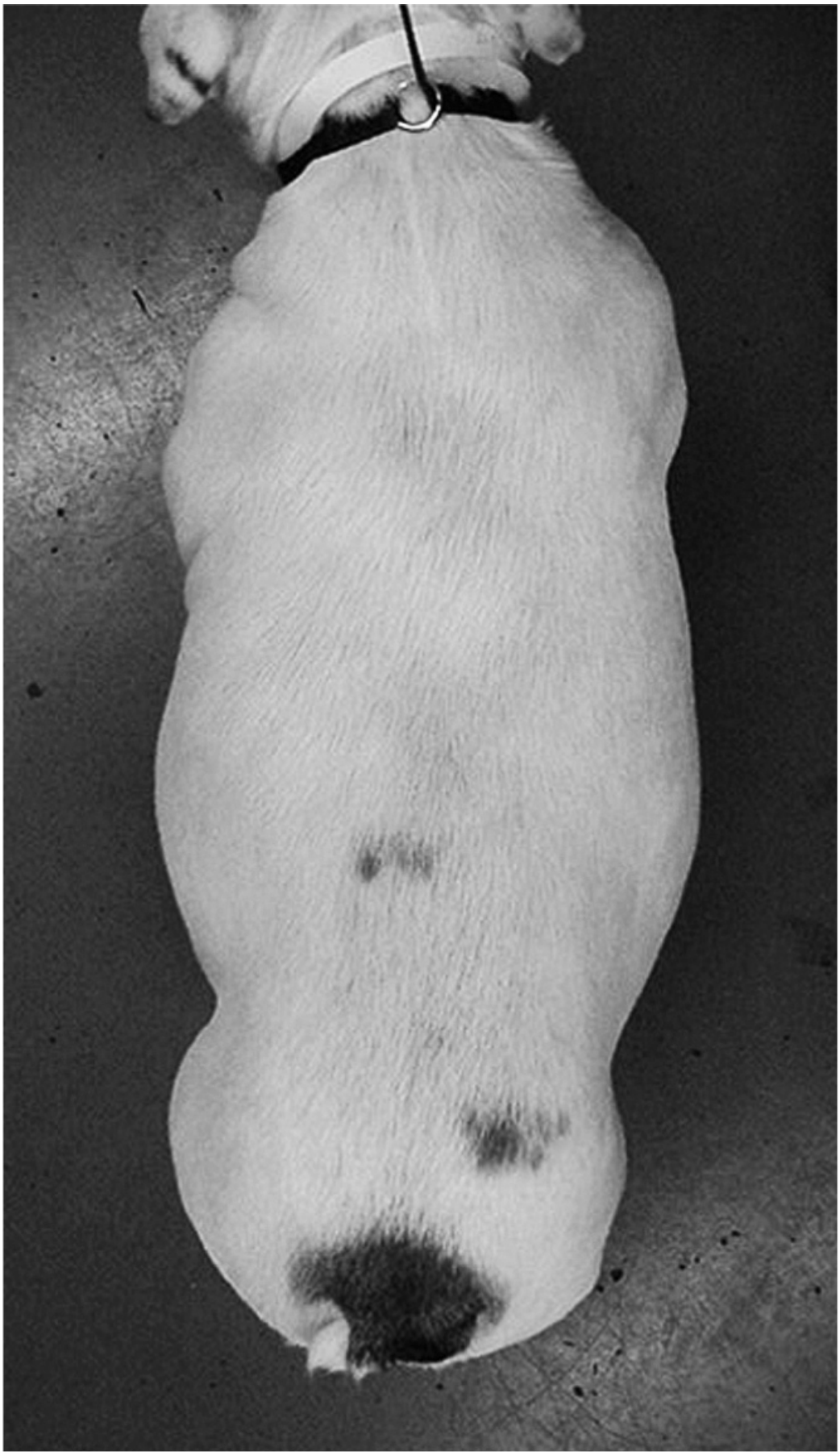
- Abdominal enlargement (rate of distention is extremely variable, varies from acute to chronic and insidious)
- Perceived weight gain
- Decreased activity
- Anorexia
- Tachypnea
- Abdominal discomfort/pain
- When ascites is present and the fluid accumulation is rapid, clinical signs of weakness and dyspnea are more likely to be apparent.
- History may include clinical signs associated with the primary disease (e.g., repeated, unproductive attempts at vomiting if gastric dilatation and volvulus; dyspnea, cough if cardiac disease; icterus if liver disease).

PHYSICAL EXAM FINDINGS

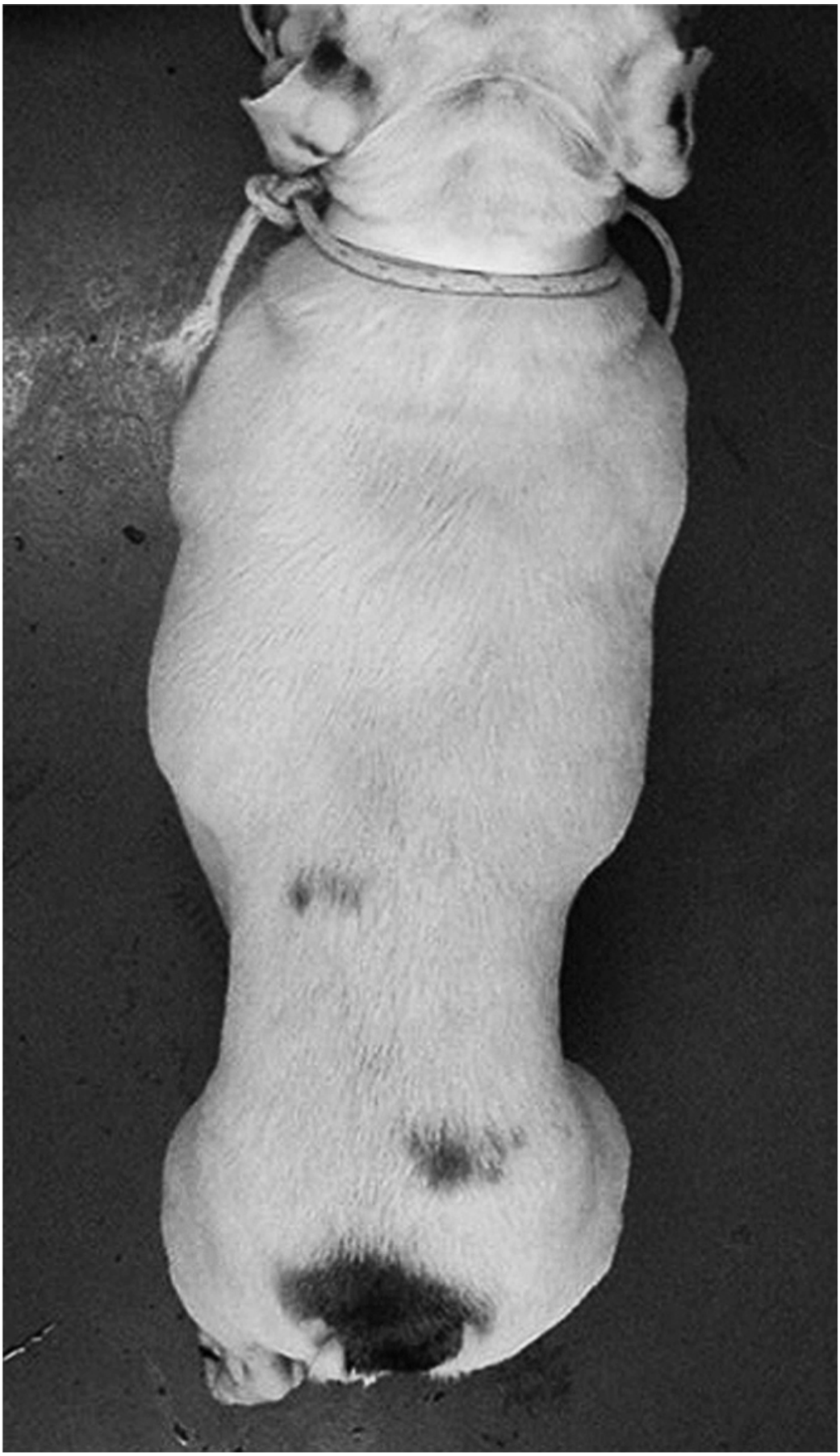
- Visible abdominal enlargement
- Abdominal palpation:
  - Fluid wave may be present (ballottement) with ascites.
  - An abdominal mass or organomegaly (liver, spleen, kidney, etc.) may be palpable.
- Physical abnormalities associated with primary disease may be present:
  - Cardiovascular abnormalities (heart murmur, arrhythmia, gallop sound, jugular distention) should warrant further investigation into the possibility of right heart failure.
  - Marked generalized lymphadenopathy may suggest lymphoma.
  - Muffled heart sounds are consistent with pericardial effusion and tamponade if ascites is present.

ETIOLOGY AND PATHOPHYSIOLOGY

- Ascites: all causes
- Hyperadrenocorticism/Cushing's disease
- Cyst (renal, hepatic)
- Gastrointestinal dilation (food, air, water, foreign material)
- Lipoma
- Lymphadenopathy
- Mass, non-neoplastic (hematoma, granuloma, abscess)
- Neoplasia



ABDOMINAL DISTENTION Dorsal view of a young English bulldog with marked ascites caused by right-sided congestive heart failure due to severe pulmonic stenosis. The abdominal distention hides the dog's weight loss and may be mistaken by the owner as an increase in lean body mass. This degree of abdominal distention was associated with poor appetite, lethargy, and dyspnea in this dog.



ABDOMINAL DISTENTION Same dog 2 hours later when large-volume abdominal drainage was complete. The dog was breathing normally, was more active, and appeared markedly more comfortable. The extent of cardiac cachexia is revealed.

- Pancreatitis
- Parasitic *(Mesocestoides)*
- Peritonitis
- Pneumoperitoneum (peritonitis or postsurgical)
- Pyometra/hydrometra
- Obstipation
- Organomegaly (hepatomegaly, splenomegaly, renomegaly)
- Torsion (splenic, gastric dilation/volvulus, etc.)
- Urinary obstruction/bladder distention

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Apparent on physical examination alone. Careful abdominal palpation and diagnostic imaging help to elucidate the cause.

DIFFERENTIAL DIAGNOSIS

- Normal variation
- Obesity
- Pregnancy

INITIAL DATABASE

- Abdominal radiographs
  - Loss of serosal detail (focal or generalized) is common if ascites is present.
  - May have “ground-glass” appearance (carcinomatosis, peritonitis)
  - Mass lesions, fat, or organomegaly may be apparent or suggested by displacement of gas-filled organs.
  - Free air may be present with peritonitis (ruptured viscus).
- Thoracic radiographs
  - Enlarged cardiac silhouette and/or caudal vena cava if congestive heart failure or pericardial effusion (rule out as cause of ascites)
  - Metastatic pulmonary disease
  - Pleural effusion
- CBC, biochemistry panel, and urinalysis are indicated for any animal with ascites or abnormal abdominal distention. Abnormalities depend on underlying cause and extent of organ damage.
- Abdominal ultrasonography
  - Confirms presence of fluid if present and differentiates fluid from soft tissue or fat
  - Identification of mass lesions, organomegaly, cyst, etc.
- Echocardiography
  - Confirms diagnosis of right heart enlargement or pericardial effusion (rule out as cause of ascites)
- Abdominal paracentesis (see p. 1194) if ascites; obtain fluid for cytology and biochemical evaluation.
- Characterize fluid based on protein concentration, specific gravity, and total cell count.
  - Transudate (pure)
    - Clear and colorless
    - Protein <2.5 g/dL
    - Specific gravity <1.018
    - Cells <1000/mm^3: neutrophils and mesothelial cells
  - Modified transudate
    - Red or pink; may be slightly cloudy
    - Protein 2.5-5.0 g/dL
    - Specific gravity >1.018
    - Cells <5000/mm^3: neutrophils, mesothelial cells, erythrocytes, and lymphocytes
  - Exudate (nonseptic)
    - Pink or white; cloudy
    - Protein 2.5-5.0 g/dL
    - Specific gravity >1.018
    - Cells 5000-50,000/mm^3: neutrophils, mesothelial cells, macrophages, erythrocytes, and lymphocytes
  - Exudate (septic)
    - Red, white, or yellow; cloudy
    - Protein >4.0 g/dL
    - Specific gravity >1.018Cells 5000-100,000/mm^3: neutrophils, mesothelial cells, macrophages, erythrocytes, lymphocytes, and bacteria
  - Hemorrhage

        - Red
        - Protein >5.5 g/dL
        - Specific gravity 1.007-1.027
        - Cells consistent with peripheral blood; usually does not clot
    - Chyle
        - Pink, straw, or white
        - Protein 2.5-7.0 g/dL
        - Specific gravity 1.007-1.040

ADVANCED OR CONFIRMATORY TESTING

- Fine-needle aspirate or needle biopsy (mass, enlarged organs, etc.). Biopsy not recommended if area is infected (abscess, pyometra) or likely to hemorrhage (e.g., suspected hemangiosarcoma).
- Prothrombin time if anticoagulant intoxication is suspected as cause of ascites (paracentesis contraindicated if coagulopathy is suspected)
- CT, MRI
- Abdominal exploratory may be indicated.

TREATMENT

TREATMENT OVERVIEW

Treatment of underlying disease and therapeutic abdominal drainage if large-volume ascites is causing the abdominal compartment syndrome (see p. 4)

ACUTE GENERAL TREATMENT

- Treatment of underlying disease:
    - Chemotherapy if lymphoma
    - Pericardiocentesis if pericardial effusion is present
    - Drug therapy for congestive heart failure
- Removal of fluid if discomfort or respiratory difficulty is present (see p. 1192).
- Surgery may be indicated for neoplasia, pyometra, peritonitis, and some causes of hemorrhage (e.g., ruptured splenic or hepatic hemangiosarcoma).

PROGNOSIS AND OUTCOME

Dependent on underlying cause

PEARLS & CONSIDERATIONS

COMMENTS

- Approach to patient with abdominal distention is to determine the nature of the primary problem.
- Thoracic radiographs should be part of the routine evaluation for a patient with ascites so as not to overlook the possibility of cardiac, pericardial, or metastatic disease–or pleural effusion.
- The cause of abdominal distention may be benign (obesity, intraabdominal lipoma, cyst).

SUGGESTED READING

Chambers G: Abdominal distension, ascites, and peritonitis. Textbook of veterinary internal medicine, ed 7, St Louis, 2010, Saunders Elsevier, pp 144–148.

AUTHOR: KIRSTIE A. BARRETT

EDITOR: ETIENNE CÔTÉ

Aberrant Adrenocortical Disease (Increased Adrenal Sex Hormone Production)

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Clinical signs of hyperadrenocorticism are present, but cortisol test results are normal, and one or more of the adrenal sex hormones is/are increased.

SYNONYMS

Atypical hyperadrenocorticism, sex hormone abnormality

EPIDEMIOLOGY

SPECIES, AGE, SEX

Middle-aged/old dogs and cats

ASSOCIATED CONDITIONS AND DISORDERS

Hyperadrenocorticism

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Pituitary dependent
- Adrenal dependent: adrenal carcinoma has mainly been reported (two cats and six dogs with hyperprogesteronism)

HISTORY, CHIEF COMPLAINT

Identical to hyperadrenocorticism (see p. 548)

PHYSICAL EXAM FINDINGS

Identical to hyperadrenocorticism (see p. 548)

ETIOLOGY AND PATHOPHYSIOLOGY

- The adrenal gland(s) secretes an excessive amount of one or more adrenal sex hormones.
- Adrenal tumors (particularly adenocarcinomas) may secrete adrenal sex hormones owing to disruption of adrenal tissue.
- Progestagens can act as glucocorticoid agonists.
- Cortisol concentrations may be normal to subnormal with sex hormone-secreting adrenal tumors, as high progestagen concentrations can suppress cortisol secretion.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The disorder is suspected when typical signs of hyperadrenocorticism are identified, but specific diagnostic tests (e.g., ACTH stimulation) are inconsistent with hyperadrenocorticism. Confirmation is obtained with identification of elevated serum levels of adrenal sex hormones.

DIFFERENTIAL DIAGNOSIS

- Polyuria/Polydipsia (see p. 902)
- Polyphagia (see p. 899)
- Alopecia (see pp. 54 and 56)

INITIAL DATABASE

Hyperadrenocorticism (see p. 548)

ADVANCED OR CONFIRMATORY TESTING

- Adrenocorticotropic hormone (ACTH) stimulation test with sex hormone panel (progesterone, 17-hydroxyprogesterone, estradiol, androstenedione, testosterone):
  - Dogs with nonadrenal illness may have mildly increased adrenal sex hormones.
  - Substantial overlap in sex hormone serum concentrations between healthy, nonadrenally ill, and hyperadrenocorticism patients make sex hormone assays ineffective screening tests for hypercortisolism.
  - Approximately 71% sensitivity and specificity for 17-hydroxyprogesterone concentrations if a cutoff greater than 8.5 ng/mL is used for diagnosing atypical hyperadrenocorticism
- Low-dose dexamethasone suppression test to rule out typical hyperadrenocorticism ± endogenous ACTH concentrations, CT, MRI (see p. 548)

TREATMENT

TREATMENT OVERVIEW

Resolution of clinical signs is the goal of treatment; medications are typically used for controlling pituitary-based disease, and surgical excision is the treatment of choice for primary adrenal tumors.

ACUTE GENERAL TREATMENT

- See Adrenal Neoplasia (Adenoma/Carcinoma), p. 43
- Pituitary-dependent (see p. 548)

CHRONIC TREATMENT

- As for hyperadrenocorticism, p. 548
- The following recommended by some, with anecdotally supported results (see http://www.vet.utk.edu/diagnostic/endocrinology/pdf/TreatmentInfoAtypicalCushingsRevised201001.pdf):
  - Melatonin (3-6 mg/dog PO q 12 h, based on body weight); inhibits aromatase and 21-hydroxylase enzymes
  - Melatonin implants (www.melatek.net) 8, 12, 18 mg for dogs weighing <25, 25-50, and >50 lb, respectively
  - Lignan (from flaxseed hulls or HMR lignan) ≈ 2 mg/kg PO q 24 h; phytoestrogenic activity inhibits aromatase
- Elimination of exogenous (e.g., hormone cream) or endogenous (ovarian remnant, cryptorchid testicle) sources of androgens

DRUG INTERACTIONS

See Hyperadrenocorticism, p. 548; Adrenal Neoplasia (Adenoma/Carcinoma), p. 43

POSSIBLE COMPLICATIONS

See Hyperadrenocorticism, p. 548; Adrenal Neoplasia (Adenoma/Carcinoma), p. 43

RECOMMENDED MONITORING

Medical therapy: ACTH stimulation testing every 3 months

- Mitotane (o,p '-DDD) therapy: sex hormone concentrations (and cortisol if also increased) should decrease to normal.
- Trilostane therapy: progesterone and 17-hydroxyprogesterone concentrations may increase concurrent with resolution of clinical signs and a decrease in cortisol concentrations.

PROGNOSIS AND OUTCOME

- Survival data unknown but subjectively similar to dogs with typical hyperadrenocorticism
- Adrenal tumor: good if surgically resectable
- Pituitary-dependent: good with treatment

PEARLS & CONSIDERATIONS

COMMENTS

- Limited information is available regarding this disease and the sensitivity and specificity of adrenal sex hormones in nonadrenal illness.
- Adrenal sex hormones are also increased in dogs with typical hyperadrenocorticism (i.e., hypercortisolemia).

TECHNICIAN TIP

On both the pre- and post-ACTH stimulated serum, 2 mL of serum are required. Centrifuge, separate, and freeze the serum as soon as possible. Avoid submission of hemolyzed samples.

SUGGESTED READING

Benitah N, Feldman EC, Kass PH, Nelson RW: Evaluation of serum 17-hydroxyprogesterone concentration after administration of ACTH in dogs with hyperadrenocorticism. J Am Vet Med Assoc 227:1095–1101, 2005.

Hill KE, Scott-Moncrieff JCR, Koshko MA: Secretion of sex hormones in dogs with adrenal dysfunction. J Am Vet Med Assoc 226:556–561, 2005.

Sieber-Ruckstuhl NS, Boretti FS, Wenger M: Evaluation of cortisol precursors for the diagnosis of pituitary-dependent hypercortisolism in dogs. Vet Rec 162:673–678, 2008.

AUTHOR: KATE HILL

EDITOR: SHERRI IHLE

Abortion, Dog

BASIC INFORMATION

DEFINITION

- The expulsion of one or more fetuses before full term pregnancy. Uncommon; in the dog, resorption is more common. Occurs more often during the fetal period.
- Induction of abortion (pregnancy termination): see p. 912.

SYNONYMS

Fetal loss, pregnancy wastage

EPIDEMIOLOGY

SPECIES, AGE, SEX

Female dog; no specific age

GENETICS & BREED PREDISPOSITION

Inbreeding (inbreeding coefficient >0.25): early embryonic death, conceptus resorption

RISK FACTORS

- History of previous pregnancy loss
- Malnutrition (pregnancy ketosis)
- Endocrinopathies (hypothyroidism, hypoluteoidism, diabetes mellitus)
- Infection *(Brucella canis, Listeria monocytogenes, Streptococcus canis, Escherichia coli, Campylobacter* sp., *Leptospira* sp. *Salmonella* sp., *Mycoplasma* sp., canine herpesvirus 1, canine parvovirus 1 [minute virus of canines], bluetongue virus, canine distemper virus, canine adenovirus [infectious hepatitis], *Toxoplasma gondii, Leishmania infantum)*
- Unsolicited treatment with endocrine disruptors, embryotoxic or teratogenic compounds (e.g., antifungal agents such as itraconazole or polyester textiles in contact with skin).
- Inadequate vaccination or deworming programs

CONTAGION & ZOONOSIS

- *Brucella canis* is zoonotic. *Salmonella* sp. and *Leptospira* sp. have zoonotic potential.
- Canine herpesvirus 1 and minute virus of canines: transmission through direct contact via aerosol or contact with aborted fetuses and/or placentas. Male-to-female venereal contact is not a significant means of viral transmission.

GEOGRAPHY AND SEASONALITY

- Canine brucellosis: endemic in parts of North and South America; eradicated in Europe since 1996.
- Canine herpesvirus: worldwide incidence; serologic prevalence of 60%-80%.

ASSOCIATED CONDITIONS & DISORDERS

Abortion may be secondary to fetal death.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Pregnant bitch whelps prematurely with live or dead pups, or no pups are born at term.
- Abnormal vulvar discharge during pregnancy (bloody or purulent discharge), fever, or signs of abdominal pain may be noted by owner.
- Usually abortion in the bitch goes unnoticed by the owner because the dam may consume the pups and the aborted tissues.
- Death may occur in one or more fetuses, whereas the remainder may continue to develop normally.
- Late-term abortions (between days 45 and 59) are typical of *B. canis*.

PHYSICAL EXAM FINDINGS

- Often unremarkable
- Vulvar discharge occurs normally in pregnant bitches and is clear to mucoid or pink-tinged and odorless; purulent, hemorrhagic, greenish, blackish, or malodorous vulvar discharge may indicate pregnancy complications that could lead to abortion.

ETIOLOGY AND PATHOPHYSIOLOGY

- Canine pregnancy requires normal luteal function throughout its duration. Any toxic or hormonal substance that induces endogenous release of prostaglandin F-2 alpha (PGF2a) and subsequent luteolysis may cause abortion (e.g., bacterial toxins [coliforms, *Staphylococcus* sp.], adrenergic agonists [e.g., phenylephrine]).
- Fetal survival requires normal placental function and placental relaxin production. Relaxin concentration declines rapidly after the death of all fetuses but may remain elevated for some days after the loss of pregnancy.
- Pathogens that influence placental function (e.g., herpesvirus placentitis) may cause abortion.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected when the pregnancy is previously confirmed on ultrasound or by radiography, and the bitch then presents nonpregnant or expelled fetuses have been observed.

DIFFERENTIAL DIAGNOSIS

- Pseudocyesis (false pregnancy). Ultrasound evaluation on days 23-25 following breeding to confirm pregnancy and fetal heart beat.
- Vulvar discharge due to vaginitis or metritis (pyometra). Ultrasound evaluation of uterine disorders may be useful on days 23-25 of anticipated gestation.

INITIAL DATABASE

- Serologic testing of affected dam.
  - *B. canis:* Rapid slide agglutination test (RSAT) is an excellent screening test, but false-positive results occur. To reduce cross-reactivity and false positive results, 2-mercaptoethanol can be added to the RSAT. Dogs in a positive kennel or household that are negative on first test should be retested once a month for 3 consecutive months to confirm negative status. Vaginal secretions or semen can be tested by PCR to determine a positive *B. canis* status before seroconversion occurs.
  - CHV-1: A serum neutralization test or ELISA test with a positive result greater than 1:16 is indicative of prior infection (exposure).
- Virus or bacterial isolation from microbial cultures from fetuses, placenta, milk, or vaginal secretions.
  - *B. canis:* Repeated samples may be necessary. Antibiotics are usually ineffective because of the intracellular location of the infectious organism.
  - In acute CHV-1 infections, viral isolation from infected tissues is possible for 2-3 weeks. Nasal or vaginal swabs may also be tested by PCR. Typically titers show 1:64-1:640. Two blood samples (acute and convalescent) at 1-month intervals are suggested to confirm a decline or rise in titer.
- Fetal gross necropsy (e.g., subcapsular hemorrhages in the kidneys indicative of CHV1) and visual inspection of associated fetal membranes
- Histologic assessment of fetal organs, liver, spleen, thymus, kidneys, adrenals, intestines and stomach, heart, lung, thymus, and brain
- Bacteriologic cultures from fetal organs and reproductive tract of the bitch
- Serum progesterone level of dam must be >2-3 ng/mL (6-9 nmol/L) to sustain pregnancy. Concentrations below this threshold for more than 48 hours may lead to pregnancy loss. Lower level at any time of pregnancy until day 55 indicates hypoluteoidism (luteal dysfunction/failure).
  - When reported, hypoluteoidism generally occurs on days 25-35 past breeding (i.e., at the initiation of the fetal period). Since low progesterone level may occur secondary to fetal death, the diagnosis of hypoluteoidism is based on a low serum progesterone level, positive effect of progesterone supplementation in a bitch that once aborted, and absence of other risk factors, such as a possible genetic etiology.
- Thyroid hormone analyses: May reveal subclinical hypothyroidism aggravated to a clinically significant disease during periods of stress, such as pregnancy (see p. 588).
- Routine laboratory testing: CBC and serum biochemistry profile
  - Normal hematocrit values: 45%-55% (nonpregnant) compared to 30%-35% (pregnant; due to an increase in plasma volume). Nonspecific
  - Mild mature neutrophilia and hemoconcentration is normal in pregnant bitches, but an elevated presence of nonsegmented neutrophils or monocytosis is abnormal.

ADVANCED OR CONFIRMATORY TESTING

- Ultrasonography may reveal fetal death before onset of abortion.
- Contact diagnostic laboratories for further recommendations for specific pathogens. For *B. canis*, blood culture with bacteriologic isolation provides a definitive diagnosis and may be attempted after 5 weeks. If the RSAT is positive, an agarose gel immunodiffusion (AGID) test on cytoplasmic protein antigens can be performed 12 weeks post infection and is the most accurate serologic test available.
- Toxicology of organs and/or blood when a specific toxin or drug is suspected

TREATMENT

TREATMENT OVERVIEW

- Acute supportive treatment of the bitch (e.g., intensive treatment of infection) is the main aim of treatment, since the prognosis for saving the ongoing pregnancy is poor.
- *B. canis*-infected dams should be euthanized or at least surgically sterilized, owing to the location of the organism in reproductive tissue. Premises should be cleaned, kennelmates should be quarantined, and humans should avoid direct contact with excretions or aborted material from potentially infected animals because of the zoonotic nature of *Brucella* sp.
- In cases of hypoluteoidism (see serum progesterone above), progesterone supplementation may be attempted to try to prevent abortion of remaining fetuses.

ACUTE GENERAL TREATMENT

- Supportive: intravenous fluids (e.g., lactated Ringer's solution) and antibiotics if fever.
- Antibiotics: empirical pending culture and sensitivity results (if clinically feasible). Typical choices include amoxicillin (22 mg/kg PO q 8 h), cephalexin or cefadroxil (20 mg PO q 8-12 h) or pivampicillin (30 mg/kg PO q 12 h). Enrofloxacin (5 mg/kg SQ, IM, or PO q 24 h) or trimethoprim/sulfadiazine (15 mg/kg PO q 12 h) are broad spectrum but potentially teratogenic.
- See p. 909

CHRONIC TREATMENT

With confirmed hypoluteoidism, options include:

- Progesterone in oil 2 mg/kg IM q 48 h until 10 days before term
- Altrenogest 0.09 mg/kg PO q 24 h is an alternative.
- Micronized progesterone (Prometrium [Solvay Medical Pharmaceuticals, Marietta, GA, USA]) has been recommended; 10 mg/kg PO q 24 h. Supplementation should be stopped at least 2 days prior to expected term (i.e., 60-61 days after the LH peak, to allow parturition).

If antibiotics are used in *B. canis*-infected dogs, antibiotic treatment should be continued for at least 4 weeks, based on culture and sensitivity results and clinical state.

NUTRITION/DIET

See p. 909. A good-quality maintenance diet is indicated.

BEHAVIOR/EXERCISE

Controlled physical activity during pregnancy

DRUG INTERACTIONS

Glucocorticoids are unpredictable abortifacient drugs in dogs.

POSSIBLE COMPLICATIONS

Supplementation with progesterone analogs (i.e., altrenogest) before sexual differentiation of the fetus is not recommended because of potential masculinization of female fetuses; nor is it recommended if the whelping date is unknown. Failure to discontinue supplementation at the appropriate time can cause prolonged gestation, fetal death, and lactation failure.

RECOMMENDED MONITORING

- If suspicious of possible abortion, weekly monitoring of progesterone concentrations and fetal viability with abdominal ultrasound examinations can be valuable.
- If abnormal vaginal discharge is observed during gestation, the pregnancy should be monitored by ultrasound to assess the viability of the fetuses, and supportive therapy should be initiated.

PROGNOSIS AND OUTCOME

- Poor for saving most ongoing pregnancies. Usually there is no problem in subsequent pregnancies, except in cases of *B. canis* infections and occasionally in herpesvirus-infected bitches with recrudescent infection.
- Bitches with hypoluteoidism may experience recurrent abortion, but the ongoing pregnancy is saved in most cases with supplementary progesterone.

PEARLS & CONSIDERATIONS

COMMENTS

- Abortion is uncommon in the bitch; embryonic death with fetal resorption or mummification is more common.
- Usually abortion in the bitch goes unnoticed by the owner, as the bitch may consume the aborted tissues.
- Infectious agents are the most common causes of canine abortion.
- The diagnosis of abortion should prompt a search for an underlying cause.

PREVENTION

- A canine herpesvirus 1 vaccine is available in Europe (Eurican herpes 205 [Merial, Lyon, France]). Vaccination should be given 1 month prior to estrus, followed by vaccination within 8 days after mating. If titers are below 1:128 at midpregnancy, a third vaccination may be given 10 days prior to parturition.
- Limit contact with external dogs at breeding and during pregnancy.
- Isolate pregnant bitches from showing or performing dogs during pregnancy, especially if herpesvirus is endemic in the area.
- Maintain an adequate vaccination and deworming program.

TECHNICIAN TIP

Educate clients on normal pregnancy (see p. 909) and preventive measures for breeding animals.

CLIENT EDUCATION

- Accurate pregnancy diagnosis should be done in bitches on days 25-30 post breeding (ultrasonography or relaxin test). See p. 909.
- Regular medical evaluation of breeding dogs
- Genetic counseling to avoid inbreeding

SUGGESTED READING

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Burns

BASIC INFORMATION

DEFINITIONS

- *Burns* are the injuries that result from exposure to flame, extreme heat, scalding, inhalation, and chemical or electrical trauma. Burns produce clinical syndromes ranging from self-limiting injury to devastating long-term incapacitation and potentially death.
- *Eschar:* a thick, coagulated crust or slough that develops as a result of a burn
- *Compartmentalization:* a condition associated with third- and fourth-degree burns in which swelling within tissue compartments creates strictures that can decrease thoracic wall motion and ventilation or cause ischemic injury to limbs
- *Transition zone:* region between completely devitalized tissue and normal tissue

EPIDEMIOLOGY

SPECIES, AGE, SEX

Animals of any signalment are susceptible to burn injury. Debilitating conditions such as chronic renal disease or immunoincompetence carry increased risks for fatal complications.

RISK FACTORS

Both temperature and duration of exposure contribute to the degree of thermal injury. Common sources of companion animal burns include heating pads, hot water bottles, fire, exhaust systems, and hot pipes.

ASSOCIATED CONDITIONS & DISORDERS

Early gram-positive and later gram-negative infections are common in burn wounds.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- First-degree (superficial) burns:
  - Epidermis
  - Typically thickened, erythematous, and desquamated
  - Typically painful
- Second-degree (deep partial thickness) burns:
  - Superficial layers of dermis
  - Typically edematous and erythematous
  - Typically wet and very painful
- Third- and fourth-degree burns:
  - Superficial layers of dermis (third-degree) and subcutaneous layers, tendon, and bone (fourth-degree)
  - Typically waxy and leathery in appearance
  - Typically less painful than first- or second-degree
  - Third- and fourth-degree burns carry a greater risk of wound sepsis, coagulation disorders, limb ischemia, or compression severe enough to cause ventilatory compromise or abdominal problems.
- Electrical burns (see p. 342):
  - High-voltage: associated with compartmental syndromes and ischemia
  - Low-voltage: seldom associated with complication
- Chemical or tar burns usually involve the superficial dermis layers.

HISTORY, CHIEF COMPLAINT

- History and chief complaint reflect acute trauma.
- Recent anesthetic procedures should prompt suspicion of heating blanket or heating lamp burn.
- With acts of malicious intent, history may be unknown.

PHYSICAL EXAM FINDINGS

- Physical examination findings depend on the location and extent of the burn.
- Burns from contact may not initially be apparent until rapid skin and hair loss occur 2-3 days later.
- Thermal burn resulting from a heating blanket or lamp will present as a defined injury reflective of the size of the blanket and the positioning of the animal during recumbency.
- Animals with extensive burns may present in hypotensive shock or with hypothermia.
- The presence of singed whiskers or burn debris in the mouth is strongly suggestive of inhalation (see p. 1027).
- Respiratory distress can occur rapidly from pharyngeal and laryngeal edema, progressive upper airway obstruction, pulmonary edema, inhalation of burn debris, or carbon monoxide toxicity.
- Corneal trauma may be present.

ETIOLOGY AND PATHOPHYSIOLOGY

- Localized wound inflammation results in release of inflammatory mediators and capillary leakage, causing extravasation of fluid.
- If systemic inflammation or vasculitis occurs, fluid losses may be severe and result in hypotension or cardiac collapse necessitating intensive IV fluid resuscitation.
- Burns are colonized initially by normal flora. Due to large volume of dead tissue and impaired blood supply and antimicrobial delivery, large burn areas are at high risk of infection. Initial organisms are gram-positive cocci, but in 3-5 days, gram-negative bacteria colonize the wound. Débridement and topical antibiotics are essential to treatment.
- Sepsis may result from wound infection, nosocomial infection due to the presence of multiple invasive catheters, or the development of pneumonia.
- Systemic inflammation may result in coagulopathy, including disseminated intravascular coagulopathy
- Inhalation injury: see Smoke Inhalation, p. 1027

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Thorough history including initial time and duration of exposure typically will be suggestive or conclusive of thermal injury; however, the full extent of burns may not be apparent immediately after the injury. Determination of the severity of the burn and appropriate treatment course requires examination of the lesion, including underlying and surrounding normal tissue. Diagnostic testing for related disorders (e.g., smoke inhalation) is applied as indicated in each case.

DIFFERENTIAL DIAGNOSIS

- Severe bacterial pyoderma
- Immune-mediated disease
- Fungal infection
- Abscess
- Aspiration pneumonia
- Sepsis

INITIAL DATABASE

- CBC, including manual platelet count
- Serum biochemistry profile
- Urinalysis
- Coagulation panel, including prothrombin and partial thromboplastin times
- Survey radiographs
- Bacterial cultures if evidence of pneumonia

ADVANCED OR CONFIRMATORY TESTING

- Wound culture if infected
- Brain CT or MRI if unexplained alteration in mentation

TREATMENT

TREATMENT OVERVIEW

Wound management is vital to preventing septic complications and minimizing tissue loss. Intravenous fluids, broad-spectrum antimicrobials, and in some cases supplemental oxygen are cornerstones of treatment. Overall goals of treatment are to maintain a patent airway, adequate mean arterial blood pressure and plasma oncotic pressure, and adequate urine production.

ACUTE GENERAL TREATMENT

- Intensive IV fluid resuscitation with crystalloid fluids (e.g., 0.9% NaCl) during the initial 8-12 hours of injury to maintain adequate mean arterial blood pressure and urine production at 1-2 mL/kg/h
- Maintenance of airway patency in presence of pharyngeal or laryngeal edema, with early elective intubation if necessary
- First- and second-degree burns may be self-limiting. Greasy or oil-based dressings (e.g., Vaseline-impregnated gauze) should be avoided.
- Third- and fourth-degree burns may require early escharotomy (débridement/burn excision) or fasciotomy to limit wound sepsis, stricture, or limb ischemia.
- In cases with concurrent smoke inhalation, supplemental oxygen provided within the first 12 hours of injury will help treat carboxyhemoglobinemia. Mechanical ventilation may be required to maintain oxygen saturation.
- Broad-spectrum antimicrobial coverage if evidence of pneumonia until culture results are available (e.g., ampicillin, 22 mg/kg IV q 8 h, plus enrofloxacin, 3 to 5 mg/kg IM or off-label use [diluted 1 : 1 in 0.9% sterile saline and given slowly IV] q 12-24 h; maximum 5 mg/kg q 24 h in cats).

CHRONIC TREATMENT

- First- and second-degree burn wounds may require little débridement. Application of antimicrobial topical creams such as silver sulfadiazine or 0.5% silver nitrate is recommended.
- Small eschars should be débrided for primary closure early in the course of wound care.
- Large eschars not amenable to primary closure should be débrided, allowed to form granulation tissue, and grafted. Open wound management presents a high potential for wound sepsis and is thus not advised if avoidable. See Shearing/Degloving Wounds (p. 1016) for details of wound treatment.
- Serious burns involving the limbs should be débrided to avoid limb ischemia, and treated with variations of splinting to avoid contracture.
- Intravenous fluid therapy should be titrated to replace losses/correct dehydration, maintain arterial blood pressure, and sustain appropriate urine production.
- Systemic inflammation and leaky vessels may result in protein loss and severe hypoalbuminemia. Judicious use of synthetic colloids (Hetastarch 20 mL/kg/24 h or Voluven 40 mL/kg/24 h) may be required to maintain colloid oncotic pressure and mean arterial blood pressure. Transfusion with fresh frozen plasma is recommended in cases of coagulopathy (see Transfusion Reactions, p. 1111). Serum electrolytes should be monitored.
- In cases of severe inhalation injury, maintenance of long-term intubation or tracheostomy may be required until resolution of burn trauma and associated pharyngeal, laryngeal, and airway edema.
- Mechanical ventilation may be required for management of direct lung injury from inhalation of carbon debris, aspiration pneumonia, or pulmonary edema.

NUTRITION/DIET

Parenteral or enteral nutrition should be instituted early in patients with large burns, as increased metabolic demand and protein losses can be significant (see p. 1267 and p. 1322).

BEHAVIOR/EXERCISE

- For third- and fourth-degree burns, especially when involving tissues affected by motion (limbs, axilla, inguinal region, flank, etc.) strict rest for 3-4 weeks may be necessary.
- Physical therapy or hydrotherapy may be beneficial to patients with large body surface regions affected.

POSSIBLE COMPLICATIONS

- Wound infection
- Aspiration pneumonia
- Nosocomial infection
- Sepsis
- Limb ischemia from wound contracture
- Coagulopathy

RECOMMENDED MONITORING

- Mean arterial blood pressure
- Central venous pressure
- Quantification of urine production
- Oxygen saturation
- CBC, serum biochemistry profile, coagulation tests

PROGNOSIS AND OUTCOME

- Outcome is generally good with first-and second-degree burns and more guarded with third- and fourth-degree burns.
- Prognosis is guarded to poor with inhalation injury.
- Prognosis relies on response to fluid resuscitation in severe burn injury. Prognosis improves with appropriate and successful wound management and worsens with development of complications like nosocomial infection and sepsis.

PEARLS & CONSIDERATIONS

COMMENTS

- Third- and fourth-degree burns, and/or inhalation, are best treated in a tertiary care facility with 24-hour intensive care management and surgeons skilled in surgical burn management, including skin grafting.
- Severe eschars causing constriction of ventilatory muscles or limb ischemia require early débridement and primary would closure or grafting to limit wound infection and reduce the risk of compartmentalization.
- Large burns resulting in marked protein loss may be best treated with fresh frozen plasma transfusion to replenish proteins for tissue repair, oncotic support, coagulation factors, and acute phase proteins.
- Respiratory distress in a patient with evidence of inhalation (e.g., burned whiskers) may be due to pharyngeal or laryngeal edema and warrants intubation to obtain and maintain airway patency.
- Iatrogenic thermal burns as a complication from heating pads or lamps during anesthetic procedures may be the most common type of burn injury not resulting in death.
- Burn injury resulting in death occurs most commonly from house fires or malicious acts.

PREVENTION

- Use of circulating warm water or warm air blankets should be used for surgical or hospitalized patients rather than electric heating blankets.
- Patients should not be placed in direct contact with hot water bottles for warming.
- Duration of time in contact with the warming device influences the extent of injury; therefore, the patient or the warming device should be repositioned frequently.

TECHNICIAN TIPS

Always place a towel or blanket between a patient and a warming device.

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Budd-Chiari-Like Syndrome and Cor Triatriatum Dexter

BASIC INFORMATION

DEFINITION

Uncommon cardiovascular defects that partially obstruct the flow of blood into or through the right atrium

- Cor triatriatum dexter (CTD):
  - Congenital cardiac defect resulting from persistence of the embryologic right sinus venosus valve
  - The result is a membranous division of the right atrium, which obstructs hepatic venous return to the heart.
  - Cranial vena caval flow is unaffected.
- Budd-Chiari syndrome (BCLS):
  - Originally described as hepatic postsinusoidal hypertension secondary to inflammation and thrombosis of small hepatic veins.
    - Result: obstruction of venous return to the heart, resulting in ascites, hepatomegaly, and abdominal pain.
  - Currently, it is often used loosely to describe obstruction of venous return to the right heart caused by such diverse entities as cor triatriatum dexter, right atrial neoplasia, and caudal vena cava obstruction secondary to masses or traumatic kinking/fibrosis.
    - These disorders are more appropriately referred to as *Budd-Chiari-like syndromes*.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Canine: most often in patients <2 years old; males more commonly affected than females
- Feline: no cases reported (see p. 259)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- CTD: membrane can cause partial or complete division of right atrium. If the membrane is complete, blood flowing into the caudal chamber must pass to the cranial chamber via a vascular connection with the azygos vein.
- Budd-Chiari-like syndrome: obstruction to venous flow may be acquired (e.g., caudal vena cava trauma and subsequent fibrosis) or congenital.

HISTORY, CHIEF COMPLAINT

- Lethargy
- Inappetence
- Severe abdominal distention

PHYSICAL EXAM FINDINGS

- Hepatomegaly
- Ascites
- Abdominal discomfort
- Distention of superficial abdominal vasculature
- Muscle wasting (cardiac cachexia)

ETIOLOGY AND PATHOPHYSIOLOGY

- Obstruction of venous return elevates intrahepatic pressure
- Increased pressure causes leakage of protein and fluid from the hepatic sinusoids, resulting in high-protein ascites (modified transudate)

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Clinical presentation of right-sided congestive heart failure should generally lead to the suspicion of other more common cardiac disorders. However, the diagnosis is established during the echocardiographic examination (generally an unexpected finding).

DIFFERENTIAL DIAGNOSIS

- Pericardial effusion
- Right atrial tumor
- Tricuspid dysplasia
- Cor pulmonale (pulmonary hypertension)
- Dilated cardiomyopathy (biventricular)
- Arrhythmogenic right ventricular cardiomyopathy

INITIAL DATABASE

- Ascites without jugular distention supports the diagnosis of CTD or BCLS over other causes of right heart failure signs.
    - Primary intraabdominal causes of ascites (e.g., hemoabdomen, portal hypertension) are important differential diagnoses.
- Fluid analysis of the ascites indicates a modified transudate: high protein (>2.5 g/dL), relatively low nucleated cell count (usually <5000 cells/mcL).
- Thoracic radiographs most often show normal cardiac silhouette and lung fields; enlargement of the caudal vena cava is expected if CTD or BCLS is causing ascites.
- Serum biochemistry panel will often show mild elevation in hepatic enzymes; complete blood count may show a stress leukogram; urinalysis is unremarkable.
- Electrocardiogram may show tall P waves consistent with right atrial enlargement.

ADVANCED OR CONFIRMATORY TESTING

- CTD: two-dimensional echocardiography will display a membrane dividing the right atrium. Doppler echocardiography will demonstrate blood flow through an opening in the membrane if the membrane is perforate.
- BCLS: two-dimensional echocardiography may reveal evidence of an obstruction or may be normal, necessitating other modalities.
- Abdominal ultrasound demonstrates ascites, hepatomegaly, distended hepatic veins, and the absence of a primary intraabdominal cause for the ascites (e.g., mass).
- Angiography is an alternate imaging technique to define blood flow and diagnose causes of BCLS other than CTD.
- Pressure measurements of the hepatic veins, caudal vena cava, and right atrium normally should be approximately equal (normal: 0-5 mm Hg). A drop in elevated pressure measured from the liver to the right heart indicates an obstruction is present.

TREATMENT

TREATMENT OVERVIEW

Correction of the underlying problem may be partial (balloon dilation) or comprehensive (open-heart surgery), with availability of appropriate facilities and barring owners' financial restrictions. Treatment of right-sided congestive heart failure aims to alleviate clinical signs of fluid retention.

ACUTE GENERAL TREATMENT

- Abdominocentesis will improve patient's comfort level (see p. 1193)
- CTD has been successfully corrected with both surgery and balloon dilation.
- Budd-Chiari-like syndromes: surgery may be indicated, depending on the underlying cause.

CHRONIC TREATMENT

If definitive treatment is not possible, furosemide (1-4 mg/kg PO q 12 h) and an angiotensin-converting enzyme inhibitor (e.g., enalapril, 0.5 mg PO q 12-24 h) should be administered along with periodic abdominocentesis to control fluid accumulation.

DRUG INTERACTIONS

Electrolyte depletion and dehydration may result from overzealous diuretic administration.

POSSIBLE COMPLICATIONS

- Surgery is highly invasive, and therefore the risk of mortality is increased with an inexperienced surgeon.
- Balloon dilation of CTD may not create a sufficient opening in the membrane to alleviate clinical signs.

RECOMMENDED MONITORING

- Ascites should resolve with successful reduction/removal of obstruction.
- Renal and hepatic function should be periodically monitored if medical therapy is chosen.

PROGNOSIS AND OUTCOME

- Excellent with successful reduction/removal of the obstruction
- Medical management alone is unlikely to be satisfactory on a long-term basis if clinical signs (e.g., marked abdominal distention from ascites) are already present.

PEARLS & CONSIDERATIONS

COMMENTS

- Jugular distention is *not* present with CTS and other BCLS, unlike other cardiovascular diseases that cause signs of right heart failure.
- Diseases that result in signs of right heart failure are the most common causes of a modified transudate in the abdomen of dogs. Therefore, a modified transudate ascites should always prompt a cardiac workup.

CLIENT EDUCATION

- Advise that surgery or balloon dilation offers the best chance for cure.
- Medical therapy is palliative but is unlikely to be satisfactory on a long-term basis.

SUGGESTED READING

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Brunfelsia Toxicosis

BASIC INFORMATION

DEFINITION

An acute poisoning resulting from the ingestion of *Brunfelsia* spp. and characterized by nervous system effects including tremors, ataxia, and seizures, often accompanied by vomiting and/or diarrhea

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs are the most commonly affected species; there is no age or sex predilection.

RISK FACTORS

All parts of the plant are toxic; berries and seeds contain more toxin.

GEOGRAPHY AND SEASONALITY

- *Brunfelsia* spp. grow best in a warm, coastal environment. Most cases in the United States are reported from coastal California, Gulf Coast states (Texas and Louisiana), and Florida. In other regions, the plant may be kept indoors as a tub plant and moved outdoors in the summer.
- The plant flowers starting in mid-spring, and berries and seeds are present from summer to fall.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Observed ingestion of the plant
- Vomiting/diarrhea containing plant material/berries/seeds
- Rapid onset of clinical signs, within 30 minutes to a few hours

PHYSICAL EXAM FINDINGS

- Initial signs include agitation or excitement.
- +/− Gastrointestinal (GI) signs such as vomiting and diarrhea
- Tremors
- Muscle rigidity
- Tonic-clonic seizures

ETIOLOGY AND PATHOPHYSIOLOGY

Source

- The genus encompasses several dozen species of shrubs or trees. The most commonly encountered are: *B. americana, B. australis, B. grandiflora*, and *B. pauciflora*.
- Common names include lady-of-the-night, yesterday-today-tomorrow, morning-noon-and-night, and kiss-me-quick.
- Several biologically active tremorgenic compounds such as hopeanine and brunfelsamidine are present in all parts of the plant.

Mechanism of Toxicosis

- Exact mechanism not known. Both hopeanine and brunfelsamidine are potent tremorgens and convulsants in laboratory animals. These compounds seem to interfere with neurotransmission in a manner similar to strychnine.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A clinical diagnosis is made based on history, presence of the plant in the environment, plant material in the vomitus or diarrhea, and rapid onset of neurologic signs (tremors, seizures, and ataxia).

DIFFERENTIAL DIAGNOSIS

- Toxicologic
  - Strychnine, metaldehyde, tremorgenic mycotoxins, stimulant toxicities (e.g. methylxanthines, amphetamines), lead
- Spontaneous, nontoxicologic
  - Seizure disorders including epilepsy, canine distemper, intracranial neoplasia, metabolic (hypoglycemia, hepatic encephalopathy)

INITIAL DATABASE

CBC, serum biochemistry profile, urinalysis. Expected to stay within normal limits. Useful for ruling out other possible causes.

TREATMENT

TREATMENT OVERVIEW

Treatment is aimed at early decontamination of the patient (inducing emesis, administration of activated charcoal), controlling tremors and seizures if present, and supportive care Decontamination can be performed but care must be taken to avoid complications (see below) from these procedures.

ACUTE GENERAL TREATMENT

- Decontamination techniques (Note: vomiting should be induced only in patients showing no clinical signs. It can also trigger seizures.)
  - Hydrogen peroxide 3%: 2 mL/kg to maximum of 45 mL. Repeat once in 15 minutes if no emesis.
  - Apomorphine: 0.03-0.04 mg/kg IV, IM. The tablet can also be crushed and mixed with water and instilled in the conjunctival sac. Rinse eye after vomiting occurs.
  - Gastric lavage (see p. 1281) or enterogastric lavage may be helpful in symptomatic animals to remove plant material, especially berries/seed pods.
  - Activated charcoal: 1-2 g/kg PO +/− a cathartic such as sorbitol. Activated charcoal can be given without first inducing emesis in patients showing clinical signs and can be instilled following gastric or enterogastric lavage. Monitor serum sodium to avoid or manage activated charcoal-associated hypernatremia.
- Control muscle tremors and seizures.
  - Diazepam: 1-2 mg/kg IV may control seizures but generally does not control tremors.
  - Methocarbamol: 100-200 mg/kg slow IV to effect and repeated as needed for tremors. Do not exceed 330 mg/kg in a 24-hour period
  - If tremors and seizures are not controlled with the above agents, pentobarbital (3-15 mg/kg slow IV to effect), propofol (4-6 mg/kg IV followed by a CRI), or gas anesthesia may be needed to avoid muscle contraction–associated hyperthermia, which can become severe.
  - Animals should be kept in a dark, quiet environment; stimulation may worsen the signs.
- Ancillary care
  - Fluid diuresis for intravascular volume and to lessen risk of pigment nephropathy from possible rhabdomyolysis associated with tremors and seizures
  - Monitor and treat hyperthermia secondary to seizures and tremors.
  - Respiratory support (intubation and ventilation) may be needed in severe cases.

PROGNOSIS AND OUTCOME

- Good prognosis if presented early; guarded if seizures are difficult to control during the initial presentation. Tremors may continue for several days.

PEARLS & CONSIDERATIONS

COMMENTS

- All species of *Brunfelsia* are considered toxic.
- The flowers on the plant change from dark purple to lavender to white over a few days, and all three colors may exist on the same plant at the same time. This change is the reason for the common names yesterday-today-tomorrow, morning-noon-and-night, or kiss-me-quick.
- The signs can be mistaken for strychnine toxicity. However, strychnine's signs rarely continue for longer than 48 hours.
- Dogs are attracted to berries and seeds.

PREVENTION

Remove the plant from pet's environment.

TECHNICIAN TIPS

Dogs, particularly large breed ones, should have well-padded bedding to avoid pressure sores due to prolonged immobility.

CLIENT EDUCATION

Make clients aware of *Brunfelsia* toxicity potential and how to avoid having their dogs come in contact with the plant.

SUGGESTED READING

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EDITOR: SAFDAR KHAN

Brucellosis, Dog

Additional Images Available on Website

BASIC INFORMATION

DEFINITION

Infection with gram-negative coccobacillus or rod-shaped bacteria, *Brucella canis*

EPIDEMIOLOGY

SPECIES, AGE, SEX

Any sexually mature canine; no gender predisposition

RISK FACTORS

Housing or breeding with infected animals

CONTAGION & ZOONOSIS

Transmission between naïve and infected dogs (including via frozen semen), whether in stray, feral, or pet population. Reportable zoonosis in some U.S. states if confirmatory tests are positive. Human cases rare but possible from close physical contact with infected dog, especially if the human is young, pregnant, or immunocompromised.

GEOGRAPHY AND SEASONALITY

Worldwide distribution

ASSOCIATED CONDITIONS & DISORDERS

Diskospondylitis, anterior uveitis, lameness, weight loss, lethargy, behavioral changes, splenomegaly, lymphadenopathy, orchitis, epididymitis, testicular atrophy, azoospermia

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Female
  - Failure to conceive
  - Abortion at 45 to 55 days of gestation, possibly with no other signs
  - Birth of stillborn, partially autolyzed, or weak pups
  - Persistent, highly infective mucopurulent or serosanguineous vulvar discharge for 1-6 weeks postpartum
  - Pattern of successive abortions followed by a normal whelping of live or dead pups
- Male: scrotal swelling, decreased libido, back pain, testicular atrophy(chronic infections), poor semen quality

PHYSICAL EXAM FINDINGS

As for History, above. Variable additional manifestations. Either gender can present with lymphadenopathy, signs of recurrent uveitis, lameness, or paraspinal pain with paresis or paralysis.

ETIOLOGY AND PATHOPHYSIOLOGY

- Bacteria penetrate exposed mucous membranes of oral cavity, conjunctiva, nasal tissue, penis, or vaginal vault.
- Organisms shed through highly contaminated vaginal discharge (following abortion), urine, milk of lactating bitch, semen, prostatic fluid, vaginal fluid during estrus, and lochia of parturition.
- Culture in rough or mucoid phase on primary isolation.
- Phagocytized, *Brucella canis* remains intracellular within regional and other lymph nodes and blood for months to years. Bacteremia within 1-4 weeks after infection; episodic for months to more than 5 years.
- Clinical signs of reproductive tract disease in bitches due to placentitis and metritis and, in male dogs, due to epididymal

inflammation and subsequent autoimmune destruction of testicular tissue.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

If exposure to *B. canis* is suspected from a reproductive history or subsequent physical examination, a blood sample is drawn for screening test, and protective care is assumed for human or canine contact with the animal. If preliminary results are positive, isolation and further client communication about treatment options continue as a precaution until confirmation test results on blood, body fluids, or tissue are received.

DIFFERENTIAL DIAGNOSIS

- Abortion: see p. 7
- Infertility/poor semen quality/azoospermia: improper timing of breeding, subclinical uterine infection, testicular or prostatic disease
- Scrotal enlargement: orchitis, epididymitis, torsion of spermatic cord, hernia, testicular neoplasia, abscess, varicocele, hydrocele, hematoma

INITIAL DATABASE

Screen blood sample with card or rapid slide agglutination test with 2-mercapto-ethanol (RSAT with 2-ME; D-Tec, Synbiotics, San Diego CA) or submit to diagnostic laboratory for overnight result (immunofluorescent assay [IFA], tube agglutination test [TAT]; see figures). Positive from 8-12 weeks post infection. Negative results reliable unless dog exposed <2 months; then retest. False positives are common. Any positive result should be sent for a confirmation test (agar gel immunodiffusion [AGID]).

ADVANCED OR CONFIRMATORY TESTING

- AGID test uses cytoplasmic antigens, is very specific, and will identify a positive dog from 8-12 weeks post infection until 3-4 years after achieving abacteremia.
- Bacterial culture of blood is definitive. Positive cultures occur 2-4 weeks post infection, whereas positive titers do not occur until 8-12 weeks post infection. Small number of circulating organisms may require multiple samples from disease-related tissue (lymph node, bone marrow, placenta, eye, fetus) or fluid (semen, lochia, urine, milk). False negatives are possible depending up on the phase of bacteremia and previous antibiotic therapy.

TREATMENT

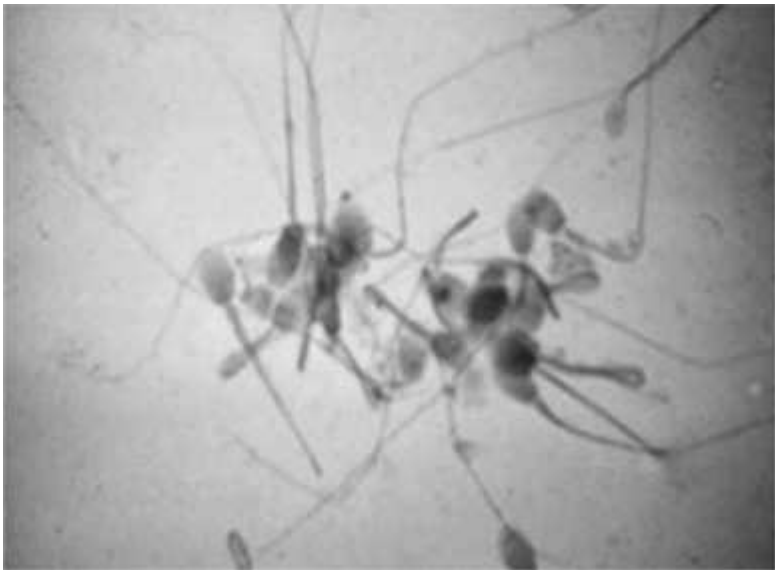
TREATMENT OVERVIEW

Goals of treatment are to:

- Minimize spread to other animals and humans through immediate quarantine, testing, and removal or euthanasia of affected dog(s).
- Stop progression of systemic disease in affected animals by surgical neuter, extended antimicrobial use, semi-isolation, and retesting.

ACUTE GENERAL TREATMENT

- Euthanasia should be treatment of choice in most cases.
- Alternatively, ovariohysterectomy/castration decreases the potential reservoirs of organisms from steroid-dependent tissues. Emphasis should be given to recurrence of symptoms and discouraging exposure of affected dogs to children, immunocompromised individuals, and pregnant women within that household or area.
- Antibiotic therapy is lengthy, expensive, and requires consistent owner compliance. Failures or relapses occur. No regimen is 100% effective. Animals should never be considered cleared of the organism. Combination of multiple drugs is better than any single antibiotic. Tetracycline (30 mg/kg PO q 12 h) or doxycycline (10 mg/kg PO q 12 h) for 1 month, in combination with gentamicin (5 mg/kg SQ q 24 h × 7 days, repeated every 3 weeks). Rifampin (5.5 mg/kg PO q 24 h) has been added in some cases. Enrofloxacin alone (5 mg/kg PO q 24 h for 4 weeks) has been reported in limited use.
- Intermittent serologic testing months after cessation of antibiotic(s).



BRUCELLOSIS, DOG Sperm agglutination.

(Courtesy Dr. Leland Carmichael.)

CHRONIC TREATMENT

- Animals should not be housed with persons susceptible to infection.
- Periodic antibiotic therapy as described previously may be beneficial in decreasing titers but not in eliminating the disease or its potential relapse.
- Quarantine kennel or facility. No animals in or out. Test all animals, including older pups. Repeat test monthly until 3 consecutive months of negative results. Remove or euthanize all positive dogs. Be aware of client's costs, financially and emotionally. Isolate any incoming animals for 8-12 weeks and test before introduction into the house or kennel.

DRUG INTERACTIONS

Cautious use with combinations of antibiotic categories; check renal function, antimicrobial sensitivities, dosages, and availability.

POSSIBLE COMPLICATIONS

Renal failure from long-term gentamicin use. Relapse or additional clinical signs as bacteremia persists.

RECOMMENDED MONITORING

Dogs diagnosed with brucellosis should be considered infected for life. Neutered dogs should be periodically treated with antibiotics to decrease risk of bacteremia and subsequent shedding. Otherwise, euthanasia is indicated for any dog that has a confirmed positive test.

PROGNOSIS AND OUTCOME

- Poor prognosis, guarded at best
- Dogs remain affected for life because of the intracellular location of *B. canis*, ongoing fluctuation of serologic titers, and ineffective bactericidal treatment.
- No infected dog should be used for breeding, even if treated with antibiotics.

PEARLS & CONSIDERATIONS

COMMENTS

- Dogs with a negative screening test (RSAT or TAT), especially those that show no overt clinical signs, are considered *not* infected with *B. canis* unless tested within 12 weeks post exposure.
- Blood samples from any dog testing positive from a preliminary test should be immediately checked by AGID. A dog with a

negative AGID result is considered *not* infected.

PREVENTION

- All intact male and female dogs should be screened for *B. canis* if accidentally bred by a stray or feral dog, exposed to aborted tissue or body fluids, and before breeding or semen shipment.
- Quarantine required by certain state regulatory agencies for facility if a positive test result occurs; enforced for minimum of 2 months until negative results reported

TECHNICIAN TIPS

- Obtain a thorough reproductive history from owners of intact dogs.
- Educate clients about annual testing with consequence of euthanasia if infected.
- Perform RSAT or Card test with in-date kit or submit blood to diagnostic laboratory.
- Test both dogs before breeding.
- Wear gloves during examination or treatment, especially mucous membranes, and isolate any dog with relevant clinical sign(s) until tested negative.

CLIENT EDUCATION

- Public health concern; incurable, zoonotic disease for intact dogs
- To reduce introduction of *B. canis* and subsequent loss of breeding stock or pet, continue regular testing annually early in the estrous cycle and before breeding or collecting semen for shipment.
- Use of common disinfectants on premises

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Bronchoesophageal Fistula

BASIC INFORMATION

DEFINITION

A communicating tract between the esophagus and a bronchus

SYNONYM

Esophageal fistula

EPIDEMIOLOGY

SPECIES, AGE, SEX

- An uncommon disease that occurs primarily in dogs; occasional cases in cats have been reported.
- Most reported cases have been described in young dogs (<7 years old) of either sex.

GENETICS & BREED PREDISPOSITION

- Most cases of bronchoesophageal fistula have been seen in small-breed dogs; this predisposition also reflects the increased prevalence of esophageal foreign bodies in small-breed dogs. Conceivably, however, any breed could be affected in the presence of appropriate risk factors.
- Congenital bronchoesophageal fistula has also been described in dogs and cats, although the genetic basis for the disease has not been established.

RISK FACTORS

An esophageal foreign body is the single biggest risk factor for the subsequent development of a bronchoesophageal fistula.

ASSOCIATED CONDITIONS & DISORDERS

- Focal pneumonia/aspiration pneumonia
- Esophageal diverticulum

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Congenital
- Acquired

HISTORY, CHIEF COMPLAINT

- Chronic cough is the most common clinical sign; coughing after drinking water is seen in some but not all cases. The cough is often responsive to therapy with antimicrobials but typically recurs at some point after cessation of antimicrobial therapy.
- Regurgitation
- Anorexia, lethargy, depression
- Tachypnea, increased respiratory effort
- Weight loss

PHYSICAL EXAM FINDINGS

- Cough
- Fever
- Tachypnea, increased respiratory effort
- Increased bronchovesicular sounds, or diminished breath sounds from pleural effusion, may be appreciated during thoracic auscultation; thoracic auscultation may also be normal.

ETIOLOGY AND PATHOPHYSIOLOGY

- Congenital:
  - Failure of tracheobronchial tree to completely separate from gastrointestinal tract during embryologic development.
- Acquired (more common form of bronchoesophageal fistula):
  - Esophageal perforation from an esophageal foreign body is the usual cause. The foreign body can perforate the esophagus itself, or perforation may result from pressure necrosis of the esophagus.
  - Esophageal diverticulum formation that predisposes to entrapment of an esophageal foreign body and subsequent perforation of the esophagus can also lead to a bronchoesophageal fistula.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis should be suspected in patients with a history of esophageal foreign bodies and recurrent bouts of antimicrobial-responsive respiratory disease.

DIFFERENTIAL DIAGNOSIS

Other causes of chronic cough include:

- Aspiration pneumonia secondary to other esophageal diseases
- Other causes of recurring pneumonia such as seen with immune deficiencies (e.g., immunoglobulin A [IgA] deficiency) or abnormalities in pulmonary defense mechanisms (e.g., ciliary dyskinesia/immotile cilia syndrome)
- Respiratory foreign bodies
- Respiratory neoplasia
- Inflammatory respiratory diseases (e.g., chronic bronchitis, eosinophilic bronchopneumopathy)

INITIAL DATABASE

- CBC: inflammatory leukogram; mild nonregenerative anemia possible (anemia of chronic inflammatory disease)
- Thoracic radiographs can have several abnormalities:
  - Localized alveolar, interstitial, or bronchial changes; the right caudal and right middle lung lobes are most commonly affected.
  - Esophageal foreign body
  - Esophageal diverticulum
  - Pleural fluid

ADVANCED OR CONFIRMATORY TESTING

- Contrast esophagrams will demonstrate the fistula in most cases. Performing a contrast esophagram with fluoroscopy is considered more sensitive for the detection of small fistulas and for differentiating a fistula from aspirated contrast agent.
- Esophagoscopy/bronchoscopy are considered less sensitive than contrast esophagrams but will be helpful in some cases. Bronchoscopy can help rule out other causes of focal pneumonia such as respiratory foreign bodies or bronchial neoplasia.
- Respiratory washes (transtracheal wash, bronchoalveolar lavage) will be important in some cases—particularly those with a history of having received multiple antimicrobials—to guide appropriate antimicrobial selections.

TREATMENT

TREATMENT OVERVIEW

- Remove or close communication between esophagus and airway.
- Control pulmonary infection.

ACUTE GENERAL TREATMENT

Surgical resection of the fistula, with primary closure of the esophageal defect; remove esophageal foreign body if present.

CHRONIC TREATMENT

Antimicrobials for pneumonia, with selection best guided by culture and sensitivity testing of respiratory washes, especially for patients that have received repeated courses of antimicrobials.

POSSIBLE COMPLICATIONS

- Complications of treatment or the primary disease have not been described for those animals that survive.
- Complications of untreated bronchoesophageal fistula include persistent or recurring pneumonia, pleuritis, and pulmonary parenchymal abscessation.

RECOMMENDED MONITORING

- Clinical signs
- Thoracic radiographs for radiographic resolution of pneumonia
    - Treating for 7-10 days beyond radiographic resolution of pneumonia is commonly recommended, as radiographic resolution often lags behind clinical resolution.

PROGNOSIS AND OUTCOME

A good prognosis is expected if respiratory complications are not serious. For patients with severe respiratory complications, the prognosis is guarded.

PEARLS & CONSIDERATIONS

COMMENTS

Administration of a dilute concentration of barium sulfate (20%-30% weight/volume) for an esophagram can facilitate demonstration of a bronchoesophageal fistula. The use of oral iodinated contrast agents for the documentation of bronchoesophageal fistulae has been discouraged because of the potential for more local adverse effects (cough, pulmonary edema) and the lower degree of radiographic contrast achieved with these substances (see Barium Esophagram, Dynamic, p. 1205; Upper Gastrointestinal Radiographic Contrast Series,p.1351).

TECHNICIAN TIPS

The presence of an esophageal foreign body poses risks of aspiration pneumonia, including during contrast studies. Changes in respiratory rate or character could signal an aspiration event.

PREVENTION

- Limit opportunities for foreign body ingestions, particularly in small-breed dogs.
- There are no means of preventing a congenital bronchoesophageal fistula, but affected dogs probably should not be bred.

SUGGESTED READING

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AUTHOR & EDITOR: RANCE K. SELLON

Bronchitis: Chronic, Sterile

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

A common noninfectious airway disease of older adult dogs. The hallmark is a chronic cough lasting longer than 2 months and not attributable to a known cause.

SYNONYMS

Chronic bronchial disease, chronic bronchitis, chronic obstructive pulmonary disease (COPD), noninfectious sterile bronchitis, old dog sterile bronchitis

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Most common in dogs; rarely reported in cats
- Mainly middle-aged to older dogs of either sex

GENETICS & BREED PREDISPOSITION

Primarily a disease of small-breed dogs but should not be overlooked in large-breed dogs

RISK FACTORS

Inhaled environmental irritants such as cigarette smoke, room deodorizers or carpet cleaners, and wood-burning stoves or fireplaces can exacerbate chronic sterile bronchitis.

GEOGRAPHY AND SEASONALITY

There may be seasonal exacerbations in individual pets, although no specific seasonality is described for all dogs.

ASSOCIATED CONDITIONS & DISORDERS

- Pneumonia
- Collapsing trachea
- Bronchiectasis
- Pulmonary hypertension and cor pulmonale

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- The primary clinical sign is a dry, hacking cough.
- Cough can be moderately productive (expectoration of mucus):
  - Not specifically diurnal or nocturnal
  - May have loud, “goose-honk” character
  - Often triggered by physical exertion, especially if it involves the dog's pulling on a leash (tracheal pressure from collars)
- Owners may note posttussive retching or gagging and mistakenly describe this as “vomiting.”
- In severe cases, signs may include:
  - Exercise intolerance
  - Syncope
  - Tachypnea
  - Cyanosis

PHYSICAL EXAM FINDINGS

- Cough:
  - The characteristic finding of this disorder
  - Commonly with sterile chronic bronchitis, the cough occurs less frequently or not at all when the dog is in a veterinary facility (sympathetically mediated bronchodilation due to anxiety).
- Tracheal sensitivity:
  - Applying light to moderate external pressure on the trachea using the fingers may elicit a cough.
  - In affected dogs, it may be possible to elicit a cough with tracheal pressure. However, many other respiratory disorders also have this feature, even if the airway is *not* the source of the problem (e.g., dogs with cardiogenic pulmonary edema virtually always cough in response to tracheal pressure). Therefore, the finding of tracheal sensitivity is nonspecific.
- Auscultatory abnormalities (increased bronchovesicular sounds, crackles, wheezes):
  - Crackles can often be heard on auscultation of the lungs in patients with sterile chronic bronchitis. They can be erroneously attributed to congestive heart failure, particularly in dogs with existing (asymptomatic) heart murmurs; therefore, both conditions should be investigated when crackles are heard, especially in a dog in which a heart murmur is auscultated.
- Tachypnea

ETIOLOGY AND PATHOPHYSIOLOGY

- Airway inflammation characterized by cellular infiltrates, glandular hyperplasia, smooth muscle hypertrophy, and loss of ciliated epithelial cells provokes cough.
- Although inhaled irritants and environmental pollutants could be partially responsible, definitive underlying causes have not been identified.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspect in middle-aged to older dogs with chronic, intermittent cough. A true diagnosis is typically made after exclusion of other causes of chronic cough.

DIFFERENTIAL DIAGNOSIS

- Pneumonia
- Collapsing trachea
- Congestive heart failure
- Respiratory neoplasia
- Heartworm disease
- Canine infectious tracheobronchitis

INITIAL DATABASE

- Thoracic radiograph abnormalities can include:
  - Mild to moderate diffuse interstitial pattern
  - Hyperinflation of lung field (“air trapping”); (see p. 98)
  - Bronchial markings (“doughnuts,” “tram lines”)
  - If pulmonary hypertension present, other possible abnormalities include:
    - Right-sided cardiomegaly
    - ± Enlarged, tortuous pulmonary arteries
- Normal thoracic radiographs do not exclude the possibility of sterile chronic bronchitis:
  - Lateral cervical radiographs should be obtained in suspected cases to avoid misdiagnosis of sterile chronic bronchitis as a result of overlooking cervical collapsing trachea.

ADVANCED OR CONFIRMATORY TESTING

- Cytologic examination of samples collected by bronchoalveolar lavage or transtracheal wash often demonstrates a predominance of nondegenerate neutrophils:
  - Occasionally, a predominance of eosinophils is seen.
  - Although bacterial infection is uncommon with this disease, quantitative culture of airway samples is recommended to exclude secondary infection or colonization exacerbating the disease.
- Bronchoscopy often reveals inflammation, hyperemia, edema, and in some patients, proliferation of the mucosa and accumulation of secretions in the tracheobronchial tree.

- Collapse or hypoplasia of the trachea or bronchi may also be appreciated in cases in which sterile chronic bronchitis coexists with collapsing trachea.
- Arterial blood gas measurement: consider if severe dyspnea/respiratory distress (uncommon). May reveal:
  - Hypoxemia
  - Hypocarbia
    - Hypercarbia from respiratory failure may be seen in advanced cases and usually signals a grave prognosis.

TREATMENT

TREATMENT OVERVIEW

The goal of therapy is to reduce cough, suppress airway inflammation, reduce airway obstructions, and minimize the potential for secondary infections. Complete resolution of cough is virtually never possible. The therapeutic goal is reduction of frequency and severity of cough so the animal is more comfortable.

ACUTE GENERAL TREATMENT

- Bronchodilators, antiinflammatory medications, and cough suppressants are indicated in acute exacerbations.
  - Cough suppressants are indicated to decrease coughing frequency and severity. Cough suppressants should not be used if the cough is moderately productive or if there is suspicion of an underlying infection.
    - Hydrocodone, 0.22 mg/kg PO q 6-12 h
    - Butorphanol, 0.25-1 mg/kg PO q 6-12 h; the higher dosage may cause sedation. The oral dosage is many times greater than the injectable dose and should *not be* used for calculating injectable doses of butorphanol.
    - Diphenoxylate hydrochloride and atropine, 0.2-0.5 mg/kg diphenoxylate PO q 12 h
- Antiinflammatory medications:
  - Prednisone/prednisolone 0.5 mg/kg q 12 h for 5-7 days to induce remission of cough
  - Decrease prednisone dose by half every 7 days and, when possible, move to alternate-day dosing to achieve minimum dose necessary to control clinical signs.
- Bronchodilators:
  - β^2 agonists:
    - Terbutaline (total amount per dose): small dogs 0.625-1.25 mgPO q 12 h, medium dogs 1.25-2.5 mg PO q 12 h, large dogs 2.5-5 mg PO q 12 h.
    - Albuterol: 0.05 mg/kg PO q 8 h.
  - Methylxanthines:
    - Not all long-acting theophylline products have equivalent bioavailability in dogs. Implications are that failure to respond to a certain product should prompt the consideration of switching bronchodilators (to a different brand of theophylline or a different class of bronchodilator altogether [e.g., a β^2 agonist]), and that certain individuals may develop signs of toxicosis when receiving doses that are well tolerated by others.
      - Extended-release theophylline (Inwood Laboratories) is recommended at 10 mg/kg PO q 12 h.
      - Aminophylline or theophylline 10 mg/kg PO q 8 h
- Oxygen therapy is indicated if hypoxemia is present (usually in patients with respiratory distress, which is uncommon).

CHRONIC TREATMENT

- Eliminate sources of airway irritation (see Risk Factors above).
- Weight loss:
  - Obesity is a common exacerbating factor, potentially leading to the Pickwickian syndrome (respiratory compromise due to obesity).
  - Weight loss helps increase lung volume and compliance.
- Bronchodilators, either oral or inhaled, are often used for decreasing airway resistance.
  - Doses for oral management are listed under Acute General Treatment above.
  - Metered-dose inhaler of albuterol (β^2-agonist): one puff (90 mcg) by inhalation q 12-24 h (see p. 1289)
- Cough suppressants decrease cough frequency and severity:
  - Antitussives should not be used if cough is moderately productive or if there is suspicion of underlying infection. Doses are listed under Acute General Treatment above.
  - For long-term use, dose is typically titrated to reduce or eliminate cough, without reaching levels that produce drowsiness.
  - Cough suppressants may be administered daily at first (days to weeks) to obtain palliation of cough, and then reduced or dosed intermittently on an as-needed basis to manage flare-ups of coughing.
- Antiinflammatory medications, either oral or inhaled corticosteroids, are often required:
  - Dose for oral management is listed under Acute General Treatment above.
  - Metered dose inhaler of fluticasone: one puff (110-220 mcg) by inhalation q 8-12 h (see p. 1289)

- The decision to incorporate antibiotic therapy should be based on cytologic evaluation and culture of airway samples.

BEHAVIOR/EXERCISE

- Minimizing the use of collars and using harnesses for restraint can help reduce cough caused by tracheal irritation.
- Eliminating/reducing possible inhaled irritants (cigarette smoke, room deodorizers, carpet cleaners) may help decrease clinical signs related to tracheal irritation.

DRUG INTERACTIONS

Fluoroquinolone antibiotics inhibit the metabolism of methylxanthine bronchodilators such as theophylline and aminophylline; their concurrent use can result in toxic plasma levels of the bronchodilator.

POSSIBLE COMPLICATIONS

- Bronchiectasis
- Pulmonary hypertension and right-sided congestive heart failure

RECOMMENDED MONITORING

Clinical signs

PROGNOSIS AND OUTCOME

- Guarded:
  - Complete resolution of the disorder (and its associated cough) is essentially never possible because sterile chronic bronchitis is a progressive disease.
  - However, it is rarely life threatening. Properly managed and treated, many or most patients with sterile chronic bronchitis can enjoy an excellent quality of life and normal life expectancy.
- Long-term complications of bronchitis can include bronchiectasis and pulmonary hypertension.

PEARLS & CONSIDERATIONS

COMMENTS

- Middle-aged to older small-breed dogs often have mitral or tricuspid endocardiosis. The combination of cough, heart murmur, and pulmonary crackles on auscultation, and some degree of cardiomegaly from valvular insufficiency radiographically, can lead to the erroneous diagnosis of a cardiogenic cause for the cough, when in fact the cause is sterile chronic bronchitis and concurrent (but compensated, clinically insignificant) mitral or tricuspid endocardiosis.
  - Dogs with sterile chronic bronchitis, in contrast to dogs with congestive heart failure, often have normal or lower than normal heart rates.
  - Similarly, dogs with sterile chronic bronchitis often have respiratory sinus arrhythmia, whereas dogs with acute pulmonary edema virtually never do (sinus tachycardia instead).
  - If pulmonary crackles are auscultated, yet there is no heart murmur, extra care should be taken to differentiate sterile chronic bronchitis from congestive heart failure (pulmonary) through radiographs, be cause the two diseases often present with very similar clinical features.
  - The diagnosis of sterile chronic bronchitis should be exclusive of any signs of pulmonary edema on thoracic radiographs. In the absence of thoracic radiographs, the diagnosis of congestive heart failure/pulmonary edema in a coughing dog cannot be made, and long-term treatment with diuretics is not supported.
- Hydrocodone cough suppressants may be difficult to obtain. Of those available, many are combined with other medications (acetaminophen, guaifenesin, and various antihistamines) that may not be safe or routinely recommended.
- Medications delivered by metered dose inhaler are now well-recognized and accepted for treating this disorder (see p. 1289).
  - The proposed advantage is minimization of the adverse effects of oral treatment.
- Obesity is a common complicating factor. For this reason (and many others related to various adverse effects of long-term use), corticosteroid administration of more than a few days' duration should be avoided as much as possible.

TECHNICIAN TIPS

When preparing for respiratory washes, be sure to use solutions that do not contain bacteriostatic additives. If available, pre-warm solutions for respiratory lavage in a 37°C incubator (or suitable alternative).

CLIENT EDUCATION

The clinical signs of sterile chronic bronchitis can be controlled in many dogs, but cure is unlikely.

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Bronchiolar and Pulmonary Neoplasia

BASIC INFORMATION

DEFINITION

Neoplastic growth originating in the bronchi or lower airways

SYNONYM

Lung cancer, primary lung tumors, primary pulmonary tumors

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Rare in dogs (1.24% of dogs at necropsy) and cats (0.38% at necropsy)
- Older animals:
  - 9.3 to 10.9 years in dogs
  - 11 to 12.5 years in cats
- No sex predilection

GENETICS & BREED PREDISPOSITION

No breed predisposition known, but increased incidence in boxer dogs and tricolor cats found in single studies

RISK FACTORS

Weak links to urban environment, secondhand smoke, brachycephalic conformation

ASSOCIATED CONDITIONS & DISORDERS

- Hypertrophic osteopathy
- Digital, ocular, or muscular signs secondary to metastasis common in the cat

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Malignant:

- Adenocarcinoma, squamous cell carcinoma, bronchial gland carcinoma, alveolar cell carcinoma
- Variety of sarcomas also possible
- Rarely carcinoids and plasma cell tumors of the airways

Benign:

- Papillary and bronchial adenoma
- Hemangioma
- Fibroma
- Myxochondroma
- Blastoma

HISTORY, CHIEF COMPLAINT

- Nonproductive cough most common complaint
- Dyspnea, lethargy, tachypnea less common
- Occasionally spontaneous pneumothorax or hemothorax
- Occasionally present for secondary problems: thickened and painful limbs or digital pain

PHYSICAL EXAM FINDINGS

- Can be normal
- Increased respiratory rate and/or effort possible
- Easily elicited cough with tracheal palpation (nonspecific)
- Lung auscultation is often normal, although silent areas may be noted over large masses.

ETIOLOGY AND PATHOPHYSIOLOGY

- Inhalation of carcinogens provoking malignant transformation is suspected.
- Dogs trained to smoke cigarettes (through a tracheostomy) or that inhaled radioactive substances developed lung tumors at a dramatically increased rate.

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

The diagnosis of pulmonary neoplasia is often suspected in a patient with a chronic cough unresponsive to antibiotics and one or more masses apparent on thoracic radiographs. The presence of such masses does not definitively establish a diagnosis of pulmonary neoplasia.

DIFFERENTIAL DIAGNOSIS

- Metastatic disease (usually multiple nodules of similar size)
- Malignant histiocytosis (usually also includes disease at other locations)
- Tumors of pleura, mediastinum, or heart base
- Abscess, fungal or bacterial disease
- Lymphoid granulomatosis
- Eosinophilic granulomatosis
- Foreign body granuloma
- Hematoma or infarct
- Lung lobe torsion
- Bronchial foreign body (causes lung lobe collapse/atelectasis)
- Mediastinal masses

INITIAL DATABASE

- CBC, serum biochemistry profile, and urinalysis are often normal.
- Thoracic radiographs:
    - Primary lung tumors usually appear as single nodules or one large nodule/mass and several smaller nodules.
    - Cats can have more diffuse infiltrative patterns within a lung lobe.

ADVANCED OR CONFIRMATORY TESTING

- Thoracic CT is the best modality to identify the full extent of disease, including detection of metastatic lesions and tracheobronchial lymph node enlargement, and assess possibility of surgical removal.
- Bronchoscopy and brush biopsy of bronchial lesions or transthoracic needle aspiration of peripheral lesions may yield sufficient cells for cytologic diagnosis.
    - Transthoracic needle biopsy carries acute risks of pneumothorax, hemothorax, and acute death, and a long-term risk of tumor seeding of the needle track.
    - Nonspecific inflammation is a common cytologic feature of respiratory samples obtained from patients with pulmonary neoplasia and thus does not rule out neoplasia.
    - Thoracoscopic lung biopsy can also be used.
    - Lung lobectomy and histopathology are often performed prior to definitive diagnosis by other means for patients with solitary lesions and no evidence of metastatic disease.

TREATMENT 

TREATMENT OVERVIEW

After appropriate staging, removal of the primary tumor is recommended for patients with solitary resectable lesions.

ACUTE GENERAL TREATMENT

- If dyspneic, give oxygen.
- Fluid or air in the thorax should be evacuated if respiration is impaired by pleural effusion or pneumothorax, respectively (see p. 1338).

CHRONIC TREATMENT

- Single nodule/mass:
  - The appropriate therapy for a single isolated nodule is surgical resection.
- If metastatic disease is identified (within lung parenchyma, pleura, hilar nodes, or distant sites), or the tumor is not removable because of size or other factors, surgery should not be attempted.
  - Incomplete removal of lung tumors will not increase quality of life or lifespan.
  - Chemotherapy can be considered for malignant tumors.
    - Vinca-alkaloid and platinum-containing drugs are most often recommended for carcinomas, but pulmonary carcinomas are generally poorly responsive to chemotherapy.
    - Doxorubicin-based protocols may be helpful for patients with sarcomas.
- Radiation therapy for palliation of clinical signs can be considered if tumor is confined to one area.

POSSIBLE COMPLICATIONS

Pneumothorax, hemothorax, pleural effusion

RECOMMENDED MONITORING

Thoracic radiographs for tumor progression, return (postoperatively), or response to therapy

PROGNOSIS AND OUTCOME

- Small tumors carry better prognosis.
  - Median survival after resection of tumors <5 cm diameter is 20 months; >5 cm diameter is 8-9 months
- Adenocarcinoma has a better prognosis than squamous cell carcinoma or undifferentiated carcinomas (median survival 251 days versus 160 days).
- Hilar lymph node enlargement is associated with a poor prognosis (median survival 60 days versus 12 months if no lymph node enlargement).

PEARLS & CONSIDERATIONS

COMMENTS

Patients with lung tumors should always be evaluated fully before attempting surgical resection. If the tumors are small, peripherally located, and there is no obvious lymph node enlargement, surgery should be recommended, and survival after resection could be greater than 1 year.

PREVENTION

There is no means of preventing the development of lung tumors in dogs and cats, although limiting exposure to second-hand smoke may help.

TECHNICIAN TIPS

- Whenever thoracic radiographs are taken, the whole thorax (don't cut off caudal lung regions, for example) should be imaged with at least two orthogonal views (e.g., lateral and ventrodorsal) to be able to examine the entire lung field so as to not miss lesions that may represent metastasis; both lateral views (three-view thorax) are better still for detection of metastasis. When solitary tumors of the lung are found at a small size, before the animal is showing signs, the prognosis will be greatly improved.
- If aspiration cytology is considered necessary to the evaluation, commonly used materials will include 22- or 23-gauge needles of 1 to 1½ inches length. If ultrasound guidance is used to aspirate, the hair over the lesion should be clipped, and skin prepped as if for surgery.

CLIENT EDUCATION

Since prognosis improves with early identification and surgical resection of lung tumors while small, surgery should not be postponed any longer than necessary. Most dogs that have a thoracotomy for lung lobe resection are able to be discharged from the hospital within 36-72 hours.

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Bronchiectasis

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Irreversible, pathologic dilation of airways due to destruction of the elastic and muscular components of the airway walls

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs are apparently affected more commonly than cats.
- Young animals are affected if associated with a congenital abnormality (rare); animals are older if associated with chronic inflammation (e.g., chronic bronchitis), infection, or neoplasia.
- Either gender can be affected.

GENETICS & BREED PREDISPOSITION

American cocker spaniels, West Highland white terriers, miniature poodles, Siberian huskies, and English springer spaniels may have an increased risk.

RISK FACTORS

- Congenital defects (e.g., primary ciliary dyskinesia)
- Acquired diseases, such as:
  - Chronic bronchitis
  - Eosinophilic bronchopneumopathy
  - Bronchopneumonia
  - Immunodeficiency diseases
  - Neoplasia

ASSOCIATED CONDITIONS & DISORDERS

- Chronic bronchitis
- Eosinophilic bronchopneumopathy
- Bronchopneumonia

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Focal, multifocal, and diffuse distribution
- Cylindrical, saccular, and cystic forms

HISTORY, CHIEF COMPLAINT

- Incidental radiographic finding in the absence of clinical signs (especially in cats)
- Cough
- Tachypnea
- Respiratory distress
- Other signs that reflect underlying disease (e.g., nasal discharge with ciliary dyskinesia)

PHYSICAL EXAM FINDINGS

- Cough may be inducible on tracheal palpation; however, an inducible cough is not specific for bronchiectasis.
- Other findings may be referable to underlying disease (e.g., fever with bacterial pneumonia).

ETIOLOGY AND PATHOPHYSIOLOGY

- Congenital or acquired conditions lead to a cycle of damage to the bronchial epithelium and/or their cilia, inflammation, impairment of mucociliary function, and secondary infection.
- Cellular damage, inflammation, and infection perpetuate the cycle of airway wall destruction, leading to bronchiectasis.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is usually accomplished by survey thoracic radiographs; however, advanced diagnostic imaging (e.g., CT) and/or histopathology may be necessary to detect subtle lesions. If a diagnosis of bronchiectasis is made, it is important to perform a thorough diagnostic workup to identify underlying/concurrent diseases.

DIFFERENTIAL DIAGNOSIS

Physical exam (cough or respiratory distress):

- Other airway diseases (e.g., chronic bronchitis, eosinophilic bronchopneumopathy, secondary bacterial bronchitis)
- Pneumonia (infectious, aspiration, eosinophilic, foreign body)
- Neoplasia
- Pulmonary thromboembolism
- Cardiogenic or noncardiogenic pulmonary edema
- Pleural effusion
- Pneumothorax
- Interstitial lung disease

INITIAL DATABASE

- CBC: neutrophilia may support underlying infection
- Eosinophilia may be present with eosinophilic bronchopneumopathy
- Thoracic radiographs:
    - Bronchiectasis has a pathognomonic radiographic appearance.
    - Morphologic classification:
        - Cylindrical form: dilated bronchi with nontapering ends; most common form (70% of canine cases)
        - Saccular form: “cluster of grapes” appearance to airways; indicates advanced disease
        - Cystic form: rounded ends of the very small bronchi; end stage of saccular form
    - Spatial classification:
        - Focal, multifocal, or diffuse distribution pattern
        - In dogs, multiple lung lobes are affected in 89% of cases; right cranial lung lobe overrepresented (93%)
    - Evidence of concurrent/underlying pulmonary disease is frequently present.
    - Radiographs may be unremarkable in the early stages of disease.

ADVANCED OR CONFIRMATORY TESTING

- CT may help detect subtle lesions.
- Bronchoscopy and bronchoalveolar lavage or fine-needle aspiration of the lung (cytology and culture) are useful in identification of underlying/concurrent diseases.
- Specialized functional and immunologic studies such as mucociliary scintigraphy, immunoglobulin A (IgA) concentrations, and others may be needed to evaluate patients for suspected congenital disease.
- Lung biopsy is sometimes needed to identify underlying/concurrent disease.

TREATMENT

TREATMENT OVERVIEW

Treatment should focus on identifying and treating an underlying cause of chronic inflammation (e.g., chronic bronchitis, infection) if present. Bronchiectasis is an irreversible dilation of the airways and is therefore not a curable disease (with the exception of focal disease treated by lobectomy). Long-term management is focused on decreasing inflammation, enhancing mucociliary clearance, and appropriate antimicrobial treatment of secondary infections.

ACUTE GENERAL TREATMENT

Address underlying illness and secondary complications (e.g., bacterial bronchopneumonia).

CHRONIC TREATMENT

- Humidification or nebulization enhances mucociliary function by increasing water content of the mucociliary blanket.
- Bronchodilators are unlikely to be helpful.
- Glucocorticoids:
  - Oral (e.g., prednisone, 0.25-0.5 mg/kg/d) preferred initially to control inflammation
  - Continuation of glucocorticoids is based clinically on the underlying disease contributing to bronchiectasis.
- If bronchiectasis is due to resolved pneumonia or obstructive disease, then glucocorticoids may not be indicated.
- If bronchiectasis is secondary to noninfectious inflammatory disease (e.g., chronic bronchitis), inflammation often will need to be controlled with long-term, low-dose glucocorticoids.
  - The metered dose inhalant glucocorticoids (e.g., flunisolide: empirically start at 110 mcg/actuation, one puff using a spacer q 12 h; decrease to 44 mcg/actuation, one puff using a spacer q 12 h thereafter) may minimize systemic side effects in the long term (see p. 1289).
- Treat recurrent secondary bacterial infections if present, ideally based on culture and sensitivity.
- In cases in which bronchiectasis is confined to a single lung lobe (e.g., due to a prior bacterial pneumonia), lobectomy may be curative.
- Cough suppressants are contraindicated, as they further impair mucociliary clearance.

BEHAVIOR/EXERCISE

- Minimize exposure to irritants such as dust, smoke, and aerosols.
- HEPA-type air filters

POSSIBLE COMPLICATIONS

Attempting to control inflammation with glucocorticoids may impair immunologic clearance of secondary infection. Additionally, bronchiectasis is itself associated with impaired mucociliary function, which also predisposes to bacterial infections. Frequent use of antibiotics may lead to development of bacterial resistance.

RECOMMENDED MONITORING

- Clinical signs at home
- Physical examination
- Thoracic radiography
- Repeated airway cultures as indicated

PROGNOSIS AND OUTCOME

- If disease is focal and the lobe removed (e.g., bronchiectasis secondary to chronic obstruction from neoplasia or a foreign body) and the underlying disease is cured, prognosis is excellent.
- Otherwise, the disease cannot be cured and must be treated chronically by balancing antibiotics for secondary infections and anti inflammatory doses of corticosteroids. In the absence of life-threatening infection or serious underlying disease (e.g., neoplasia), long-term survival is possible.

PEARLS & CONSIDERATIONS

COMMENTS

- Bronchiectasis is always secondary to an underlying condition, although the primary disease may have resolved by the time of evaluation (e.g., bacterial pneumonia).
- Management of secondary bacterial infections should be done on the basis of culture and sensitivity whenever possible to prevent development of antibiotic resistance.

PREVENTION

The best means of preventing bronchiectasis is early identification and treatment of the diseases that predispose to its development.

TECHNICIAN TIPS

- When preparing for respiratory washes, be sure to use solutions that do not contain bacteriostatic additives. If available, pre-warm solutions for respiratory lavage in a 37°C incubator (or suitable alternative).
- Needle aspiration of the lung is commonly performed with 23-gauge needles and a 6- or 12-mL syringe in the dorsal lung fields defined by rib spaces 6-8.

CLIENT EDUCATION

Owners must understand that aside from focal disease treated with lobectomy, this is not a curable disease; in multifocal and diffuse cases, recurrent secondary bacterial infections are common and can potentially be life threatening.

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AUTHORS: CAROL REINERO AND LAURA NAFE

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Bromethalin Toxicosis

BASIC INFORMATION

DEFINITION

A neurotoxic syndrome resulting from ingestion of bromethalin rodenticide.

SYNONYMS

(2,4-dinitro-*N*-methyl-*N*-[2,4,6-tribromo-phenyl]-6-[trifluoromethyl] benzeneamine). Sold under numerous trade names, including: Assault mouse/rat Place Pack, Fastrac Mouse Seed Place Pacs, Green thumb mouse killer, Hot Shot Sudden Death Brand Mouse Killer, Purina Assault Meal, Rampage Rodenticide Place Pacs, Real-Kill Mouse Killer Placepacs, Real-Kill Rat and Mouse Killer All Weather Bars, Real-Kill Rat and Mouse Killer Pellets, Real-Kill Rat Killer Placepack, Top Gun Pellet Rodenticide Place Pack, Vengeance, Trounce, No Pest

EPIDEMIOLOGY

SPECIES, AGE, SEX

Cats much more sensitive than dogs; ingestion more common in dogs than cats; all breeds, both sexes susceptible; young animals may be more sensitive

GEOGRAPHY AND SEASONALITY

Intoxication common year round but more prevalent during fall or winter months

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Dogs ingesting doses close to or greater than the LD50 (dog, 2.4-5.6 mg/kg; cat, 0.4-0.7 mg/kg bait formulation) may develop a convulsant syndrome (acute form) with onset of seizures within 24 hours.
- Dogs consuming less than the LD50 can manifest a paralytic syndrome (subacute/chronic form) in 1-7 days.
- Cats typically develop a paralytic syndrome regardless of amount ingested.

HISTORY, CHIEF COMPLAINT

- History or evidence of exposure
- Central nervous system (CNS) depression, hind limb weakness, or ataxia without evidence of pain
- Twitching, seizures

PHYSICAL EXAM FINDINGS

- Convulsant syndrome (acute form):
  - Focal or generalized seizures (possibly triggered by environmental stimuli)
- Tremors:
  - +/− Hyperthermia
- Paralytic form (sub-acute form):
  - Hind limb weakness, ataxia
  - Depression, tremors, areflexic hind limb paralysis, decreased proprioception, seizures
  - Cats may also show nystagmus, anisocoria, opisthotonos, and occasionally abdominal distension from paralytic ileus

ETIOLOGY AND PATHOPHYSIOLOGY

- Baits are sold as bars, pellets, seed, and worm. Mole baits sold as 5-g worm (0.025%, or 1.25 mg bromethalin in 5 g). Other commercial products contain 0.01% bromethalin, or 2.84 mg bromethalin per 1 oz of bait.
- Bromethalin and its major metabolite, desmobromethalin, are potent uncouplers of oxidative phosphorylation.
- Cerebral and spinal edema secondary to decreased ATP production and failure of Na^+/K^+-ATPase pumps.

- Elevated cerebrospinal fluid pressure causes neurologic dysfunction.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is generally presumptive and based on history of observed or suspected exposure to the bait followed by typical neurologic effects within 1-7 days after the exposure. Advanced or confirmatory tests are rarely conclusive for this intoxication.

DIFFERENTIAL DIAGNOSIS

- Convulsant form:
  - Primary CNS disease
  - Metaldehyde toxicosis
  - Strychnine toxicosis
  - Zinc phosphide toxicosis
  - Ethylene glycol toxicosis
  - Tremorgenic mycotoxins (moldy food ingestion)
- Paralytic form:
  - Neuromuscular disease (polyradiculoneuritis, tick paralysis, botulism, myasthenia gravis)
  - 2,4 D or other phenoxyacetic acid herbicide exposure in dogs
  - Copperhead snake envenomation in cats
  - Spinal cord/CNS trauma
  - Intervertebral disk disease

A/C, Activated charcoal.

RECOMMENDATIONS FOR DOGS

Time Since Exposure (Hours)	Dose Ingested (mg/kg)	Treatment
<4	0.1-0.49	Emesis or 1 dose of A/C
>4	0.1-0.49	One dose of A/C
<4	0.5-0.75	Emesis and 3 doses of A/C over 24 hours
>4	0.5-0.75	3 doses of A/C over 24 hours
<4	>0.75	Emesis and 3 doses of A/C a day for 48 hours
>4	>0.75	3 doses of A/C a day for 48 hours

A/C, Activated charcoal.

RECOMMENDATIONS FOR CATS

Time Since Exposure (Hours)	Dose Ingested (mg/kg)	Treatment
<4	0.05-0.1	Emesis or 1 dose of A/C
>4	0.05-0.1	1 dose of A/C
<4	0.1-0.3	Emesis and 3 doses of A/C over 24 hours
>4	0.1-0.3	3 doses of A/C over 24 hours
<4	>0.3	Emesis and 3 doses of A/C a day for 48 hours
>4	>0.3	3 doses of A/C a day for 48 hours

INITIAL DATABASE

- The diagnosis is generally presumptive, based on clinical presentation, physical examination, and history if available.
- CBC, serum biochemistry panel, diagnostic imaging: no significant changes

ADVANCED OR CONFIRMATORY TESTING

Rarely performed

- CSF tap: increased pressure; no inflammatory changes
- CNS edema, demyelination, and vacuolization on histopathologic exam
- Bromethalin can be detected in tissues postmortem (liver, kidney, brain, and fat).

TREATMENT 

TREATMENT OVERVIEW

In patients presented prior to the onset of clinical signs: induction of emesis followed by administration of activated charcoal. If signs are present, treatment is based on need (e.g., control seizures if present, provide supportive care).

ACUTE GENERAL TREATMENT

Emesis and/or activated charcoal (A/C) treatment recommendations (see Pearls, below, for concentration in products):

CHRONIC TREATMENT

Treatment for subacute cases

- Supportive care for clinically ill patients (fluids, nutritional support, seizure control, etc.)
- Cerebral edema may not respond well to furosemide, mannitol, or corticosteroids.
- Diazepam, barbiturates, and other anticonvulsants for CNS signs

POSSIBLE COMPLICATIONS

Permanent CNS damage/dysfunction due to demyelination and vacuolization

RECOMMENDED MONITORING

Animals with a suspected or confirmed exposure to bromethalin but without overt clinical signs need to be monitored for an onset of hind limb weakness or other CNS signs for 7 days postexposure.

PROGNOSIS AND OUTCOME 

- Good with decontamination of patient prior to the onset of signs
- Guarded if signs develop; recovery may take days to weeks
- Poor if paralysis or seizures develop

PEARLS & CONSIDERATIONS 

COMMENTS

- Commercial products contain 0.01% bromethalin or 2.84 mg/oz bromethalin.
- Presence of blue-green to turquoise dye in the stool over the past few days may provide evidence of ingestion, especially if exposure was not witnessed. However, presence of dye in the stool is not specific for the type of rodenticide (bromethalin, anticoagulant, vitamin D analog, etc.) involved.
- Doses of 0.95-1.05 mg/kg in dogs and 0.24 mg/kg in cats can be lethal.
- Vitamin K1 therapy, used for anticoagulant rodenticides, is not indicated for bromethalin ingestion.
- Potential for relay toxicosis (intoxication through consumption of prey that has itself ingested the toxin) appears low except for those cats whose diet consists largely of rodents.

TECHNICIAN TIP

The various rodenticides (see p. 83), bromethalin, and cholecalciferol (see p. 200) cannot be differentiated by appearance alone (in vomitus or even prior to ingestion).

PREVENTION

Placement of baits in areas not accessible to dogs and cats

SUGGESTED READING

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AUTHOR: MICHAEL KNIGHT

EDITOR: SAFDAR A. KHAN

1ST EDITION AUTHOR: ERIC DUNAYER

Breeding Management

BASIC INFORMATION

DEFINITION

Diagnostic and treatment approaches that optimize a bitch's reproductive performance

SYNONYMS

Breeding timing, estrus monitoring

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs, postpubertal, female

GENETICS & BREED PREDISPOSITION

- Breeding animals should be tested for heritable disorders; >400 genetic diseases have been identified in dogs.
- Bitches requiring elective caesarean section (e.g., brachycephalics) require intense monitoring to establish the time of their luteinizing hormone (LH) surge during estrus.

RISK FACTORS

- Advanced age of dam and/or sire
- Use of cooled or frozen semen
- Dam's or sire's history of unsatisfactory fertility
- Degenerative and/or infectious conditions within the reproductive tract

CONTAGION & ZOONOSIS

Brucella canis (see p. 162)

GEOGRAPHY AND SEASONALITY

Bitches cycle at any time of the year (except basenji—late summer/early fall).

ASSOCIATED CONDITIONS & DISORDERS

Estrus induction, artificial insemination, pregnancy diagnosis.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

Owner desires litter from dam and wants to maximize fertility and fecundity.

PHYSICAL EXAM FINDINGS

Physical exam should be unremarkable. Overt signs of estrus should be evident:

- Swollen, edematous vulva
- Serosanguineous vaginal discharge
- Perineal stimulation results in lateral deviation of the tail (“flagging”), elevation of the vulva, and lordosis

ETIOLOGY AND PATHOPHYSIOLOGY

- Developing follicles secrete estradiol initially (proestrus), followed by progesterone after the LH surge has occurred (estrus).
- Follicles ovulate 2 days after the LH surge, and oocytes are fertile another 2 days later.
- Oocytes remain fertile for 4 days.
- Breeding should occur between 3 and 8 days after the LH surge.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

For optimal timing of breeding, determine the day of the preovulatory LH surge by detecting the first day on which serum progesterone concentration exceeds 2 ng/mL or by measuring serum LH concentrations directly. Additional value may be found in vaginal cytology and vaginoscopy (see p. 1361), both of which are inexpensive, provide immediate results, and may be performed on site but are less accurate than hormone assays. Therefore, a typical protocol for a bitch whose signs of estrus are subtle involves daily vaginoscopy or vaginal cytology until characteristic changes of early estrus are noted at which time serum progesterone is measured q 24-48 h.

DIFFERENTIAL DIAGNOSIS

- Persistence of estrous behavior: granulosa cell tumor, endocrine-secreting anovulatory follicle(s)
- Discharge from an open pyometra
- Vaginal or uterine trauma resulting in bleeding

INITIAL DATABASE

- Vaginal cytologic evaluation:
  - Start 0 to 5 days after the onset of vaginal bleeding and continue q 48 h to monitor estrogenization of the vaginal mucosa.
  - Use a cotton swab moistened with saline, and extended with hemostat or artificial insemination pipette to reach through a vaginal speculum for collection of cells from cranial vagina.
  - The vaginal cytology will contain 100% superficial cells (cornified; large, angular, often with folded edges) during estrus, many of which still have nuclear remnants or pyknotic nuclei.
  - Presence of 50% or more cornified cells can be used as the threshold for beginning measurement of serum progesterone levels.
- Serum progesterone concentration
  - Start determining serum progesterone concentration once there is maximal development of the squamous epithelium and/or the vaginal cytology contains 100% superficial cells.
    - Refrigeration of whole blood during the first 2 hours after sample collection significantly decreases measured serum progesterone concentrations in dogs.
    - When whole clotted blood is not centrifuged immediately after collection, it must not be refrigerated for at least 2 hours, because this will affect serum progesterone concentrations.
  - The day of LH surge (d0) is the day preceding the first day on which serum progesterone concentration exceeds 2 ng/mL.
  - Progesterone can be measured by laboratory assays (RIA or chemiluminescence) or by patient-side semiquantitative ELISA assay.
- *Brucella canis* testing is essential (see p. 162).

ADVANCED OR CONFIRMATORY TESTING

- Vaginoscopy (see p. 1361)
  - Start 0 to 5 days after onset of vaginal bleeding; continue q 48 h to monitor estrogenization of the vaginal mucosa.
  - Tubular Plexiglas speculum, 10-20 mm inner diameter, 15-25 cm length.
  - Maximal development of the squamous epithelium (evident as paleness) and edema (evident as swollen, rounded folds) of the vaginal mucosa coincides with peak estradiol concentrations, just before LH surge.
- Serum LH concentration
  - Commercial kits are available for semiquantitative assessment of serum LH concentrations.
  - Once- or twice-daily testing is required; LH concentrations will only remain elevated for 18-24 h.

TREATMENT

TREATMENT OVERVIEW

Breeding management is preventive. Therefore, under most circumstances, treatment as such is not indicated. Proactive strategies help to optimize efficacy of breeding.

ACUTE GENERAL TREATMENT

- Breeding strategies
  - Natural service, fresh or shipped (cooled) semen artificial insemination:
    - Breed on days 4 and 6 after LH surge.
    - Inseminate vaginally, using a 5-mm-thick plastic pipette that is advanced to the caudal end of the cervix (confirm placement by abdominal palpation).
    - Once the pipette is placed, the semen is injected slowly through a syringe attached to the pipette, the pipette is withdrawn, and a finger is placed into the vestibulum and used to massage the floor of the cranial vestibulum ("feathering") for 1-10 minutes (vaginal contractions result and facilitate movement of semen through the cervix).
    - Elevation of the bitch's hindquarters (theoretical benefit of gravity) is often practiced but does not improve fertility.
  - Artificial insemination with frozen or poor-quality fresh/cooled semen:
    - Breed between days 5 to 7 after LH surge.
    - Perform laparotomy and inject semen through uterine wall into the uterine lumen, or perform transcervical catheterization and inject semen directly into uterine lumen (see p. 1346).
      - Transcervical catheterization can be performed either via an endoscopically guided transcervical catheter (dedicated equipment) or with a Norwegian catheter that can be guided through the cervix using abdominal palpation (advanced skill and experience needed).
      - Transcervical catheterization allows for repeat inseminations on multiple days.
      - With frozen semen, more than one insemination at daily intervals and a lower sperm dose produces better results than a single, well-timed insemination with a high sperm dose.
    - Two to four daily vaginal inseminations with frozen-thawed semen extended with prostatic fluid have yielded excellent results as well.
    - Natural copulation can be simulated by the use of a dedicated insemination catheter that allows for the insufflation of a large cuff that seals the vagina to prevent backflow of semen after insemination (MAVIC, Minitube of America).

BEHAVIOR/EXERCISE

- Unrestricted exercise
- To prevent unintentional matings, estrous bitches must not have contact with intact male dogs.

POSSIBLE COMPLICATIONS

- For surgical artificial insemination, clients must be warned that no anesthetic protocol is totally safe, and about 8% of all elective soft-tissue surgeries result in postoperative complications (e.g., infection, wound dehiscence, delayed healing) despite the use of modern techniques and procedures aimed at preventing such complications.
- Inappropriate timing of artificial insemination or use of poor-quality semen can result in a reduction of expected litter size.

PROGNOSIS AND OUTCOME

Average pregnancy rates after artificial insemination with fresh, chilled, or frozen-thawed semen vary greatly between 45% and 90%.

PEARLS & CONSIDERATIONS

COMMENTS

- Animals should be tested for brucellosis and heritable disorders before breeding.
- Semen quality should be assessed in advance of insemination.
- In-house test kits for semiquantitative determination of serum progesterone and luteinizing hormone concentrations of bitches are available for use when veterinary diagnostic laboratory services are not available.
- The day of LH surge (d0) is the day preceding the first day on which serum progesterone concentration exceeds 2 ng/mL.

TECHNICIAN TIP

Follow instructions very carefully when performing in-house or patient-side serum progesterone or LH tests, as results are a cornerstone of success.

CLIENT EDUCATION

- Days 3-8, or days 4 and 6, after the LH surge are the most fertile days for breeding bitches, but pregnancies can result from breeding up to 3 days earlier or 2 days later using fresh semen.
- Estrus monitoring is also used to predict the most likely whelping date: 65 (±1) days after the LH surge or 57 (±1) days after cytologic diestrus (D1).

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Brain Neoplasia

BASIC INFORMATION

DEFINITION

- Primary brain tumors include meningioma (discussed separately; see p. 715), glioma (astrocytoma, oligodendroglioma), choroid plexus tumor, ependymoma, medulloblastoma, olfactory neuroblastoma, and primitive neuroectodermal tumor.
- Secondary brain tumors include pituitary tumors, tumors that invade by direct extension into the brain (e.g., nasal tumors), and metastatic tumors to the brain (e.g., hemangiosarcoma, lymphoma [latter is discussed separately]; see p. 671).

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Occurs in both dogs and cats of both sexes
- Incidence reported as high as 2.6% in dogs and 2.8% in cats
- Brain tumors typically occur in older dogs (most > 5 years old) and cats. Median age: 9 years (dogs), 11 years (cats).

GENETICS & BREED PREDISPOSITION

- Canine: Dolichocephalic breeds (e.g., golden retriever, German shepherd dogs) tend to develop meningiomas. Brachycephalic breeds (e.g., boxer, Boston terrier) appear prone to developing gliomas.
- Feline: no breed predisposition. Meningioma is the most common brain tumor in cats.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Meningioma: tumor of the arachnoid membrane
- Glioma: tumor of the cells that form the interstitial tissue of the central nervous system (CNS)
- Choroid plexus papilloma: tumor of the cells of the choroid plexus, the intracranial vascular structure responsible for the formation of cerebrospinal fluid
- Ependymoma: tumor of the ependymal cells that line the ventricular system

HISTORY, CHIEF COMPLAINT

- A brain tumor should be suspected in any older patient with an insidious onset of slowly progressive neurologic signs, and in any patient older than 5 years with a recent onset of seizures.
- Historic findings depend on lesion location. Clinical signs are often insidious and progressive; however, recent onset of clinical signs is possible.
- The most common chief complaints include seizures, circling, behavior change (aggression), altered consciousness, and nonspecific signs such as inappetence and lethargy.

PHYSICAL EXAM FINDINGS

- Neurologic exam findings vary depending on lesion location (see p. 1311).
- Findings generally reflect a focal lesion with asymmetric clinical signs. However, a large case series found that half of canine brain tumors occupy more than one anatomic region of the brain (e.g., forebrain and brainstem).
- Cerebral brain tumors: seizures, contralateral menace and postural reaction deficits, behavior change, contralateral hemiparesis, altered mental status
- Brainstem brain tumors: ipsilateral cranial nerve deficits, hemiparesis or tetraparesis or tetraplegia, altered mental status, central vestibular dysfunction
- Cerebellar brain tumors: hypermetria, intention tremors, truncal sway, broad-based stance, paradoxical vestibular dysfunction

ETIOLOGY AND PATHOPHYSIOLOGY

- Etiology is unknown.
- Usually occur as solitary masses. Multiple tumors may be seen with metastatic disease.

- Most commonly reported in the supratentorial compartment (rostral to the tentorium cerebelli, including the cerebrum and diencephalon)
- Biological behavior (benign versus malignant) is generally irrelevant because neoplasia of the brain is detrimental via space-occupying effects.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Neoplasia of the brain is suspected based on signalment, history, and neurologic examination results. Confirmation requires intracranial imaging (CT or MRI).

DIFFERENTIAL DIAGNOSIS

- Infectious diseases (bacterial, viral, fungal, protozoal)
- Inflammatory diseases (e.g., granulomatous meningoencephalomyelitis)
- Cerebrovascular infarction if clinical signs are acute, nonprogressive, and asymmetric
- Toxin and metabolic diseases if clinical signs are acute, nonprogressive, and symmetric

INITIAL DATABASE

- CBC, serum biochemistry profile, urinalysis: usually normal
- Thoracic and abdominal radiographs: usually normal but performed to rule out extracranial neoplasia

ADVANCED OR CONFIRMATORY TESTING

- CT or MRI:
  - MRI is markedly superior for soft-tissue detail (brain, spinal cord) and has higher resolution than CT. As a result, this is the current gold standard for brain imaging.
  - CT is an adequate imaging modality, is superior for bone lesions (e.g., skull tumors), much faster, and may be cheaper than MRI.
  - Focal mass identified for most brain tumors; however, multiple tumors may be identified with metastatic neoplasia.
  - CT and MRI features are variable between tumor types.
- Cerebrospinal fluid (CSF) analysis:
  - Used as an adjunct to advanced imaging, primarily to assess encephalitis
  - With brain neoplasia, results are generally nonspecific and reveal normal to mildly elevated protein.
  - Albuminocytologic dissociation (elevated CSF protein with normal white blood cell count) can occur but is not pathognomonic.
  - Neoplastic cells are rarely identified within the CSF; however, the presence of lymphoblasts within the CSF supports a diagnosis of CNS lymphoma.
- Histopathologic analysis of tissue is required for definitive diagnosis. Tissue samples can be obtained via surgical excision or stereotactic brain biopsy.

TREATMENT

TREATMENT OVERVIEW

Definitive treatment involving surgical excision and/or radiation therapy and/or chemotherapy

ACUTE GENERAL TREATMENT

- Surgical excision: used for removing or debulking the tumor, if accessible, and for providing a definitive histologic diagnosis
- Radiation therapy: used as an adjunctive treatment to surgery or as a primary treatment
- Chemotherapy: most agents are not effective because the blood-brain barrier (BBB) prevents chemotherapeutic agents from entering the brain and spinal cord. The exception to this is nitrosourea drugs.
  - Nitrosourea agents such as lomustine (CCNU; 60-90 mg/m^2 PO q 6 wk) or carmustine (BCNU 50 mg/m^2 IV q 6 wk), which can cross the BBB, appear to have some effect in canine gliomas and canine CNS lymphoma.
  - The most serious potential adverse effects are bone marrow suppression (anemia, thrombocytopenia, leukopenia) and hepatotoxicity.
  - The use of hydroxyurea (20 mg/kg PO q 24 h) has been shown to significantly increase survival times in dogs with

meningiomas, compared with use of prednisone alone. Side effects at this dose are typically mild to nonexistent.

- Cluster seizures or status epilepticus: diazepam, 0.5 mg/kg IV (can be repeated at 5-minute intervals for a maximum of three doses). If diazepam is initially effective, but seizures recur, consider diazepam IV constant rate infusion (0.25-0.5 mg/kg/h) or loading dose of phenobarbital IV (to effect, up to 16-20 mg/kg total dose). A seemingly effective newer alternative therapy is intravenous levetiracetam.
- Cerebral edema/brain herniation: mannitol, 0.5 g/kg IV slowly over 10-15 minutes; furosemide (2 mg/kg IV) has synergistic effects with mannitol and can be given if needed.

CHRONIC TREATMENT

- Seizures: anticonvulsants should be used if there is more than one seizure every 6-8 weeks.
  - Phenobarbital: 2-4 mg/kg PO or IV q 12 h
  - Potassium bromide: 20-50 mg/kg PO q 24 h; dose can be divided q 12 h to reduce nausea and vomiting. (See p. 1009 and p. 353 .) Use with caution in cats; frequently causes reversible clinical signs consistent with bronchial asthma, but in rare cases has been fatal.
- Cerebral edema: prednisone, 0.5 mg/kg PO q 12 h initially, then taper to lowest dose that will control clinical signs.

DRUG INTERACTIONS

- Drug interactions or altered metabolism of medications have been reported between corticosteroids and amphotericin B, furosemide, thiazide diuretics, digitalis glycosides, cyclosporine, phenytoin, phenobarbital, and mitotane.
- Corticosteroids should not be given concurrently with nonsteroidal antiinflammatory drugs or other potentially gastric ulcerogenic medications.
- Phenobarbital may cause excessive sedation in dogs with intracranial mass lesions, even at low doses.

POSSIBLE COMPLICATIONS

Progression of clinical signs, including status epilepticus, brain herniation, and sudden death

RECOMMENDED MONITORING

- Serial neurologic exam every 4-6 weeks
- Serum phenobarbital blood level 2 weeks after starting medication, or any change in dosage, or immediately after loading dose
- Serum bromide blood level 3-4 months after starting medication, or any change in dosage in dogs and 2 months in cats, or immediately after loading dose

PROGNOSIS AND OUTCOME

- In general, the prognosis is fair to guarded in both dogs and cats.
- In dogs, several small-scale reports have shown a median survival time of approximately 2-4 months with supportive care and nonspecific treatment only, 6-12 months with surgery alone, 7-24 months with radiation therapy alone, 6 months to 3 years with surgery and radiation, and 7-11 months with chemotherapy alone.
- There are no large-scale reports of survival times in cats, with the exception of meningiomas (see p. 715). However, the long-term prognosis for cats with other brain tumors is likely similar to that for dogs.

PEARLS & CONSIDERATIONS

COMMENTS

With neoplasia of the brain, asymmetric neurologic deficits are much more common than symmetric deficits. Symmetric neurologic deficits make other diagnoses more likely.

TECHNICIAN TIPS

Postoperative craniotomy patients are very vulnerable to brain trauma, and comprehensive care (e.g., padding of cage walls, prevention of self-trauma through gentle restraint and padding over the surgical site) can make the difference between a excellent outcome and a life-threatening complication.

PREVENTION

No known method to prevent disease

CLIENT EDUCATION

- Warn owner of corticosteroid side effects (e.g., polyuria, polydipsia, polyphagia, weight gain, gastrointestinal ulceration, iatrogenic hyperadrenocorticism).
- Phenobarbital and KBr: Short-term side effects include sedation/lethargy and pelvic limb weakness and ataxia. Long-term side effects include polyuria, polydipsia, polyphagia, weight gain. Less common adverse effects include hepatotoxicity and blood dyscrasias for phenobarbital and pancreatitis for KBr.
- See other sources for additional information.

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Brachycephalic Airway Syndrome

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

A syndrome of anatomic and functional abnormalities of the upper airway found in brachycephalic (short-nosed) dogs; results in variable degrees of upper airway distress

SYNONYMS

Brachycephalic syndrome; brachycephalic upper airway syndrome; upper airway syndrome

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Brachycephalic airway syndrome occurs almost only in dogs.
- Mean age at presentation: 3 to 4 years.
- Age at presentation variable:
  - Young dogs (3-12 months old); clinical signs often associated with stenotic nares
  - Middle-aged dogs with increasingly severe respiratory problems over several years

GENETICS & BREED PREDISPOSITION

Breeds predisposed: English and French bulldogs, Boston terrier, pug, boxer, Pekinese, shih tzu (shih tzu: rarely elongated soft palate, frequently stenotic nares).

RISK FACTORS

Deterioration/decompensation producing severe dyspnea:

- Hot, humid weather
- Hot ambient temperature (e.g., in car with inadequate ventilation)
- Exertion

GEOGRAPHY AND SEASONALITY

More likely to trigger owner concern during summer, when increased ambient temperatures and activity can lead to episodes of severe dyspnea.

ASSOCIATED CONDITIONS & DISORDERS

- Three primary anatomic components of the brachycephalic airway syndrome:
  - Stenotic nares
  - Elongated soft palate
  - Hypoplastic trachea
  - Any or all may be present in any given brachycephalic dog
- Secondary airway changes that can develop due to increased airway resistance include:
  - Laryngeal saccule eversion
  - Laryngeal collapse
    - Seen in older dogs with chronic, severe, untreated brachycephalic syndrome
- Obesity: aggravating factor
- Noncardiogenic pulmonary edema (see p. 933), acute respiratory distress syndrome (see p. 34):
  - Occurs if patient inspires forcefully and excessively against severe upper airway obstruction
  - Can cause persistence of cyanosis/hypoxemia despite relief of upper airway obstruction

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- History of exercise intolerance, cyanosis, or collapse
- Gagging or coughing
- Stertor (heavy snoring) most common, stridor (high pitched) less common

PHYSICAL EXAM FINDINGS

- Stenotic or narrowed nares
- Stertor or stridor; increased inspiratory sounds
- Increased expiratory sounds on auscultation if concurrent pneumonia, bronchitis, or noncardiogenic pulmonary edema
- If in severe respiratory distress: cyanosis, stridor or apnea, hyperthermia

ETIOLOGY AND PATHOPHYSIOLOGY

- Breeding selection has led to dorsoventral flattening and rostrocaudal shortening of the skull and nasal passages of these dogs. The result is increased negative pressure in the nasal passages and pharynx during inspiration.
- These anatomic characteristics coupled with redundant and edematous nasopharyngeal and oropharyngeal soft tissues contribute to increased airway resistance and obstruction.
- If untreated, stenotic nares and an elongated soft palate increasingly interfere with breathing.
- Excessive negative nasopharyngeal pressure results in laryngeal saccule eversion and laryngeal collapse (inward folding of the epiglottis and arytenoid cartilages).
- As the nasopharyngeal mucosa becomes edematous and inflamed, it contributes to upper airway obstruction.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The characteristic inspiratory stertor in brachycephalic breeds is suggestive of the diagnosis on physical examination alone. Confirmation requires a sedated oropharyngeal examination and cervical and thoracic radiographs.

DIFFERENTIAL DIAGNOSIS

- Upper airway mass: neoplasia, polyp, granuloma, foreign body, abscess
- Laryngeal paralysis
- Cervical or laryngeal trauma
- Coagulopathy resulting in laryngeal hematoma
- Collapsing trachea

INITIAL DATABASE

- CBC, serum biochemistry profile, urinalysis: generally unremarkable
- Lateral cervical radiographs: length of soft palate, hypoplastic trachea
- Inspiratory and expiratory thoracic radiographs (to assess for complications and rule out differential diagnosis):
    - Tracheal collapse
    - Chronic small airway disease
    - Pneumonia
    - Noncardiogenic pulmonary edema

ADVANCED OR CONFIRMATORY TESTING

Rapid-acting anesthetic induction and oropharyngeal/laryngeal examination (e.g., propofol, 4-6 mg/kg given slow IV to effect): be prepared to intubate and ventilate if necessary, given propofol's apnea-inducing qualities:

- Determine if soft palate excessively long
- Presence of laryngeal saccule eversion
- Presence of laryngeal collapse

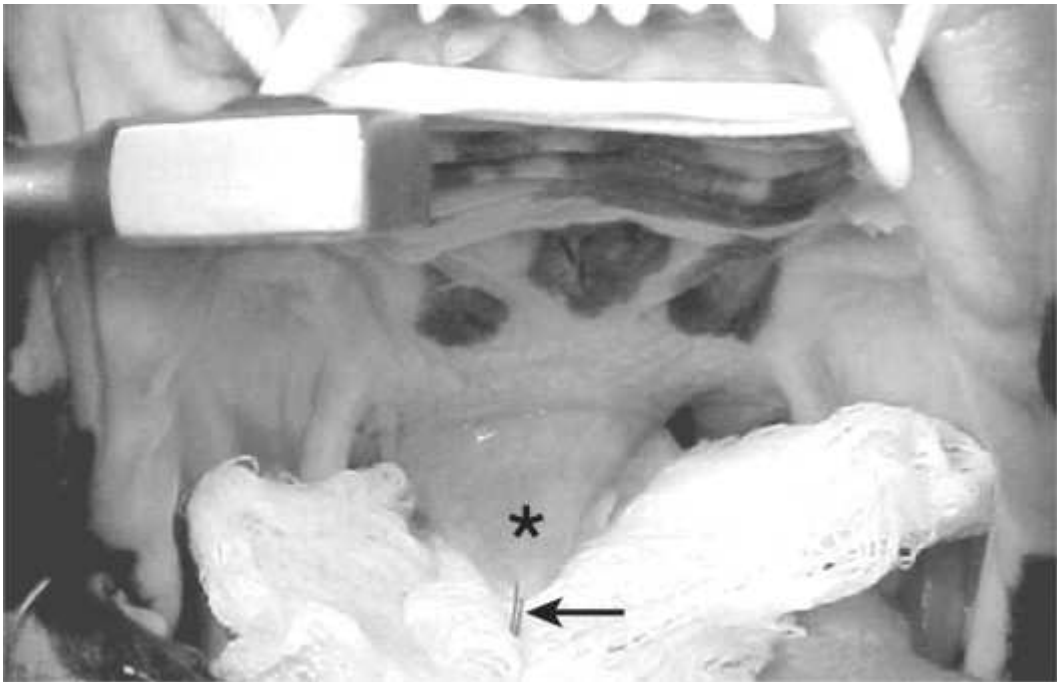
TREATMENT

TREATMENT OVERVIEW

- Immediately, if severe dyspnea:
  - Relieve upper airway obstruction via sedation with or without endotracheal intubation or tracheostomy.
  - Minimize patient's anxiety, and thus reduce the risk of noncardiogenic pulmonary edema, hyperthermia, and worsening dyspnea.
- Long-term:
  - Relieve upper airway obstruction via surgical correction.

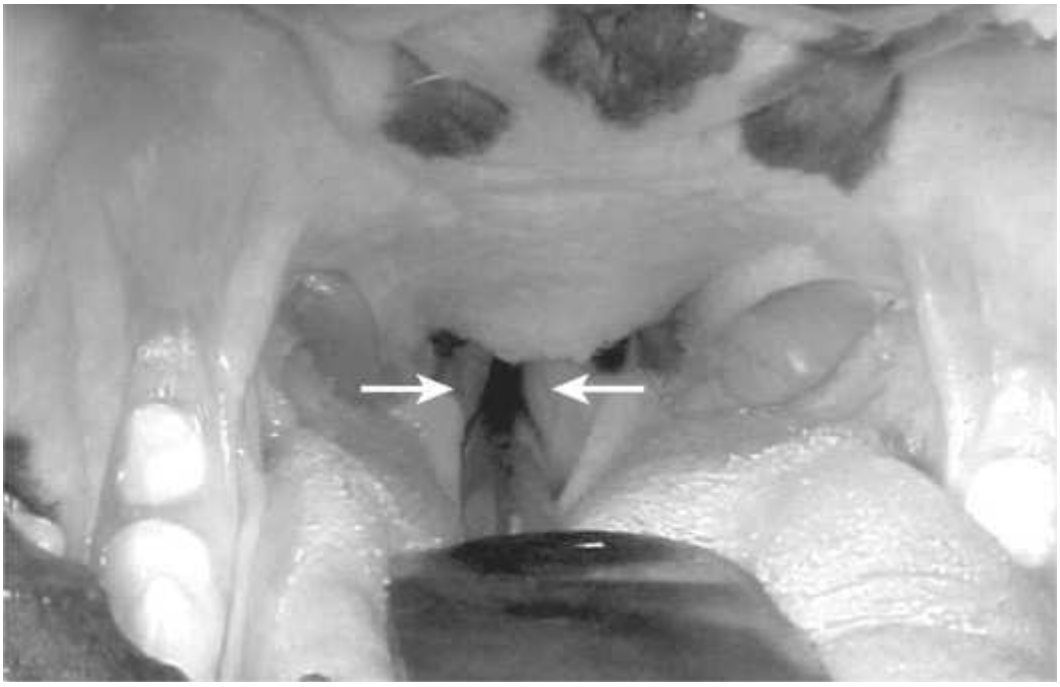
ACUTE GENERAL TREATMENT

- Stenotic nares:
  - Remove excessive cartilaginous tissue of alae (wings) of nostrils by excision.
- Elongated soft palate:
  - Shorten soft palate by removing excessive or redundant palatal tissue to improve glottal airflow, eliminate excessive negative pressure, and improve functional glottal size.
  - Soft palate resection using sharp transection and suture, or CO2 laser
- Everted laryngeal saccules: excise everted mucosal tissue.
  - Traction and amputation of everted mucosa with scissors, scalpel, or CO2 laser
- Laryngeal collapse:
  - Cannot be surgically corrected
  - Permanent tracheostomy may be necessary
- Hypoplastic trachea: no surgical treatment
- Complications: treatment as required should they occur



BRACHYCEPHALIC AIRWAY SYNDROME Preoperative open-mouth view of the elongated soft palate *(asterisk)* of a French bulldog with brachycephalic airway syndrome. A stay suture *(arrow)* is placed through the caudal tip of the soft palate in preparation for resection.

(Courtesy Dr. Richard Walshaw.)



BRACHYCEPHALIC AIRWAY SYNDROME Postoperative view of the same dog. Resection of the elongated soft palate is complete, creating a pharynx with a more normal conformation. Consequently, the larynx *(arrows)* is more easily seen, illustrating the improvement brought by the soft palate resection.

(Courtesy Dr. Richard Walshaw.)

CHRONIC TREATMENT

- Avoid exposure to high ambient temperatures and humidity and other sources of stress.
- Maintain optimal body weight.

POSSIBLE COMPLICATIONS

- Hyperthermia (see p. 480)
- Noncardiogenic pulmonary edema (see p. 933). Sedate early to reduce the risk of this complication.
- Aspiration pneumonia (see p. 885)
- Excessive shortening of soft palate may result in nasal reflux of food or water or, more rarely, aspiration pneumonia.
- Laryngeal saccule eversion and collapse may develop if upper airway obstruction persists.

RECOMMENDED MONITORING

Owner should be aware of any recurrent signs of upper airway obstruction (exercise intolerance, coughing, gagging, stridor, or stertor), which might indicate progressive degenerative changes in upper airway (laryngeal collapse).

PROGNOSIS AND OUTCOME

- Guarded prognosis if acute, severe dyspnea: a life-threatening state may exist, but with a good response to treatment, full resolution of signs is possible.
- Good to excellent long-term prognosis after correction of stenotic nares and resection of elongated soft palate, provided secondary changes have not developed
- Variable (poor to good) prognosis if laryngeal collapse has developed or if dog has a hypoplastic trachea, depending on degree of airway obstruction

PEARLS & CONSIDERATIONS

COMMENTS

- Early detection and surgical treatment are recommended for best outcome and avoidance of secondary changes/complications.
- Lifestyle modifications are often necessary to minimize episodes of airway distress:
  - Maintain ideal body weight.
  - Avoid stressful situations.
- Hypoplastic trachea is often a subclinical problem, but if severe it may affect long-term prognosis and outcome after surgery.

PREVENTION

- Because brachycephalic syndrome is breed-associated and heritable, it is not preventable in a given patient.
- Episodes of respiratory distress may be minimized by avoiding stress, moderating exercise, preventing obesity, avoiding exposure to high ambient temperatures, and early surgical treatment for elongated soft palate and stenotic nares.
- Correction of stenotic nares in the puppy may reduce the severity of brachycephalic syndrome later in life.

TECHNICIAN TIPS

Hospitalized patients with brachycephalic syndrome require preoperative and postoperative intensive care and constant monitoring. Respiratory obstruction is a potential problem at any time. Technicians caring for these patients perioperatively should be familiar with and comfortable performing:

- Orotracheal intubation in a brachycephalic dog
- Oxygen administration
- Administration of prescribed sedative and analgesic drugs
- Tracheostomy care
- Cardiopulmonary resuscitation

CLIENT EDUCATION

- Discuss breed association and heritability in brachycephalic dogs.
- Syndrome is progressive and exacerbated by stress, obesity, and exposure to high ambient temperatures.
- Early surgical intervention is important for most successful outcome.

SUGGESTED READING

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Brachial Plexus Abnormalities

BASIC INFORMATION

DEFINITION

Dysfunction of the peripheral nerves or nerve roots of the brachial plexus (C6-T2 spinal segments)

EPIDEMIOLOGY

RISK FACTORS

Dependent on disease subtype:

- Trauma
- Antigenic stimulation/allergy

ASSOCIATED CONDITIONS & DISORDERS

With concurrent traumatic injuries:

- Shock, hypotension, head trauma, pneumothorax
- With neoplasia, intervertebral disk disease: +/− signs of unilateral C6-T2 myelopathy

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Traumatic brachial plexus injury:
  - Neurotmesis: complete avulsion of brachial plexus nerves
  - Unilateral or bilateral; can involve some or all nerves in the brachial plexus
    - Axonotmesis: partial brachial plexus avulsion (endoneurium remains intact)
    - Neurapraxia: stretching/transient damage to nerve(s), without avulsion
- Brachial plexus neuritis:
  - Idiopathic inflammatory neuropathy of the brachial plexus
- Nerve sheath tumors (see p. 763)
- Lymphoma (rare)

HISTORY, CHIEF COMPLAINT

- Thoracic limb lameness, paresis, or paralysis (acute or chronic onset)
- History of trauma or antigenic stimulation (e.g., vaccination, allergic hypersensitivity [see p. 64 and p. 402])

PHYSICAL EXAM FINDINGS

- Variable, depending on nerve root(s) affected
- Abnormalities may include:
  - Focal muscle atrophy
    - Evident 5-10 days post injury
  - Neurologic deficits in thoracic limb(s): normal pelvic limbs
    - Thoracic limb monoparesis/monoplegia, or bilateral thoracic limb paresis/plegia
    - Proprioceptive deficit of affected limb(s)
    - Hyporeflexia/areflexia
    - Loss of nociception (superficial or deep pain sensation) to various autonomous zones of thoracic limb(s): evaluate all autonomous zones and all digits for sensory loss (see p. 1412)
  - Ipsilateral loss of cutaneous trunci reflex
    - May occur with lateral thoracic nerve injury (C8-T1 spinal nerve roots)
  - Ipsilateral Horner's syndrome
    - May occur with injury of the sympathetic pathway (T1-T3 spinal nerve roots)

ETIOLOGY AND PATHOPHYSIOLOGY

- Brachial plexus injury/avulsion: trauma to the thoracic limb(s) that results in abduction, caudal displacement, or extreme flexion/extension of the shoulder joint; results in traction injury to the nerve roots of the brachial plexus as they attach to the spinal cord
- Complete avulsion more common than partial, caudal nerve root avulsion more common than cranial
- Brachial plexus neuritis: idiopathic inflammatory response; theories include antigenic stimulation by vaccination, allergic reactions, or diet hypersensitivities (particularly diets containing horse meat).
- Neoplasia

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on evidence of thoracic limb hypotonic and hyporeflexive monoparesis/monoplegia with normal pelvic limbs. History may include trauma or recent vaccination. Electrodiagnostic testing and advanced imaging (CT/MRI) may confirm etiology and provide prognostic information.

DIFFERENTIAL DIAGNOSIS

- Neoplasia
- Musculoskeletal injury:
  - Fractures
  - Dislocations
  - Muscle avulsions
- Central cord syndrome:
  - Injury or dysfunction of the central spinal cord parenchyma (grey matter)
  - Very rare; reported sporadically with spinal trauma, disk herniation, intramedullary neoplasia, syringomyelia
- Other focal neuropathies (e.g., early stages of rabies encephalomyelitis or acute canine polyradiculoneuritis/Coonhound paralysis)

INITIAL DATABASE

- Neurologic examination (see p. 1311)
- Cutaneous sensory evaluation (autonomous zones) and deep pain assessment (see p. 1412)

ADVANCED OR CONFIRMATORY TESTING

- Electrodiagnostic testing (see online chapter: Electromyography and Nerve Conduction Velocity): may confirm loss of function but generally not essential for diagnosis
  - Abnormal spontaneous muscle activity seen with electromyography
  - Decreased motor or sensory nerve conduction velocities
- Myelography, CT, and MRI: often not effective in diagnosing brachial plexus injury; however, may rule out other compressive myelopathies or neuropathies
- Brachial plexus ultrasonography: not effective for diagnosing brachial plexus injury; may be useful to localize neoplasia located within the brachial plexus

TREATMENT

TREATMENT OVERVIEW

Treatment mainly consists of maintaining joint mobility and preventing muscle contracture and self-mutilation of affected limb(s) while awaiting return of neurologic function and ability to ambulate.

ACUTE GENERAL TREATMENT

- Supportive care/trauma resuscitation
- Prevent self-mutilation and external trauma to affected limb(s):
  - Booties to protect paw from abrasions and scuffing
  - E-collar to prevent licking, chewing, or other self-mutilation

- Neuropathic analgesia (i.e., gabapentin 10 mg/kg PO q 8 h) may help prevent paresthesia and self-mutilation.
- Corticosteroids may be beneficial in brachial plexus neuritis; however, insufficient information exists to confirm their efficacy.

CHRONIC TREATMENT

- Prevent self-mutilation.
- Physical therapy (see p. 1329): prevent muscle contracture and maintain range of motion/extensor ability should neurologic function return:
  - Target-all joints, including carpus and digits.
  - Perform range of motion (ROM) exercises for 10-15 minutes 3-5 times daily.
- Limb amputation: treatment of choice for permanent unilateral brachial plexus avulsion or if documented or highly suspected nerve sheath tumor
- Euthanasia is warranted in permanent bilateral avulsions.
- Limb-sparing treatments for brachial plexus avulsion have been attempted, including nerve root transplantation, transposition, neurotization, and muscle transposition. Treatment results are generally unsatisfactory. Transposition and neurotization of the intact contralateral C8 ventral root in dogs shows some promise, but at this time, recovery of neurologic function remains limited.

NUTRITION/DIET

Avoid diets containing horse meat.

POSSIBLE COMPLICATIONS

- Paresthesias/sensory nerve injuries promote self-mutilation.
- Abrasions may occur on the dorsum of the paw from scuffing/dragging the affected limb during ambulation, creating a potential portal for infection.
- Peripheral nerve sheath tumor that goes on to invade the vertebral canal

RECOMMENDED MONITORING

Serial assessment of cutaneous sensation and motor function every 2-4 weeks

PROGNOSIS AND OUTCOME

- Loss of deep pain sensation suggests avulsion and warrants a grave prognosis for return of function.
- Preservation of deep pain sensation warrants a guarded to good prognosis for return of function over weeks to months.
- Lack of any neurologic improvement over a 4-week period suggests permanent deficit.
- Brachial plexus neuritis has a guarded prognosis; recovery is possible.

PEARLS & CONSIDERATIONS

COMMENTS

- Physical therapy is imperative in cases with potential for recovery.
  - Splints or bandages are generally not recommended because they impair mobility.
- Evaluate all digits for deep pain sensation; peripheral nerve deficits may be localized and identified in only one digit.
- Neoplasia may present as an acute onset/trauma event.

PREVENTION

Minimize risk of motor vehicle trauma (e.g., riding in open truck beds where pets could jump or be thrown from the vehicle).

CLIENT EDUCATION

- If recovery is possible/attempted, train clients to perform effective physical therapy or encourage referral for formal rehabilitation.
- If amputation is necessary, discuss benefits of amputation and how well pets adapt.
- Discuss importance of maintaining pet at a lean body weight and the negative impact of concurrent osteoarthritis or hip dysplasia on their pet's ability to ambulate.

SUGGESTED READING

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Botulism

BASIC INFORMATION

DEFINITION

An acute, rapidly progressive generalized lower motor neuron (LMN) paralytic disorder caused by ingestion of an exotoxin produced by the bacterium *Clostridium botulinum*

EPIDEMIOLOGY

SPECIES, AGE, SEX

Any breed, either sex. Cats appear highly resistant to botulism (no natural cases reported).

RISK FACTORS

Ingestion of contaminated food or carrion.

CONTAGION & ZOONOSIS

There are seven antigenically identified types of botulinum neurotoxins (A-G). Dogs: type C. Large animals: type B. Humans: types A, B, F.

ASSOCIATED CONDITIONS & DISORDERS

Aspiration pneumonia, ventilatory failure (respiratory arrest)

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Lower motor neuron paresis/paralysis that is often ascending
  - Begins as weakness in the pelvic limbs and can progress to quadriplegia
- History of ingestion of carrion or other source of anaerobic bacterial contamination
  - The incubation period after ingestion ranges from hours to 6 days.
  - Botulism is especially likely if multiple animals are affected.

PHYSICAL EXAM FINDINGS

- Decreased LMN reflexes (patellar, others) and muscle tone in all limbs
- Cranial nerve abnormalities (decreased/absent palpebral and menace, decreased jaw tone and gag, mydriasis, voice change)
- Level of consciousness maintained, pain perception preserved
- In severely affected animals, decreased abdominal and intercostal muscle tone is observed, which can require ventilation or lead to death from ventilatory failure.
- Tail wag is maintained.
- Parasympathetic dysfunction can also be observed (heart rate changes, regurgitation due to megaesophagus).

ETIOLOGY AND PATHOPHYSIOLOGY

- *C. botulinum* is a gram-positive, saprophytic, spore-forming bacterial rod in soil.
- Clinical signs develop after ingestion of the preformed toxin; it is absorbed from the stomach and small intestine and enters the lymphatics, where it is transported by an unknown mechanism to the neuromuscular junction of cholinergic nerves.
- A metalloprotease (botulinal toxin) prevents the presynaptic release of acetylcholine at the neuromuscular junction. Toxin binding is quick, irreversible, and independent of temperature and neural activity. Cell membrane receptors have a high affinity for the toxin (species and individual variation in sensitivity to toxin).
- The severity of the signs varies with the amount of toxin ingested and individual susceptibility.
- The blockage of release of acetylcholine from the presynaptic membrane results in progressive, symmetric, ascending lower

motor neuron paresis/paralysis.
- Duration of illness in the dog: 14-24 days

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is based on a history suggestive of toxin ingestion and the resultant clinical signs. Toxin identification may be undertaken to confirm the diagnosis, but treatment, which is supportive and may be urgently required, is initiated based on neurologic deficits and history.

DIFFERENTIAL DIAGNOSIS

- Early tick paralysis
- Early polyradiculoneuritis

INITIAL DATABASE

- CBC, serum biochemical analysis, and urinalysis: usually normal
- Neurologic examination consistent with diffuse lower motor neuron dysfunction
- Thoracic and abdominal radiographs may occasionally reveal megaesophagus (with or without signs of aspiration pneumonia) and carrion skeletal remains in the gastrointestinal tract, respectively, but radiographic abnormalities are not required to make the diagnosis of botulism.

ADVANCED OR CONFIRMATORY TESTING

- Confirmatory diagnosis is based on finding the toxin in serum, feces, vomitus, or food samples.
- Preferred method of toxin identification is the mouse neutralization test.
- Other in vitro tests (radioimmunoassay, passive hemagglutination, enzyme-linked immunosorbent assay and polymerase chain reaction) exist but have not replaced the mouse test to date.
- Electrophysiologic testing (see p. 1255):
    - Marked reduction in muscle action potential amplitude evoked by electrical stimulation of the motor nerve
    - Normal or only mildly reduced nerve conduction velocities
    - Normal electromyography

TREATMENT

TREATMENT OVERVIEW

Treatment consists principally of supportive care during spontaneous recovery.

ACUTE GENERAL TREATMENT

- Antitoxin (type specific) must be administered before the botulinal toxin binds to receptors at the myoneural junction.
    - Type C polyvalent antitoxin (dog): 10,000-15,000 IU/dog IV or IM, 2 doses given 4 hours apart
    - Anaphylaxis (see p. 64) is a potential risk; intradermal skin testing is recommended prior to administration.
    - Antitoxin may be effective to prevent further toxin binding if ongoing intestinal absorption/circulation.
- Antibiotic use is debated; penicillin and metronidazole have been given to dogs and humans to reduce potential intestinal growth of *C. botulinum*, but use is controversial (disease occurs due to ingestion of preformed toxin; these drugs could alter gastrointestinal flora).
- Antibiotics if secondary infection (i.e., aspiration pneumonia; based on culture and sensitivity testing).

CHRONIC TREATMENT

Long-term physical rehabilitation (see p. 1329), frequent turning, and soft bedding are essential.

DRUG INTERACTIONS

Avoid aminoglycosides (associated with neuromuscular blockade)

POSSIBLE COMPLICATIONS

- Aspiration pneumonia
- Decubital ulcers
- Muscle atrophy and fibrosis
- Ventilatory failure

RECOMMENDED MONITORING

- Respiratory rate and character; temperature and pulse
- Chest radiographs
- Serial neurologic examinations

PROGNOSIS AND OUTCOME 

- Good to guarded.
- Recovery usually occurs 2-3 weeks after regrowth of terminal motor branches; dependent on severity of signs and complications.
- Complete recovery can occur spontaneously in moderately affected animals.

PEARLS & CONSIDERATIONS 

COMMENTS

- The index of suspicion for botulism increases markedly if more than one animal is affected simultaneously.
- Referral may be necessary if long-term supportive care and ventilatory support are needed.

PREVENTION

- Prevention of access to carrion and spoiled food
- Thorough cooking of any foods fed to dogs and cats
- Botulinal toxin is destroyed by heating to 80°C for 30 minutes or 100°C for 10 minutes.

CLIENT EDUCATION

See Prevention above.

SUGGESTED READING

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Borreliosis

BASIC INFORMATION

DEFINITION

Borreliosis is a bacterial disease that infects humans, mammals, and birds. It is caused by a unicellular, spiral-shaped, gram-negative spirochete, transmitted primarily by *Ixodes* ticks.

SYNONYMS

Lyme disease, Lyme borreliosis

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Susceptibility: humans, dogs, cats
- Younger dogs more commonly affected.

GENETICS & BREED PREDISPOSITION

- Breeds associated with outdoor activities
- Labradors, golden retrievers, and Shetland sheepdogs appear predisposed to Lyme nephropathy.

RISK FACTORS

Tick exposure in endemic areas

CONTAGION & ZOONOSIS

- Direct transmission does not occur from pets to humans.
- Seropositive dogs/cats are sentinel carriers.

GEOGRAPHY AND SEASONALITY

- In 2005, 89% of human cases reported in the US were from 10 northeastern and mid-Atlantic states (PA, NY, NJ, MA, CT, RI, MD, DE, VA, NH); 6% were from upper Midwest states (WI, MN).
- Most cases are reported between May and November.

ASSOCIATED CONDITIONS & DISORDERS

Lyme nephropathy can develop in predisposed animals. Tickborne co-infections are common, especially anaplasmosis (p.66).

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- History of tick exposure in a Lyme-endemic area
- Most seropositive dogs (95%) show no clinical signs. In highly endemic areas, 70%-90% of healthy dogs are seropositive. Illness in seropositive cats is rare.
- Less than 5% of seropositive dogs show the syndrome “Lyme arthritis” (anorexia/fever/arthritis). This occurred 2-5 months after tick exposure in experimental beagle puppies (self-limiting), whereas adults showed no clinical signs.
- No experimental model exists for the less common syndrome “Lyme nephropathy” (protein-losing nephropathy [PLN] with glomerulotubular damage). Patients with this syndrome may present with signs of nephrotic syndrome, hypertension, thromboembolic events, and/or renal failure signs (vomiting/anorexia).

PHYSICAL EXAM FINDINGS

- No abnormalities is most common.
- Lyme arthritis: warm, swollen, painful joint(s), fever (103-106°F, [40-41°C]), lymphadenopathy.
- Lyme nephropathy: dehydration (renal failure), ascites/edema (nephrotic), aortic thromboembolism/dyspnea (thromboembolic events), retinal hemorrhage/detachment (hypertension).

ETIOLOGY AND PATHOPHYSIOLOGY

- *Borrelia burgdorferi* is a small micro-aerophilic spirochete.
- The agent in North America is *B. burgdorferi sensu stricto*.
- The organism multiplies in the tick, entering the host at the end of the tick's bloodmeal (when it regurgitates) after 48-72 hours of attachment.
- Replication in the skin at the tick bite site is followed by interstitial tissue migration.
- Clinical signs appear to be due to an immune-mediated pathogenesis (e.g., Lyme-specific antigen-antibody complexes are in glomeruli of dogs with Lyme nephropathy).
- A persistent carrier state is likely both in healthy-appearing carriers and clinically ill patients.
- Vectors are *I. scapularis* (deer tick) in the eastern United States and *I. pacificus* in the western United States. The white-footed deer mouse is the main reservoir and preferred host of larval and nymphal ticks. There is no transovarial transmission. Migratory birds are also carriers and disseminate infective ticks.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

- A presumptive diagnosis of borreliosis includes (1) evidence of natural exposure antibodies, (2) clinical signs consistent with borreliosis, (3) consideration of other differentials, and (4) response to treatment, although Lyme nephropathy may not respond well.
- Overdiagnosis should be avoided; in endemic areas, many dogs with no clinical signs are seropositive. Response to treatment does not confirm diagnosis and may occur by inadvertent treatment of causative co-infections (e.g., Rocky Mountain spotted fever [RMSF], anaplasmosis, ehrlichiosis, bartonellosis, leptospirosis), or the antiinflammatory/antiarthritic properties of doxycycline.
- All seropositive (clinical and nonclinical) dogs should be monitored for proteinuria. Treatment is not recommended for nonclinical, nonproteinuric seropositive carrier dogs. The dog's sentinel status is an opportunity to educate the owner about tick control and public health aspects of Lyme disease.

DIFFERENTIAL DIAGNOSIS

- Lyme arthritis versus other causes for lameness
  - Septic arthritis, tickborne arthritides (anaplasmosis, ehrlichiosis, RMSF, bartonellosis), immune-mediated polyarthritis, systemic lupus erythematosus, rheumatoid arthritis
  - Degenerative joint disease, intervertebral disk disease, trauma
  - Panosteitis, osteomyelitis, polymyositis, neoplasia
  - Cardiopulmonary, metabolic, neurologic disease
- Lyme nephropathy
  - Proteinuria: urinary tract infection, neoplasia, calculi
  - PLN: genetic, infectious, immune-mediated, amyloidosis, neoplasia
  - Other causes for hypertension, hypercoagulable state, edema/effusions, and/or renal failure

INITIAL DATABASE

To confirm exposure and rule out other causes of lameness/fever or PLN:

- CBC and serum biochemistry profile: no specific findings expected unless Lyme nephropathy: hypoalbuminemia, hypercholesterolemia, ± azotemia, hyperphosphatemia, anemia, thrombocytopenia possible.
- SNAP-4Dx (IDEXX Laboratories) for heartworm antigen and antibodies to C6 peptide (specific for natural exposure to *B. burgdorferi*), *E. canis/chaffeensis*, and *A. phagocytophilum/A. platys*. This test replaces previous two-tier testing with Western blot for differentiating natural exposure from vaccine-induced antibodies, because the C6 peptide of the VlsE antigen is not found in any Lyme vaccines.
- IgM/IgG titers are not warranted. Experimentally infected dogs did not show signs of Lyme disease until 2-5 months, well after seroconversion (there is no acute stage when they are seronegative), so paired acute/convalescent titers are unnecessary.
- All Lyme-positive dogs should be screened for proteinuria by urinalysis, microalbuminuria testing, or urine protein/creatinine ratio. Lyme nephropathy cases may also have glycosuria and/or active sediment due to tubular damage.
- Radiographs of leg(s) involved (nonerosive arthritis)

- Arthrocentesis: nonseptic suppurative inflammation
- Abdominal ultrasound and chest radiographs to rule out neoplasia

ADVANCED OR CONFIRMATORY TESTING

- Serology: C6 Quant (IDEXX Laboratories). C6 antibody is detected 3-5 weeks post exposure, before clinical signs appear; paired titers are not necessary. C6 > 30 proves natural exposure (not cause) and is not an indication for treatment in nonclinical, nonproteinuric dogs. Magnitude of titer is not predictive of or correlated with illness.
- PCR or paired serology for other infectious diseases: RMSF (if acute presentation), anaplasmosis/ehrlichiosis, bartonellosis, babesiosis, leptospirosis.
- Renal biopsy: glomerulonephritis, tubular necrosis/regeneration, interstitial lymphoplasmacytic inflammation.

TREATMENT

TREATMENT OVERVIEW

Goals of treatment are:

- Avoidance of treating patients that have positive titers alone (exposure) in the absence of compatible clinical abnormalities
- Resolution of lameness and fever if present
- Palliative/supportive care for complications of PLN

ACUTE GENERAL TREATMENT

- Doxycycline (10 mg/kg PO q 12-24 h)or amoxicillin (11 mg/kg PO q 8-12 h). Treatment for clinical cases is continued for 4 weeks to try to eliminate the carrier state. Treatment is not recommended for nonclinical, nonproteinuric carriers.

CHRONIC TREATMENT

- The length of time antibiotics are needed to clear the carrier state is unknown.
- Treatment for Lyme nephropathy often includes long-term combination doxycycline, angiotensin-converting enzyme inhibitor (e.g., enalapril, 0.5 mg/kg PO q 12-24 h), low-dose aspirin (0.5 mg/kg PO q 12 h), and omega-3 fatty acids. Immunosuppressive therapy protocols are being studied.
- Supportive care of renal disease may include antiemetics, phosphate binders, intravenous fluids/colloids, antihypertensives, and other agents
- Some dogs with Lyme arthritis do not improve with antibiotics alone. Corticosteroids are added for suspected immune-mediated polyarthritis (e.g., prednisone, 1 mg/kg PO q 12 h, tapering to 0.5 mg/kg PO q 48 h).

RECOMMENDED MONITORING

- Lyme nephropathy is uncommon even in seropositive retrievers, but it is recommended to continue screening (duration/frequency unknown) all Lyme-positive dogs for proteinuria whether treated or not.
- If treated, C6 Quant is recommended at 0 and 6 months; the new baseline is for comparison if signs recur. High pretreatment titers usually drop > 50%; lower titers may not. Qualitative C6 (SNAP-4Dx) often remains positive post treatment.
- For Lyme nephropathy: Monthly monitoring of hematocrit, serum creatinine, serum albumin, urine protein/creatinine ratio, and blood pressure measurement are decreased to every 3-6 months if clinically stable.

PROGNOSIS AND OUTCOME

- Prognosis is good for Lyme arthritis. Most dogs respond immediately without recurrence.
- Prognosis is guarded to poor for Lyme nephropathy, especially in hypoalbuminemic/dehydrated/azotemic cases; life expectancy may be days to weeks.

PEARLS & CONSIDERATIONS

COMMENTS

In humans, the *Borrelia* vaccine was removed from the market because of poor sales over concern about possible immune-mediated

sequelae in genetically predisposed individuals.

PREVENTION

- Tick prevention and control are paramount.
- Lyme disease vaccines are controversial because the most serious forms of Lyme disease in dogs have an immune-mediated pathogenesis.

CLIENT EDUCATION

Proper tick removal and tick control.

SUGGESTED READING

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Boric Acid Toxicosis

BASIC INFORMATION

DEFINITION

Toxicosis resulting from ingestion of inorganic compounds of boron used in ant or roach baits, flea products for dogs and cats, cleaning compounds, buffering agents, eye washes, and as an anticaking agent. While ingestions are common, toxicosis is uncommon because of the relatively large amount of product that needs to be ingested. However, clinically significant ingestions are characterized by vomiting, diarrhea, anorexia, lethargy, and (rarely) renal damage.

SYNONYMS

Borax, boric acid, orthoboric acid, sodium biborate, sodium borate, sodium perborate, sodium pyroborate, sodium tetraborate

EPIDEMIOLOGY

SPECIES, AGE, SEX

- All breeds of cats and dogs are susceptible.
- Cats may be exposed after walking through the agent when it is placed on small pieces of cardboard or in small cups in cupboards or closets, or when flea powders containing boric acid are used topically.

RISK FACTORS

Preexisting kidney disease may increase the risk of nephrotoxicosis from large ingestions.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- History of using a boric acid–containing product on the animal or in the house (for fleas or control of other insects)
- Vomiting
- Hypersalivation
- Anorexia
- Lethargy

PHYSICAL EXAM FINDINGS

- Findings tend to be nonspecific
- Common:
  - Hypersalivation
  - Lethargy
  - Vomiting, diarrhea
- Possible:
  - Oliguria/anuria
  - Anorexia
  - Ataxia (rare)
  - Seizures (rare)

ETIOLOGY AND PATHOPHYSIOLOGY

Source:

- Some ant baits may contain less than 1% boric acid, whereas some roach products can contain 100% boric acid.
- Boric acid–containing formulations are available as powders, liquids, or gels.
- Borates have been used in pharmaceutical preparations (mouthwash, toothpastes, cosmetics), as toiletries, in cleaning compounds, and as insecticides.

Mechanism of Toxicosis:

- The exact mechanism is unknown. Boric acid is considered cytotoxic to all cells.
- Rapidly absorbed after oral ingestion through mucous membranes, as well as through abraded skin.
- Concentrated in the kidneys before excretion, excreted unchanged in the urine.
- Half-life in dogs is 12 hours, but total elimination may take up to 7 days.
- No death or serious systemic toxicosis reported in dogs when given 1.54-6.51 g/kg of borax or 1-3 g/kg of boric acid. Examples:
  - 20 ounces (570 g) of a 5.4% boric acid ant bait would have to be ingested by a 20-kg dog to reach a dose of 1.5 g/kg.
  - Similarly, 1.1 ounces (31 g) of a 99% boric acid agent would need to be ingested by a 20-kg dog to reach a dose of 1.5 g/kg.
  - In either case, systemic signs are not likely, except for possibly vomiting and diarrhea.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis rests on history and physical exam: suspected or witnessed exposure and presence of gastrointestinal disturbance signs (vomiting, diarrhea) that are typically self-limiting.

DIFFERENTIAL DIAGNOSIS

Toxicologic:

- Garbage toxicosis
- Dietary indiscretion
- Nephrotoxic agents (ethylene glycol, pharmaceuticals, lilies [cats], grapes and raisins [dogs])

Spontaneous Nontoxicologic:

- Infectious enteritis (parvoviral, coronaviral, bacterial, etc.)
- Foreign body

INITIAL DATABASE

- CBC: microcytic hypochromic anemia
- Serum biochemistry panel: azotemia, hyperchloremia, hypernatremia, hyperkalemia, and metabolic acidosis may be noted in severe cases; rarely, elevated liver enzymes.
- Urinalysis: in severe cases causing oliguria or anuria with tubular necrosis, albuminuria, hematuria, proteinuria, and epithelial casts (acute renal failure), or isosthenuria concurrently with azotemia (chronic kidney disease) may be noted

ADVANCED OR CONFIRMATORY TESTING

Boric acid may be detected in the urine, cerebrospinal fluid, blood, and plasma.

TREATMENT

TREATMENT OVERVIEW

Treatment is aimed at inducing emesis in large exposures and providing supportive care as needed, notably in uncommon instances of systemic effects. Most cases are self-limiting (signs resolve within a few hours).

ACUTE GENERAL TREATMENT

- Decontamination of patient:
  - Emesis (see p. 1364): induce vomiting in cases involving large ingestions. Activated charcoal not useful in binding boric acid.
  - Bathe the animal for dermal exposures, using diluted liquid dishwashing detergent.
- Supportive care:
  - Control excessive vomiting with metoclopramide at 0.022-0.044 mg/kg PO, SQ, or IM, barring gastrointestinal

obstruction
- Gastrointestinal protectants: sucralfate, 0.5-1 g q 8 h PO, and famotidine, 0.5 mg/kg PO, SQ, or IM q 12-24 h for 5-7 days
- IV fluid diuresis for 24-48 hours in cases involving large ingestions
- Treat renal failure as needed (see p. 31).
- Control seizures with diazepam, 0.5-2 mg/kg IV unless underlying cause is metabolic (e.g., hypoglycemia, hypocalcemia, hepatic encephalopathy)

CHRONIC TREATMENT

- Chronic problems not expected
- Renal injury is uncommon and when it occurs, generally responds to fluid therapy and supportive care.

POSSIBLE COMPLICATIONS

May exacerbate preexisting kidney disease

RECOMMENDED MONITORING

- Recheck renal parameters (blood urea nitrogen, creatinine, urinalysis) at 24 and 48 hours postexposure.
- If renal parameters are within normal limits at that time, further problems not expected.

PROGNOSIS AND OUTCOME

Excellent in animals with signs limited to vomiting/diarrhea after a low-dose exposure

PEARLS & CONSIDERATIONS

COMMENTS

- Activated charcoal adsorbs boric acid poorly (boron compounds do not adhere well to charcoal). A 30:1 ratio of activated charcoal to boric acid was needed to absorb 38% of boric acid in an in vitro study; 5 to 10 times the normal activated charcoal dose would be required to be effective (risk of severe hypernatremia), so activated charcoal is not recommended as a routine part of treatment of boric acid toxicosis.
- In general, boron compounds have a wide margin of safety, and in most cases of toxicity, only vomiting and diarrhea are noted.
- Ant baits containing 1%-5% boric acid are not expected to cause a serious problem in dogs or cats.
- Concentrated boric acid product greater than 50% should be avoided, but products containing less than 5.4% concentration are considered relatively safe.

PREVENTION

Avoid using highly concentrated boric acid products directly on animals or in the house (on the carpet especially if cats are around) where direct exposure to pets is likely.

SUGGESTED READING

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Bordetellosis

BASIC INFORMATION

DEFINITION

An inclusive term for diseases caused by *Bordetella bronchiseptica*, a highly contagious aerobic gram-negative cocco-bacillus that is a primary respiratory pathogen for dogs and cats and can cause acute or chronic respiratory disease

SYNONYMS

Infectious tracheobronchitis, kennel cough, canine respiratory disease complex. *B. bronchiseptica* is considered a contributing agent in the acute canine respiratory disease syndrome known by these names.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs, cats, rabbits, pigs
- Young animals more susceptible to disease, especially severe disease, than adults

RISK FACTORS

Increased incidence in dogs and cats exposed to other animals with respiratory infection or housed with large numbers of other animals (shelters, boarding kennels, breeding facilities)

CONTAGION & ZOONOSIS

- *B. bronchiseptica* is highly contagious: animal-to-animal contact, aerosol, or fomites. Infected animals shed the organism in nasal and oropharyngeal secretions for 3 months or longer post infection. Infection can be transmitted between species. *B. bronchiseptica* is a rare cause of zoonotic disease: human infection can occur opportunistically (respiratory disease, pleuritis, meningitis, peritonitis) in infants or immunocompromised people.
- *B. bronchiseptica* can be isolated from the upper respiratory tract of healthy dogs and cats: up to 10% of healthy household dogs and 5%-11% of healthy household cats are *Bordetella* positive.

GEOGRAPHY AND SEASONALITY

Probable worldwide distribution, occurs year-round

ASSOCIATED CONDITIONS & DISORDERS

- Bordetellosis is often part of a disease complex that can include co-infections with canine parainfluenza, canine adenovirus-2, canine distemper, *Mycoplasma* spp., and/or *Streptococcus* spp. in dogs and feline rhinotracheitis (feline herpesvirus), feline calicivirus, and other pathogens in cats.
- Bordetellosis is generally limited to the upper respiratory tract; in some cases, pneumonia can occur.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Typically includes exposure to multiple non-housemate animals (kennel/animal shelter, dog show) several days before onset of coughing
- Chief complaint in dogs is usually acute-onset nonproductive hacking cough, including fits of coughing that result in terminal retch.
- Chief complaint in cats is sneezing and oculonasal discharge + cough.
- Severe or complicated cases may be dyspneic, anorectic.

PHYSICAL EXAM FINDINGS

- Spontaneous or inducible cough
- ± Conjunctivitis
- ± Nasal or ocular discharge
- ± Submandibular lymphadenomegaly
- ± Mild to moderate fever, increased lung sounds (pneumonia) in severe cases

ETIOLOGY AND PATHOPHYSIOLOGY

- The organism colonizes respiratory epithelium of the nasal cavity and trachea and can establish persistent (often subclinical) infections.
- Infection occurs via contact of the organism with the upper airway and attachment/adherence to the respiratory epithelium by direct binding to cilia, inducing stasis of the cilia and reducing mucociliary escalator clearance of bacteria and other particulate matter from the airways.
- Airway colonization induces an inflammatory response and increased mucus production.
- *Bordetella* spp. produce multiple factors, allowing *Bordetella* to persist chronically and predispose the host to secondary infections.

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

Bordetellosis often is a suspected diagnosis that goes unconfirmed. Since many infections are mild and self-resolving, the urgency of establishing a diagnosis of bordetellosis specifically is low, and treatment is often initiated based only on clinical signs of upper respiratory infection.

DIFFERENTIAL DIAGNOSIS

Dogs:

- Other agents of infectious tracheobronchitis: canine parainfluenza, canine influenza, canine adenovirus, canine herpesvirus, canine distemper, *Mycoplasma* spp. infection, *Streptococcus* spp. infection
- Chronic bronchitis
- Collapsing trachea
- Traumatic tracheitis
- Airway foreign body
- Mechanical or chemical airway irritant
- Other causes of pneumonia: fungal infection, aspiration

Cats:

- Other upper respiratory infections/agents: feline rhinotracheitis (feline herpesvirus 1), feline calicivirus infection, *Chlamydophila felis* infection, other pathogenic causes of pneumonia

INITIAL DATABASE

- CBC: often unremarkable; neutrophilia with left shift or toxic neutrophil changes may be seen with pneumonia.
- Thoracic radiographs: usually unremarkable; pneumonia in severe/complicated cases

ADVANCED OR CONFIRMATORY TESTING

- Bacterial culture and sensitivity: many healthy animals are culture positive.
  - Nasal or oropharyngeal swabs for bacterial culture: should be plated on selective medium to decrease overgrowth by other respiratory flora.
  - Transtracheal wash or bronchoalveolar lavage if pneumonia or lower airway disease suspected
- Serologic testing not helpful; many healthy animals have positive titers
- PCR assays available that differentiate *Bordetella* spp. including *B. bronchiseptica;* no routine clinical application

TREATMENT 

TREATMENT OVERVIEW

- Treatment goals are initiation of appropriate antibiotic therapy and supportive care.
- Cough suppressants are often indicated to break the cough cycle but are contraindicated in cases with pneumonia or productive cough.

ACUTE GENERAL TREATMENT

- Antimicrobials:
  - Should be based on culture/sensitivity, especially since *Bordetella* spp. show high level of antimicrobial resistance
  - Options for empirical treatment pending culture results:
    - Doxycycline (5 mg/kg PO q 12 h) is the antimicrobial of choice (most *Bordetella* isolates are susceptible). Treat adults for 14-21 days, young (growing) animals for 7-9 days (reduces risk of discoloration of teeth); *or*
    - Amoxicillin-clavulanate (12.5-25 mg/kg PO q 12 h); *or*
    - Trimethoprim-sulfonamide (15-30 mg/kg PO q 12 h); *or*
    - In severe cases, other options include gentamicin, enrofloxacin, and cefazolin.
    - Antimicrobial therapy helps alleviate clinical signs but does not alter shedding in recovered carriers.
- Antitussives:
  - For suppression of dry, nonproductive cough in milder cases (animal is otherwise well); titrate dose to reduce cough without causing sedation
    - Butorphanol 0.05-1 mg/kg PO q 8-12 h; *or*
    - Hydrocodone 0.22 mg/kg PO q 8-12 h
  - Contraindicated with pneumonia
- Bronchodilators:
  - May be indicated in patients with pneumonia
- Nebulization therapy:
  - Nebulization with sterile saline may help hydrate airway secretions and facilitate clearance, but patient must have adequate systemic hydration as a prerequisite.
  - Nebulization with antibiotic solutions (gentamicin, kanamycin, or polymyxin B) has been suggested for refractory cases to reduce *Bordetella* populations in the trachea and bronchi, but unpredictable dose delivery to airways.
- Glucocorticoids:
  - Antiinflammatory doses administered short term may reduce cough.
  - E.g., prednisolone 0.25-0.5 mg/kg PO q 12-24 h for 3-5 days
  - Does not shorten course of disease
  - May exacerbate disease in immunocompromised animals
  - Do not use in cases with severe/complicated disease
- Adequate systemic hydration very important to facilitate clearance of respiratory secretions

DRUG INTERACTIONS

Reduce dose of trimethoprim-sulfa and avoid gentamicin in patients with renal disease. Tetracyclines may cause discoloration of dental enamel in young animals.

POSSIBLE COMPLICATIONS

Pneumonia may develop secondary to *Bordetella-induced* impairment of respiratory defenses. Sulfonamides (trimethoprim-sulfonamide) may induce keratoconjunctivitis sicca, hypersensitivity reactions, crystalluria, renal tubule obstruction, polyarthritis, and GI signs.

RECOMMENDED MONITORING

- Serial thoracic radiographs, CBC, and arterial blood gas to monitor patients with pneumonia
- Monitor tear production before and during treatment in patients receiving sulfonamides.
- Monitor BUN, creatinine, and urinalysis in patients receiving gentamicin.

PROGNOSIS AND OUTCOME

- Disease is usually self-limiting; uncomplicated cases resolve within approximately 2 weeks.
- Severe (potentially fatal) pneumonia may occur in young or debilitated animals.

PEARLS & CONSIDERATIONS

COMMENTS

- Shedding of organisms may continue for 3 months or more after resolution of clinical signs. Transmission of infection to other animals and immunocompromised people may continue during that time; suitable precautions (avoidance of direct or indirect contact) should be taken.
- *B. bronchiseptica* is the evolutionary progenitor of *B. pertussis*, a human-specific pathogen that is the causative agent of whooping cough.

TECHNICIAN TIP

Caution is warranted when preparing a vaccine: erroneous SQ injection of intranasal vaccine in dogs has caused severe acute hepatic injury.

PREVENTION

- Limit transmission by quarantine of new animals and isolation of infected animals.
- Decrease stress, provide adequate hygiene and care.
- Disinfect cages and other surfaces (1:32 dilute bleach solution).
- Vaccination:
    - Parenteral and intranasal (IN) vaccinations are available for dogs, intranasal for cats.
    - Effective in reducing infection rate and severity of clinical signs
    - IN: rapid onset of immunity within 72 hours post vaccination; duration 1 year
    - Vaccinate at least 5 days prior to anticipated exposure (boarding) if possible.
    - Some IN vaccines may be used as early as 2 weeks of age.
    - Intranasal vaccines may induce cough and/or nasal discharge.
    - Animals receiving live vaccines will shed bacteria that may cause infection ± disease in susceptible animals and humans.
- Natural immunity lasts at least 6 months post infection.

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Blue-Green Algae Toxicosis

BASIC INFORMATION

DEFINITION

Syndrome of sudden-onset neurologic signs or acute liver failure in dogs caused by ingestion of blue-green algae (BGA) toxins

SYNONYM

Cyanobacteria toxicosis

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs: all breeds, ages, and both sexes susceptible
- Cats: none reported

RISK FACTORS

BGA blooms are favored by stagnant water, warm water temperatures, ample sunlight, and high nutrients from fertilizer, animal waste, and sewage runoff.

GEOGRAPHY AND SEASONALITY

Blooms occur mostly in summer or fall.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Acute neurotoxic syndrome
- Subacute hepatotoxic syndrome

HISTORY, CHIEF COMPLAINT

- History of swimming in or drinking water from a pond, lake, or river
- Vomiting, diarrhea, weakness, and collapse (>6 hr after exposure): hepatotoxic syndrome
- Salivation, vomiting, diarrhea, dyspnea, tremors, muscle fasciculations, ataxia, weakness, seizures, and death (>15 min after exposure): neurotoxic syndrome

PHYSICAL EXAM FINDINGS

- Presence of algae on the muzzle or on the fur elsewhere on the body is common. Bluish-green and slimy, or may be dried if later presentation.
- Hepatotoxic syndrome: see History, Chief Complaint above; plus pale mucous membranes, poor capillary refill time, tachycardia or bradycardia, signs of abdominal pain, rapid weak pulse, hypothermia, and shock
- Neurotoxic syndrome: see History, Chief Complaint above

ETIOLOGY AND PATHOPHYSIOLOGY

- BGA are microscopic organisms that form colonies visible to the naked eye, rely on photosynthesis for energy, and have a cell wall similar to gram-negative bacteria.
- Accumulations of large amounts of BGA in lakes, ponds, or rivers are known as *waterblooms*. BGA blooms exist worldwide and are light to dark green or sometimes reddish-brown. Wind propels toxic algae to the shoreline, where animals are exposed to the organism by ingestion when they drink BGA-contaminated water.
- Common toxin-producing genera of fresh and brackish water BGA include *Microcystis*, *Anabaena*, *Oscillatoria*, *Aphanizomenon*, *Nodularia*, and *Nostoc* spp.

- Acute hepatotoxic syndrome:
  - Most commonly described poisoning by BGA; caused by low-molecular-weight cyclic heptapeptides and pentapeptides known as *microcystins* and *nodularins*. Microcystin-LR (MCLR) is the most toxic and the most frequently encountered of approximately 50 similar peptides.
  - After ingestion, BGA toxins are released from the cells and preferentially absorbed from the ileum.
  - Once inside hepatocytes, toxins inhibit protein phosphatases (PP) types 1 and 2A (PP1 and 2A), causing hyperphosphorylation of cytosolic and cytoskeletal proteins, leading to cytoskeletal disruption, damage, and necrosis.
  - Death is possibly due to massive intrahepatic hemorrhage, hypovolemia, and liver failure.
- Peracute neurotoxic syndrome; responsible toxins are:
  - Anatoxin-a: an alkaloid and potent postsynaptic depolarizing neuromuscular blocking agent that affects nicotinic and muscarinic acetylcholine receptors
  - Anatoxin-a(s): inhibits peripheral (but not central) cholinesterase irreversibly and is the only known naturally occurring organophosphorus cholinesterase inhibitor (similar to organophosphate pesticides)

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A tentative diagnosis is based on history of exposure (drinking or swimming in a pond) and rapid onset of clinical signs (vomiting, shock, liver failure, or neurologic signs). Given the potential speed and intensity of progression, treatment may be initiated on this basis. Toxicosis can be confirmed by purification and identification of toxins, but turnaround time means these methods are not clinically useful to an affected patient (e.g., rather for preventative purposes or medicolegal reasons).

DIFFERENTIAL DIAGNOSIS

- Differentiate from other hepatotoxic agents: amanita mushroom, sago palm, acetaminophen
- Primary hepatic diseases (see p. 503)

INITIAL DATABASE

- Hepatotoxic syndrome:
  - CBC: leukocytosis and thrombocytopenia
  - Serum biochemistry panel: increased levels of all liver enzymes, glucose, and possibly creatine phosphokinase. Hypoglycemia is possible after hyperglycemia.
  - Serum bile acids: increase commonly occurs early.
  - Coagulation profile: whole blood clotting time may be normal; prothrombin time and activated thromboplastin times increase twofold to fourfold.
- Neurotoxic syndrome:
  - Owing to rapid effect of the toxins, no significant serum biochemical changes are expected.

ADVANCED OR CONFIRMATORY TESTING

- Postmortem (hepatotoxicosis): rounding of hepatocytes, disruption of hepatic cords, loss of sinusoidal integrity, intrahepatic hemorrhage, and centrilobular necrosis
- Microscopic identification of toxigenic algae. Obtain large specimen (1-2 L) of the algae by straining the cells out of the water with cheesecloth. Specimens can be sent for identification, purification, and quantification of algal toxins, for mouse bioassay, or for ELISA to Dr. Wayne Carmichael's laboratories. Call before shipping specimens. Information available at: http://www.wright.edu/biology/faculty/carmichael/labhome/labhome.htm.

TREATMENT

TREATMENT OVERVIEW

Early decontamination (induce emesis and give charcoal) of patients not showing clinical signs. For overtly ill patients, treatment of muscarinic and central nervous system (CNS) signs, prevention/treatment of liver damage, and supportive care are cornerstones of therapy.

ACUTE GENERAL TREATMENT

- Decontamination of patient:

- Emesis: only in animals not showing any clinical signs (see p. 1364)
- Activated charcoal 2-4 g/kg PO
- Cholestyramine (200-300 mg/kg PO) may be more effective than charcoal (more expensive and must be obtained from a pharmacy).
- The noncompetitive bile-acid transport inhibitors, rifampicin, and bile salts such as cholate and deoxycholate can inhibit uptake of microcystins. Their utility, however, in clinical algal toxicoses has yet to be determined.

- Control muscarinic and neurologic signs:
  - Atropine sulfate for muscarinic signs (0.04-0.1 mg/kg IV PRN)
  - Diazepam for seizures 0.5-2 mg/kg IV PRN; other antiseizure medications (e.g., barbiturates) if diazepam is ineffective
- Supportive care:
  - Control severe vomiting with metoclopramide (0.1-0.4 mg/kg PO, SQ, or IM q 6 h), only if intestinal obstruction has been ruled out (if present, usually unrelated to BGA) or use maropitant 1 mg/kg SQ q 24 h or 2 mg/kg PO q 24 h for 5 days.
  - Treat signs of acute hepatic failure (see p. 503, and p. 501). Typical therapeutics may include:
    - Lactulose
    - *S*–adenosyl methionine (SAMe)
    - Dietary management
    - Vitamin K1
    - Plasma and/or whole blood transfusions as needed
    - IV fluids (possibly including 5% dextrose)
    - Broad-spectrum antibiotics for secondary infection

POSSIBLE COMPLICATIONS

Permanent hepatic insufficiency

RECOMMENDED MONITORING

- Serum chemistry profile, especially liver-specific enzymes (ALT, AST, GGT, alkaline phosphatase)
- Serum bile acids
- CBC
- Hematocrit
- Body temperature
- Blood glucose

PROGNOSIS AND OUTCOME

Poor prognosis with systemic signs of acute hepatic damage or severe neurologic dysfunction

PEARLS & CONSIDERATIONS

COMMENTS

- In dogs, BGA poisoning is a sporadic but recurrent cause of acute illness and death.
- Lethal doses of purified MCLR: rat, 160 mg/kg IP; mouse, 100 mg/kg

IP; LD50 of purified anatoxin-a in mouse = 200 mg/kg IP and anatoxin-a(s) = 30 mg/kg IP.

SUGGESTED READING

Beasley VR, et al: Diagnostic and clinically important aspects of cyanobacterial (blue-green algae) toxicoses. J Vet Diag Invest, 1:359–365, 1989.

Khan SA, et al: Comparative pathology of microcystin-LR in cultured hepatocytes, fibroblasts, and renal epithelial cells. Nat Toxins 3:119–128, 1995.

Puschner B, Hoff B, Tor E: Diagnosis of ana-toxin-a poisoning in dogs from North America. J Vet Diagn Invest 20:89–92, 2008.

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Blindness

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Loss of vision

SYNONYMS

Amaurosis, central blindness: loss of vision due to a lesion in the central nervous system

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs and cats; any age and sex may be affected, depending on etiology.

GENETICS & BREED PREDISPOSITION

Several, depending on causative disorder (see p. 448, p. 644, p. 985)

RISK FACTORS

- Age: older animals may be predisposed to diseases associated with blindness, including neoplasia (intracranial, intraocular, optic chiasmal), cataracts, and retinal detachment (see p. 985)
- Outdoor access may predispose to infectious diseases associated with blindness (see p. 141)

CLINICAL PRESENTATION

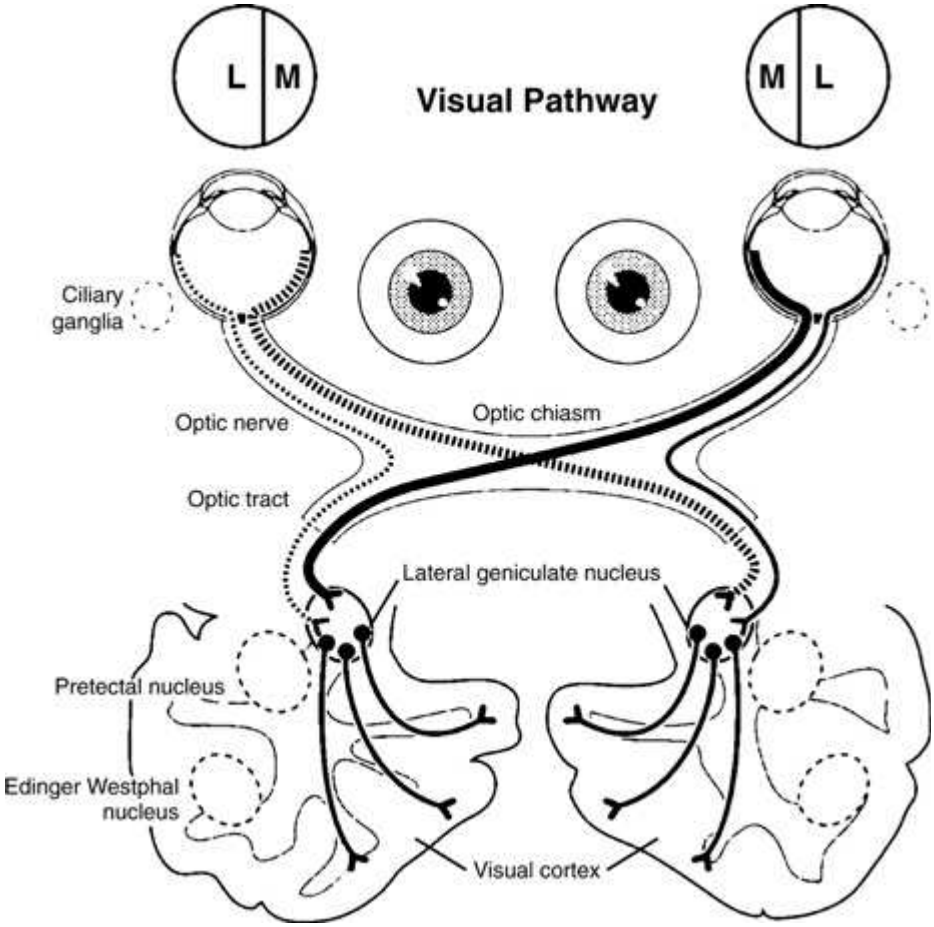
DISEASE FORMS/SUBTYPES

- Unilateral or bilateral
- Sudden or progressive
- "Red eye" blindness: associated with visible conjunctival redness on physical examination:
  - Glaucoma (see p. 448), severe uveitis (see p. 1151), cataracts (see p. 181), lens luxation (see p. 644), complex corneal ulceration (see p. 250), orbital disease (see p. 790)
- Non-red, noninflamed eye ("quiet eye") blindness: no conjunctival or scleral redness is observed in the blind eye(s):
  - Prechiasmal/chiasmal blindness
    - Lesion affecting retina, optic nerve, optic chiasm
    - Associated with dilated pupils and pupillary light reflex (PLR) abnormalities
  - Postchiasmal/cortical blindness
    - Lesion affecting optic tracts, lateral geniculate nucleus (LGN), optic radiations, or visual cortex of the cerebrum
    - Pupil size and PLRs usually normal unless optic tracts affected along portions common to PLR and vision pathways (see figure) and/or unrelated, concurrent iris condition (see p. 944)
    - The PLR fibers split from the vision pathway just before the LGN.

HISTORY, CHIEF COMPLAINT

- Variable depending on the underlying cause, whether the blindness is unilateral or bilateral, and sudden or progressive in onset
- In cases of sudden blindness, all or some of the following may be reported:
  - Disorientation (see p. 314)
  - Suddenly starts bumping into objects within familiar or unfamiliar environments
  - Inability to find food bowl, toys, and the like
  - Lethargy
  - Anxiety
- In cases of progressive blindness, all or some of the following may be reported:
  - Occasionally bumping into objects in own environment

- Frequently bumping into objects in unfamiliar or suddenly altered environment
- Vision deficits in dim light and/or darkness (loss of night vision/nyctalopia) (e.g., progressive retinal degeneration/atrophy; see p. 983)
- Patients may be lethargic and/or anxious but generally adjust and compensate better with progressive vision loss, especially if slowly progressive.



BLINDNESS Anatomy of visual pathway from the eye to the visual cortex of the cerebrum. Circles adjacent to "Visual Pathway" title indicate visual fields. *M*, Medial; *L*, lateral.

PHYSICAL EXAM FINDINGS

- See also: Ophthalmic Examination p. 1313, ; Neurologic Examination,p. 1311
- "Red eye" blindness (see p. 448 ,p. 1151 , and p. 790)
- Non-red, quiet eye blindness
  - Prechiasmal/chiasmal blindness:
    - Menace response (blink in response to hand motion toward the eye) absent
    - Dazzle reflex (blink in response to a bright light) absent
    - Pupil(s) dilated or fixed and dilated
    - PLR(s) decreased (i.e., sluggish and incomplete) or absent
    - ± Anisocoria (asymmetry between the size of the pupils), especially seen in unilateral lesions where only the affected pupil is more dilated)
  - Postchiasmal/cortical blindness:
    - Menace response variable depending on localization and severity of lesion
    - Menace response absent or decreased in contralateral eye if a unilateral lesion present
      - Small percentage of contralateral nasal/medial visual field may be preserved, owing to undecussated (those not crossed over) lateral optic nerve fibers.
    - Menace response absent in both eyes in bilateral/diffuse optic tract, lateral geniculate nucleus, optic radiation, or visual cortical lesions
    - Pupil size and PLRs normal unless certain portions of optic tract(s) affected that are common to both the PLR and visual pathways and/or unrelated, concurrent iris condition (see p. 944)
    - Dazzle reflex(es) normal (like the PLR, the dazzle reflex does not involve the visual cortex.)

ETIOLOGY AND PATHOPHYSIOLOGY

- "Red eye" blindness: the lesion is ocular or intraocular:
  - Opacity of the ocular media (e.g., cornea, aqueous humor, lens, vitreous) in cases of corneal edema/ulceration /pigmentation, uveitis, cataract and vitreal debris or hemorrhage
  - Retinal degeneration with or without detachment and optic nerve atrophy in glaucoma (see p. 448)
  - Retinal detachment in cases of chorioretinitis (see p. 985)
- Non-red, quiet eye blindness:
  - Prechiasmal/chiasmal: the lesion lies along the retinaoptic nerveoptic chiasm pathway
    - Retinal diseases (see p. 983 and p. 985)
    - Optic nerve lesions (e.g., congenital optic nerve hypoplasia, inflammation [see p. 784]), neoplasia (e.g., meningioma), or atrophy (e.g., glaucoma, trauma)
    - Optic chiasmal lesions (e.g., neoplasia, abscess)
  - Postchiasmal/cortical: the lesion affects the optic tract and/or radiations to and including the visual (occipital) cerebral cortex
    - Encephalitis (extension to bilateral optic tracts via cerebrospinal fluid)
    - Cerebral edema
    - Cerebral infectious, inflammatory, neoplastic or traumatic disease

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Lesion localization is the cornerstone of accurate diagnosis and treatment of causes of blindness. A complete cranial nerve and general neurologic examination () are an essential first diagnostic step. If the cause of blindness is not readily apparent, prompt referral of affected patients to a veterinary ophthalmologist is advised. Early diagnosis is key to determining whether or not return of vision with therapy is possible.

DIFFERENTIAL DIAGNOSIS

- "Red eye" blindness:
  - May be confused with disorientation due to causes other than blindness (see p. 314) and concurrent non–vision-threatening cause(s) of "red eye," including: conjunctivitis (see p. 237 and p. 239), episcleritis (see p. 356), and corneal disease (see p. 250)
- Non-red, noninflamed eye ("quiet eye") blindness:
  - May be confused with disorientation due to causes other than blindness
- Blindness may also be characterized as unilateral or bilateral. Note: unilateral processes listed more commonly affect only one eye but can affect both eyes in some cases; disorders that affect one or both eyes with equal frequency are listed in both categories.
  - Unilateral: corneal trauma, complex corneal ulceration, lens luxation, cataract, severe uveitis, retinal detachment, subretinal hemorrhage, glaucoma, cerebral lesions (optic radiation/visual occipital cortex)
  - Bilateral: cataracts, retinal detachment, subretinal hemorrhage, severe uveitis, glaucoma, optic neuritis, optic chiasm lesions, sudden ac quired retinal degeneration, progressive retinal degeneration/atrophy, diffuse cerebral/visual cortex disease

INITIAL DATABASE

- In order to accurately diagnose and treat causes of blindness, it is imperative to first localize the lesion causing the blindness. A thorough cranial nerve and general neurologic examination must be performed. Additional diagnostic tests may be indicated based on the site of the lesion.
- Cranial nerve (CN) examination:
  - Menace response (CN II & VII), assessment of pupil symmetry and size and direct and consensual PLRs (CN II & sympathetic and parasympathetic innervation), dazzle reflex (blinking in response to bright light; CN II & VII), palpebral (CN V & VII) and corneal (CN V & VII) reflexes, assessment of physiologic nystagmus (i.e., vestibuloocular reflex or "Doll's eye;" CN III, IV, VI & VIII), evaluation of facial sensation (CN V) and motor function (CN VII)
    - Normal PLRs: lesion usually postchiasmal/cortical (with a "non-red, noninflamed eye" ["quiet eye"] blindness) or due to opacity of ocular media
    - Sluggish, incomplete/absent PLR and dilated pupil: lesion involves retina, optic nerve, optic chiasm (causes bilateral blindness), or optic tract; or a separate, primary lesion of the pupil is present
- General neurologic examination (see p. 1311)
- Complete ophthalmic examination including:
  - Intraocular pressure assessment

- Examination of anterior segment
  - Evaluate for opacity of the cornea, aqueous humor, lens, or vitreous
- Posterior segment/fundic examination after pharmacologic pupil dilation (1% tropicamide)
  - Pharmacologic pupil dilation is contraindicated with glaucoma
  - Evaluate optic nerve (size, shape, color; see p. 448and p. 784)
  - Evaluate tapetum (dorsal reflective structure) for brightness and/or color changes
    - Appears hyperreflective/bright with retinal degeneration and/or certain forms of retinal detachment
    - Appears hyporeflective/dull grey to pigmented with subretinal inflammation and/or certain forms of retinal detachment
  - Evaluate nontapetal fundus (located ventrally and typically pigmented) for whitish or grey discoloration (e.g., edema, inflammatory exudate or depigmentation from active or past inflammation or retinal detachment) or hemorrhages
  - Evaluate vasculature of retina (should see small arteries and larger veins coming from the optic disk and coursing peripherally), and look for changes in vessel direction to indicate detachment or attenuation (thinning) to indicate degeneration.
- CBC, serum chemistry profile, urinalysis to assess systemic status
- +/− Blood pressure (see p. 985 , p. 1068, and p. 1209) if retinal hemorrhage and/or detachment is/are noted

ADVANCED OR CONFIRMATORY TESTING

- Thoracic radiographs (screen for neoplasia or systemic infectious disease if intraocular mass or uveitis, chorioretinitis are noted and/or if optic neuritis is suspected)
- Serologic titers for infectious diseases unique to geographic area:
  - Rickettsial diseases (particularly if intraocular hemorrhage is noted)
  - Blastomycosis, cryptococcosis, histoplasmosis, coccidioidomycosis (particularly if chorioretinal lesions with uveitis and/or optic neuritis are detected)
  - Lyme disease (if history of tick exposure + uveitis)
  - Bartonellosis (if history of flea exposure + uveitis)
  - Toxoplasmosis (if history of rodent exposure + chorioretinal lesions)
- Aspiration of enlarged lymph nodes for cytologic evaluation
- Ocular ultrasonography if opacity of ocular media precludes fundic examination
- Histopathologic study in cases when eye is blind and painful and enucleation is advised
- Referral is advisable for all cases of blindness of undetermined cause for additional workup, including one or more of the following:
  - Electroretinography to assess retinal function
  - Visual-evoked potentials
  - Cerebrospinal fluid tap
  - MRI or CT
  - Vitreous centesis with cytologic study, culture, titers

TREATMENT

TREATMENT OVERVIEW

- Treatment is directed at addressing any underlying cause of blindness such as hypertensive retinopathy, uveitis, cataracts, and so forth
- In general, administration of empirical therapy is not recommended until a tentative or final diagnosis has been reached.
  - Administration of systemic corticosteroids prematurely may preclude diagnosis of neoplasia and some inflammatory disorders and may exacerbate systemic infectious diseases.

ACUTE GENERAL TREATMENT

Depends on underlying etiology

CHRONIC TREATMENT

- Manage any underlying conditions such as chronic renal failure, systemic hypertension, systemic infectious disease.
- Systemic mycoses and immune-mediated disorders typically require long-term therapy.
- Treat primary cause of blindness when possible (e.g., refer for surgery of mature cataracts).

RECOMMENDED MONITORING

- Monitor for return of vision, PLR, dazzle reflex after commencing therapy.
- Serial fundic examinations

PROGNOSIS AND OUTCOME

- Variable depending on underlying cause
- Restoration of vision after acute vision loss may be possible after rapid diagnosis of underlying condition and intensive appropriate therapy.
- In many cases, however, blindness is irreversible, and long-term management aims to provide comfort if pain is likely (e.g., glaucoma).

PEARLS & CONSIDERATIONS

- Assessment of the direct and consensual PLRs and dazzle reflexes is imperative in evaluation of blindness.
    - Absence of the PLR and/or dazzle reflex is a poor prognostic indicator, because minimal retinal function is required to retain these reflexes.
- The PLR and dazzle reflexes are subcortical pathways (do not involve the cerebral cortex) and therefore are normal with blindness caused by optic radiation and cortical lesions.
- A PLR is dependent only on *quantity* of light; vision is dependent on *quality* of light; therefore, the PLR should remain intact despite opacity of the ocular media (such as nuclear sclerosis) if there is no concurrent retinal or optic nerve damage.

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EDITOR: CHERYL L. CULLEN

Blastomycosis

BASIC INFORMATION

DEFINITION

Systemic mycotic infection affecting many mammalian species. Animals usually have lung, skin, eye, and bone lesions.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Occurs most often in people and dogs. Has been reported in domestic cats, lions, tigers, sea lions, wolves, ferrets, and a polar bear.
- Usually seen in 1- to 5-year-old large-breed male dogs

GENETICS & BREED PREDISPOSITION

Doberman pinschers may be at increased risk.

RISK FACTORS

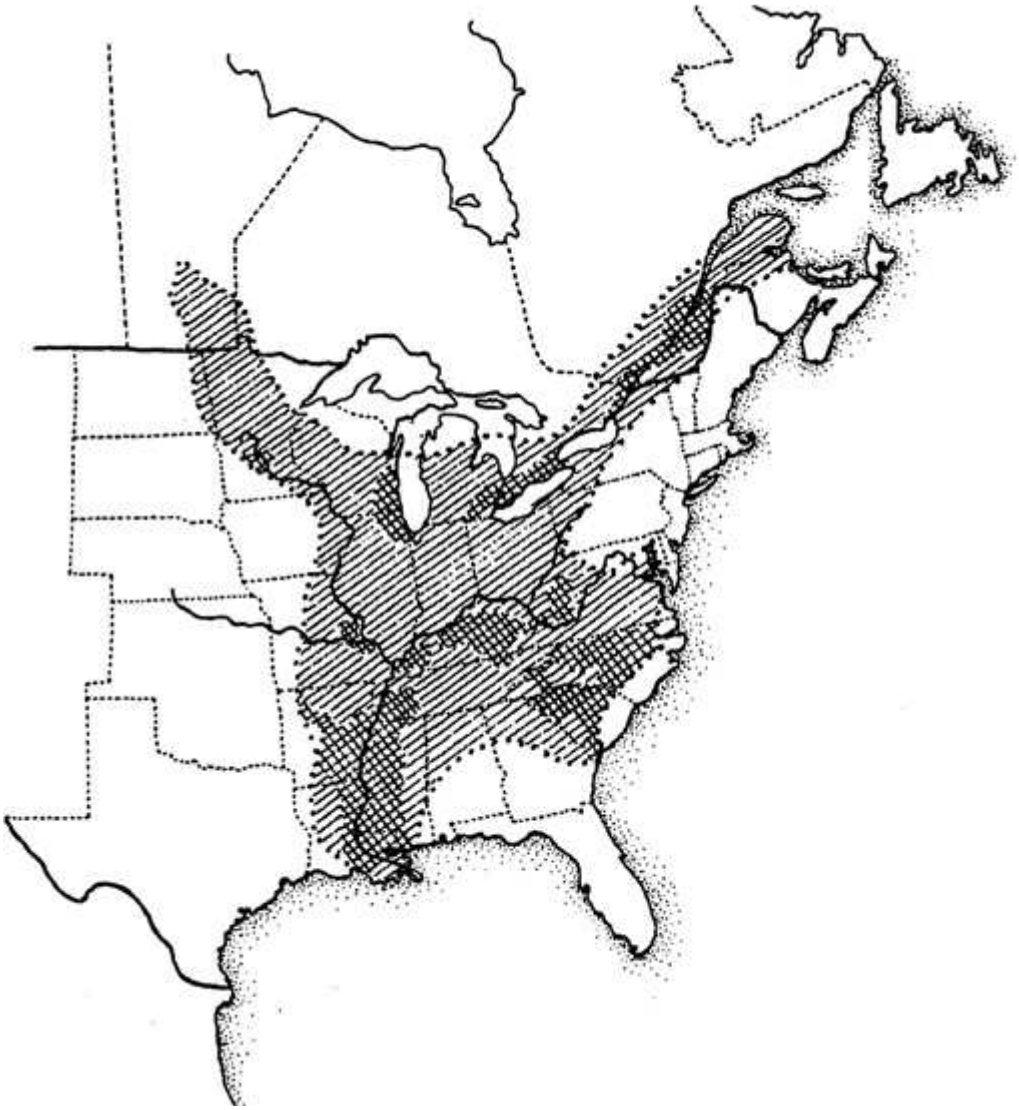
- Outdoor, roaming dogs in endemic areas living near a waterway are at increased risk.
- Exposure to sandy, acidic soil disrupted by construction involving earthmoving or excavation

CONTAGION & ZOONOSIS

- Bites, needlesticks while doing aspirates, and cuts during necropsies of infected dogs have caused infection in people.
- Organisms can be transmitted when cultured (aerosol) if plates are opened outside a hood.
- Direct airborne animal-human or human-animal transmission does not occur, because the yeast phase in the infected patient is too large to be transmitted by aerosol.
- Dogs and people may become infected from the same environmental source, but illness usually occurs first in the dog. The dog can serve as a sentinel for human disease.

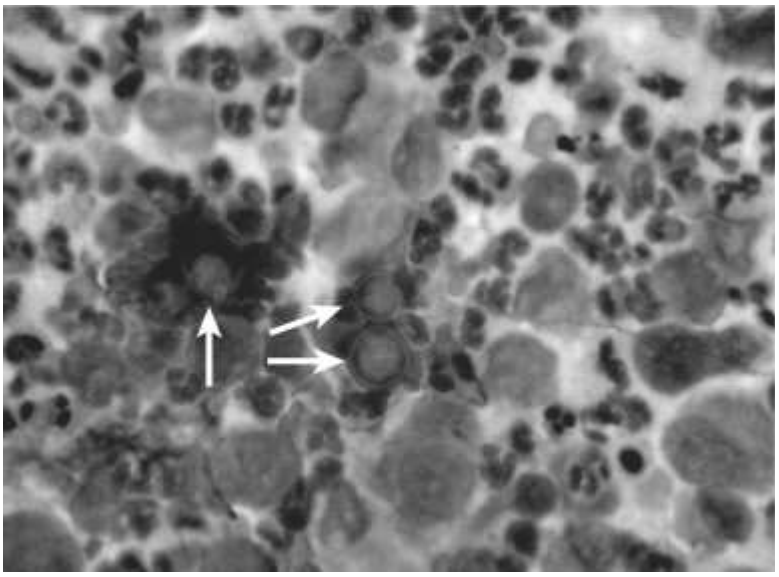
GEOGRAPHY AND SEASONALITY

- *Blastomyces dermatitidis* is present in North America, Africa, and Central America. Endemic areas include the Mississippi, Missouri, and Ohio River valleys; mid-Atlantic states; and the Canadian provinces of Alberta, Manitoba, Ontario, and Quebec.
- No seasonal distribution in the southeastern United States
- May be seasonally distributed in the U.S. Midwest, with more cases seen during late spring through late fall in Wisconsin
- The specific location of the fungus in soil is unknown; the fungal colonies are not grossly visible and are difficult to isolate from the environment.
- A "microfocus" model for the ecology of *B. dermatitidis* suggests that environmental pockets of fungal growth occur when a suitable combination of soil type and moisture is present. Rain, physical disruption of soil, or both, may promote release of spores.
- Proximity of the face to soil increases likelihood of inhalation/infection.



BLASTOMYCOSIS Geographic area in which blastomycosis is endemic. Areas of highest prevalence are cross-hatched.

(From Rippon JW: Medical mycology, ed 3. Philadelphia, 1988, Saunders, pp 474–505. Reprinted with permission.)



BLASTOMYCOSIS Cytologic evaluation of a fine-needle aspiration from a patient with blastomycosis. The cytologic diagnosis is

made based on the thick-walled, basophilic, spherical *B. dermatitidis (arrows)*. The intense inflammatory infiltrate surrounding the yeasts is typical.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Cutaneous, pulmonary, ocular, and osseous forms.

HISTORY, CHIEF COMPLAINT

Any combination of anorexia, weight loss, cough, dyspnea, exercise intolerance, ocular changes, lameness, skin lesions, and neurologic signs is possible.

PHYSICAL EXAM FINDINGS

- Fever, lethargy, emaciation, lymphadenomegaly
- Pulmonary involvement:
  - Harsh, dry lung sounds; cough; dyspnea at rest
- Ocular changes: signs of uveitis (see p. 1151), endophthalmitis, corneal edema, glaucoma
- Skin lesions (nasal planum, face, nail beds): subcutaneous abscesses, ulcerated draining lesions, or granulomatous proliferative lesions
- Bone involvement: lameness due to fungal osteomyelitis, toe involvement

ETIOLOGY AND PATHOPHYSIOLOGY

- *Blastomyces dermatitidis* is a dimorphic fungus that exists in the mycelial form in the soil and as a yeast in the tissues.
  - The mycelial form grows in soil, especially in manure-enriched soil, and produces infective spores which are released into the air. Soil disruption exposes organisms from deep within the soil.
  - The yeast phase grows at body temperature and is too large for aerosol transmission/contagion
- The route of infection is by inhalation of mycelial spores that enter the terminal airways from the environment.
- At body temperature, the spores become yeasts and establish an infection in the lungs which disseminates throughout the body via blood and lymphatics.
- Organisms cause a pyogranulomatous inflammation with a predilection for the skin, eyes, bones, lymph nodes, subcutaneous tissues, mouth, nares, brain, mammary tissues, prostate and testes.
- Cats are less commonly infected but develop a similar spectrum of lesions as dogs, and may also have pharyngeal lesions.
- Direct inoculation into a wound from soil is uncommon.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Characteristic lesions on chest films of a patient having been in an endemic area alert the clinician to the possibility of fungal infection. Identification of organisms by cytology, culture, or histopathology is best. A urine antigen test for blastomycosis is more sensitive than serologic testing.

DIFFERENTIAL DIAGNOSIS

- Pulmonary form: metastatic tumors, especially hemangiosarcomas; bacterial or viral pneumonia.
- Bone form: bacterial osteomyelitis, primary or metastatic bone tumors
- Cutaneous form: bacterial, fungal, parasitic, autoimmune dermatitis
- Other systemic mycoses

INITIAL DATABASE

- CBC:
  - Mild normocytic normochromic anemia
  - Moderate leukocytosis (17,000 to 30,000 white blood cell/µL), left shift, lymphopenia
- Serum biochemistry panel:
  - Hyperglobulinemia
  - Hypoalbuminemia
  - Hypercalcemia (occasionally)

- Thoracic radiographs:
  - Diffuse, nodular interstitial and bronchointerstitial lung patterns common
  - Solitary to multiple nodules may be seen
  - Tracheobronchial lymphadenomegaly
  - Less commonly: pleural effusion, pneumomediastinum
- Radiographs of bones: osteolytic or periosteal proliferation with soft-tissues welling

ADVANCED OR CONFIRMATORY TESTING

- Identification of the organism in more than half the cases by cytologic examination of lymph node aspirates, draining exudates, skin impression smears, or vitreous aspirates
  - A thick-walled, broad-based budding yeast is characteristic of *Blastomyces* (see figure).
- Lung aspirates (see p. 1275) often identify the organism but pneumothorax may occur. Tracheal wash (see p. 1350) is less sensitive than a lung aspirate.
- Urine *Blastomyces* antigen test has >90% sensitivity and is the preferred approach when organisms are not found. The *Blastomyces* urine antigen test is done by Mira Vista Labs in Indianapolis, IN (http://www.miravistalabs.com/services.aspx?o=veterinary).
- Agar-gel immunodiffusion test: a positive test result is very specific, but the test is not sensitive early in the disease process.

TREATMENT

TREATMENT OVERVIEW

Itraconazole is the treatment of choice because of efficacy, low toxicity, and ease of treatment. Dogs with neurologic disease need to be treated with amphotericin B. Corticosteroids may be indicated in dogs with dyspnea.

ACUTE AND CHRONIC TREATMENT

- General supportive care to include supplemental oxygen to dyspneic patients. Dogs with dyspnea at rest or dogs that become dyspneic after starting antifungal treatment require corticosteroid therapy (prednisone/prednisolone 0.5 mg/kg q 12 h × 5-7 days) to reduce pulmonary inflammation. Corticosteroids should not be used before antifungal therapy is started.
- Antifungal drugs:
  - Itraconazole is considered the drug of choice in most cases.
  - Amphotericin B may be superior in severe disease and in dogs with neurologic involvement.
- Itraconazole:
  - Dogs: 5 mg/kg q 12 h PO for 3 days, then 5 mg/kg PO q 24 h for at least 60 days and for 30 days after all signs of disease have resolved. The capsules should be given with canned food for maximal absorption. Brand-name itraconazole is preferred; poor absorption can occur with compounded itraconazole. Itraconazole is expensive in large dogs.
  - Cats: 5 mg/kg PO q 12 h
    - The pellets from the capsules can be mixed with palatable food for ease of administration.
    - Oral liquid formulation available (10 mg/mL)
- Amphotericin B (IV):
  - Dogs: 0.5 mg/kg IV in 5% dextrose 3 times a week at evenly spaced intervals. A cumulative dose of amphotericin B of 9 mg/kg is usually required. Amphotericin B should be temporarily discontinued when the blood urea nitrogen concentration (BUN) reaches 40 mg/dL (metric: 14 mmol/L). Therapy is continued until signs have resolved. When acute signs of blastomycosis have resolved, the treatment can be changed to itraconazole.
  - Cats: 0.25 mg/kg IV 3 times weekly. Monitor closely for nephrotoxicosis.
  - Animals must be adequately hydrated before receiving amphotericin B. The amphotericin B is usually given over a 30-minute period if there are no problems with nephrotoxicosis. Administration times of 3 hours will reduce the likelihood of nephrotoxicosis. Amphotericin B is light sensitive; therefore, the fluid bag containing the drug should be covered.
- Lipid-soluble amphotericin B:
  - Dogs, cats: 1 mg/kg IV 3 times weekly at evenly spaced intervals. The lipid formulations are costly and usually not required for blastomycosis unless there is preexisting renal disease.

DRUG INTERACTIONS

Itraconazole and ketoconazole should not be administered with drugs that inhibit cytochrome P450, such as some anticoagulants.

POSSIBLE COMPLICATIONS

- Itraconazole may cause hepatotoxicity and anorexia in dogs and cats but has fewer adverse effects than amphotericin B. Itraconazole at doses of 10 mg/kg/d may produce vasculitis, with ulcerative skin lesions that may resemble lesions of blastomycosis.
- BUN concentrations need to be monitored before every dose of amphotericin B, because the degree of nephrotoxicity varies greatly from dog to dog.
- Lung disease often worsens initially with treatment, owing to inflammation secondary to dying organisms. Corticosteroid therapy can be life saving in dyspneic dogs but should be given only after starting antifungal drugs.

RECOMMENDED MONITORING

- Liver enzymes should be monitored every 2-4 weeks during treatment in animals treated with itraconazole and measured if the patient develops anorexia.
- Assess BUN before each amphotericin B treatment. When BUN concentrations reach 40 mg/dL (metric: 14 mmol/L), treatment needs to be discontinued until BUN returns to normal.
- Thoracic radiographs should be done monthly to assess response to treatment in dogs with respiratory involvement.

PROGNOSIS AND OUTCOME

- Animals with severe lung involvement (dyspnea) or CNS involvement have a guarded prognosis. Most deaths occur in the first week of treatment.
- About 60% of dogs can be cured with the initial course of treatment.
- The mortality rate is about 20%.
- Recurrence of blastomycosis occurs in 20%-25% of treated dogs within a few months to a year after completion of treatment. Most dogs with recurrence are cured when given another course of treatment.
- Eyes that have anterior uveitis usually become glaucomatous and blind. Retinal lesions are more likely to be cured. Blind eyes should be enucleated because they can harbor organisms.
- The value of repeated urinary antigen testing in monitoring response to treatment and assessing duration of treatment is unclear but appears to be helpful.

PEARLS & CONSIDERATIONS

COMMENTS

- Early recognition is critical for successful treatment. Comprehensive diagnostic testing should be done initially in suspect cases.
- Obtaining a travel history when dogs have signs suspicious of blastomycosis is an important step for raising or lowering the disease on the differential diagnosis.

PREVENTION

- No vaccine exists
- Restrict activity in endemic areas, particularly lakes, creeks, and heavily shaded areas with moist soil in endemic areas.

TECHNICIAN TIP

- Although the disease is infectious (acquired by inhalation in the wild), it is not transmitted by inhalation from an infected patient to other animals or humans.
- Never culture a lesion or exudate in-house if it could harbor *Blastomyces;* the spores aerosolize from culture medium and are highly infectious in this context.
- Bandages contaminated with exudates should be disposed of as infectious waste, but the likelihood of aerosolization is low, owing to the specific conditions *Blastomyces* organisms require to grow.

CLIENT EDUCATION

- Long-term treatment is necessary.
- Can be fatal despite treatment
- Yeast form found in animal tissues is not directly transmissible.
- Can be transmitted via penetrating wounds

SUGGESTED READING

Spector D, Legendre AM, Wheat J, et al: Antigen and antibody testing for the diagnosis of blastomycosis in dogs. J Vet Intern Med 22:839–843, 2008.

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EDITOR: DOUGLASS K. MACINTIRE

1ST EDITION AUTHOR: LISA TIEBER NIELSON

Bilious Vomiting Syndrome

BASIC INFORMATION

DEFINITION

A disorder resulting in vomiting of a bile-stained fluid, most likely due to gastric hypomotility or gastroduodenal reflux

SYNONYMS

Gastroduodenal reflux, idiopathic gastric hypomotility

EPIDEMIOLOGY

SPECIES, AGE, SEX

Only reported in dogs, but likely occurs in cats

RISK FACTORS

Concurrent gastric, pancreatic, or intestinal disease (i.e., outflow obstruction) possible, but usually affects otherwise normal dogs.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Gastric hypomotility causing vomiting when stomach is empty, otherwise healthy
- Gastric hypomotility causing chronic-vomiting and weight loss

HISTORY, CHIEF COMPLAINT

- Vomiting, typically in the morning (especially in animals fed once daily)
- Abdominal discomfort or increased “stomach noises” (borborygmi)
- Nausea
- Anorexia
- Weight loss
- Some or all of these may be present

PHYSICAL EXAM FINDINGS

- Typically normal; abdominal palpation is unremarkable
- Dehydration and lethargy (chronic vomiting)

ETIOLOGY AND PATHOPHYSIOLOGY

- Presumed to be caused by gastroduodenal reflux that occurs when the dog's stomach is empty for long periods or due to abnormal gastroduodenal motility
- Classically, the pet vomits bile-stained fluid, usually late at night or in the morning just before eating, but otherwise feels well.
- Anatomic abnormalities or pyloric obstruction are not present, and there are no inflammatory changes in the gastrointestinal mucosa.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A working diagnosis is made based on presenting signs (vomiting when the stomach is likely empty in an otherwise well dog) and response to treatment. Diagnostic testing is warranted if features of the case suggest other disorders.

DIFFERENTIAL DIAGNOSIS

- Outflow obstruction (e.g., pyloric stenosis, foreign bodies, polyps, neoplasia)
- Dietary intolerance or hypersensitivity
- Defective propulsion
- Gastric disorders (gastritis, gastroenteritis)
- Metabolic (hypokalemia, hypocalcemia, hypoadrenocorticism)
- Nervous inhibition (trauma, stress)
- Drugs (anticholinergics, others)

INITIAL DATABASE

- CBC, serum biochemistry profile, urinalysis usually unremarkable. Hypokalemia, hypochloremia, and metabolic alkalosis possible with voluminous or chronic vomiting.
- Abdominal radiographs:
  - Normal
- Retention of food or fluid in the stomach longer than 8 hours, and often 12-16 hours after a meal, is suggestive of outflow obstruction or a motility disturbance.

ADVANCED OR CONFIRMATORY TESTING

- Motility studies are frequently difficult to perform, are not routinely available outside referral centers, and the repeatability and sensitivity of these studies are often questioned.
- Positive contrast radiography:
  - Typically normal
  - Incomplete gastric emptying following 4 hours (wide variability)
- Fluoroscopy:
  - Often normal
- Decreased frequency of gastric contractions and incoordination of antropyloric movement (objective criteria are lacking)
- Abdominal ultrasound:
  - Normal
  - Abnormal contractile activity (subjective)
- Scintigraphy:
  - Handling of radioisotopes limits the availability of scintigraphy to referral institutions.
- Gastroduodenoscopy is suggested to help rule out inflammatory, infectious, or structural causes of vomiting. The presence of an open pylorus with large amounts of bile reflux present in the stomach can be suggestive, but it is important to remember that certain anesthetic drugs can alter GI motility, creating the impression of reflux.

TREATMENT

TREATMENT OVERVIEW

Treatment goals consist of increasing gastric peristalsis and promoting gastric emptying. Nutrition and medical management using prokinetic therapy are important components of therapy.

ACUTE GENERAL TREATMENT

Management/resolution of systemic disorder if present, including fluid and electrolyte disturbances or acid-base abnormalities

CHRONIC TREATMENT

- Medical management: structural disease first must be ruled out.
  - Metoclopramide (0.2-0.4 mg/kg PO or SQ q 8 h); increases gastric peristalsis in some but not all affected dogs, *or*
  - Cisapride (0.5-1 mg/kg PO q 24 h); accelerates gastric emptying in dogs by stimulating pyloric motor activity
  - Erythromycin (1 mg/kg PO q 8-12 h); accelerates gastric emptying by inducing antral contractions, *or*
  - Ranitidine (1-2 mg/kg PO or SQ q 12 h) or nizatidine (2-5 mg/kg PO q 12 h); stimulate gastric antral contractions

NUTRITION/DIET

- Feeding small, frequent meals (especially late at night) to prevent the stomach from being empty for long periods and to encourage normal gastric motility
- Diets low in fat and fiber promote gastric emptying and may be helpful to reduce gastric retention.

- Canned or liquefied diets (solids are retained in the stomach longer) are also beneficial in animals with abnormal gastric retention of foods.

POSSIBLE COMPLICATIONS

- Acid-base or electrolyte disorders may occur secondary to chronic vomiting.
- Weight loss

PROGNOSIS AND OUTCOME

Prognosis is typically excellent; most dogs respond well to dietary and/or prokinetic therapy.

PEARLS & CONSIDERATIONS

COMMENTS

- Differential diagnoses for bilious vomiting syndrome include primary and secondary disorders of gastric emptying.
  - Primary disorders of gastric emptying may arise from mechanical obstruction or defective propulsion.
  - Secondary disorders of gastric emptying include metabolic and electrolyte disturbances.
- Weight loss should prompt a complete diagnostic evaluation, because it is not a common feature of uncomplicated bilious vomiting syndrome.

SUGGESTED READING

Hall JA, et al: Diagnosis and treatment of gastric motility disorders. Vet Clin North Am Small Anim Pract 29:377–395, 1999.

Washabau RJ, et al: Diagnosis and management of gastrointestinal motility disorders in dogs and cats. Compend Contin Educ Pract Vet 19(6):721–737, 1997.

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EDITOR: DEBRA L. ZORAN

Bile Duct Obstruction, Extrahepatic

BASIC INFORMATION

DEFINITION

Pathologic obstruction of the extrahepatic bile duct system

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dependent on the underlying cause. Dogs (middle-aged to older adults): pancreatitis; less commonly, neoplasia. Cats (middle-aged to older adults): neoplasia

RISK FACTORS:

Dogs:

- Pancreatitis

Cats:

- Pancreatitis
- Cholangitis/cholangiohepatitis
- Inflammatory bowel disease
- Neoplasia

ASSOCIATED CONDITIONS & DISORDERS

Dogs:

- Cholecystitis
- Gallbladder mucocele

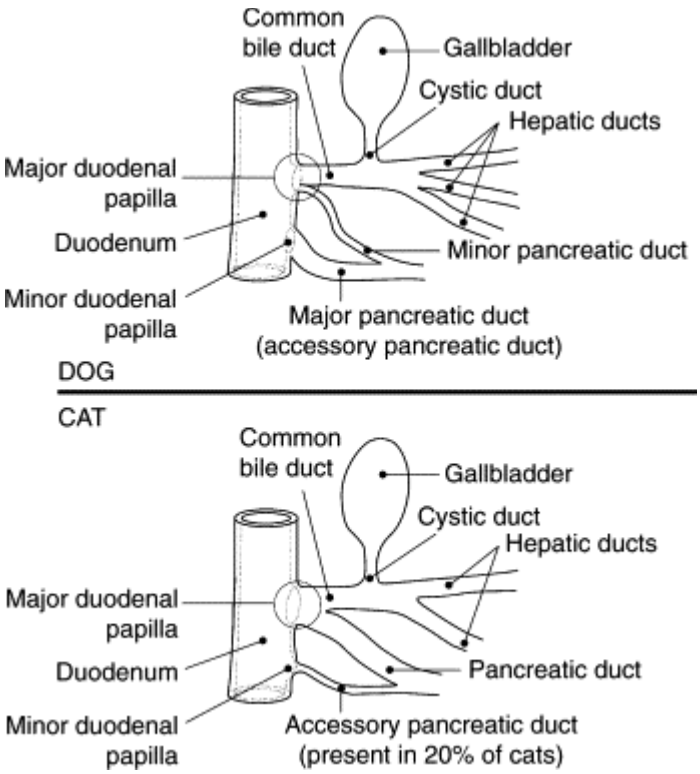
Dogs and cats:

- Coagulopathy possible due to lack of absorption of fat-soluble vitamin K
- Cholelithiasis
- Bile peritonitis
- Neoplasia

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

Dogs: anorexia, lethargy, vomiting, diarrhea. *Cats:* anorexia, lethargy, weight loss, vomiting



BILE DUCT OBSTRUCTION Comparative anatomy of the canine and feline biliary systems.

(Courtesy Glenda Clements-Smith.)

PHYSICAL EXAM FINDINGS

Dogs: icterus, fever, tachycardia.

Cats: icterus, dehydration, fever or hypothermia

ETIOLOGY AND PATHOPHYSIOLOGY

Dogs:

- See Pancreatitis, Dog, p. 820
- Cholelithiasis: etiology poorly understood

Cats:

- Extrahepatic biliary obstruction often associated with a “triad” of diseases: cholangitis, pancreatitis, and inflammatory bowel disease
- Common opening of the pancreatic and common bile ducts into the duodenum and the increased duodenal bacterial content may predispose cats to ascending cholangitis and pancreatitis after vomiting associated with inflammatory bowel disease.

Dogs and Cats:

- Lack of bile entering intestinal tract:
  - Decreases absorption of fat and fat soluble vitamins, notably vitamin K: potential coagulopathy. May also result in increased absorption of endotoxin from the gut.
- Other possible etiologies include neoplasia, stricture in biliary system, duodenal obstruction by a foreign body, diaphragmatic hernia, and parasitic infection.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on presenting history and physical examination findings. Confirmation requires demonstration that the icterus is caused by an obstructed common bile duct rather than inherent liver disease, typically involving abdominal ultrasound exam.

DIFFERENTIAL DIAGNOSIS

- Hyperbilirubinemia:
  - Rule out hemolysis:
    - Immune-mediated hemolytic anemia, toxicity (zinc, onions, etc.) and other diseases causing hemolytic anemia
  - Rule out hepatic disease:
    - Hepatitis: acute, chronic
    - Cirrhotic/fibrosing liver disease
    - Neoplasia
    - Copper and other toxins in dogs, acetaminophen toxicosis in cats

INITIAL DATABASE

- CBC:
  - Possible anemia; generally very mild if any (unless concurrent gastrointestinal ulceration). By contrast, hyperbilirubinemia/icterus caused by hemolysis generally produces moderate to marked anemia
  - Inflammatory leukogram
- Serum biochemistry profile:
  - Elevated bilirubin concentration
  - Elevated liver enzyme concentrations
  - Possible elevated amylase and lipase concentrations
  - Hypokalemia
- Urinalysis: bilirubinuria is common in both species (but mild bilirubinuria is also normal in healthy dogs)
- Survey abdominal radiographs:
  - Cranial abdominal detail may be decreased in cases with biliary leakage and peritonitis.
  - May delineate radiopaque choleliths
- Survey thoracic radiographs:
  - Rule out metastatic disease if neoplasia is suspected.

ADVANCED OR CONFIRMATORY TESTING

- Abdominal ultrasound examination:
  - Common bile duct dilation
    - >5 mm diameter: diagnostic of bile duct obstruction in the cat
  - Visible contraction of the gallbladder is not expected in either healthy or diseased states.
- Peritoneal fluid analysis (obtained during abdominal ultrasound examination):
  - Elevated bilirubin concentration: bile peritonitis
  - Cytologic analysis and microbiologic (aerobic and anaerobic) culture and sensitivity testing: septic peritonitis
- Coagulation profile

TREATMENT

TREATMENT OVERVIEW

Patients require surgical correction of the problem along with appropriate intensive and supportive care. A major exception is transient biliary obstruction caused by acute pancreatitis, provided the patient's clinical course is mild and improves rapidly (few days) with medical therapy alone.

ACUTE GENERAL TREATMENT

- Rehydration by intravenous administration of balanced electrolyte solution
- Parenteral antibiotics effective against gram-negative bacteria and anaerobes:
  - Empirical therapy:
    - Cefoxitin, 30 mg/kg IV q 2 h perioperatively, then q 6 h, *or*
    - Metronidazole, 7.5-15 mg/kg IV q 12 h with
    - Enrofloxacin, 2.5-5 mg/kg IV q 12 h (5 mg/kg q 24 h maximum in cats, owing to risk of retinal toxicity)
  - Specific long-term therapy based on culture and sensitivity test results
- Possible administration of fresh frozen plasma:

    - Hypoproteinemia
    - Possible coagulopathy
- Vitamin K administration: 2.5 mg/kg SQ q 12 h × 3-5 days, then once weekly
- Relief of extrahepatic biliary obstruction—surgical intervention:
    - Duodenotomy and retrograde and antegrade flushing of biliary system: all cases
    - Common bile duct stenting: if temporary or dynamic obstruction likely (i.e., pancreatitis) and severe persistent hyperbilirubinemia
    - Cholecystoduodenostomy/jejunostomy: if advanced or permanent obstruction
    - Tube cholecystostomy
    - Cholecystectomy: if gallbladder wall is devitalized
    - Gastrointestinal biopsies: association of biliary disease with inflammatory bowel disease in cats
- Relief of intragallbladder luminal hypertension has been achieved via ultrasound-guided centesis of the gallbladder in dogs with pancreatitis-associated biliary obstruction

CHRONIC TREATMENT

Maintenance of bile flow: Ursodeoxycholic acid, 10-15 mg/kg PO q 24 h. Contraindicated if biliary obstruction is still present.

NUTRITION/DIET

Provide enteral feeding (e.g., gastrostomy tube; see p. 1270 and p.1267) if patient is anorexic

POSSIBLE COMPLICATIONS

Ongoing pancreatitis, bile leakage, peritonitis, endotoxemia, sepsis, death

RECOMMENDED MONITORING

- Clinical and laboratory parameters assessing perfusion, including capillary refill time, pulse rate and quality, blood pressure, urine output, arterial pH, and lactate concentrations
- Respiratory function
- Serum liver enzyme and bilirubin concentrations
- Coagulation profile

PROGNOSIS AND OUTCOME

- Poor if biliary obstruction associated with neoplasia: 100% mortality in cats
- Guarded if biliary obstruction associated with nonneoplastic causes in cats
- Guarded to fair if biliary obstruction associated with nonneoplastic causes in dogs

PEARLS & CONSIDERATIONS

COMMENTS

- Given the association of biliary obstructive disease in cats with cholangitis/cholangiohepatitis and inflammatory bowel disease, a liver biopsy and culture, bile culture, and small-intestinal biopsies must be obtained at the time of surgery in this species. A convenient site for duodenal biopsy is the edge of the duodenotomy performed to cannulate the duodenal papilla(e) or to perform a cholecystoduodenostomy.
- In assessing hyperbilirubinemia, total bilirubin concentration is important. Conjugated versus unconjugated bilirubin is not linked to the source of hyperbilirubinemia in dogs and cats as it is in humans.

SUGGESTED READING

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Aguirre AL, Center SA, Randolph JF, et al: Gallbladder disease in Shetland sheepdogs: 38 cases (1995-2005). J Am Vet Med Assoc 231:79–88, 2007.

Herman BA, Brawer RS, Murtaugh RJ, Hackner SG: Therapeutic percutaneous ultrasoundguided cholecystocentesis in three dogs with extrahepatic biliary obstruction and pancreatitis. J Am Vet Med Assoc 227(11): 1753, 1782–1786, 2005.

AUTHOR: DAVID HOLT

EDITOR: RICHARD WALSHAW

Bicipital Tenosynovitis

BASIC INFORMATION

DEFINITION

Inflammation of the biceps brachii tendon and surrounding synovial sheath

SYNONYM

Bicipital bursitis (inaccurate)

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs
- Medium and large breeds
- Middle-aged to older

RISK FACTORS

Trauma, overuse of muscle, shoulder joint osteoarthritis

ASSOCIATED CONDITIONS & DISORDERS

Osteoarthritis or osteochondrosis of shoulder joint, supraspinatus tendonitis

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

Forelimb lameness exacerbated by exercise and unresponsive to nonsteroidal antiinflammatory drugs (NSAIDs); caused by trauma to shoulder or insidious in onset

PHYSICAL EXAM FINDINGS

- Shortened forelimb stride, with head lifted as affected forelimb is advanced
- Pain on palpation of the bicipital tendon in the intertubercular groove
- Pain on flexion of shoulder and extension of the elbow while placing tendon and muscle under tension

ETIOLOGY AND PATHOPHYSIOLOGY

- Can be caused by blow to cranial aspect of shoulder during flexion
- Tendon may be strained or stretched with disruption of fibers
- In chronic conditions, dystrophic mineralization occurs in tendon
- Secondary to shoulder joint osteoarthritis or osteochondrosis if cartilage fragments collect within the communicating tendon sheath and cause inflammation
- Adhesions between tendon sheath and tendon can occur secondary to trauma.
- Tendon can also be avulsed from supraglenoid tubercle

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Forelimb lameness raises the possibility of this diagnosis; pain on deep palpation of the bicipital tendon is characteristic.

DIFFERENTIAL DIAGNOSIS

- Supraspinatus tendonitis
- Supraglenoid tubercle fracture
- Biceps muscle tearing at the distal musculotendinous junction
- Shoulder joint collateral ligament injury
- Shoulder joint osteoarthritis
- Cervical nerve root compression

INITIAL DATABASE

- Patient database as indicated by stability and American Society of Anesthesiologists classification (p.1372)
- Medial to lateral radiograph of the scapulohumeral joint
- Skyline radiographic view of the intertubercular groove

ADVANCED OR CONFIRMATORY TESTING

- Contrast arthrography may reveal irregularity of tendon surface or sheath.
- Arthrocentesis may be consistent with osteoarthritis (increase nucleated cell counts 1500-4800 cells/mcL, primarily mononuclear; aseptic).
- Ultrasonography of the biceps tendon will identify irregular fiber arrangement and increased synovial sheath fluid content.
- MRI may be considered to identify tendon and sheath lesions.
- Arthroscopy for direct visualization of tendon and sheath

TREATMENT

TREATMENT OVERVIEW

Relieve pain due to tenosynovitis.

ACUTE GENERAL TREATMENT

- Local injection with methylprednisolone acetate (10-40 mg) followed by 2 weeks of rest. Repeat at 2-week intervals for 3 treatments; if no improvement, surgery is considered.
- Surgical treatment:
  - Preserve tendon and release transverse humeral ligament if it is restricting biceps tendon excursion.
  - Tenotomy via arthrotomy or arthroscopy
  - Tenodesis to the proximal humerus by screw/washer or passing tendon through a bone tunnel and suturing to the periosteum

CHRONIC TREATMENT

Exercise restriction for 6-8 weeks

POSSIBLE COMPLICATIONS

- Poor response to steroid treatment
- Chondromalacia in shoulder joint or biceps tendon rupture secondary to steroid injection
- Persistent lameness due to inadequate tenodesis

RECOMMENDED MONITORING

- Short-term postoperatively for seroma
- Long-term for restoration of limb function

PROGNOSIS AND OUTCOME

- Fair to good after steroid injection and rest
- Good after tenodesis or tenotomy (arthroscopic)

PEARLS & CONSIDERATIONS

COMMENTS

- Establishing a diagnosis of bicipital tenosynovitis can be difficult.
- Disease of the supraspinatus tendon can be a conflicting cause of shoulder joint pain. This condition is best evaluated by MRI or arthroscopy to identify tendon impingement into the groove; splitting this tendon resolves pain and lameness.
- The synovial sheath of the biceps tendon is continuous with the shoulder joint capsule.
- Transverse humeral ligament thickening may constrict the tendon and cause pain.

SUGGESTED READING

Lafuente MP, Fransson BA, Lincoln JD, et al: Surgical treatment of mineralized and nonmineralized supraspinatus tendi nopathy in twenty-four dogs. Vet Surg 38:380–387, 2009

AUTHOR: JAMES D. LINCOLN

EDITOR: JOSEPH HARARI

Behavior Problems, Miscellaneous

BASIC INFORMATION

DEFINITION

Species-typical and normal behaviors that may inconvenience clients

Dogs:

- Coprophagy (see p. 244)
- Digging
- Mounting/humping
- Roaming
- Fence running/scratching

Cats:

- Scratching of furnishings
- Late night activity, climbing on counters

EPIDEMIOLOGY

SPECIES, AGE, SEX

Younger animals more likely to exhibit exploratory and play behaviors that may irritate clients. Intact males may roam more frequently and greater distances.

GENETICS & BREED PREDISPOSITION

- Hounds and northern dog breeds (e.g., husky, malamute, Samoyed) are anecdotally reported to look more readily for opportunities to roam.
- Highly active breeds or individuals with inadequate stimulation and exercise to satisfy their behavioral and cognitive needs may look for alternatives for behavioral expression, which may be intolerable to owners.

RISK FACTORS

Management practices that decrease enrichment (both mental and physical) or fail to establish a humane rule structure that meet a pet's physical, social, developmental, behavioral, and cognitive needs. Examples are lengthy confinement within a day for dogs (e.g., 8 of 24 hours), lack of interactive toys, lack of basic training, inadequate aerobic exercise, and inadequate social exposure.

CONTAGION & ZOONOSIS

Multiple-dog and multiple-cat households may experience social facilitation that fosters many of these behaviors. In social facilitation, the behaviors of one individual in a group stimulate others to do the same or similar behaviors.

GEOGRAPHY AND SEASONALITY

Access (e.g., digging in soil) and the level of provocative stimuli (e.g., other cats outside) may vary seasonally.

ASSOCIATED CONDITIONS & DISORDERS

Obsessive-compulsive disorders (see p. 775).

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Bouts of behaviors that can be interrupted and that seem only to occur opportunistically may be normal but annoying behaviors or management-related behavior problems. If the behaviors cannot be easily interrupted, or if the animal is constantly seeking ways to get access to do them, a more serious disorder should be suspected (e.g., obsessive-

compulsive disorder, see p. 775)

HISTORY, CHIEF COMPLAINT

Behavior that is annoying (e.g., cat walking on counters) or disgusting (e.g., dog rolling in feces) to the client, but not threatening or dangerous. The first step in eliciting relevant information is to get a good and complete description of the behaviors and the context in which they occur. Context is critical for assessment of whether the behaviors are “normal” or species-typical ones that can be redirected or managed while still meeting the animal's needs. For example, a cat's scratching at an inanimate object (e.g., furniture) is part of normal behavior and can be redirected, but scratching at humans or other cats may represent aggression.

PHYSICAL EXAM FINDINGS

Usually unremarkable, although history or evidence of minor self-trauma acquired during exploratory or escape behaviors may be present.

ETIOLOGY AND PATHOPHYSIOLOGY

- Clients must understand that animals do not undertake these behaviors to “spite” them or out of “jealousy;” attention-seeking is commonly involved, but the key to managing these disorders is having clients understand the significance of the behaviors in terms of normal dog and cat behavior.
- Most of these behaviors are normal behaviors in context, intensity, and frequency, at least at first.
- With time, if behaviors become increasingly abnormal, the context, intensity, and frequency with which they are exhibited will change, as will the animal's focus, interactions with humans and other animals, and daily time budget.
- Effective behavior modification: positive behaviors are encouraged and repeated if they result in a pleasurable outcome. This repetition leads to learning at the neurochemical level where new proteins at synapses are made. These more efficient neuronal connections make it more likely that the dog or cat will continue with the behavior. This sequence explains the importance of early identification and intervention.

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

Many “nuisance” behaviors are actually within the species repertoire of normal behaviors. A problem exists when their expression is undesirable to owners, but even then, they may not be a sign of abnormal behavior. Therefore, the history is diagnostic; the context in which the specific behavior occurs will determine whether the behavior is normal but inconvenient, or indicative of a true disorder.

DIFFERENTIAL DIAGNOSIS

- If any of the signs are excessive, repetitive, and performed to the exclusion of other comfort, social, and maintenance behaviors, an anxiety disorder such as obsessive-compulsive disorder (see p. 775) must be considered.
- Late-night activity in middle-aged to older cats that is new and uncharacteristic based on the pattern of previous nocturnal behavior could be a sign of feline cognitive dysfunction (see p. 225).
- Hyperthyroidism also should be ruled out whenever an adult cat's activity level increases uncharacteristically.

INITIAL DATABASE

- CBC, serum biochemistry profile, urinalysis: generally unremarkable
- Ingestion of feces or other nonnutritive items: fecal flotation, trypsin-like immunoreactivity (see p. 372)

TREATMENT 

TREATMENT OVERVIEW

Provide an acceptable outlet for the unmet behavioral, cognitive, and species-typical needs that lead the pet to engage in the behavior the client finds objectionable.

ACUTE GENERAL TREATMENT

- Increase aerobic activity through exercise and interactive play with humans or fellow dogs/cats. Play with compatible conspecifics, particularly for dogs, usually provides more effective exercise with greater aerobic scope than does play with

humans.
- Environmental modification should be used for preventing access to or limiting the repetition of the undesirable behavior, and to foster alternative, acceptable behaviors.

CHRONIC TREATMENT

- Behavior modification can provide outlets or encourage substitute behaviors that allow acceptable expression of the individual's mental and social needs. Depending on the problem, this may consist of continued aerobic exercise, goal-oriented activities (obedience, agility, tracking, coursing training in dogs; interactive predatory play in cats). Rewards—verbal, physical (e.g., petting or stroking), food—should be given for all spontaneous and calm behaviors (e.g., chewing on chew-toys, clawing on provided surfaces, digging in a sandbox provided for this purpose, pouncing on cat toys).
- Attention-seeking behaviors such as jumping or “playful” whining or biting need to be ignored completely. Elimination of the reward (of attention) will extinguish the behavior if, and only if, the client is consistent in not responding.
- In mild cases, devices that interrupt the behavior with an aversive stimulus can be useful early in the course of the problem, only if the animal is not afraid of the stimulus, and only if appropriate outlets to which the behavior can be redirected are also provided.
- Examples of aversive but not harmful or fear-inducing disruptive stimuli include inverted plastic carpet runners (spike side up), static electricity mats for surfaces the client wants to be off-limits to the pet, and pressurized air blasts triggered by motion-detector sensors. Note that some animals will be afraid of these stimuli. If this is the case, the devices should not be used. The purpose of a disruptive stimulus is to stop the behavior in a way that encourages the animal to seek information and engage in an alternative behavior that can be rewarded. If the animal is afraid, it cannot do this.

POSSIBLE COMPLICATIONS

Poor client compliance can lead conversely to continued self-reinforcement and worsening of the problem, and deterioration of the pet-client relationship. Therefore a cornerstone of treatment is owner understanding of the basis for the behavior and the intention of the proposed treatment.

RECOMMENDED MONITORING

- Frequent follow-up will help many clients comply more reliably.
- Demonstrations that show clients new ways to interact with their pet are essential.
- By dedicating these tasks to one staff member, continuity and consistency in advice and follow-up are maintained. Clients also feel that their veterinarians care more about them under these conditions.

PROGNOSIS AND OUTCOME 

- Excellent if the clients understand the pets' needs and are willing and able to meet them
- Poor if clients have unrealistic expectations, consider pets recyclable, feel guilty about discussing the issue with their vet, or are unwilling or unable to meet their pets' needs

PEARLS & CONSIDERATIONS 

COMMENTS

- In extreme forms that interfere with normal physical and social functioning, most of these “annoyance” behaviors are also characteristic of obsessive-compulsive disorder and other anxiety-related conditions. This does not mean that exhibition of these miscellaneous concerns will lead to obsessive-compulsive disorders. It does mean that the nonspecific signs and complaints can be similar, and clients should be aware of this and not dismiss unusual behaviors out of hand as just “bratty” behaviors without having them evaluated first. Referral to a veterinary behaviorist may be very helpful in such situations.
- Relinquishment and euthanasia are frequent sequelae to behaviors clients find undesirable, whether or not the behaviors were the pet's “fault.” The effect of this pattern on veterinary economics and veterinary staff morale is huge and often preventable.
- This is a quality of life (QoL) issue for pets.

PREVENTION

Puppy and kitten classes, basic obedience and agility training, and understanding of basic behavioral, physical, and social needs of dogs and cats will help clients to intervene before behaviors become problems.

CLIENT EDUCATION

Veterinarians are encouraged to keep a loaning library of books, newsletters, videos covering basic behaviors of dog and cats, and a list of trainers and facilities that a staff member has verified use humane training techniques. This will provide the atmosphere of caring that will make it easier for clients to seek and get the help they need. A useful source of video and other training and behavioral material is http://abrionline.org/.

SUGGESTED READING

Donaldson J: The culture clash. Berkeley, Calif., 1996, James and Kenneth Publishers.

Miller P: The power of positive dog training. Dog Wise, 2003.

Seksel K: Training your cat. Melbourne, Australia, 2001, Hyland House.

AUTHOR: SORAYA V. JUARBE-DIAZ

EDITOR: KAREN L. OVERALL

Behavior Problem Prevention, Puppies

BASIC INFORMATION

DEFINITION

The first few puppy visits set the stage for future veterinary visits. They educate the new puppy owner about normal canine behavior and social systems and help prevent problems with toilet training, digging, jumping up, barking, mouthing and chewing.

SYNONYMS

Puppy socialization; puppy training; Puppy Preschool

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs <6 months old, both sexes; consider as 2 age groups (£3 months; >3 months) and multiple activity appropriate groups.
- Problematic behavior often becomes more pronounced at social maturity (“18-24 months of age).

RISK FACTORS

Dogs not adequately exposed to varied stimuli, especially during the sensitive socialization period (3-12 weeks old; later for ongoing novel experiences), are at increased risk of neophobia (fear of humans, other dogs).

CONTAGION & ZOONOSIS

Dog bites are a public health risk.

ASSOCIATED CONDITIONS & DISORDERS

- Increased risk of abandonment and euthanasia if owners do not understand normal canine behaviors and social structure and use this understanding to meet the dog's needs.
    - Risk factors for surrender/abandonment include absence of castration, lack of housetraining, no veterinary attention, and no obedience/manners training.
    - The average client with a problem dog keeps the dog 3 months before relinquishment.
- Dogs with inherited neurologic disorders (e.g., lissencephaly) often present with abnormal puppy behavior as the nonspecific complaint.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

The owner may not report any difficulties with the puppy or may report some problems with toilet training, digging, jumping up, barking, mouthing, or chewing.

PHYSICAL EXAM FINDINGS

If there are no medical problems, it should be unremarkable.

ETIOLOGY AND PATHOPHYSIOLOGY

Certain behaviors are normal for the individual/species and misunderstood by, or out of context for, an uninformed owner. Other behaviors are truly abnormal and warrant intervention.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Detailed history, discussion of expectations, and observation of interaction between owner and puppy are usually sufficient to identify potential misunderstandings and anticipate problems, allowing early intervention.

DIFFERENTIAL DIAGNOSIS

Normal behavior that may not be acceptable to the owner versus behavioral disorder

INITIAL DATABASE

History and physical exam are usually sufficient.

TREATMENT

TREATMENT OVERVIEW

Cornerstones of treatment are to identify the exact features of behaviors the owner considers abnormal, annoying, or troublesome and determine whether these are normal or pathologic; to counsel owners on behaviors that are normal for dogs; and to increase positive interaction between owner and puppy. The goal is to maximize positive interaction between puppy and owner, and with perceived or real behavioral disorders, to reduce the risk of surrender.

ACUTE AND CHRONIC TREATMENT

- Preventive health care for dogs should always include information about canine behavior. Many issues that lead to abandonment may be preventable with client education.
- Every veterinary visit should include an assessment of a puppy's behavior, thus educating the client about age-specific normal behavior and allowing early intervention. Sample questions could include: Does your puppy urinate in the house? Does your puppy avoid other dogs or strangers and/or appear concerned about them? Does your puppy vocalize when left alone? Does your puppy have any behaviors that concern you or that you do not like?
- Rewards (e.g., treats, pats, verbal praise) should be given for appropriate behaviors, including during veterinary visits.
- Inappropriate behaviors should be redirected and more appropriate behaviors substituted consistently and long term (e.g., the dog grabs a toy at the door, not the human's hand)
- Dogs should not be verbally or physically punished for inappropriate behaviors.
- Dogs should be taught to sit and settle/relax on cue.
- Head collars can help owners manage their puppy better with less need for “corrections.”
- Choke chains, prong collars, and electronic collars have no place in modifying or preventing unacceptable behaviors.
- Many behaviors such as jumping up, digging, or mouthing are normal behaviors that owners dislike or do not understand. They are best resolved by ignoring the behavior and teaching the dog an alternative response instead (response substitution), such as sitting for petting rather than jumping up and being pushed down.
- Many of these problem behaviors may be addressed by referral to a good positive-reinforcement trainer.

NUTRITION/DIET

- Dogs eat during the day and would naturally eat three meals. Using foraging devices/food toys can be used as way of enriching the dog's environment.
- Advice on prevention of obesity is important; use of only small treats and accurate exercise requirements must be explained.

BEHAVIOR/EXERCISE

- Age-appropriate physical and mental stimulation is necessary. These can include walking, swimming, games, interactive toys, agility, and tracking.
- Jumping up (see p. 133):
    - May start inadvertently as the puppy seeks attention
    - Puppy should be taught to sit on cue and quietly praised.
    - The owner should not pay attention to the dog when he/she jumps up. Instead, the owner should stand still or turn his/her back on the dog and wait until all of the dog's four feet are firmly placed on the ground and the dog is quiet and attending to the owner. The dog should then be given quiet, calm praise immediately.
    - Interactions only occur when the dog is calm.
    - Making eye contact, pushing the dog down, kneeing, pinching the toes, or saying “no” will encourage jumping as the dog gains attention.
- Chewing objects (see also p. 654).

    - Dogs use the mouth to investigate their environment, so it is important owners recognize this is a normal behavior.
    - Dogs may also chew when they are anxious or distressed, and chewing may be a sign of such problems as separation anxiety (see and p. 654).
    - Puppies need to be given suitable, safe toys to chew. Rotating toys or odors associated with toys may increase interest for some dogs.
    - Foraging devices such as Kongs, Treat Balls, the Busy Buddy line of toys, and Buster Cubes are useful for puppies to chew. The toys should be as indestructible as possible and must be checked and cleaned regularly.
    - The puppy should not have access to potentially valuable or unacceptable items. Puppies should not be given old shoes or other belongings of the owner to chew, as dogs cannot always tell the difference between what is a new shoe and what is an old shoe.
- Digging
    - Many dogs dig, and this is a normal behavior. The dog may be given a digging pit (the size of a child's size sandpit) filled with loose sand or soil to encourage digging in this area.
    - Burying bones, toys, and other treats in this area “rewards” the dog for digging there.
- Mouthing (see also p. 654)
    - Puppies mouth to investigate their environment. They may also mouth in play. It is important for owners not to use hands to play with puppies, as that may encourage mouthing.
    - Appropriate toys should be available for the puppy to chew and can be offered to the puppy if it mouths or bites.
    - If a puppy uses its mouth excessively in play or bites, play should stop immediately and the person should walk away. Once the puppy is calm, play can resume.
    - If the puppy persists in play biting, the owner needs to entirely discontinue any interaction or play for that session.
    - Owners should not to use hands to hit the puppy or push him/her away, as this may encourage mouthing or biting. Puppies may perceive this as a game and will persist in biting.
- Barking: see p. 127

RECOMMENDED MONITORING

Weekly phone call to monitor progress and help with troubleshooting for the first months of intervention.

PROGNOSIS AND OUTCOME

New puppy owners often are very open to learning about their puppy's development. Encourage this by asking about behavior and viewing photos/videos with clients.

PEARLS & CONSIDERATIONS

COMMENTS

- Educate owners often that rewarding appropriate behaviors while ignoring or redirecting inappropriate behaviors is the best way to manage potential problem behaviors.
- If behavior problems persist, refer to a veterinary behaviorist early in their development. Most dogs do not “grow out of it,” but instead learn to become more distressed and problematic with time.

PREVENTION

- Offer pre-pet selection advice, especially pertaining to size and grooming and exercise needs.
- Attendance at puppy socialization and training classes (Puppy Preschool) or puppy manners classes helps puppies to behave politely in society. The classes also help owners understand their dog's behavior and to have realistic expectations of their dog.

TECHNICIAN TIPS

Regular contact with owners to educate them and assist them with any behavior modification advice will increase client compliance. Participation in Puppy Preschool and routine manners classes are great ways of building client trust and confidence.

CLIENT EDUCATION

Exposing puppies to many stimuli in a manner where they are not distressed, or can easily overcome their distress, maximizes their chances to grow into well-behaved and accepted members of their households and society.

SUGGESTED READING

Brammeier S, et al: Good trainers: how to identify one and why this is important to your practice of veterinary medicine. J Vet Behav: Clin Appl Res 1:47–52, 2006.

Seksel K: Preventative behavioral medicine for cats. In Horwitz D, Mills D, editors: BSAVA manual of canine and feline behavioral medicine, Gloucester, UK, 2002, British Small Animal Veterinary Association, pp 75–82.

Landsberg G, Hunthausen W, Ackerman L: Handbook of behavior problems of the dog and cat. Oxford, 2003, Butterworth-Heineman.

Overall KL: Clinical behavioral medicine for small animals. St Louis, Missouri, 1997, Mosby.

AUTHOR: KERSTI SEKSEL

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Behavior Problem Prevention, Kittens

BASIC INFORMATION

DEFINITION

The first few kitten visits set the stage for future veterinary visits. They help the new kitten owner understand normal feline behavior and social systems and help prevent problems with litter box usage, scratching furniture, biting, and chewing.

SYNONYMS

Kitten kindergarten, Kitten Kindy, kitten socialization, kitten training

EPIDEMIOLOGY

SPECIES, AGE, SEX

Cats <3 months of age of both sexes

RISK FACTORS

Increased risk of abandonment and euthanasia if owners do not understand normal feline behaviors and social structure and meet the cat's needs.

CONTAGION & ZOONOSIS

Cat scratch fever (bartonellosis) is most commonly transmitted with fleas. Exposure of 2- to 8-week-old kittens to humans helps adaptation and reduces future risk of aggression.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

The owner may not report any difficulties with the kitten or may report some difficulties with litter box usage, chewing undesirable or inappropriate objects, or scratching and/or biting humans or other animals.

PHYSICAL EXAM FINDINGS

If there are no medical problems, it should be unremarkable.

ETIOLOGY AND PATHOPHYSIOLOGY

People keep cats approximately 2 years after they start to exhibit behavior problems, which often occurs at the onset of social maturity (2-4 years old).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

- Preventive health care for cats should always include information about feline behavior so the cat's long-term health and welfare are maximized, and owners have realistic expectations of their cats. Many issues that lead to abandonment and euthanasia may be preventable with client education.
- Make veterinary visits as stress free as possible for the cat, owner, and veterinary staff.

DIFFERENTIAL DIAGNOSIS

Based on the presenting signs and complaints of the owner

INITIAL DATABASE

As appropriate; often, no evaluation is needed beyond history and physical exam

TREATMENT

TREATMENT OVERVIEW

Treatment goals are:

- To educate owners about normal feline behavior
- To advise clients how to prepare the home for their kitten, including bedding, feeding, exercise, and health care requirements
- To reduce the risk of surrender or euthanasia in the future
- To help veterinary visits to be as stress free as possible for the owner, the cat, and the veterinary staff
- Early recognition of behavior problems and referral to a veterinary behaviorist as soon as concern becomes apparent, to decrease risk of surrender or euthanasia

ACUTE AND CHRONIC TREATMENT

- Rewards (e.g., treats, pats, verbal praise) should be given for appropriate behaviors.
- Inappropriate behaviors should be redirected and more appropriate behaviors substituted (e.g., chase the toy, not the human's foot).
- Cats should not be verbally or physically punished for inappropriate behaviors.
- Cat “carry-basket” training so the cat associates the cat basket with pleasant experiences
- Feliway diffusers in the consulting room and spray applied to hands and consultation table surface may decrease anxiety.
- Appropriate behaviors must be reinforced long term in order for them to be maintained.
- All veterinary visits should be as pleasant as possible. Use rewards and low-stress handling techniques, with minimal restraint. If profound distress occurs, consider use of panicolytic medication early in its development.
- Many behaviors such as scratching furniture are not true behavior problems but normal behaviors that are viewed as a problem by the owners.

NUTRITION/DIET

- Cats eat during the day and night and often graze. Using foraging devices can be a way of enriching the cat's environment.
- Obesity prevention is important (only small treats).
- Place water bowls apart from food bowls to encourage water consumption.
- Newer food toys may encourage more species-typical eating patterns and exercise if used for meal feeding.

BEHAVIOR/EXERCISE

Age-appropriate physical and mental stimulation are necessary, especially for indoor cats. These can include:

- Scratching posts: stable/anchored; horizontal and vertical [individual cat preferences]; large to allow stretching; can be homemade.
- Indoor garden box: growing grass, catnip or catmint for cats to nibble on can provide enrichment for many cats.
- Tunnels, paper bags, and cardboard boxes provide good hiding places, especially if placed up high.
- Commercially available toys such as the Bizzy Kitty, Cat Track, Kitty Kong, and Cat Dancer can provide enrichment, both physically and mentally.
- Two kittens: in some cases this can be appropriate, as they may keep each other company and play together while the owners are at work.
- Hiding the cat's dry food around the house so the cat “hunts” for its dinner. Food toys can also play this role.
- Training behaviors on cue: example, cats can be trained to come on cue, sit, or roll over.
- Agility training: cats are taught similar techniques to dogs, such as negotiating various stimuli.

RECOMMENDED MONITORING

Weekly phone call for the first month to monitor progress and troubleshoot can help increase owner compliance.

PROGNOSIS AND OUTCOME

New kitten owners often are very open to learning about them, so the outcome should be favorable. Encouraging questions and sharing of photos/videos will help.

PEARLS & CONSIDERATIONS

COMMENTS

- Educate owners that rewarding appropriate behaviors and ignoring or redirecting inappropriate behaviors is the best way to manage potential behavioral problems.
- If behavior problems persist, referral to a veterinary behaviorist early is preferable to waiting to see if the cat "will grow out of it."

PREVENTION

- Offer pre-pet selection advice, including information on what grooming the adult cat will entail.
- Attendance at kitten socialization and training classes (Kitten Kindy) can help owners to have realistic expectations of their cat.

TECHNICIAN TIPS

Regular contact with owners to educate and assist them with any behavior modification advice increases client compliance. Kitten Kindy is a great way to get to know and earn the respect of clients.

CLIENT EDUCATION

It is just as important to socialize and train kittens as it is puppies so they to grow up into well-behaved and accepted members of society.

SUGGESTED READING

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AUTHOR: KERSTI SEKSEL

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Bee and Other Insect Stings

BASIC INFORMATION

DEFINITION

Stings from insects such as bees, wasps, and hornets. Spider envenomation is discussed separately (see p. 1035).

SYNONYM

Insect bites

EPIDEMIOLOGY

SPECIES, AGE, SEX

Bites and stings are more likely to occur in young, inquisitive animals. Cats may be more tolerant than dogs to many insect toxins.

GENETICS & BREED PREDISPOSITION

Boxers seem especially prone to insect reactions.

GEOGRAPHY AND SEASONALITY

Bee stings are more common during warm weather when the insects are active.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

Bees, wasps, hornets (order Hymenoptera): Animals frequently present with no known history of an insect sting. Instead, they present for clinical signs associated with allergic reaction (see p. 64). Severity of signs will depend on the type of venom, location of the sting, number of stings, and sensitivity of the animal receiving the sting.

PHYSICAL EXAM FINDINGS

- Bees, wasps, hornets:
  - Local reaction associated with an immunologic response is the most common finding. This may include a swollen head/face or diffuse urticaria. Cases with severe facial swelling can develop respiratory distress from upper airway obstruction and occlusion.
  - Less commonly, an animal may develop anaphylaxis (see p. 64). Signs of anaphylaxis may develop within 15 minutes of a sting. Anaphylaxis in dogs can manifest as vomiting, defecation, urination, muscular weakness, respiratory depression, or seizures. Cats most often show signs of pruritus, dyspnea, salivation, incoordination, and collapse. Animals with massive envenomation may show signs of acute respiratory distress syndrome or disseminated intravascular coagulation.

ETIOLOGY AND PATHOPHYSIOLOGY

- Most systemic signs result from an immunoglobulin E (IgE)-mediated allergic reaction (see p. 1399).
- A small number of dogs and cats may develop anaphylaxis.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis of insect envenomation is frequently presumptive and made based upon clinical signs and history of possible (but unwitnessed) exposure.

DIFFERENTIAL DIAGNOSIS

- Cellulitis
- Peripheral edema
- Acute abdomen (black widow spider)
- Nonhealing wound (brown recluse spider)

INITIAL DATABASE

- Packed cell volume
- Serum total protein
- Blood glucose
- Blood urea quick-assessment test (Azo stick)

TREATMENT

TREATMENT OVERVIEW

- Relief of discomfort
- Prevent further edema/urticaria formation

ACUTE GENERAL TREATMENT

- Facial edema/urticaria:
  - Remove stinger if present. Use fine forceps/tweezers or a flat object (e.g., dull side of a scalpel blade), taking care not to press on the stinger's sac (if present) to avoid injecting the remaining contents of the stinger into the patient
  - Diphenhydramine 1-2 mg/kg IM
  - Dexamethasone sodium phosphate 0.2 mg/kg IV slowly
- Anaphylaxis (see p. 64):
  - Epinephrine 0.01 mg/kg IV
  - Intravenous fluid support
  - Diphenhydramine 1-2 mg/kg IM
  - Dexamethasone SP 0.2 mg/kg IV slowly

RECOMMENDED MONITORING

Animals with facial swelling or urticaria should be monitored for 20-30 minutes after therapy to ensure clinical signs are not progressing.

PROGNOSIS AND OUTCOME

Most animals with insect bites and stings have an excellent prognosis. Animals with severe systemic signs have a more guarded short-term prognosis as dictated by the severity of signs.

PEARLS & CONSIDERATIONS

COMMENTS

Animals with facial edema of unknown origin should have the face and lips closely examined for the presence of a stinger.

PREVENTION

Avoid insects and spiders.

SUGGESTED READING

Cowell AK, Cowell RL: Management of bee and other Hymenoptera stings. In Bonagura JD, editor: Current veterinary therapy XII. Philadelphia, 1995, WB Saunders, pp 226–228.

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EDITOR: ELIZABETH ROZANSKI

Baylisascaris Infection

BASIC INFORMATION

DEFINITION

A rare but potentially devastating zoonosis involving parasitic infection with the raccoon roundworm, *Baylisascaris procyonis*

SYNONYMS

Ocular or neural larval migrans; raccoon roundworm, visceral

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Raccoons are the natural host for the mature enteric parasite. However, larval stages of *B. procyonis* can infect more than 90 species of birds and mammals, including dogs.
- Cats appear to be only marginally susceptible or even resistant to disease caused by *Baylisascaris* larva migrans.

RISK FACTORS

- Zoonosis occurs when humans acquire the parasite by the fecal-oral route. Therefore, exposure to “aged” raccoon feces harboring embryonated eggs (eggs which contain infective second-stage larvae) of *B. procyonis* is a major risk factor (e.g., in uncovered outdoor sandboxes or similar “latrines,” which are areas where raccoons specifically choose to defecate).
- Dog feces have also been shown to contain *Baylisascaris* eggs when the dog is infected with intestinal adult *B. procyonis*.
- The tissues of transport or paratenic hosts (e.g., small rodents) may contain encysted/arrested second-stage larvae. If a raccoon or other suitable mammalian host (e.g., the dog) ingests this infected transport or paratenic host, the ingested larvae will excyst and migrate, thus infecting the gut (or other host tissues) of the definitive host.

CONTAGION & ZOONOSIS

Infective eggs within the environment can cause an often fatal meningoencephalitis in humans. Children younger than 2 years are at highest risk.

GEOGRAPHY AND SEASONALITY

More common in the Midwestern and Northeastern United States and California. Infected raccoons have also been reported in Georgia.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Clinical illness due to *B. procyonis* is extremely uncommon in small animal medicine; neurologic and ocular signs are theoretically possible.
- Rather, the greatest concern is regarding the zoonotic potential of *B. procyonis* eggs passed in raccoon or (rarely) canine feces.
- In humans, visceral larval migrans (VLM), ocular larval migrans (OLM), and neural larval migrans (NLM) may be observed.

HISTORY, CHIEF COMPLAINT

- Dogs infected with *B. procyonis* generally show no clinical signs, harboring the parasite without outward evidence of infection. Rarely, dogs may sustain larva migrans that causes overt clinical signs as early as 9-10 days after ingestion of raccoon feces containing ova with infective larvae.
- Signs often progress rapidly over several days.

PHYSICAL EXAM FINDINGS

- NLM: Depression, ataxia, head tilt, circling, nystagmus, opisthotonos, recumbency, coma
- OLM: Blindness, signs of uveitis (red eye, photophobia, etc.), observable larvae within the eye/retina
- VLM: Usually an incidental finding without clinical signs

ETIOLOGY AND PATHOPHYSIOLOGY

- Eggs of *B. procyonis* become embryonated and infective (contain infective second-stage larvae) 24-48 hours after being passed by the raccoon. Infective eggs are highly stable and may remain viable within the environment for years; however, they can be destroyed by heat.
- All animals (including dogs and humans) are infected by ingesting the embryonated/larvated eggs of *Baylisascaris procyonis*. Raccoons originally become infected in the same manner or by ingesting transport or paratenic hosts (see Risk Factors).
- Once ingested, the larvae emerge from the eggs within the host's intestine and begin to migrate *(larva migrans)* through the liver, lungs, brain, and eyes as early as 3 days post-infection.
- Migration of only one or two larvae through the brain can cause destruction of the white matter (leukomalacia) and severe inflammation and necrosis.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Infection of the definitive host with *B. procyonis* is of great public health significance. If humans become infected with neural larva migrans, the consequences can be fatal. *B. procyonis* rarely poses a significant threat to dogs.

DIFFERENTIAL DIAGNOSIS

In dogs and raccoons, signs of central nervous system dysfunction are very uncommonly due to *Baylisascaris* infection. Causes that are much more common include:

- Other infectious causes of encephalitis: toxoplasmosis, tickborne diseases, *Neospora*, canine distemper virus, rabies
- Granulomatous meningoencephalitis
- Toxin exposure
- Neoplasia
- Metabolic disease (e.g., hepatic encephalopathy, hypoglycemia)

INITIAL DATABASE

- CBC: possible eosinophilia
- Serum biochemistry profile, urinalysis: may rule out toxic or metabolic diseases
- Complete neurologic and ocular examination: asymmetry of deficits is expected if any deficits are present.
- Fecal flotation and examination: more than 20 dogs in the Midwest have been shown to have a mature intestinal infection of *Baylisascaris* with infective eggs shed in their feces
- Cerebrospinal fluid tap with cytology: meningoencephalitis with increased eosinophils

ADVANCED OR CONFIRMATORY TESTING

- Virtually never performed in small animal medicine, given the rarity of clinical disease in dogs and cats
- MRI (brain): preferential destruction of white matter
- Serologic testing is available for humans but is not commercially available for veterinary patients.
- Definitive diagnosis may not be possible until postmortem.

TREATMENT

TREATMENT OVERVIEW

It is critical to remove all adult stages of this parasite from the small intestine of the infected host (dog) with anthelminthic therapy prior to treating neurologic signs with corticosteroids. All feces should be removed promptly from the cage or kennel and properly disposed of. Gloves should be worn at all times when there is contact with infected feces. Handwashing is essential. The therapeutic goal is rapid identification and treatment to prevent progression of leukomalacia and neurologic signs

ACUTE GENERAL TREATMENT

- Anthelmintics: when *Baylisascaris* eggs are found incidentally on a fecal flotation
  - Albendazole (50 mg/kg PO q 24 h × 10 days or more): traditionally the anthelmintic of choice. Administration for >3 days may risk myelosuppression.
  - Milbemycin oxime (0.5-1 mg/kg PO): *B. ascaris* infection is a newer application of this treatment. About 75% effective at eliminating *Baylisascaris* infection in dogs with one dose.
- Neurologic larva migrans (rare in dogs and cats): Corticosteroids (e.g., dexamethasone 0.1-0.2 mg/kg IV q 8-24 h) are essential to stabilize the inflammatory component of the encephalitis.
- Ocular larvae within the retina may be killed using laser photocoagulation or removed via enucleation.

CHRONIC TREATMENT

- Patients surviving the initial neurologic disease may be permanently handicapped and require supportive and nursing care.
- A long course of corticosteroids may be necessary to control the necrosis and inflammation associated with larval migration and death.

PROGNOSIS AND OUTCOME

- Severity of signs and speed of progression are related to the egg burden ingested.
- Prognosis is poor if clinical signs are advanced at time of diagnosis or treatment. Fair to good if signs are mild and treated quickly.

PEARLS & CONSIDERATIONS

COMMENTS

- Consider larval migrans in an animal with acute onset of neurologic dysfunction consistent with encephalitis, especially if recent contact with raccoon environments is possible.
- *B. procyonis* does not usually cause any outwardly observable clinical signs in raccoons.

PREVENTION

- Prevention is the most effective therapy.
- Preventing exposure to raccoons and their feces is paramount. Covering sandboxes when unused and avoiding raccoon latrines are essential.

TECHNICIAN TIPS

- It is important for the technician to make clients aware that raccoons should never be considered to be family pets, indoors or outdoors. They should always be considered to be wild animals, and therefore unsuitable to be in or around human habitats, particularly those with small children.
- Technicians should always wash hands when handling feces of suspect animals.

CLIENT EDUCATION

- People and pets should avoid raccoon latrines (bases of trees, fallen logs or large rocks, forks of trees, and also attics, haylofts), which may contain raccoon feces with millions of infective eggs.
- Raccoons are attracted to sources of food. People should not attempt to feed them.
- Young children should be closely observed when outside to avoid ingestion of infective eggs.

SUGGESTED READING

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Bartonellosis

BASIC INFORMATION

DEFINITION

An emerging vector-transmitted disease of humans and domestic and wild mammals caused by bacteria of the genus *Bartonella*. These organisms are fastidious, pleomorphic, aerobic, gram-negative rods. In vivo *Bartonella* spp. can cause intracellular infections and are known to infect erythrocytes and endothelial cells.

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs and cats: any age and either sex

GENETICS & BREED PREDISPOSITION

Dogs: herding dogs may be at increased risk, whereas toy breeds may have a decreased risk for infection (possibly owing to environment).

RISK FACTORS

Exposure to vectors such as sand flies, lice, keds, biting flies, fleas, and ticks. Immunocompromised individuals may also be at increased risk of infection.

CONTAGION & ZOONOSIS

Many *Bartonella* spp. or subspecies infect humans, including via cat scratches (e.g., cat scratch disease).

- *B. henselae:* cat scratch disease, endocarditis, bacillary angiomatosis
- *B. vinsonii* subsp. *berkhoffi:* endocarditis
- *B. vinsonii* subsp. *arupensis:* endocarditis
- *B. koehlerae:* endocarditis
- *B. alsatica:* endocarditis, granulomatous lymphadenitis
- *B. elizabethae:* endocarditis
- *B. washoensis:* myocarditis
- *B. quintana:* trench fever, endocarditis, bacillary angiomatosis
- *B. bacilliformis:* Carrion's disease, Oroya fever, verruca peruana

GEOGRAPHY AND SEASONALITY

Seroprevalence is increased in warm, humid climates, although *Bartonella* spp. are being identified worldwide. Seasonality of disease may be associated with vector exposure.

ASSOCIATED CONDITIONS & DISORDERS

Dogs: Endocarditis, myocarditis and arrhythmias, peliosis hepatis, granulomatous and lymphocytic hepatitis, granulomatous lymphadenitis, epistaxis, granulomatous rhinitis, polyarthritis. Evidence of *Bartonella* exposure has been identified in patients with the following disorders, but a cause/effect relationship has not been established: immune-mediated hemolytic anemia, cutaneous vasculitis, anterior uveitis and choroiditis, meningoencephalitis.

Cats: Endocarditis (rare), osteomyelitis (rare). The high prevalence of *Bartonella* infections in cats makes clinical associations with diseases difficult. A correlation with some conditions such as stomatitis and uveitis has been suggested but remains unproven.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Dogs: naturally infected with *B. vinsonii* subspecies *berkhoffi, B. henselae, B. clarridgeiae, B. elizabethae, B. washoensis, B. quintana, B. rochalimae*.

Cats: can become infected or serve as a reservoir for numerous *Bartonella* species such as *B. henselae, B. clarridgeiae, B. koehlerae, B. quintana*, and *B. bovis*. They can also become infected with *B. vinsonii* subspecies *berkhoffi*. Cats may be bacteremic for several weeks to more than a year.

HISTORY, CHIEF COMPLAINT

Dogs: Affected individuals may have one or more of the following presentations:

- Weakness, lethargy, anorexia
- Nasal discharge and/or epistaxis
- Lameness
- Other reported signs include vomiting, diarrhea, cough, and seizures
- Subclinical and nonspecific signs are also possible

Cats: Affected individuals may have one or more of the following presentations:

- Lethargy, anorexia
- Reproductive difficulty
- Subclinical infections are very common.

PHYSICAL EXAM FINDINGS

Dogs: Affected individuals may have one or more of the following findings:

- Fever
- Splenomegaly
- Lameness
- Evidence of vasculitis
- Heart murmur
- Lymphadenopathy
- Hepatomegaly
- Neurologic dysfunction
- Uveitis
- Nasal discharge/epistaxis
- Some affected dogs have no abnormal findings detected during physical examination.

Cats: Affected individuals may have one or more of the following findings:

- Many cats have no abnormal findings.
- Fever
- Lymphadenitis
- *Bartonella*-associated stomatitis, uveitis, and neurologic dysfunction have also been reported.
- Coinfection with feline immunodeficiency virus (FIV) may be associated with stomatitis and lymphadenopathy.

ETIOLOGY AND PATHOPHYSIOLOGY

Dogs: A tick vector (*Rhipicephalus sanguineus, Dermacentor* spp., or *Ixodes* spp.) is the likely source of *B. vinsonii* subspecies *berkhoffi* and possibly other *Bartonella* infections. *Bartonella* spp. infect endothelial cells and are periodically released into the circulation, resulting in a waxing and waning course of infection. Infections are associated with a cyclical CD8+ cell lymphopenia, modulation of adhesion molecules on CD4+ T cells, defective monocytic phagocytosis, and impaired B-cell antigen presentation within lymph nodes.

Cats: B. henselae is believed to be transmitted via the inoculation of infected flea *(Ctenocephalides felis)* feces rather than flea bites. Direct or vertical transmission from cat to cat has not been identified. The sources of other feline *Bartonella* infections are unknown.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Understanding the clinical picture is paramount. In dogs, serologic and PCR testing is insensitive. As reservoir hosts, healthy cats may be bacteremic. Diagnosis can only be made by matching a clinical picture with a battery of serologic and molecular testing combined with culture.

DIFFERENTIAL DIAGNOSIS

- Bacterial endocarditis
- Other vector-borne diseases, including *Rickettsia, Ehrlichia, Babesia*, and *Borrelia* infections
- Systemic fungal infections, including histoplasmosis, blastomycosis, and coccidioidomycosis
- Neoplasia
- Immune-mediated disease
- Feline leukemia virus and feline immunodeficiency virus (cats)
- Polyarthritis

INITIAL DATABASE

- CBC
  - *Dogs:* Thrombocytopenia, anemia, neutrophilic leukocytosis, monocytosis, and eosinophilia: most common with *B. vinsonii* subspecies *berkhoffi*.
  - *Cats:* transient anemia and persistent eosinophilia possible.
- Serum biochemistry panel
  - *Dogs:* Often unremarkable or indicative of end-organ damage. Increased liver enzymes and hypoalbuminemia: most common specific abnormality.
  - *Cats:* No consistent abnormalities
- Urinalysis: no consistent abnormalities
- Arthrocentesis
  - *Dogs:* neutrophilic, lymphocytic, or mononuclear polyarthritis.
- Cerebrospinal fluid: no consistent abnormalities (dogs)

ADVANCED OR CONFIRMATORY TESTING

Dogs:

- IFA for immunoglobulin G (IgG) antibodies widely used; confirm exposure; cross reactivity (particularly with *Rickettsia* species) or nonreactivity are pitfalls; titers ≥1:64 are considered seroreactive.
- PCR from blood and tissue samples: also effective; risk for false positive and false negative
- Routine microbiological techniques usually inadequate (30-60 days to note detectable growth).
- Liquid media preparation (*Bartonella*-alphaproteobacteria growth medium, [BAPGM]) followed by *Bartonella* identification via PCR has resulted in faster, more sensitive detection of *Bartonella* and is currently the standard recommended by the Vector Borne Disease Diagnostic Laboratory at North Carolina State University.

Cats:

- Definitive identification of *Bartonella* as a causative agent of disease is difficult, given the large number of chronically infected healthy cats. Pursuing diagnostic testing for bartonellosis is currently only recommended in cats presenting for unexplained or clinically consistent illness.
- Antibody testing is only recommended on adopting new cats, especially kittens that immunocompromised individuals wish to adopt. Seronegative antibody tests have a strong correlation with the lack of bacteremia.
- Serologic testing is otherwise of limited utility in cats.
- Both IFA and Western blot testing for anti-*B. henselae* antibodies are widely available.
- PCR can accurately identify *Bartonella* infections in cats but does not necessarily indicate that bartonellosis is the cause of disease.
- Definitive isolation via culture on agar plates is still considered the gold standard for confirming bacteremia.

TREATMENT

TREATMENT OVERVIEW

There is no current treatment consensus. Treatment should be considered in bacteremic individuals, particularly if clinical signs are apparent. A lack of resolution of disease after treatment should prompt clinicians to consider alternative diagnoses. Seroreactive patients (titers >1:64) should be treated only after first considering the *Bartonella* species identified and the antibody prevalence

within the population before instituting therapy.

ACUTE GENERAL TREATMENT

- By extrapolation from human medicine: prolonged use of tetracyclines, erythromycin, rifampin, azithromycin, doxycycline, or a combination of these antibiotics could be effective (but efficacy and safety unproven in dogs and cats).
- *Dogs:* Azithromycin has been used: small dogs, 10 mg/kg; medium dogs, 7 mg/kg; large dogs, 5 mg/kg. Give PO q 24 h × 7 days, then q 48 h × 5 weeks. Doxycycline (10 mg/kg PO q 24 h) or enrofloxacin could possibly be beneficial; unproven in clinical veterinary medicine. In principle, prolonged treatment for 4-6 weeks is recommended, but the high rate of incidentally discovered infections in otherwise normal animals indicates that treatment should be considered only if compatible clinical signs are present and other possible causes have been ruled out.
- In dogs suffering from a life threatening *Bartonella* infection such as endocarditis, the use of aminoglycosides in the initial phase of treatment may be warranted. This class of antibiotics should only be considered if renal function is stable and kidney perfusion is going to be supported with intravenous fluid therapy.
- *Cats:* Azithromycin has been used: 10 mg/kg PO q 24 h × 7 days, then q 48 h × 5 weeks. However, there is no antibiotic protocol that has been shown to clear cats of infection. At the present time, there are no definitive recommendations for treatment of cats.

CHRONIC TREATMENT

- There are no clear recommendations for chronic relapsing disease in dogs and cats. Alternative diagnoses should be strongly considered in patients that “fail” treatment.
- Dogs that remain bacteremic after an initial treatment course of azithromycin may respond to combination therapy of continued azithromycin with the addition of rifampin (5 mg/kg PO q 24 h) for an additional 6 weeks.
- Development of antibiotic resistance is a risk and should be considered before deciding to institute therapy.

POSSIBLE COMPLICATIONS

Recurrent/persistent infection

RECOMMENDED MONITORING

- Resolution of clinical signs after therapy
- Antibody titers can be followed during treatment (at 1 month) and post treatment (at 6 months) to follow antibody trends. A resolution of detectable antibodies is generally considered a positive outcome. Since persistently infected dogs may fail to have an increased antibody titer, serology in combination with BAPGM culture and PCR is recommended to ensure bacterial clearance. The significance of persistent antibody titers after treatment is unknown.

PROGNOSIS AND OUTCOME

Depending on the clinical presentation, the prognosis can vary widely.

PEARLS & CONSIDERATIONS

COMMENTS

- Coinfection with multiple *Bartonella* spp. and subtypes, as well as with other vector transmitted infections, is possible and should be considered.
- Defining bartonellosis as a clinical entity is still in its infancy.
- It remains unknown in many circumstances whether *Bartonella* is a primary pathogen, opportunistic invader, or incidental finding.
- It is well established that *B. vinsonii* subspecies *berkhoffi* is an important infective agent in dogs, but the clinical implications of *B. henselae* bacteremia in both dogs and cats remains to be elucidated.

PREVENTION

Consistent use of flea and tick preventatives is recommended.

CLIENT EDUCATION

- Monitor for recurrence of presenting signs.
- Since the current understanding of the pathology and treatment of bartonellosis is far from complete, clients should be cautioned that treatment may not eliminate clinical disease.
- Zoonosis is possible, and immunocompromised individuals should be particularly cautious when adopting new pets.

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Barking, Excessive

BASIC INFORMATION

DEFINITION

Either a normal amount of barking that is deemed unacceptable to humans or a pathologic amount of barking as part of an anxiety or other behavioral disorder

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs of any age and either sex. Puppy vocalizations: more often associated with care-seeking behaviors. Adult vocalizations: more often associated with care-giving behaviors, social interaction, cohesion.

GENETICS & BREED PREDISPOSITION

None; body size may affect the pitch.

RISK FACTORS

In breeds that have been selected for specific vocalization behaviors, such vocalizations may become more annoying to the clients and/or their neighbors and still be normal.

CONTAGION & ZOONOSIS

Naïve/newly added puppies or adults may learn barking by observation.

GEOGRAPHY AND SEASONALITY

Dogs kept outdoors, especially if confined and not walked, are more likely to use barking to communicate with other dogs in the vicinity.

ASSOCIATED CONDITIONS & DISORDERS

Barking may be a nonspecific sign in any anxiety-based disorder, including separation anxiety, aggression, obsessive-compulsive disorder, and noise, storm, and social phobias.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Excessive barking is noted by client at home. In some cases, however, clients may not know about the barking unless neighbors complain.
- Barking can appear indiscriminate or as a response to external stimuli. For example, barking associated with an anxiety disorder may also be characterized by hypervigilant behavior (continuous monitoring of the social and physical environments). In these cases, dogs may scan at windows, along fences, and at doors. Clients may also describe the patient as unable to rest or settle down for any considerable amount of time.
- Important elements of the history that should be elicited include whether it occurs in the owner's real or virtual absence (e.g., associated with separation anxiety) and whether it ends with the owner's inadvertently rewarding the behavior, as with a treat to “silence” the dog (i.e., learned behavior).

PHYSICAL EXAM FINDINGS

- Generally unremarkable
- If barking represents a change in behavior, vocal cords and surrounding tissue may become edematous;
- A change in quality of bark may be associated with oropharyngeal lesions (laryngeal paralysis, mass, and so on).
- Rarely, a source of pain or other physical abnormality can be identified as a trigger for barking or whining.

ETIOLOGY AND PATHOPHYSIOLOGY

- Barking may be used for making contact with other individuals (including when reuniting after being apart), to signal alarm, to signal concern or distress, and to solicit information from other dogs (depending on pitch, tone, frequency, and pattern).
- Spectrographic analysis of canine barks has shown that their structure varies predictably according to context; barks can likely be divided into contextual subtypes and are thought to convey complex information to both canine and human listeners.
- Recent studies support the observation that people can distinguish between barks and can correctly identify the context in which a bark was given, even when the dogs are unfamiliar to the human listeners and the humans have never owned dogs.
- Barking can also be a sign of an anxiety disorder, including obsessive-compulsive disorder (see p. 1012 and 775).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is made based on history. The context in which the barking occurs will determine whether the behavior is normal but inconvenient, or indicative of a mood disorder.

DIFFERENTIAL DIAGNOSIS

- Normal barking, especially alarm barking by watch and guard dogs selected to alert by barking, reactive barking in terrier and hound breeds, and working barking in some herding breeds. These barking behaviors can be modified with humane training and are typically context-appropriate, although inconvenient or undesirable for some clients.
- Learned behavior: barking that elicits a response/reward from the client (e.g., the client lets the dog out when it barks, or pets it to “calm it down”)
- Separation anxiety
- Thunderstorm phobia
- Noise phobia
- Obsessive-compulsive disorder

Change in vocalization:

- Laryngeal paralysis, laryngeal masses, and thyroid neoplasia can result in changes in bark quality (see p. 1172), which must be differentiated from barking-induced hoarseness and from owner-induced trauma to the cervical region through leash, choke chain, or pinch collar “corrections.”

INITIAL DATABASE

Minimum database: complete blood count, serum chemistry profile, and urinalysis to rule out any underlying contraindications for psychotropic medication, if their use is warranted. Other laboratory or imaging procedures should address any other concurrent physical exam findings.

ADVANCED OR CONFIRMATORY TESTING

Learned behaviors are ruled out if they are extinguished by complete removal of the reward. Extinction is a gradual waning in occurrence of a behavior in the absence of a reward. The longer the behavior has been ongoing, reinforced, or rewarded, the longer eradication of the learned behavior will usually take.

TREATMENT

TREATMENT OVERVIEW

The goal is to treat the disorder or modify the behavior (if normal) based on accurate identification of cause.

ACUTE GENERAL TREATMENT

- If barking is within the normal behavioral repertoire, given triggers and context, the dog can be taught when and when not to bark by rewarding “good barking” and not “bad barking” and coupling both to words used only in those situations.
    - When the dog barks in a context that is unacceptable to the owner, redirecting the dog to an incompatible behavior (such as catching a toy with the mouth or playing tug) stops barking and rewards an alternative behavior. The offered alternative behavior must be of higher value to the dog.

- If barking is pathologic, the anxiety state that leads to the abnormal vocalization must be treated.
  - Identify triggers and limit exposure to them whenever possible.
  - When barking occurs, redirect the dog's attention and activity to alternative behaviors (play, relaxation) and reward for compliance; use a leash or head collar if necessary; reward all decreases in barking in response to triggers.
  - A neutral stimulus (noise, citronella spray burst) may be used for interrupting the behavior, followed by positive engagement in a different, non barking-related behavior that can be rewarded.
  - Treatment with psychotropic medication (amitriptyline, fluoxetine, or clomipramine) is only appropriate if barking is a manifestation of a behavioral disorder (e.g., anxiety); consider referral to a behaviorist.
  - Punishment, yelling, and use of shock collars should be avoided. Aversive responses serve only to increase, rather than decrease, arousal and may exacerbate the barking behavior.

CHRONIC TREATMENT

- Dogs should be taught to relax while making eye contact with the clients as a preferred default/substitute behavior when the dog encounters a situation about which it is anxious or unsure.
- Systematic desensitization can be used if the triggers can be identified and manipulated (e.g., Manners Minder [www.premier.com]).
- Alternate ways of alerting (sitting in a designated spot or in front of the clients) should be taught so the dog is still allowed to signal information.

DRUG INTERACTIONS

Amitriptyline, fluoxetine, and clomipramine should not be used with mono-amine oxidase inhibitors (e.g., some tick collars and flea, tick, and mite dips, and some medications used for treating cognitive dysfunction). Combinations of different classes of psychotropic medications at lowered doses are usually safe other than for the potential for sedation, in which case dosages can be adjusted downward.

- Fluoxetine, paroxetine, and possibly sertraline, if given with tramadol, which has a weak but similar effect, may increase the risk of serotonin syndrome. If coadministration is necessary, start both at reduced dosages, titrate each to effect, and monitor for serotonin syndrome.

POSSIBLE COMPLICATIONS

Clients who try to work with behavior modification too quickly (e.g., rewarding sitting even if the dog is distressed, instead of working to teach the dog to relax), with force, or inconsistently (in a multiperson household) may experience slow or no progress. Leash, choke chain, or pinch collar “corrections” can damage the esophagus, trachea, larynx, thyroid, and recurrent laryngeal nerves, altering quality of vocalization +/− swallowing and respiratory functions.

RECOMMENDED MONITORING

Frequent follow-up with the clients—at least weekly—is helpful. Medications should be monitored for cardiac, renal, or hepatic side effects (uncommon) or sedation (more common).

PROGNOSIS AND OUTCOME

- For species-appropriate but inconvenient barking, prognosis is very good to excellent when owners understand the diagnosis.
- For pathologic barking, prognosis ranges from fair to very good depending on severity and chronicity of disorder.
- Both are influenced by client compliance, environmental circumstances, and response to psychotropic medication in the case of pathologic barking.

PEARLS & CONSIDERATIONS

COMMENTS

Shock collars have no place in the treatment of any behavioral condition. They will always exacerbate anxiety, even if they may suppress some aspects of behavioral signs; the behavior of dogs trained with a shock collar changes even outside the context of the training environment (display of signs of anxiety). Assessment for the potential risk of physical abuse of pets, spouses, and children should be made in any case in which such techniques have been used or the clients wish to use them (see online chapter: Abuse).

TECHNICIAN TIP

Verbal reprimands serve no useful purpose. If a dog is barking excessively in the hospital, changing stimuli (e.g., moving the dog to an area with less/more activity or different animals in surroundings) is far better.

PREVENTION

Early intervention. When dogs are added to the home, education of the dog as to what level of barking is acceptable to the client should be instituted on the first episode of unwanted barking.

CLIENT EDUCATION

- Yelling at a dog to be quiet will increase arousal and is therefore counterproductive.
- Clients can teach their dog the level of alarm barking they will tolerate by calmly taking the barking dog away from the trigger (using a leash if necessary), asking for an alternative behavior (sitting while looking at the client in a relaxed fashion), and then rewarding the quiet response.
- Clients can also thank their dog for barking when the barking is appropriate (e.g., someone is in the driveway), and then reward them for stopping, which the dog will do when he or she looks at the client in response to the client's praise.

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Barbiturates Toxicosis

BASIC INFORMATION

DEFINITION

Barbiturates are hypnotic, sedative, anticonvulsant drugs derived from barbituric acid (2,4,6-trioxohexahydropyrimidine). *Barbiturate toxicosis* refers to the onset of clinical signs caused by an acute, excessive exposure by ingestion or injection to this class of substances. The chronic effects of therapeutic phenobarbital use are discussed in greater detail elsewhere (see p. 871).

EPIDEMIOLOGY

SPECIES, AGE, SEX

All species, breeds, and both sexes of companion animals are susceptible; dogs are more likely to be involved.

GENETICS & BREED PREDISPOSITION

Greyhounds and other sight hounds: prolonged duration of action

RISK FACTORS

- Underlying liver disease (decreased metabolic capacity)
- Patients with kidney disease may accumulate parent drug (may require dose adjustment) or decompensate with barbiturate-induced hypotension.
- Cardiorespiratory disease (regarding arrhythmogenicity, potential hypoxemia)
- Puppies, kittens, starved animals (decreased metabolic capacity)

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- History/evidence of exposure
- Rapid onset of central nervous system (CNS), respiratory, and cardiovascular (CV) depression, ataxia, hyporeflexia

PHYSICAL EXAM FINDINGS

- Decreased response to stimuli, obtunded mentation/coma
- Slow, shallow respirations
- Hypotension: poor pulse quality, prolonged capillary refill time
- Bradycardia
- Hypothermia

ETIOLOGY AND PATHOPHYSIOLOGY

Source

- Based on their half-lives, barbiturates are divided into ultra-short-acting, short-acting, and long-acting drugs:
- Ultra-short-acting: methohexital (Brevital), thiamylal (Surital), thiopental (Pentothal)
- Short-acting: amobarbital, butabarbital (Buticaps, Butisol, Barbased, Butolan), butalbital (marketed in combinations with aspirin, acetaminophen, caffeine, codeine, and anticholinergic alkaloids), hexobarbital (Evipal), pentobarbital (Nembutal), secobarbital (Seconal)
- Long-acting: phenobarbital (Donnatal, in combination with anticholinergic alkaloids), primidone (metabolized to phenobarbital), metharbital (not available in United States)

Mechanism of Toxicosis

- Toxicosis occurs when animals accidentally eat large amounts of prescription medication (phenobarbital), from an overdose or accidental administration of injectable solution (pentobarbital, euthanasia solution), or from eating flesh of an animal that

had been euthanized with a barbiturate.
- Barbiturates cause nonselective depression of both presynaptic and postsynaptic excitability via several mechanisms (GABA and glutamate receptors, sodium channels).
- Toxicosis is characterized by hyporeflexia, ataxia, hypothermia, hypotension, coma, slow shallow respirations, and death.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Barbiturate toxicosis is suspected from a history of possible or confirmed exposure, and suspicion is heightened by the presence of one of more overt signs (ataxia, depression, coma, hypothermia, hyporeflexia, and CV and respiratory depression). In most instances, this is sufficient to proceed to treatment and monitoring. The diagnosis can be definitively confirmed by identification of drug in bodily fluids or tissues.

DIFFERENTIAL DIAGNOSIS

- Toxicologic: alpha-2 agonists (amitraz, detomidine, medetomidine, xylazine, etc.), benzodiazepines, cardiac drugs causing hypotension (calcium channel blockers, high doses of ACE inhibitors, and beta blockers), ethanol or other alcohols, essential oils, ethylene glycol, isoxazole mushrooms, ivermectin and other avermectins, marijuana, muscle relaxants (baclofen, methocarbamol, guaifenesin), opioids, phenothiazines, trazodone (tetracyclic antidepressant)
- Nontoxicologic disorders: hepatic encephalopathy, hypoglycemia, primary intracranial disorder (encephalitis, neoplasia, etc.), shock (septic, hypovolemic), trauma

INITIAL DATABASE

- CBC
- Serum chemistry profile
- Blood pressure
- Heart rate and rhythm
- Acid-base status: monitor for acidosis

ADVANCED OR CONFIRMATORY TESTING

Barbiturates can be analyzed antemortem in stomach contents/vomitus, urine, serum, or plasma. Postmortem, barbiturates can be detected in liver, heart, or kidney.

TREATMENT

TREATMENT OVERVIEW

Treatment is aimed at decontamination of the patient (emesis, activated charcoal) if no clinical signs are seen. Supportive care—intravenous fluids to maintain blood pressure, thermoregulation, oxygen supplementation/assisted ventilation, and enhanced elimination of barbiturates—is implemented according to anticipated (ingested dosage known to be large) or visible (marked clinical signs) severity of toxicosis.

ACUTE GENERAL TREATMENT

- Decontamination of patient:
  - Emesis (see p. 1364): Useful within 2 to 4 hours only in animals not showing clinical signs (3% hydrogen peroxide 2 mL/kg PO up to maximum of 45 mL/dose, may be repeated once if no results within 15 minutes)
  - Activated charcoal (1-2 g/kg PO once, with sorbitol or other cathartic); repeating charcoal (half of the original dose; omitting the cathartic) q 6 to 8 hours until improvement of depression will help decrease severity and duration of signs. May be ingested by patient if conscious and stable or given by stomach tube in a recumbent animal if the airway is protected (see p. 1281).
  - Gastric lavage: consider if large toxic doses have been ingested (see p. 1281) and the animal is not already comatose.
  - Enema (5 mL/lb, lukewarm water) may help promote gastrointestinal evacuation; administer 1-2 hours after administration of activated charcoal.
  - Peritoneal or hemodialysis may be considered if hemodynamic compromise occurs, but likely not any more helpful than fluids and repeated doses of activated charcoal.
  - Lipid emulsion therapy: Intravenous administration of lipid emulsion is a potential new method of enhanced elimination

of lipophilic barbiturates; efficacy/safety of this has not been established. Use when other measures fail. Risk of hyperlipidemia from therapy (see p. 127).

- Supportive care:
  - Intravenous administration of isotonic crystalloid fluids (warmed if animal is hypothermic), rate titrated to support blood pressure
  - If hypothermia: external warmth (see p. 587)
  - If hypoventilation or apnea:
    - Supplemental oxygen
    - Cuffed endotracheal tube to protect airway (always with mouth gag/speculum in place to avoid tube chewing). Monitoring of tube and airway care are essential (tube cleaning, deflating, and repositioning PRN; avoid pressure injury from overinflated cuff).
    - Positive-pressure ventilation (see p. 1362)

CHRONIC TREATMENT

(See p. 871)

DRUG INTERACTIONS

- Drugs that can increase barbiturate action: any CNS depressant, valproic acid, chloramphenicol
- Decreased efficacy of oral anticoagulants, chloramphenicol, corticosteroids, doxycycline, beta blockers, quinidine, theophylline, and metronidazole
- Rifampin may induce P450 enzymes and reduce the half-life of phenobarbital
- Increased risk of hypotension with concurrent furosemide

POSSIBLE COMPLICATIONS

- Aspiration pneumonia
- Renal impairment secondary to hypotension
- Cardiorespiratory arrest

RECOMMENDED MONITORING

- Oxygenation
- Blood pressure
- Body temperature
- Mentation

PROGNOSIS AND OUTCOME

With coma, prognosis is guarded to poor if intensive supportive care is not pursued.

PEARLS & CONSIDERATIONS

COMMENTS

- Induction of emesis at home should be considered only if no clinical signs are present, if an observed ingestion took place, or if the pet was found with the container.
- Boiling or freezing of meat does not destroy barbiturates. Barbiturate-contaminated meat is a high risk source of relay (secondary) toxicity for scavengers.
- Acute signs of toxicosis (depending on the dose and the type of agent involved) can last several days.
- Repeated doses of activated charcoal are useful even when overdose occurs from barbiturate injection, since plasma barbiturates diffuse into the acidic stomach environment. Be aware of possible hypernatremia from multiple doses of activated charcoal.

PREVENTION

- Keep medications out of animal's reach.
- Prevent unsupervised roaming of animals.
- To prevent secondary acute poisoning, animals euthanized with barbiturates should not be used for animal (or human)

consumption.
- Proper disposal of euthanized carcasses

CLIENT EDUCATION

- Control and monitor pet's environment.
- Do not feed barbiturate-contaminated meat/euthanized animal to pets.

SUGGESTED READING

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Baclofen and Other Centrally Acting Muscle Relaxants Toxicosis

BASIC INFORMATION

DEFINITION

Syndrome developing following the ingestion of one of several centrally-acting skeletal muscle relaxants (SMR) and characterized mainly by central nervous system (CNS) depression.

SYNONYMS

Generic Name	Trade Name(s)
Baclofen	Lioresal, Kemstro
Carisoprodol	Soma
Chlorphenesin carbamate	Maolate
Chlorzoxazone	Parafon Forte
Cyclobenzaprine	Flexeril
Guaifenesin	Gecolate
Metaxalone	Skelaxin
Methocarbamol	Robaxin, Robaxin-V
Orphenadrine	Norflex
Tizanidine	Zanaflex

EPIDEMIOLOGY

SPECIES, AGE, SEX

All species susceptible; dogs more likely because of indiscriminate eating habits.

RISK FACTORS

- Availability of muscle relaxants in the animal's environment
- Many people taking skeletal muscle relaxants for diseases of spasticity (e.g., multiple sclerosis) take other medication as well, increasing the risk for accidental exposures to multiple drugs by pets (polypharmacy).

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

History of exposure to muscle relaxants or presence of drugs in environment (see Table).

Drug	Chief Complaint
Baclofen	• Onset of signs within 15 minutes to 7 hours following ingestion • *Dogs:* vomiting, ataxia, hypersalivation, depression, vocalization, disorientation/agitation, recumbency, coma, seizure • *Cats:* vomiting, depression, ataxia, weakness, hypothermia, recumbency, coma, mydriasis, diarrhea

PHYSICAL EXAM FINDINGS

- Baclofen:
  - As above
  - Hypothermia (if recumbent), hyperthermia (if seizing)
  - Hypertension or hypotension
  - Tachycardia or bradycardia

    - Hypoventilation
    - Miosis (dogs) or mydriasis (cats)
    - Muscular hypotonia, weakness
- Cyclobenzaprine and orphenadrine
    - Depression or agitation, hyperesthesia (cats), vocalization
    - Miosis (dogs) or mydriasis (cats), nystagmus (occasional, dog and cat)
    - Muscle weakness, tremors, fasciculation
    - Panting
    - Tachycardia or bradycardia
    - Hyperthermia
- Tizanidine
    - Depression, weakness, ataxia
    - Hypotension, bradycardia
    - Pale mucous membranes, prolonged capillary refill time
    - Hypothermia
- Other SMR
    - Depression, somnolence, weakness
    - Hypoventilation, cyanosis
    - Tachycardia, hypotension
    - Hypothermia (if recumbent), hyperthermia (if seizuring)

ETIOLOGY AND PATHOPHYSIOLOGY

Source

- Most centrally acting SMRs are used for controlling spasticity in humans with neuromuscular disorders. May also be prescribed for relief of musculoskeletal pain.

Mechanism of Toxicosis

- Baclofen: Mimics gamma-aminobutyric acid (GABA) within the spinal cord, blocking excitatory responses to sensory input and causing flaccid paralysis. Baclofen-induced seizures may be due to interference with GABA release from presynaptic neurons, resulting in excessive postsynaptic nerve firing.
- Cyclobenzaprine: Structurally and functionally related to tricyclic antidepressants. Skeletal muscle relaxation may be related to sedative effects as well as inhibition of brainstem and spinal cord gamma and alpha motor neurons. In overdose situations, anticholinergic and antihistaminic effects become exaggerated.
- Tizanidine has a mechanism of action similar to that of xylazine and clonidine, in that it stimulates alpha-adrenoreceptors in the brainstem, causing decreased vascular resistance, heart rate, and blood pressure. At therapeutic levels, skeletal muscle effects predominate, but in overdose situations, pronounced cardiovascular effects occur.
- Orphenadrine has pronounced anticholinergic and antihistaminic effects.
- Chlorphenesin carbamate, guaifenesin, and methocarbamol may act by blocking nerve impulse transmission within the brainstem, spinal cord, and subcortical levels of the brain. Some of the skeletal muscle relaxant effect is due to sedation.
- Carisoprodol causes skeletal muscle relaxation via depression of postsynaptic spinal reflexes. Some of the skeletal muscle relaxant effect is due to sedation.
- Chlorzoxazone and metaxalone have no direct effect on skeletal muscles; muscle relaxant properties are likely due to sedative effects.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is based on history of exposure or presence of drugs in animal's environment along with appropriate clinical signs (ataxia, depression, coma, vocalization).

DIFFERENTIAL DIAGNOSIS

Toxicologic:

- Other CNS depressants: barbiturates, benzodiazepines, opioids, ivermectin, ethylene glycol, tick paralysis, botulinum toxin, ionophore ingestion (dogs).
- Other causes of seizures: amphetamines, ethylene glycol, metaldehyde, strychnine, methylxanthines, zinc phosphide, tricyclic

antidepressants, serotonergic drugs.

Nontoxicologic, Spontaneous:

- Spinal trauma
- Polyradiculoneuritis, tick paralysis
- Organic brain disease (neoplasia, inflammation, etc.)

INITIAL DATABASE

- CBC, serum biochemistry profile: minimal alterations expected from SMR (identify preexisting liver or kidney dysfunction that may interfere with drug elimination)
    - Orphenadrine overdose in humans has been associated with hypokalemia, hypoglycemia, liver enzyme elevations, and bleeding disorder.

ADVANCED OR CONFIRMATORY TESTING

- Baclofen, carisoprodol, chlorzoxazone, cyclobenzaprine, guaifenesin, and methocarbamol levels can be determined in urine and/or serum; presence will confirm exposure.
    - Turnaround time may limit usefulness in dealing with an acute intoxication.
    - Cyclobenzaprine will result in a positive serum or urine assay for amitriptyline.

TREATMENT

TREATMENT OVERVIEW

Treatment is aimed at early decontamination of the patient (emesis induction then administration of activated charcoal) when clinical signs are absent, and supportive care to address overt signs when they are present.

ACUTE GENERAL TREATMENT

- Stabilize patient
    - Maintain respiration: endotracheal intubation and positive-pressure mechanical ventilatory support may be required.
    - Control seizures: diazepam (0.5-1 mg/kg slow IV, to effect); propofol or isoflurane may be considered in cases refractory to diazepam (induce, keep anesthetized 5-10 minutes, then recover). Barbiturates should be considered a last resort, as their use may result in severe exacerbation of CNS depression; diazepam also generally useful for managing agitation.
- Manage cardiovascular abnormalities: most arrhythmias and blood pressure irregularities resolve during supportive care. Nitroprusside constant-rate IV infusion (1-2 mcg/kg/min [dogs] or 0.5 mcg/kg/min [cats], increased incrementally q 3-5 min until target BP is obtained) has been successfully used to manage baclofen-induced hypertension in dogs. Use of atropine to manage bradycardia is contraindicated in orphenadrine or cyclobenzaprine toxicosis, because it exacerbates anticholinergic effects.
- Supportive care:
    - Intravenous fluid therapy: as needed for hypotension/hypovolemia and to promote urine formation; may enhance excretion of baclofen
    - Atipamezole (50 mcg/kg, give ¼ to ⅓ of dose IV, remainder IM) or yohimbine (0.025 mg/kg slow IV) can be helpful to reverse hypotension from tizanidine.
    - Cyproheptadine (1.1 mg/kg PO or per rectum q 6 h) has been helpful in reducing vocalization in dogs.
    - Thermoregulation is essential, especially in comatose or recumbent animals.
- Decontamination of patient (no clinical signs):
    - Emesis (see p. 1364): Because of the potential for rapid onset of clinical signs, induction of emesis is best done under veterinary supervision (hydrogen peroxide 3%: 0.25-0.5 mL/kg PO once [dogs] or xylazine hydrochloride 0.44 mg/kg IM [cats]). Emesis is contraindicated in animals showing overt clinical signs.
    - Gastric lavage (see p. 1281): Consider for large ingestions (many tablets); protect airway with cuffed endotracheal tube.
    - Activated charcoal (see p. 1322): dose according to packaging label of product (e.g., 10 mL/kg of activated charcoal suspension PO made from 2 g activated charcoal suspended in 10 mL kg tap-water). Repeated doses of activated charcoal q 8 h × 24 h and a cathartic, given every 3rd charcoal dose, are recommended for cyclobenzaprine and orphenadrine; single doses are recommended for all other SMRs.

CHRONIC TREATMENT

Ventilatory support may be required for several days (particularly with baclofen)

NUTRITION/DIET

For animals requiring long-term ventilatory support, parenteral nutrition may be considered (see p. 1322).

DRUG INTERACTIONS

Use caution when administering drugs to sedated agitated animals.

RECOMMENDED MONITORING

Respiratory rate and rhythm, heart rate, blood pressure, body temperature, blood gases, electrolyte status, hydration status, fluid ins/outs

PROGNOSIS AND OUTCOME

- Signs can persist for hours to several days, depending on the SMR involved and the dose ingested.
- Most animals with mild to moderate signs and receiving prompt and appropriate veterinary attention have an excellent prognosis.
- Animals exhibiting respiratory depression requiring ventilatory support have a more guarded prognosis, depending on the availability of mechanical ventilators.
- Seizuring or comatose animals have a more guarded prognosis.

PEARLS & CONSIDERATIONS

COMMENTS

- Because the primary effect of these drugs is CNS depression, when treating animals showing paradoxical excitation, it is important to use the lowest sedative dose necessary to relieve the stimulation in order to avoid oversedation once the agitation has resolved.
- Baclofen, cyclobenzaprine, and tizanidine have narrow margins of safety, and significant (potentially life-threatening) signs can be seen at low doses.
    - Baclofen: doses >1 mg/kg can cause signs; doses 8-16 mg/kg can be fatal to dogs.
    - Cyclobenzaprine: doses as low as 0.07 mg/kg have resulted in clinical signs in dogs.
    - Tizanidine: doses as low as 0.05 mg/kg have been associated with clinical signs in dogs, with hypotension occurring at doses as low as 0.08 mg/kg.
- Methocarbamol, guaifenesin, and chlorphenesin carbamate have fairly wide margins of safety, and overdoses rarely cause life-threatening problems.
- Anecdotally, intravenous lipid solutions have hastened recovery of dogs with baclofen toxicosis. This treatment modality is new and considered experimental.
    - Use 20% intravenous lipid solution (normally used for parenteral nutrition, readily available from pharmacies, human hospitals)
    - Bolus 1.5 mL/kg, then constant rate infusion of 0.25 mL/kg/min for 30-60 minutes. Can repeat in 6-8 h if serum is not lipemic and animal is still showing clinical signs.
    - More information on this treatment method may be found at www.lipidrescue.org.

TECHNICIAN TIP

Be prepared for paradoxical excitement when a sedative is given to patients with this type of intoxication: be sure doors are closed to prevent escape, have the patient on a surface clear of sharp or breakable objects, and take precautions to avoid being injured.

PREVENTION

Keep medications out of reach of pets.

CLIENT EDUCATION

- When taking medication, do so in a room away from pets with the door closed to prevent pets from ingesting an accidentally dropped tablet.
- Never administer human medications to pets without first consulting a veterinarian.

SUGGESTED READING

Gwaltney-Brant SM: Skeletal muscle relaxants. In Plumlee KH, editor: Clinical veterinary toxicology. St Louis, 2004, Mosby, p 324.

AUTHOR: SHARON GWALTNEY-BRANT

EDITOR: SAFDAR A. KHAN

Back Pain

BASIC INFORMATION

DEFINITION

Pain localized to the thoracolumbar spinal column

SYNONYMS

Spinal hyperesthesia, spinal hyperpathia

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dependent on the underlying cause
- Dogs: middle-aged (type I intervertebral disk disease), older adults (type II intervertebral disk disease, neoplasia)
- Cats: older adults (neoplasia), males more commonly represented (aortic thromboembolism)

GENETICS & BREED PREDISPOSITION

Dogs: chondrodystrophic breeds (type I intervertebral disk disease)

RISK FACTORS

Cats: thromboembolism associated with cardiomyopathy

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Vocalization, reluctance to movement or activity, pain elicited if patient touched or moved

PHYSICAL EXAM FINDINGS

- Hunched posture (kyphosis), pain elicited on epaxial palpation; ataxia, paresis, or paralysis; heat or swelling in epaxial region; splinting and pain on abdominal palpation
- Fever, if back pain is associated with infection (e.g., diskospondylitis)
- Heart murmur, diminished femoral pulses, cyanosis of toenails if back pain is associated with aortic thromboembolism

ETIOLOGY AND PATHOPHYSIOLOGY

- Neurogenic: compression, inflammation, or traumatic disruption of spinal cord, spinal roots, spinal nerves, dorsal root ganglia, or meninges
- Vertebral column: trauma, inflammation, or lysis of vertebral bone, intervertebral disks, or articular facets
- Epaxial muscle: inflammation, abscessation, ischemia, or trauma

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Back pain often presents nonspecific physical signs (or absence of any observable deficits) and gentle, thorough physical manipulations during the physical examination are used for eliciting signs of back pain. Diagnostic imaging and specific techniques then help to elucidate the source of the pain.

DIFFERENTIAL DIAGNOSIS

- Intervertebral disk disease (IVDD)

- Vertebral fracture or luxation
- Meningitis or meningomyelitis (granulomatous)
- Polyarthritis (immune-mediated or infectious)
- Diskospondylitis
- Vertebral osteomyelitis
- Spondylosis deformans/degenerative joint disease of articular facets
- Neoplasia (primary or metastatic)
- Polymyopathy (traumatic or inflammatory myositis)
- Fibrocartilaginous embolism (FCE; acute but transient pain, resolving within hours)
- Pain not localized to the spinal column: aortic thromboembolism, abdominal pain

INITIAL DATABASE

- Neurologic examination (see p. 1311)
- CBC, serum biochemistry, urinalysis: often unremarkable unless systemic disease or infection present
- Radiographs: bone lysis or proliferation (neoplasia, osteomyelitis), vertebral fracture or luxation (trauma), intervertebral disk mineralization, disk space narrowing, wedging or displacement (IVDD), vertebral endplate lysis or proliferation (diskospondylitis), articular facet sclerosis and malformation, spondylosis

ADVANCED OR CONFIRMATORY TESTING

Selection based on history, clinical signs, and results of initial database:

- Cerebrospinal fluid tap: cytologic evaluation, culture, serologic testing for immunoglobulin A (IgA) or infectious agents
- Myelogram: identify and discern between extradural compression (IVDD), intradural/extramedullary lesion (meningioma), or intramedullary lesion (other neoplasia or cord swelling [e.g., due to FCE])
- Urine culture (diskospondylitis)
- Blood culture and sensitivity (discospondylitis, osteomyelitis, bacterial meningitis)
- Needle aspirate of intervertebral disk (diskospondylitis)
- Serology: *Brucella canis* (discospondylitis), rickettsial diseases (polyarthritis, meningitis)
- Arthrocentesis: cytology (polyarthritis), culture (septic polyarthritis or meningitis)
- Advanced imaging: CT or MRI if lesion is suspected but not identified on myelogram
- Biopsy of vertebral bone (neoplasia, osteomyelitis)

TREATMENT

TREATMENT OVERVIEW

- Elimination of infectious or noninfectious paraspinal inflammatory causes
- Elimination of any compressive lesion on spinal cord or nerve roots
- Stabilization of vertebral column

ACUTE GENERAL TREATMENT

Address the underlying cause.

CHRONIC TREATMENT

- Degenerative joint disease may require persistent or recurrent nonsteroidal antiinflammatory drug (NSAID) administration.
- Chronic intervertebral disk disease or immune-mediated disease may require intermittent or persistent corticosteroid treatment.
- Antibiotic therapy for diskospondylitis (see p. 312) or vertebral osteomyelitis continued for 6 weeks beyond resolution of clinical signs.

DRUG INTERACTIONS

Corticosteroids and NSAIDs must not be administered concurrently, owing to the risk of severe gastrointestinal ulceration.

POSSIBLE COMPLICATIONS

- Worsening or recurrence of signs
- Progression of spinal cord lesions

- Myelomalacia
- Valvular endocarditis, for infectious conditions

RECOMMENDED MONITORING

- Repeat physical and neurologic examination within 12 to 24 hours of treatment
- Follow-up examination and radiographs as needed

PROGNOSIS AND OUTCOME

Variable, depending on underlying cause

PEARLS & CONSIDERATIONS

COMMENTS

- Localization of pain requires thorough physical and neurologic examination.
- Acute back pain with neurologic deficits may represent a surgical emergency and should be evaluated immediately.

CLIENT EDUCATION

- Owner should monitor for recurrence of signs.
- Acute worsening of signs warrants emergency evaluation and treatment.

SUGGESTED READING

Lorenz MD, Kornegay JN: Handbook of veterinary neurology. St Louis, 2004, WB Saunders, pp 345–353.

AUTHOR: PETER MOAK

EDITOR: ETIENNE CÔTÉ

Babesiosis

BASIC INFORMATION

DEFINITION

Canine babesiosis is a tickborne disease caused by a hemoprotozoan parasite that infects red blood cells of dogs causing hemolytic anemia and thrombocytopenia. Two primary species have been identified: *Babesia canis* (large *Babesia*) and *Babesia gibsoni* (small *Babesia*).

SYNONYMS

- Babesiosis: piroplasmosis
- *Babesia annae: B. microti*-like parasite
- *Babesia gibsoni: B. gibsoni* (Asian genotype)
- *Babesia conradae:* Referred to in some literature as *B. gibsoni* (USA genotype)

EPIDEMIOLOGY

GENETICS & BREED PREDISPOSITION

- American pit bull terriers (APBT) and Tosa Inus at risk for *B. gibsoni*
- Greyhounds at risk for *B. canis vogeli*

RISK FACTORS

- Dog fights (particularly bites by an APBT)
- Tick infestation
- Blood transfusion
- Shared needles or surgical instruments
- Vertical transmission in affected breeds

CONTAGION & ZOONOSIS

- Transmission is through blood contamination or arthropod infestation (*Rhipicephalus, Haemaphysalis*, or *Dermacentor* spp.).
- Canine babesiosis is not a documented zoonotic disease; *B. microti* is a small *Babesia* infecting human red blood cells. Canine species of *Babesia* causing infections in humans have not been well documented.

GEOGRAPHY AND SEASONALITY

- Since babesiosis can be either acute or chronic, it can be diagnosed at any time of year.
- Small babesias:
  - *B. gibsoni* was once limited to Asia but now has a worldwide distribution.
  - *B. annae:* Spain
  - *B. conradae:* southern California
- Large babesias:
  - B. canis vogeli: worldwide
  - B. canis canis: Europe
  - B. canis rossi: southern Africa

One of the novel large *Babesia* sp. has been diagnosed in the United States and the other in the United Kingdom.

ASSOCIATED CONDITIONS & DISORDERS:

- Some patients with babesiosis have been concurrently diagnosed with other tickborne diseases.
- The novel large *Babesia* sp. identified in United States has been primarily diagnosed in dogs that have previously undergone splenectomy or are undergoing chemotherapy.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Babesiosis can cause severe, life-threatening disease in some dogs; others show few or no outward clinical signs. *B. annae* is commonly associated with azotemia and proteinuria.

HISTORY, CHIEF COMPLAINT

Owners may observe weakness, lethargy, anorexia, pallor, icterus, or discolored urine (bilirubinuria or hemoglobinuria). Other historic findings may include tick exposure, recent blood transfusion, or recent dog fight (especially with an APBT).

PHYSICAL EXAM FINDINGS

Pallor and splenomegaly, +/− lymphadenopathy, fever or icterus.

ETIOLOGY AND PATHOPHYSIOLOGY

- Sporozoites in tick salivary glands transmitted to dog during feeding (requires 2-3 days)
- Sporozoites enter red blood cells (RBCs), where they become merozoites and undergo asexual reproduction.
- Intravascular and extravascular hemolysis occur.
- Secondary immune-mediated destruction of RBCs and platelets may occur.
- Azotemia and proteinuria are presumed to be secondary to glomerulonephritis and are most commonly seen with *B. annae* infections.

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

Most dogs with babesiosis have one or more of the following abnormalities: thrombocytopenia, anemia, hyperglobu linemia or splenomegaly. PCR assays have become the primary means of accurately diagnosing *Babesia* infections.

DIFFERENTIAL DIAGNOSIS

- Immune-mediated hemolytic anemia
- Immune-mediated thrombocytopenia
- Zinc toxicity
- Splenic torsion
- Ehrlichiosis
- Leptospirosis
- Dirofilariasis with caval syndrome
- Neoplasia: lymphoma or hemangiosarcoma

INITIAL DATABASE

One or more of the following may be identified in dogs with babesiosis:

- Regenerative anemia: It is important to note that not all dogs with *Babesia* infections have anemia.
- Thrombocytopenia: This is the most common hematologic abnormality in dogs with babesiosis; platelet counts can be as low as <5000 platelets/µL.
- Blood smear: identification of *Babesia* organisms
    - Small babesiosis: 1-3 mcm signet ring forms.
    - Large babesiosis: 3-6 mcm single or paired tear drop forms, but other more ameboid forms can predominate.
- Serum bilirubin: may be increased.
- Hyperglobulinemia: a polyclonal gammopathy is frequently detected.
- Urinalysis: +/− bilirubinuria or hemoglobinuria
- Coombs' test: positive in up to 85% of cases

ADVANCED OR CONFIRMATORY TESTING

- PCR test: only way to determine species or subspecies. More sensitive than blood smear

- False-positive, false-negative results recognized
- Tests vary between laboratories.
- Not always able to detect all species (check with laboratory about sensitivity and specificity)
- IFA test >1 : 64 is considered positive.
    - Cannot differentiate species
    - False-negative results can occur with acute or peracute disease or severe immunosuppression.

TREATMENT

TREATMENT OVERVIEW

It may not be possible to completely eradicate the parasite in all cases, but clinical signs usually improve with supportive care and antiparasitic therapy. The treatment of choice is dependent upon which *Babesia* species is identified. Currently, most data are available for treatment of *B. canis* and *B. gibsoni*.

ACUTE GENERAL TREATMENT

Supportive treatment may require blood transfusion or hemoglobin polymer (e.g., Oxyglobin) for animals that are anemic:

- IV fluids may be required in animals that are febrile and dehydrated.
- Imidocarb diproprionate (6.6 mg/kg IM once, repeat in 7-14 days). Pretreatment with atropine (0.04 mg/kg IM or SQ 30 minutes before imidocarb injection) may reduce cholinergic side effects. This drug appears to reduce morbidity and mortality for nearly all *Babesia* spp. but is not effective for the clearance of *B. gibsoni*. It is the treatment of choice for *B. canis vogeli*.
- Atovaquone (13.5 mg/kg PO q 8 h with fatty meal for 10 days) plus azithromycin (10 mg/kg PO q 24 h for 10 days) is the treatment of choice for *B. gibsoni*. Results in elimination or reduction of the parasite below the limit of detection of PCR testing in ≈82% of cases. Resistance to atovaquone has been identified.
- Clindamycin (25 mg/kg PO BID for 14 days) has been associated with clinical improvement but not clearance of *B. gibsoni*.
- A combination of clindamycin (25 mg/kg PO BID), metronidazole (15 mg/kg PO BID), and doxycycline (5 mg/kg PO BID) had been associated with elimination or reduction of the parasite below the limit of detection of PCR testing. Unfortunately, a well-defined treatment course has not been established, with treatment times ranging from 24-92 days.
- Concurrent immune suppression should be avoided whenever possible, as it may reduce the ability to clear the infection with antiprotozoal drugs.

CHRONIC TREATMENT

- Vector control: topical acaricide (e.g., fipronil) plus flea/tick collar
- Dogs with positive *Babesia* titers or PCR should not be used as blood donors.

POSSIBLE COMPLICATIONS

Prolonged immunosuppressive therapy before specific antibabesial treatment can worsen outcome and should not be used in sick, hospitalized dogs.

RECOMMENDED MONITORING

- Monitor hematocrit and platelet count daily until improvement is seen and then every 1-3 weeks until anemia and thrombocytopenia resolve.
- PCR should be negative 60 and 90 days post treatment if the parasite has been successfully eradicated.

PROGNOSIS AND OUTCOME

- Good prognosis with early diagnosis and treatment
- Animals may remain subclinically infected for life
- Severely anemic animals may die without supportive care such as blood transfusions or hemoglobin based oxygen carrying solutions.

PEARLS & CONSIDERATIONS

COMMENTS

B. gibsoni is an emerging infectious disease in North America. New species are being identified through molecular techniques.

TECHNICIAN TIP

The characteristic features of *Babesia* make them identifiable on a blood smear with little practice.

PREVENTION

- Effective tick control, particularly topical acaricides, are likely to reduce the risk of infection.
- Screening blood donors for *Babesia* infections will reduce the chances of iatrogenic infections.

CLIENT EDUCATION

- In endemic areas, use both a topical acaricide and a repellent tick collar. Avoid blood transmission (shared needles, vaccines, etc.).
- *Babesia* spp. can be transmitted vertically and should be considered in puppies with weakness and pallor.

SUGGESTED READING

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Cytauxzoonosis

BASIC INFORMATION

DEFINITION

Cytauxzoon felis is a protozoal organism transmitted by ticks that causes potentially fatal illness in domestic cats.

EPIDEMIOLOGY

SPECIES, AGE, SEX

C. felis infects only domestic and wild cats. There is no age or sex predilection.

RISK FACTORS

Outdoor cats with tick exposure in endemic areas are at risk. Specific risk factors include urban-edge habitats and close proximity to wooded or unmanaged areas. It is common for multiple cats from the same household to become infected.

CONTAGION & ZOONOSIS

Extensive investigation of *C. felis* has shown that many nonfelidae species cannot be infected. There is no evidence of human infections.

GEOGRAPHY AND SEASONALITY

C. felis infection has been reported in the south central and southeastern United States, but its range appears to be expanding north and east, corresponding to changes in distribution of the tick, *Amblyomma americanum*. Nearly all cases occur between April and September. The majority of cases are diagnosed between March and June, with a second wave of infections occurring in August and September.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Historically, almost all reported cases of *C. felis* in domestic cats were fatal, but many cats are now surviving infection. Some cats are even incidentally diagnosed with *C. felis* erythroparasitemia.

HISTORY, CHIEF COMPLAINT

Clinical signs are acute and nonspecific and include anorexia, lethargy, dyspnea, icterus, and pallor.

PHYSICAL EXAM FINDINGS

Affected cats are usually febrile (103°F-107°F [39.4°C-41.7°C]), but hypothermia is seen in moribund cats. Abdominal palpation reveals splenomegaly and hepatomegaly. Tachypnea, tachycardia, altered mentation, vocalization, seizures, and coma can be seen in the later stages of disease. Most cases exhibit a rapid course, with death occurring within 1 week of onset of signs if left untreated.

ETIOLOGY AND PATHOPHYSIOLOGY

- The natural host is thought to be the eastern bobcat *(Lynx rufus rufus),* which develops a mild or subclinical infection compared to the rapidly progressive and usually fatal disease seen in domestic cats.
- The organism is transmitted by the *Dermacentor variabilis* or *Amblyomma americanum* ticks during feeding.
- Sporozoites released from the tick salivary glands infect macrophages.
- Asexual reproduction occurs within the host macrophage during the schizont phase, causing infected cells to grow to enormous size (=250 m in diameter). These schizont-laden macrophages then occlude arterioles, venules, and capillaries, causing organ failure and clinical illness.
- When the schizonts rupture, merozoites are released to infect erythrocytes. Merozoites are minimally pathogenic.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Early diagnosis through aspiration of lymph nodes, spleen, or bone marrow is indicated when a clinical suspicion exists (via history and physical exam); earlier diagnosis is associated with better response to treatment. Identification of the organism on a blood smear is a relatively late finding.

DIFFERENTIAL DIAGNOSIS

- Toxoplasmosis
- Cholangitis/cholangiohepatitis
- Pancreatitis
- Hemotropic *Mycoplasma* infection
- Feline infectious peritonitis
- Immune-mediated hemolytic anemia
- Feline leukemia virus infection
- Feline immunodeficiency virus

INITIAL DATABASE

- Blood smear: pleomorphic (round, oval, anaplasmoid, bipolar [binucleated], or rod-shaped) organism; the round and oval piroplasm forms are most common (0.8-2.2 m in diameter). Infected macrophages may also be seen on the feathered edge and may be mistaken for platelet clumps at low power.
- If cytauxzoonosis is suspected but not immediately detected by examination of a blood smear, tissue aspirates of lymph node, liver, and spleen are indicated to identify infected macrophages. These cells range in size from 15-250 m in diameter, typically have a large distinct nucleolus, and their cytoplasm is filled with numerous small (1-2 m) basophilic particles (i.e., developing merozoites).
- CBC: pancytopenia (normocytic, normochromic, nonregenerative anemia, leukopenia, and thrombocytopenia) is the classic finding, but mono- or bicytopenias may occur.
- Serum biochemistry profile: elevated liver enzymes (frequently lower than expected for the degree of hyperbilirubinemia), hyperbilirubinemia (mild to moderate), and hyperglycemia are the most common findings.
- Abdominal radiographs or ultrasound reveal splenomegaly and hepatomegaly but do not contribute directly to the diagnosis.
- Urinalysis reveals bilirubinuria.
- Coagulation testing may be consistent with disseminated intravascular coagulation (DIC).

ADVANCED OR CONFIRMATORY TESTING

- PCR testing can be used for confirming infection.
- Necropsy of cats presented with consistent signs should be performed. This is usually the first method of identification of cytauxzoonosis in regions that were previously considered non-endemic.

TREATMENT

TREATMENT OVERVIEW

New treatments with antiprotozoal therapy have proven effective along with supportive care in this disease that was previously considered universally fatal. Since the disease progression can be very rapid, specific treatment should be instituted immediately in cases suspected of having cytauxzoonosis.

ACUTE GENERAL TREATMENT

- Crystalloid fluids: to correct dehydration, restore intravascular volume, and maintain perfusion
- In anemic animals, oxygen delivery to tissues must be restored with a transfusion of whole blood (20 mL/kg IV administered over 4 hours), packed red blood cells (20 mL/kg IV administered over 4 hours), or polymerized hemoglobin (e.g., Oxyglobin; 5 mL/kg IV administered over 4 hours).
- Some clinicians treat/prevent DIC with heparin (100-300 IU/kg SQ q 8 h or 18 IU/kg/h IV CRI [constant rate infusion]).
- Animals with respiratory compromise may require supplemental oxygen.
- Minimal stress and handling is recommended.
- Antiprotozoal therapy should be started immediately.

- Atovaquone (15 mg/kg PO q 8 h administered with a fatty meal for 10 days) and azithromycin (10 mg/kg PO q 24 h for 10 days) associated with survival rates of approximately 65%.
- Imidocarb dipropionate (Imizol [Schering-Plough, Kenilworth, N.J.]): 2-5 mg/kg IM repeated in 7-14 days after pretreatment with atropine (0.04 mg/kg SQ) to minimize cholinergic side effects. Survival estimates with imidocarb range from 0%-50%. In the author's hospital, survival with imidocarb therapy is approximately 25%.
- Diminazene aceturate (Ganaseg [ER Squibb, Princeton, NJ]) 2 mg/kg IM repeated in 7 days. A small case series showed this to be a promising treatment, but it is not FDA approved or currently available in the United States.
- Doxycycline (5 mg/kg PO q 12-24 h × 14 days) is recommended as treatment for coinfection with other tick-borne pathogens.
- Antiinflammatory medications may be helpful in reducing fever: meloxicam (only given after rehydration in nonazotemic patients), 0.1 mg/kg PO q 24 h; or prednisolone, 1 mg/kg PO q 24 h

CHRONIC TREATMENT

- Some cats that survive infection remain chronically infected but do not exhibit clinical signs of illness.
- No treatments have been demonstrated to consistently clear the carrier phase.

PROGNOSIS AND OUTCOME

- With early diagnosis and treatment (atovaquone and azithromycin), survival rates are approximately 65%.
- It is important to note that even with early diagnosis and treatment, some cats that survive infection develop severe clinical disease that lasts for 5–7 days.
- Progressive hemolysis (presumably associated with antibody production against parasite antigens) is frequently detected during the second or third week of treatment and may require treatment with blood products, but immune suppression has not been required in the author's hospital.
- All clinical, hematologic, and biochemical abnormalities resolve within 4–6 weeks.
- Chronic infection does not appear to be associated with decreased lifespan.
- Recurrent severe infections appear extremely rare in surviving animals, suggesting some degree of protective immunity.
- Without treatment, death usually occurs within 1–3 weeks after infection or within 1 week of developing clinical signs.
- Hypothermia, icterus, severe anemia, and collapse warrant a poor prognosis.

PEARLS & CONSIDERATIONS

COMMENTS

Clinical suspicion and early diagnosis through tissue aspiration and cytology have resulted in successful response to treatment.

PREVENTION

In endemic areas, an effective acaricide and tick repellent should be used to prevent exposure to ticks. Since infections have occurred despite acaricide treatment, keeping cats indoors is also recommended.

CLIENT EDUCATION

Outdoor cats in areas where bobcats roam are at risk for this deadly disease.

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Cystitis, Fungal/Algal

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Rare infection of the urinary tract caused by fungal or algal organisms (most often *Candida* sp.). Infections can be primary (confined to the urinary tract) or secondary (systemic or disseminated infection with secondary shedding of organisms into the urine).

SYNONYMS

Candiduria, fungal urinary tract infection (UTI), funguria

EPIDEMIOLOGY

SPECIES, AGE, SEX

Reported in dogs and cats. Secondary algal infections only reported in dogs. No age predilection, but associated risk factors more common in older animals. Females possibly at increased risk.

RISK FACTORS

Diabetes mellitus, urinary tract stoma formation (e.g., perineal urethrostomy), urinary tract catheterization, concurrent lower urinary tract disease (e.g., neoplasia, recurrent bacterial cystitis), prolonged antibiotic administration, immunosuppressive drug administration (e.g., glucocorticoids, chemotherapeutics)

CONTAGION & ZOONOSIS

No zoonotic risk because organisms are ubiquitous in the environment.

ASSOCIATED CONDITIONS & DISORDERS

Fungal pyelonephritis, fungal septicemia, disseminated/systemic fungal or algal infection

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Primary fungal cystitis: infection confined to bladder/lower urinary tract
- Fungal pyelonephritis: infection of renal pelvis and parenchyma, usually due to ascending lower UTI
- Secondary fungal/algal cystitis: urinary shedding of fungal or algal organisms due to systemic/disseminated infection with renal involvement

HISTORY, CHIEF COMPLAINT

- Primary fungal cystitis may be asymptomatic.
- Lower urinary tract disease signs (dysuria, pollakiuria, stranguria) possible.
- Clinical signs associated with renal failure (see pp. 205 and 207) may accompany fungal pyelonephritis or secondary fungal cystitis.
- Signs of other organ system disease may occur with secondary fungal/algal cystitis.

PHYSICAL EXAM FINDINGS

- Primary fungal cystitis or pyelonephritis: usually unremarkable
- Secondary fungal/algal cystitis: depends on organism and distribution (see Aspergillosis, p. 96; Blastomycosis, p. 138; Cryptococcosis, p. 266; Protothecosis, p. 926)

ETIOLOGY AND PATHOPHYSIOLOGY

- Primary fungal cystitis: disruption of urinary tract defense mechanisms allows ascending infection from genital mucosa and environment.
  - Pyelonephritis results when organisms ascend from the bladder to renal pelvis.
  - Reported primary fungal infections include those caused by *Aspergillus* spp., *Candida* spp., *Cryptococcus neoformans*, *Trichosporon* sp., *Rhodotorula* sp.
- Secondary fungal/algal cystitis: disseminated/systemic infection that includes colonization of the kidneys results in urinary shedding of organisms.
  - Fungal organisms isolated from urine in dogs or cats with disseminated infections: *Acremonium* sp., *Aspergillus* spp., *Blastomyces dermatitidis*, *Candida* spp., *Cryptococcus neoformans*, *Paecilomyces* sp., *Penicillium* sp., *Phialemonium obovatum*, *Trichosporon* sp.
  - Algal organisms isolated from urine in dogs with disseminated infections: *Prototheca wickerhamii*, *Prototheca zopfii*.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Identification of fungal organisms on urine sediment examination allows presumptive diagnosis of fungal cystitis, but definitive diagnosis and identification of the infective organism requires fungal urine culture. Identification of the infecting species is required for determining whether primary or secondary infection is more likely, and for determining the most effective antifungal therapy.

DIFFERENTIAL DIAGNOSIS

Differentials for fungal elements in urine: contamination from genital mucosa, contamination from skin, primary or secondary fungal infection

INITIAL DATABASE

- CBC and chemistry profile:
  - Primary fungal cystitis: unremarkable
  - Fungal pyelonephritis: +/- azotemia
  - Disseminated infection: variable; depends on extent and location of infection
- Urinalysis:
  - Organisms often seen on urine sediment examination or urine cystospin preparations
  - Often lack pyuria, hematuria despite active infection

ADVANCED OR CONFIRMATORY TESTING

- Urine culture:
  - Identification of fungal or algal organisms in urine sediment should be followed by urine culture (cystocentesis).
  - Most fungal and algal organisms grow readily on standard culture media.
    - *Candida* sp. (most commonly isolated agent) grows on blood agar within 2-3 days.
    - Other fungal organisms may require culture for longer periods.
  - Speciation requires culture on specific media (e.g., Sabouraud's).
- Antifungal drug susceptibility testing
  - Recommended for *Candida albicans* infections that do not respond to standard therapy
  - Recommended for all non –*C. albicans* fungal infections (including non –*C. albicans* candidal infections) because of increased likelihood of resistance
  - Recommended for *Prototheca zopfii* infections, because reported cases have had widely varying susceptibility patterns

TREATMENT

TREATMENT OVERVIEW

- Successful resolution of primary fungal cystitis requires identification and elimination or control of any predisposing conditions. Fluconazole is the recommend first-line antifungal drug, but many infections recur.

ACUTE GENERAL TREATMENT

- Primary *C. albicans* infections: fluconazole 5-10 mg/kg PO q 12 h for 4-6 weeks

- Primary non –*C. albicans* candidal infections, other fungal agents, and secondary/systemic fungal and algal infections: therapy based on susceptibility testing
    - Primary infections: start fluconazole while waiting for susceptibility results.
    - Secondary/systemic infections: start itraconazole while waiting for susceptibility.

CHRONIC TREATMENT

- Primary fungal infections should always be treated as "complicated" UTIs:
    - To assess efficacy, reculture urine 1-2 weeks after starting therapy.
    - Continue treatment until two successive negative urine cultures 2 weeks apart.
- If infection does not respond or recurs, repeat susceptibility testing.
- Intravesicular clotrimazole infusion may be attempted:
    - Comparative trials are lacking.
    - Can be performed in dogs (easy) or cats.
        - Place Foley catheter, empty bladder.
        - Infuse 7.5-10 mL/kg 1% clotrimazole solution.
        - Solution should be retained for a minimum of 30 minutes if possible.
        - Repeat q 1 wk for 3-4 weeks.
        - Continue oral antifungal therapy during infusions.
- Other treatment options (e.g., systemic or intravesicular amphotericin B, fluconazole, and terbinafine cotherapy) or benign neglect (absent clinical signs) have not been evaluated in pet animals.

POSSIBLE COMPLICATIONS

Primary infections may progress to pyelonephritis or disseminated/systemic infection.

RECOMMENDED MONITORING

Culture urine regularly (q 2-4 mon) after resolution to monitor for recurrence.

PROGNOSIS AND OUTCOME

- Primary fungal infections may be very difficult to treat; prognosis is fair.
    - Intravesicular clotrimazole infusion protocol may improve treatment success.
- Prognosis for secondary fungal or algal cystitis due to disseminated/systemic infections is poor.

PEARLS & CONSIDERATIONS

COMMENTS

- Control or elimination of predisposing factors is critical for resolution of fungal infections.
- Patients with primary fungal cystitis should be screened for diabetes mellitus and concurrent lower urinary tract diseases.
- Urine culture in animals suspected of having disseminated or systemic fungal or algal disease, even when organisms are not identified on urine sediment examination, may be a noninvasive method of diagnosis.

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Cystitis, Bacterial

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Bacterial infection of the urinary bladder occurs very commonly in dogs and less commonly in cats.

SYNONYM

Lower urinary tract infection (UTI)

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs affected more often than cats.
- Females affected more often than males.

RISK FACTORS

- Bladder disease, including cystic calculi and neoplasia
- Congenital or acquired structural defects of the lower urinary tract
- Conditions causing formation of dilute urine, including diabetes mellitus and hyperadrenocorticism
- Immunosuppressive drug therapy, including glucocorticoids
- Disorders of micturition, including urine retention (physical or functional causes), urinary incontinence, and vulvar (or, rarely, preputial) conformational abnormalities
- Bacteremia
- Prostatitis, vaginitis, pyometra, pyelonephritis
- Urinary catheterization, especially indwelling catheters
- Perineal urethrostomy

CONTAGION & ZOONOSIS

Occasionally, clonally identical strains of uropathogenic *Escherichia coli* are transmitted between human and animal members of a household.

ASSOCIATED CONDITIONS & DISORDERS

Struvite urolithiasis, pyelonephritis, emphysematous cystitis

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Uncomplicated: infection in the absence of structural or functional host defects
- Complicated: infection in a host with structural or functional defects (see Risk Factors)
- Recurrent: repeated infections with the same or different species of bacteria
- Persistent: continued infection with the same bacteria despite antibiotic treatment

HISTORY, CHIEF COMPLAINT

- Clinical signs may be absent.
- When present, the signs encountered most commonly include:
  - Pollakiuria
  - Stranguria/dysuria
  - Hematuria
  - Inappropriate elimination
  - Malodorous urine

- Perivulvar dermatitis

PHYSICAL EXAM FINDINGS

- Usually unremarkable
- Occasionally: findings related to associated illness or condition (e.g., findings suggestive of endocrine disorder, urolithiasis, prostatitis)
- Rarely:
  - Painful bladder
  - Palpably thickened urethra on rectal exam (if concurrent urethritis)

ETIOLOGY AND PATHOPHYSIOLOGY

- Infecting bacteria usually ascend through the urethra to the bladder, but hematogenous infection or infection from pyelonephritis is possible.
- Bacterial virulence factors influence likelihood of infection. Flora adapted for preputial and vaginal environments are protective from uropathogenic infection.
- Multiple physical (e.g., intact uroepithelium, voiding action of urination, urethral pressure and length), chemical (e.g., urine osmolality, urea content, pH), and immunologic host defenses protect from infection. Disruption or defects in these defenses predispose to infection.
- The most common pathogens are *E. coli, Staphylococcus, Proteus, Enterococcus, Klebsiella, Streptococcus, Enterobacter, and Pseudomonas.* Only ~20% of infections involve more than one species.
- Bacterial resistance to antibiotics can be problematic. Resistance may be inherent or may result from genetic transfer of resistance factors or from mutation and selection pressures.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

UTI is often recognized on routine urinalysis as bacteriuria and pyuria; results should be confirmed on a "clean" sample (cystocentesis, catheter, or midstream catch). Urine culture and susceptibility are indicated for all complicated, recurrent, or persistent UTIs. Absence of bacteriuria cannot rule out UTI, especially when urine is poorly concentrated.

DIFFERENTIAL DIAGNOSIS

- Urolithiasis
- Prostatitis
- Lower urinary tract neoplasia
- Feline lower urinary tract signs/disease; interstitial cystitis
- Obstructive uropathy

INITIAL DATABASE

- CBC: unnecessary for uncomplicated UTI; may reflect predisposing illness or condition in complicated infections
- Serum biochemistry profile: unnecessary for uncomplicated UTI; may reflect predisposing illness or condition in complicated infections
- Urinalysis: bacteriuria, pyuria, hematuria, proteinuria. Sample should be obtained via midstream catch, clean catheterization, or cystocentesis (ideal).
  - May reflect predisposing illness or condition (e.g., crystals, glucosuria)
  - Sediment exam may be inactive despite infection, especially with diabetes mellitus, hyperadrenocorticism, or other conditions producing dilute urine.
  - "Leukocyte" squares on urine dipstick are notoriously inaccurate
- Gram stain of urine sediment
- Urine culture/sensitivity:
  - Samples should be collected via clean catheterization or cystocentesis (ideal). If urine is collected via catheter, bacterial number should be quantified to distinguish contamination ($<10^3$ bacteria/mL) from infection.
  - Although preferred, culture is not necessary for first occurrence of uncomplicated infection.
  - Culture/sensitivity should always be obtained from complicated, recurrent, or persistent infection.
  - An inactive sediment does not eliminate the need for culture and sensitivity when UTI is suspected, because many concurrent disorders produce dilute urine, limit leukocyte responses in the urine, or both, producing a negative microscopic sediment exam despite active cystitis.

ADVANCED OR CONFIRMATORY TESTING

Reserved for complicated, recurrent, or resistant infection, primarily with the intention of identifying risk factors for UTI

- Abdominal radiographs: radiopaque uroliths, prostatomegaly, rarely emphysematous cystitis
- Abdominal ultrasound: identify radiolucent uroliths, thickened bladder wall or mass, evidence of pyelonephritis or prostatic disease
- Urinary contrast studies: identify radiolucent uroliths, bladder mass, evidence of pyelonephritis, urethral abnormalities

TREATMENT

TREATMENT OVERVIEW

Most uncomplicated UTIs respond readily to a short course of antimicrobial drugs. Complicated, recurrent, and persistent UTI may be very difficult to cure. In such cases, the primary goal is resolution of clinical signs and prevention of complications of infection rather than elimination of all urinary microbes.

ACUTE GENERAL TREATMENT

Several antibiotic choices are appropriate for empirical treatment of uncomplicated infection, or pending culture/sensitivity results in complicated infection:

- Gram-positive infections: amoxicillin (15-20 mg/kg PO q 8-12 h) or amoxicillin-clavulanic acid (10 mg/kg PO q 12 h).
- Gram-negative infections: trimethoprim/sulfadiazine ([TMS]; 15-30 mg/kg q 12 h) or enrofloxacin (5-10 mg/kg q 12 h).
    - In cats, a maximum enrofloxacin dosage of 5 mg/kg/day is recommended to reduce the risk of ocular toxicity (permanent retinal degeneration).
    - Cefovecin (8 mg/kg SQ once) has been used off-label with good success (*Enterococcus* spp. and *Pseudomonas* spp. will be resistant).

CHRONIC TREATMENT

- Predisposing illnesses or conditions should be addressed.
- Duration of antibiotic therapy:
    - Uncomplicated: 7-14 days
    - Complicated: 4 weeks or more
- Antibiotic therapy is adjusted based on in vitro susceptibility results while considering cost-effectiveness, potential adverse reactions, and the likelihood of developing resistance.
- Multidrug resistant *E. coli* infections may be encountered in complicated or persistent infections. Susceptibility may be limited to expensive, potentially toxic, or parenterally administered antibiotics:
    - Amikacin (5-10 mg/kg SQ [or IV, IM] q 24 h) or gentamicin (2-6 mg/kg SQ [or IV, IM] q 24 h):
        - Nephrotoxic
        - Avoid use in dehydrated animals or those with compromised renal function.
    - Meropenem (8.5 mg/kg SQ [or IV] q 12 h) or imipenem-cilastatin (2-5 mg/kg SQ [or IV,IM] q 8 h)
        - Although not an approved route of administration, the 250- or 500-mg imipenem-cilastatin powder for injection may be diluted in 10 mL of saline and the appropriate dose of the resultant solution given SQ. The vial may be kept refrigerated for up to 24 hours.
- Fosfomycin tromethamine may be useful for *E. coli* UTI (3-g packet divided into 3 equal oral daily doses, repeated in 1 week).
- Other therapies may be used to reduce recurrence (see Prevention).

POSSIBLE COMPLICATIONS

- Emphysematous cystitis: rare complication resulting in gas formation in bladder wall; most often identified in diabetic animals.
- Pyelonephritis: vesicoureteral junction usually prevents bacterial ascension to kidneys.
- Urolithiasis: especially struvite
- Adverse reactions to antibiotics are possible (e.g., TMS may cause ker-atoconjunctivitis sicca, gentamicin is nephrotoxic, enrofloxacin is detrimental to cartilage in growing dogs and, in high doses, may irreversibly damage the feline retina).

RECOMMENDED MONITORING

- For uncomplicated infection, urinalysis should be repeated just before discontinuing antibiotic. If sediment is inactive, antibiotic may be stopped, and analysis should again be evaluated 2-3 weeks later.
- For recurrent or relapsing infection, urine culture is repeated 3-5 days after initiation of appropriate antibiotic and again 2-3

weeks after completion of course. Urine sediment should be inactive just before discontinuing antibiotic. If it is not, culture is repeated.
- For animals with continuing predisposing illness or conditions, periodic urine culture may be warranted even without signs of lower urinary tract disease. Inactive sediment exam cannot be substituted for urine culture in animals with diabetes mellitus, hyperadrenocorticism, or dilute urine from any cause.

PROGNOSIS AND OUTCOME

- Prognosis of uncomplicated infection is excellent.
- Prognosis of complicated infection depends on ability to correct predisposing illness or condition.

PEARLS & CONSIDERATIONS

COMMENTS

- Any bacterial cystitis in a male dog should be viewed as a complicated infection.
- Struvite crystalluria in dogs is most commonly due to bacterial UTI or delayed microscopic examination of the sediment, and virtually never is related to diet.
- Lower urinary tract signs in cats are seldom caused by bacterial cystitis (<5% of cats age 10 years or younger with lower urinary tract signs have bacterial cystitis), making empirical antibiotic therapy inappropriate in cats. Therefore, urine from such cats should first be cultured to rule out an infectious contribution.
- Concurrent pyelonephritis commonly occurs in the absence of "classic" signs such as lumbar pain, intermittent fever, or neutrophilia. The absence of these signs in a patient with recurrent bacterial cystitis should not defer an evaluation for pyelonephritis (e.g., abdominal ultrasound) when pyelonephritis is otherwise suspected (e.g., azotemia).
- Many antibiotics are present in high concentration in the urine as a result of renal excretion:
    - Disk diffusion assays of sensitivity evaluate expected serum drug concentration, so sensitivity of a uropathogen in vivo may be greater than that predicted in vitro.
    - If expected urine concentration of antibiotic exceeds minimum inhibitory concentration by four times, the antibiotic should be effective.
- Persistent bacterial cystitis usually results from either inappropriate choice of antibiotic or inadequate dose/duration of administration, emergence of bacterial resistance to the chosen antibiotic, or failure to correct underlying illness or condition allowing infection to occur.

PREVENTION

- Correction of predisposing illness or conditions is the most effective strategy to prevent infection.
- For animals in which predisposing factors cannot be corrected and recurrent infections are problematic, prophylactic antibiotic use or urinary antiseptics may be warranted:
    - Antibiotics:
        - One-third to half of usual daily dose of amoxicillin, TMS, or fluoroquinolone, administered once daily before bed
        - Fosfomycin tromethamine (⅓ packet orally once weekly)
    - Antiseptics (dogs):
        - Methenamine mandelate (10 mg/kg PO q 6-8 h) or methenamine hippurate (500 mg PO q 12 h)
            - Both effective in acidic urine; may require addition of ammonium chloride as acidifying agent (60-100 mg/kg q 12 h). Caution: urinary acidification may precipitate formation of certain uroliths.
    - Alternative (unproven) therapies
        - Cranberry juice concentrate, D-mannose, *Coleus forskohlii* (an herb)

CLIENT EDUCATION

Antibiotics should be given as prescribed to completion even if clinical signs resolve quickly.

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Cystadenoma, Hepatobiliary

BASIC INFORMATION

DEFINITION

Benign hepatic tumor primarily seen in older cats; may occur as focal or multifocal cystic lesions of the liver. The cysts are lined by cuboidal, occasionally vacuolated, epithelium. Histogenesis remains uncertain.

SYNONYM

Bile duct adenoma

EPIDEMIOLOGY

SPECIES, AGE, SEX

Primarily cats older than 10 years. No sex predisposition. Rare in dogs.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Focal or multifocal hepatic lesions are most common.
- Solitary masses are far less common.

HISTORY, CHIEF COMPLAINT

Abdominal enlargement, lethargy, vomiting, and polydipsia. Patients may show no overt clinical signs, with cystadenomas identified as incidental findings on abdominal palpation, radiographs, abdominal ultrasound, or necropsy.

PHYSICAL EXAM FINDINGS

Generally unremarkable. Cranial abdominal organomegaly may be noted with very large cystadenomas.

ETIOLOGY AND PATHOPHYSIOLOGY

Etiopathogenesis remains unknown.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A tentative diagnosis can be made by a skilled ultrasonographer; histopathologic evaluation of a biopsy is required for a definitive diagnosis.

DIFFERENTIAL DIAGNOSIS

Congenital or acquired hepatic cysts, hepatic abscess, malignant hepatobiliary tumors (e.g., cystadenocarcinoma), metastatic hepatic neoplasia

INITIAL DATABASE

- Serum biochemical profile, CBC, and urinalysis are generally unremarkable.
- Abdominal radiographs may prove useful with large cysts that displace surrounding structures.
- Ultrasonography is the diagnostic test of choice. It reveals fluid-filled mass(es) with internal septae, with a variable tissue component. The mass can appear hypoechoic or anechoic due to the cystic nature of the lesion.
- Aspiration of the cystic fluid yields an acellular fluid with a low total protein concentration (<2.0 g/dL).

ADVANCED OR CONFIRMATORY TESTING

- Advanced imaging is generally not indicated.
- Histopathologic evaluation is required for a definitive diagnosis; a presumptive diagnosis may be made by a skilled ultrasonographer.

TREATMENT

TREATMENT OVERVIEW

Surgical excision is advised if possible, as complete excision can be curative. Many cases do not require therapy (small lesions not causing clinical signs). These patients should then be monitored by ultrasonography.

ACUTE GENERAL TREATMENT

- Surgical removal to prevent progressive enlargement and associated clinical signs
  - The decision to excise the mass must be weighed against the condition of the patient (e.g., patients with comorbid conditions in which cystadenoma is an incidental finding).
- Enteral feeding should be considered postoperatively in patients that are anorectic (esophagostomy or gastrostomy tubes).

POSSIBLE COMPLICATIONS

Hemorrhage and bile leakage and resultant bile peritonitis are potential postoperative complications.

RECOMMENDED MONITORING

Follow-up hepatic ultrasound may be considered to monitor for recurrence in cases with incomplete excision or in patients that do not undergo surgery.

PROGNOSIS AND OUTCOME

- Complete tumor excision warrants an excellent prognosis.
- Given the slow-growing nature of the tumor, surgical debulking of nonresectable lesions may provide long-term palliation.
- Hepatobiliary cystadenomas are not known to have malignant potential in veterinary medicine.

PEARLS & CONSIDERATIONS

COMMENTS

- Given the potential for malignancy, histopathologic evaluation should be advised for all cystic hepatic lesions in general.
- Malignant transformation has been reported in humans with hepatobiliary cystadenoma.

TECHNICIAN TIPS

The most common perioperative complication associated with liver surgery is hemorrhage. Increasing heart rate, decreasing blood pressure, decreasing pack cell volume/total solids and decreasing body temperature can be suggestive of hemorrhage in the immediate postoperative period.

CLIENT EDUCATION

Percutaneous cyst drainage may be palliative in select cases; however, given the excellent prognosis associated with complete excision, surgical intervention is advised.

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Cyclic Thrombocytopenia

BASIC INFORMATION

DEFINITION

A tickborne disease characterized by periodic parasitemia of platelets, leading to intermittent episodes of thrombocytopenia.

SYNONYM

Anaplasma platys (formerly *Ehrlichia platys*) infection

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs; no sex or age predilection

RISK FACTORS

Increased tick exposure

CONTAGION & ZOONOSIS

Transmitted by tick vectors, primarily *Rhipicephalus sanguineus* (brown dog tick); possible transmission via other arthropods. Not reported in humans.

GEOGRAPHY AND SEASONALITY

Reported worldwide. United States strains typically less pathogenic.

ASSOCIATED CONDITIONS & DISORDERS

Concurrent or previous infection with other tickborne organisms (e.g., *Babesia*, *Borrelia*, *Ehrlichia* spp.) is common and can potentiate severity of both diseases.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

The organism found in the United States rarely causes any clinical signs or hematologic abnormalities other than thrombocytopenia itself. A more virulent strain causing overt clinical disease exists outside the United States. For less pathogenic strains, history and physical exam are often unremarkable. Thrombocytopenia may be an incidental finding on workup for other disease.

HISTORY, CHIEF COMPLAINT

- Commonly none
- Otherwise, presenting complaint may include lethargy, anorexia, ocular changes, epistaxis, petechiae/ecchymoses.

PHYSICAL EXAM FINDINGS

- Commonly none (e.g., organism may be incidental hematologic finding)
- When present, may include pallor, fever, petechiae/ecchymoses, postoperative hemorrhage, uveitis/hyphema, lymphadenopathy, mucopurulent nasal discharge

ETIOLOGY AND PATHOPHYSIOLOGY

- Ribosomal RNA sequencing has led to reclassification of causative organism. Formerly *Ehrlichia platys* (family

Rickettsiaceae). Renamed *Anaplasma platys* (family Anaplasmataceae).
- Two mechanisms of platelet destruction:
  - Direct injury from replicating organisms
  - Immune-mediated destruction and clearance
- Incubation period is 8-15 days after tick bite, followed by a rapid decline and rebound in platelet numbers.
- Cycles occur every 1-2 weeks, lessening in severity with each recurrence.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Definitive diagnosis requires verification of *A. platys* exposure via serologic titer or genetic isolation in an animal with proven thrombocytopenia.

DIFFERENTIAL DIAGNOSIS

- Other tickborne diseases:
  - *Ehrlichia canis*
  - *Rickettsia rickettsii* (Rocky Mountain spotted fever)
- Immune-mediated thrombocytopenia
- Toxin- or drug-induced thrombocytopenia (cisplatin, cyclophosphamide, chlorambucil, doxorubicin, hydroxyurea)
- Bone marrow suppression
- Disseminated intravascular coagulation (DIC)
- Platelet consumption due to internal or external hemorrhage or vasculitis
- Modified live canine distemper vaccine can rarely cause a transient, nonclinical thrombocytopenia.
- Canine cyclic hematopoiesis of gray collie dogs (see Color Disorders of the Skin and Haircoat, p. 233)

INITIAL DATABASE

- CBC:
  - Thrombocytopenia of varying severity (as little as <10,000 to near-normal >100,000 platelets/mcL)
  - Giant platelets often noted
  - ± Regenerative anemia if extensive hemorrhage
  - Mild nonregenerative anemia with repeated disease cycles
  - Mild leukopenia (occasional)
- Serum biochemistry panel: often unremarkable
- Activated clotting time and buccal mucosal bleeding time will be prolonged with severe thrombocytopenia; other coagulation tests normal.
- Bone marrow exam: megakaryocytes normal or increased in number
- Diagnostic imaging of thorax and abdomen is often unremarkable but should be performed to rule out other causes of thrombocytopenia such as internal hemorrhage or neoplasia.

ADVANCED OR CONFIRMATORY TESTING

- Giemsa-stained blood smear may show dark-staining morulae, representing organisms within platelets, but these are found in fewer than 10% of affected animals.
- Serology: indirect immunofluorescent antibody test is available. Monitor convalescent titers every 2-3 weeks.
- An in-house ELISA (Idexx Snap 4DX) that tests for exposure to heartworms, *E. canis*, *B. burgdorferi*, and *Anaplasma phagocytophilum* is now available, but cross-reaction with *A. platys* occurs. A positive result should be followed up with PCR testing for speciation.
- PCR has become the diagnostic test of choice. PCR is highly specific (false positives rare). Sensitivity is also good, but a negative result does not rule out *A. platys* infection.

TREATMENT

TREATMENT OVERVIEW

Treatment should focus on elimination of organisms and providing supportive care for complications of thrombocytopenia.

ACUTE GENERAL TREATMENT

- Drugs of choice: doxycycline (5-10 mg/kg PO or IV q 12 h) or tetracycline (20-30 mg/kg PO q 8 h) for 21 days
- Administration of blood or oxygen-carrying solutions, intravenous crystalloids/colloids as indicated for acute hemorrhage
- Platelet-rich plasma may be administered for severe thrombocytopenia. Expensive, poorly available (refrigerated shelf life = 2-3 days), and often unsuccessful.
- Vincristine: induces thrombocytosis via an unknown mechanism. Give 0.02 mg/kg IV once, maximum once weekly.

CHRONIC TREATMENT

Tick control is imperative to prevent reinfection.

DRUG INTERACTIONS

- Many oral drugs and foods can decrease absorption of oral tetracyclines: aluminum- or calcium-containing antacids, iron, kaolin-pectin, bismuth salicylate, milk products. Theophylline may enhance adverse gastrointestinal side effects.
- Doxycycline has fewer issues with the listed drug interactions than tetracycline.

POSSIBLE COMPLICATIONS

- Common side effects of tetracyclines are anorexia, vomiting, and diarrhea.
- Doxycycline is caustic to the esophageal mucosa and can cause esophageal strictures. Ensure the pill reaches the stomach by following with water or a small food bolus after administration.
- Vincristine can cause sloughing of soft tissues if extravasation occurs during intravenous injection. CBC is indicated 5-7 days after administration to monitor for a neutrophil nadir. If neutrophils are less than 1500/mcL, prescribe broad-spectrum antibiotics.

RECOMMENDED MONITORING

Serial CBCs q 1-2 weeks posttreatment to monitor recurrence

PROGNOSIS AND OUTCOME

- Good with effective treatment and less pathogenic strains
- Guarded if severe hemorrhage, DIC

PEARLS & CONSIDERATIONS

COMMENTS

Since coinfection with other tickborne diseases is common, diagnostics should include workup for multiple causative agents.

TECHNICIAN TIP

Depending on prevalence, this disease may be first identified during examination of a blood smear; examination of platelet morphology (looking for the organism) is important, especially in thrombocytopenic patients.

PREVENTION

Tick control is most important.

CLIENT EDUCATION

Has not been reported to affect humans

SUGGESTED READING

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AUTHOR: SHANNON T. STROUP

EDITOR: DOUGLASS K. MACINTIRE

Cyanosis

BASIC INFORMATION

DEFINITION

A bluish or grayish discoloration of the mucous membranes or skin due to hypoxemia.

SYNONYMS

Oxidized hemoglobin: oxygenated hemoglobin. Reduced hemoglobin: deoxygenated hemoglobin.

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dog or cat of any age and either sex

GENETICS & BREED PREDISPOSITION

Predispositions for underlying causes

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Generalized cyanosis: all mucous membranes have a bluish tinge.
- Regional cyanosis: due to localized hypoxia. Not discussed further.

HISTORY, CHIEF COMPLAINT

- Dyspnea
- Exercise intolerance
- Collapse; hind limb collapse (described by owners as unexplained periods of sitting during walks) in cases of cyanosis affecting only the caudal half of the body (differential cyanosis)
- Syncope
- Visible cyanosis noted by owner

PHYSICAL EXAM FINDINGS

- Dyspnea may range in severity from mild to severe, in positive correlation to the severity of the underlying problem.
    - An exception is right-to-left shunting heart disease, which may cause pronounced cyanosis even in a patient with minimal dyspnea.
- Heart murmur possible with some right-to-left shunts (e.g., tetralogy of Fallot)
- Stunted growth if congenital right-to-left cardiac shunts

ETIOLOGY AND PATHOPHYSIOLOGY

ETIOLOGY

- Severe pulmonary disease (e.g., pneumonia, pulmonary edema, hemorrhage):
    - Ventilation/perfusion (V/Q) mismatch
    - Pulmonary diffusion disorder
- Severe bronchial disease (e.g., asthma)
- Airway obstruction (laryngeal paralysis, elongated soft palate/brachycephalic airway syndrome, foreign body, mass)
- Hypoventilation
- Pulmonary arterial disease (pulmonary hypertension, pulmonary thromboembolism)
- Diminished lung capacity (severe pleural effusion, pneumothorax, intrathoracic mass, obesity)
- Right-to-left shunting heart disease:

- Cyanosis is usually generalized (tetralogy of Fallot, Eisenmenger's complex, others).
- Differential cyanosis, with pink oral and conjunctival mucous membranes and cyanotic vulvar/preputial mucosa, is characteristic of right-to-left shunting patent ductus arteriosus.

PATHOPHYSIOLOGY

- Reduced (deoxygenated) hemoglobin is blue, whereas oxidized (oxygenated) hemoglobin is red.
- Cyanosis appears when there is a substantial quantity of reduced hemoglobin in the blood:
  - The deep blue color of a reduced hemoglobin molecule overwhelms the red color of an oxidized hemoglobin molecule.
  - Therefore, when cyanosis first appears, there is less reduced hemoglobin than oxidized hemoglobin.
  - Typically, in a patient with a normal hematocrit, the presence of cyanosis indicates a blood concentration of reduced hemoglobin of >5 g/dL (normal total blood hemoglobin concentration: 12.4–19.1 g/dL [dog], 8.5–14.4 g/dL [cat]).
- When cyanosis is observed, severe hypoxemia is present. In a patient with a normal hematocrit, cyanosis begins to appear when Pao2 < 50 mm Hg, which corresponds to SaO2 < 80%, (normal Pao2 = 90-100 mm Hg when breathing room air; normal SaO2 > 95%).
- It is the *absolute* amount of reduced hemoglobin that determines the presence of cyanosis, not the proportion of total hemoglobin that is reduced. Therefore, anemic animals are cyanotic only when they have a very severe degree of hypoxemia, whereas polycythemic animals can be cyanotic with proportionally less oxidized hemoglobin, or even under normal conditions.
- Carboxyhemoglobin, which is elevated in carbon monoxide poisoning, confers a “cherry-colored flush” to the skin and mucous membranes, and this may mask cyanosis in a severely hypoxemic, carbon monoxide–intoxicated patient.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Cyanosis is recognized on physical exam. Beyond a history to suggest recent causes (e.g., smoke inhalation), a CBC (including examination of whole blood for methemoglobinemia, if relevant) and thoracic radiographs are usually the most important initial diagnostic tests.

DIFFERENTIAL DIAGNOSIS

- Methemoglobinemia from oxidative injury to red blood cells (e.g., acetaminophen toxicosis in cats):
  - Methemoglobin gives a “muddy” color to the mucous membranes, which may be indistinguishable from cyanosis.
  - Differentiation is possible based on the gross appearance of the blood. A drop of blood is applied to a white paper towel. With cyanosis, the blood is dark blue, whereas with methemoglobinemia, it is chocolate-brown.
- Normal pigmentation/melanin. Differentiation involves evaluation of other, nonpigmented mucous membranes or measurement of an arterial blood gas sample for oxygen content.
- Normal pink mucous membranes observed in certain lighting conditions (e.g., fluorescent lights) may falsely appear cyanotic.

INITIAL DATABASE

- Thoracic and lateral cervical radiographs: identify airway or lung structural lesions
- CBC: identify clues indicating cause (e.g., polycythemia with right-to-left shunts or chronic lung disease)
- Arterial blood gas: confirm hypoxemia
- Echocardiography: identify cardiac shunts
- Oral and pharyngeal exam if upper airway dyspnea or apnea: identify and correct obstruction

TREATMENT

TREATMENT OVERVIEW

Correct critical hypoxemia.

ACUTE GENERAL TREATMENT

Oxygen supplementation (see p. 1318). Beneficial effect expected in most cases, although right-to-left shunts are minimally to poorly responsive to oxygen supplementation.

CHRONIC TREATMENT

Management or correction of the underlying cause

POSSIBLE COMPLICATIONS

Worsening hypoxemia leading to respiratory arrest

RECOMMENDED MONITORING

- Observation of respiratory effort
- Mucous membrane color
- Pulse oximetry and/or arterial blood gas measurements help quantify response to treatment but are not a replacement for careful observation of respiratory effort and monitoring of underlying cause.

PROGNOSIS AND OUTCOME

- Short term: always guarded, because severe hypoxemia is present.
- Long term: varies widely, depending on underlying cause. Ranges from excellent (e.g., with good response to treatment for lung disease) to poor (e.g., with end-stage heart disease).

PEARLS & CONSIDERATIONS

COMMENTS

- Cyanosis depends on the absolute amount of reduced, or deoxygenated, hemoglobin in the circulation. Therefore, anemic animals or animals with hypoperfusion (e.g., shock) are less cyanotic despite severe hypoxemia, whereas polycythemic animals may show cyanosis with minimal hypoxemia.
- A patient with marked cyanosis and minimal dyspnea should be suspected of having right-to-left shunting or a hematologic problem (e.g., methemoglobinemia from oxidative red blood cell injury).

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AUTHOR & EDITOR: ETIENNE CÔTÉ

Cutaneous Neoplasia

BASIC INFORMATION

DEFINITION

Benign or malignant tumor arising from cells within the skin and adnexa. The most common cutaneous neoplasms in dogs are, in descending order of frequency, lipoma, sebaceous gland hyperplasia/adenoma, mast cell tumor, histiocytoma, and papilloma. In cats, basal cell tumors are the most common, followed by squamous cell carcinoma and fibrosarcoma. Squamous cell carcinoma (p. 1045) and mast cell tumor (canine, ; feline,) are discussed separately.

SYNONYMS

Basal cell tumor: basal cell epithelioma Infundibular keratinizing acanthoma: keratoacanthoma, intracutaneous cornifying epithelioma

EPIDEMIOLOGY

SPECIES, AGE, SEX

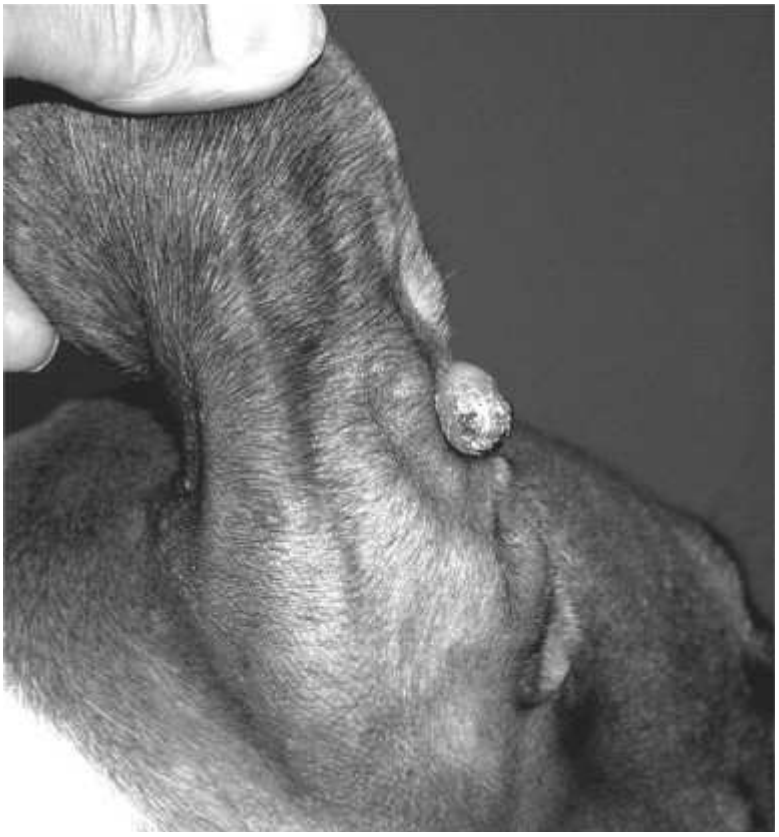
- Dogs: 30% of all tumors arise within the skin
- Cats: 20% of all tumors arise within the skin
- Median age for cutaneous neoplasia is 10.5 years for dogs and 12 years for cats
- Predilection for histiocytoma in young dogs

GENETICS & BREED PREDISPOSITION

- Canine breeds with highest incidence of skin tumors include the boxer, Scottish terrier, bull mastiff, basset hound, Kerry blue terrier, and Norwegian elkhound.
- Shar-peis tend to develop mast cell tumors at a younger age (mean 4 years).
- Feline breeds with highest incidence are the Siamese and Persian.
- Infundibular keratinizing acanthoma: generalized form may have a hereditary basis in Norwegian elkhound and keeshond.

RISK FACTORS

- Basal cell carcinoma: a strong correlation in humans exists with exposure to ultraviolet light and development. This association has not been established in dogs and cats.
- Cutaneous hemangioma/hemangiosarcoma: short-coated dogs with nonpigmented skin in sun-exposed areas such as the glabrous (hairless) skin of the ventral abdomen and white cats are at higher risk.



CUTANEOUS NEOPLASIA Histiocytoma on the pinna of a 1-year-old beagle.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Basal cell tumors: benign or malignant (basal cell carcinoma) tumors arising from the pluripotential basal epithelial cells in the epidermis and adnexa
- Hemangioma/hemangiosarcoma: benign or malignant neoplasms arising from endothelial cells of blood vessels
- Histiocytoma: benign neoplasm that arises from epidermal Langerhans cells
- Infundibular keratinizing acanthoma: benign neoplasms of hair follicle origin
- Trichoepithelioma: benign neoplasms that arise from keratinocytes that differentiate toward all three segments of the hair follicle
- Sebaceous gland hyperplasia/adenoma: epithelial growths arising from sebocytes

HISTORY, CHIEF COMPLAINT

Solitary to multiple cutaneous masses

PHYSICAL EXAM FINDINGS

- Basal cell tumor: solitary, well-circumscribed, firm to cystic, alopecic, commonly ulcerated, often pigmented mass, typically located on the head, neck, shoulders, or thorax. In cats, malignant lesions also can occur on the nasal planum and eyelids.
- Cutaneous hemangioma/hemangiosarcoma: dermal or subcutaneous, solitary or multiple, oval masses or red to dark red plaques, usually located along the limbs and ventral abdomen. In cats: bluish to reddish-black nodules to plaques.
- Histiocytoma: solitary, well-circumscribed, firm, erythematous, intradermal nodule found most frequently on the head, limbs, and thorax. Fast growing but benign. Occasionally observed as multiple cutaneous nodules or plaques.
- Infundibular keratinizing acanthoma: most commonly found on the back, neck, thorax, and limbs. Well-circumscribed dermal or subcutaneous masses with a pore opening to the skin surface; pore usually consists of a keratin plug. Not metastatic.
- Trichoepithelioma: usually solitary, solid or cystic, elevated, round, and well circumscribed; frequently become ulcerated and alopecic.
- Sebaceous gland tumors: solitary or multiple, raised, wartlike to smooth, may ulcerate; most commonly found on limbs, trunk, eyelids, head.

ETIOLOGY AND PATHOPHYSIOLOGY

- Neoplastic transformation relies on changes within specific growth-regulating genes
- Principal growth-regulating genes include:
  - Oncogenes that code for proteins that increase growth
  - Tumor-suppressor genes that decrease proliferation and differentiation

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The only way to distinguish benign neoplasms from malignant neoplasms and nonneoplastic proliferative skin disease is histopathologic examination of biopsied tissue. Malignant lesions show rapid invasive growth, infiltration, and metastasis.

INITIAL DATABASE

- CBC, serum biochemistry profile, urinalysis (if indicated): assess systemic abnormalities if any
- Cytologic exam (fine-needle aspirate):
  - Basal cell tumor: small, round to cuboidal epithelial cells arranged in groups or ribbons. Basal cell carcinomas are difficult to differentiate cytologically from benign lesions.
  - Histiocytoma: sheets of round cells with a pale blue cytoplasm and variable size and shape to the nuclei; variable numbers of neutrophils and lymphocytes, depending on stage of growth and involution
  - Sebaceous gland hyperplasia: clusters of lipid sebocytes
- Histopathologic exam (biopsy):
  - Basal cell tumor: well-circumscribed, symmetric proliferation of basal epithelial cells that has a broad zone of connection to the overlying epidermis
  - Basal cell carcinoma: circumscribed, irregular dermal mass comprising multiple epithelial cell aggregates embedded in a fibrous stroma that may extend into the underlying subcutis
  - Hemangioma: proliferation of blood-filled vascular spaces lined by single layers of well-differentiated endothelial cells
  - Hemangiosarcoma: invasive proliferation of atypical endothelial cells with areas of vascular space formation
  - Histiocytoma: uniform sheets and cords of histiocytes infiltrating the dermis and subcutis; characteristic high mitotic index
  - Infundibular keratinizing acanthoma: keratin-filled crypt in the dermis that has an opening to the skin surface

ADVANCED OR CONFIRMATORY TESTING

Abdominal and cardiac ultrasonography to determine whether hemangiosarcoma lesions are primary or metastatic

TREATMENT

TREATMENT OVERVIEW

Treatment typically should be localized for local disease. Systemic attack on cancer should be reserved for generalized disease or disease in which local therapy alone is not likely to be curative. Treatment options include surgery, chemotherapy, radiation, cryosurgery, electrosurgery, immunotherapy, combinations thereof, or observation.

ACUTE GENERAL TREATMENT

- Basal cell tumor: surgical excision is curative.
- Hemangioma: surgical excision, cryotherapy, or electrosurgery usually curative
- Hemangiosarcoma: aggressive surgical excision is treatment of choice; complete excision of subcutaneous tumor is difficult.
- Histiocytoma: spontaneous remission may occur within 3 months. Surgical excision is curative for lesions that do not regress.
- Infundibular keratinizing acanthoma: may resolve spontaneously. Surgical excision, cryosurgery, or observation without treatment are also options.
- Trichoepithelioma: surgical excision, cryosurgery, electrosurgery, or observation without treatment
- Sebaceous gland hyperplasia/adenoma: surgical excision, cryotherapy, or observation without treatment. May recur after surgery. Sebaceous gland carcinomas rarely metastasize.

CHRONIC TREATMENT

Hemangiosarcoma: chemotherapy can be used before surgery to reduce tumor size; median postsurgical survival of 425 days with the use of a regimen including doxorubicin, cyclophosphamide, and vincristine (study of six dogs). See p. 483.

POSSIBLE COMPLICATIONS

Hemangiosarcoma: local recurrence and metastasis are common in dogs; metastasis is rare in cats.

PROGNOSIS AND OUTCOME

- Excised basal cell tumor and trichoepithelioma: generally very good
- Intradermal hemangiosarcoma: excellent
- Subcutaneous hemangiosarcoma: poor
- Excised solitary histiocytoma: excellent

PEARLS & CONSIDERATIONS

COMMENTS

- The most effective way to separate benign neoplasms from malignant neoplasms and nonneoplastic proliferative skin disease is histopathologic examination of biopsied tissue.
- The key to successful management is an accurate diagnosis.
- Cytologic evaluation of smears may provide valuable information about the cell type.
- Immunohistochemistry has markedly improved our ability to determine progenitor cells for many skin neoplasms, with a positive impact on treatment selection and in some cases on prognostication.

TECHNICIAN TIP

Fine-needle aspirates of subcutaneous masses cannot reliably be interpreted without a microscope. The water-droplet appearance on a glass slide of “classic adipose tissue” is also observed with mast cell tumors and other malignant tissues, not just lipomas; routine staining and microscopic assessment are essential.

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AUTHOR: EDWARD JAZIC

EDITOR: MANON PARADIS

Cutaneous Lymphoma

BASIC INFORMATION

DEFINITION

A malignant neoplasm of lymphoid origin involving the skin or oral cavity. It may be primary or secondary to other forms of lymphoma.

SYNONYMS

Epitheliotropic lymphoma, mycosis fungoides

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Uncommon in dogs and rare in cats
- Usually affects older animals
- No gender predisposition

ASSOCIATED CONDITIONS & DISORDERS: Sézary syndrome, a concurrent tumor cell population in peripheral blood

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Epitheliotropic lymphoma: the more common form; lesions most commonly involve epidermis, superficial dermis, and periadnexa; oral mucosal form also described; T-cell origin; characteristic histologic feature is Pautrier's microabscesses (small aggregates of epitheliotropic lymphoid tumor cells in epidermis); protracted clinical course.
- Nonepitheliotropic lymphoma: uncommon; subcutaneous nodules; B-cell origin; more rapid onset and progression

HISTORY, CHIEF COMPLAINT

- Epitheliotropic lymphoma may be divided into three stages:
  - Premycotic stage: erythematous lesions with varying degrees of depigmentation and alopecia over the trunk and neck which may progress to other body locations
  - Mycotic stage: erythematous, raised, firm plaques which may be ulcerated and exudative
  - Tumor stage: progressive thickening and proliferation of plaque lesions with ulceration; lymph node and/or other organ involvement possible
- Nonepitheliotropic lymphoma in dogs presents as rapidly progressing and frequently multiple subcutaneous nodules.
- Cutaneous lymphoma in cats presents as progressive solitary or disseminated ulcerated plaques or nodules.

PHYSICAL EXAM FINDINGS

- Typical presentation of epitheliotropic lymphoma involves chronic, progressive, generalized exfoliative dermatitis with crusting, ulceration, and alopecia.
- Epitheliotropic lymphoma may present as solitary or multiple ulcerated plaques or nodules involving oral mucosa.
- Variably sized subcutaneous nodules are characteristic of nonepitheliotropic lymphoma.
- In cats, plaquelike lesions are most common; nodules and erythroderma are also possible; solitary lesions may be present initially, with additional lesions developing as the disease progresses.

ETIOLOGY AND PATHOPHYSIOLOGY

Neoplastic lymphocytes in epitheliotropic lymphoma are T cells; CD3 and CD8 phenotype most common in dogs.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Immune-mediated disease (e.g., pemphigus vulgaris, bullous pemphigoid, discoid lupus erythematosus)
- Allergic skin disease with pyoderma
- Infectious disease (e.g., dermatophytosis)

INITIAL DATABASE

- CBC, serum biochemistry panel, urinalysis: typically unremarkable. Occasionally, circulating lymphoblasts may be present, consistent with Sézary syndrome.
- Skin biopsy: test of choice for establishing the definitive diagnosis of cutaneous lymphoma

ADVANCED OR CONFIRMATORY TESTING

- Lymph node aspirate cytologic evaluation: to assess enlarged lymph nodes for lymphoma infiltration versus inflammation/reaction if severe dermatopathy
- Thoracic radiographs: to assess for pulmonary infiltration, intrathoracic lymph node enlargement
- Abdominal ultrasound: to identify changes consistent with hepatic or splenic involvement, lymphadenopathy, or other sites of lymphoma
- Bone marrow aspirate cytologic evaluation: to identify bone marrow involvement, particularly in cases with suspected Sézary syndrome (prognostic value)
- Phenotyping (flow cytometry, immunocytochemistry, immunohistochemistry): if uncertainty exists regarding the histologic diagnosis

TREATMENT

TREATMENT OVERVIEW

Treatment goal: complete remission with resolution of lesions

ACUTE GENERAL TREATMENT

Canine epitheliotropic lymphoma:

- Oral differentiating agents:
  - Vitamin A analogs (isotretinoin, 1-3 mg/kg PO q 24 h): 45% response rate for 5 to 15 months
- Topical agents:
  - Nitrogen mustard (25% solution applied once daily): anecdotal response reported; use is *not recommended* because of concern over human contact dermatitis and carcinogen exposure.
- Radiation therapy:
  - Total skin electron beam therapy may prove beneficial; however, current limited availability precludes wide application.
  - Other forms of radiation therapy may benefit patients with localized oral lesions or those with more generalized disease needing palliation of specific discrete skin lesions.
- Chemotherapy: special handling requirements and potentially severe or life-threatening adverse patient effects exist with many of these chemotherapeutic drugs; such concerns and rapid evolution of protocols warrant consultation with/referral to an oncologist. Chemotherapeutic drug options may include:
  - Chloroethyl-cyclohexyl-nitrosurea (CCNU [lomustine]), 60-70 mg/m^2 PO q 21 days: 15%-30% CR rate and 50%-60% PR rate for median duration of 3-4 months; *or*
  - Prednisone alone, 20-40 mg/m^2 PO q 24-48 h: 25%-35% response rate
  - Combination chemotherapy (see Lymphoma, Dog [Multicentric], p. 675) has limited activity; response durations range from 2-16 weeks.
- Surgery:
  - May be beneficial for patients with solitary resectable oral lesions

Canine nonepitheliotropic lymphoma:

- Treat as for other forms of canine multicentric lymphoma.

Feline cutaneous lymphoma:

- Consider treatment as for canine epitheliotropic lymphoma.

POSSIBLE COMPLICATIONS

See Lymphoma, Dog (Multicentric), p. 675.

RECOMMENDED MONITORING

Regular monitoring of remission status (see Lymphoma, Dog [Multicentric], p. 675).

PROGNOSIS AND OUTCOME

Biological behavior and response to treatment vary widely. Solitary epitheliotropic lymphoma oral lesions may respond well to local therapy (surgery, radiation therapy). Generalized epitheliotropic lymphoma may benefit from chemotherapy, and early results from the administration of oral CCNU are promising.

PEARLS & CONSIDERATIONS

COMMENTS

- Although rapid complete responses to treatment are uncommon, and standard therapy in human medicine (topical chemotherapy or total skin electron-beam therapy) is not currently feasible in veterinary medicine, CCNU alone or in combination with prednisone may be considered a reasonable option for veterinary patients with epitheliotropic lymphoma.
- Most cases of cutaneous lymphoma are epitheliotropic, such that the terms *cutaneous lymphoma* and *epitheliotropic lymphoma* are often used interchangeably.
- Mycosis fungoides is cutaneous lymphoma, not a fungal disease.

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Cutaneous Lupus Erythematosus

BASIC INFORMATION

DEFINITION

Cutaneous lupus erythematosus (CLE) is a chronic inflammatory autoimmune disease with a broad spectrum of clinical manifestations and a variable course. Discoid lupus erythematosus (DLE) is a relatively benign skin disease with no systemic involvement. Two other forms, exfoliative cutaneous lupus erythematosus (ECLE) and vesicular cutaneous lupus erythematosus (VCLE), can be debilitating and potentially fatal.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Uncommon in dogs; very rare in cats
- No age or clear sex predilection

GENETICS & BREED PREDISPOSITION

Breed predispositions include German shepherd, Siberian husky, Brittany spaniel, collies, and Australian herding breeds (DLE). German shepherds may have been excessively represented, as many alleged cases were probably affected with mucocutaneous pyoderma instead. German short-haired pointer (ECLE); rough collie and Shetland sheepdog (VCLE).

RISK FACTORS

Breed, exposure to ultraviolet light.

GEOGRAPHY AND SEASONALITY

More common in summer months and sunny climates.

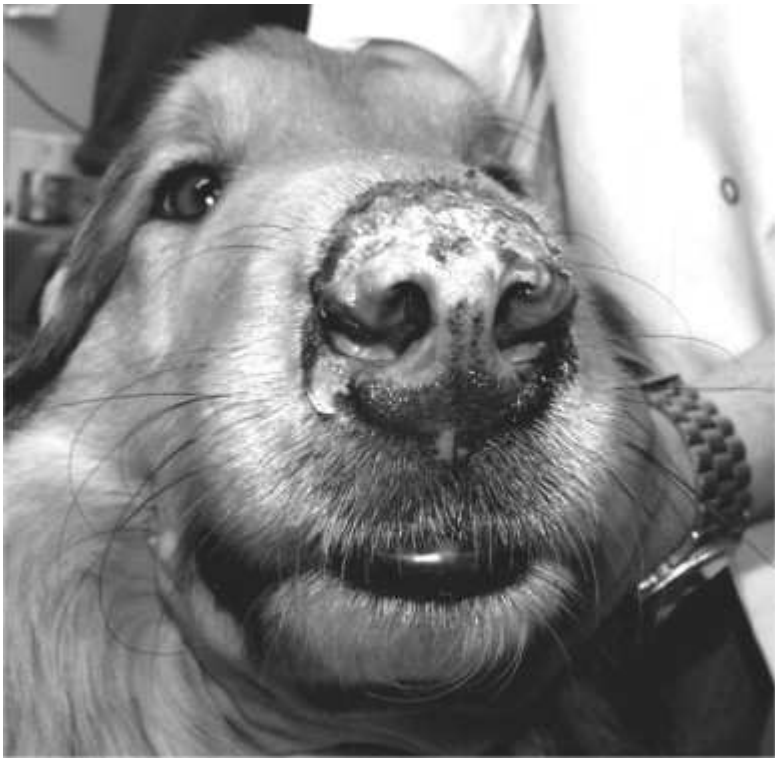
CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

Lesions on the nasal planum +/− bridge of the nose (DLE), generalized scaling (ECLE), or ulcerative skin lesions of the axillae and groin (VCLE).

PHYSICAL EXAM FINDINGS

- DLE: Usually localized to the nasal planum (unhaired, rostral surface of the nose). Less commonly, lesions affect other sites, including lip folds, oral cavity, periocular area, pinnae, genitalia and rarely distal limbs.
  - Erythema, depigmentation, and scaling of the nasal planum with or without involvement of the bridge of the nose. Early depigmentation manifests as a change in color from normal black to gray/white; there is also a change in surface texture of the nasal planum from the normal rough “cobblestone”-like appearance to a smooth, shiny surface.
  - Scaling and crusting may be present at the junction between nasal planum and haired skin. When other sites are affected; crusting, erosions, and ulceration may be noted. Dogs with DLE are otherwise healthy.
- ECLE: Initially there is scaling on the face, pinnae, and dorsum, progressing to a more generalized distribution. Peripheral lymphadenopathy and fever may be present.
- VCLE: Characteristic lesions include annular, polycyclic, and serpiginous ulcerations distributed over sparsely haired areas of the body, specifically the ventral abdomen, axilla, groin, and concave aspects of the pinna.



CUTANEOUS LUPUS ERYTHEMATOSUS Discoid lupus erythematosus in a collie. Note the depigmentation, erosion, and crusting of the nasal planum.

(Copyright Dr. Manon Paradis.)

ETIOLOGY AND PATHOPHYSIOLOGY

- Pathogenesis is thought to involve autoreactive T cells that stimulate B cells to produce antibodies to a number of different nuclear proteins.
- Ultraviolet light may initiate the process of expression in photosensitive individuals (50% of cases).
- Antibodies are deposited in the basement membrane, and subsequently, epidermal basal layer cells are damaged. This results in subepidermal vesicle formation and immune complex deposition in the basement membrane zone.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A strong suspicion exists on physical examination alone. The differential diagnosis varies according to the type of CLE. Biopsy for histopathologic evaluation is the confirmatory test of choice.

DIFFERENTIAL DIAGNOSIS

- Bacterial infection: mucocutaneous pyoderma (DLE), staphylococcal folliculitis
- Immune-mediated diseases: systemic lupus erythematosus, pemphigus foliaceus and erythematosus
- Drug reaction, uveodermatologic syndrome
- Vitiligo
- Neoplasia: squamous cell carcinoma, epitheliotrophic lymphoma (DLE)
- Trauma
- Dermatophytosis
- Demodicosis
- Dermatomyositis (collie and Shetland sheepdog)
- Nasal parakeratosis in Labrador retriever (DLE)

INITIAL DATABASE

- Deep skin scrapings

- Skin cytology (impression smear)
- Dermatophyte culture
- Routine hematology, chemistry profile, and urinalysis: generally unremarkable
- Serum antinuclear antibody test: usually negative (helps rule out SLE)

ADVANCED OR CONFIRMATORY TESTING

- Biopsy (under general anesthesia for DLE) for histopathologic evaluation, which is the gold standard for diagnosis. The typical lesional patterns are a lymphocyte-rich interface dermatitis along the dermoepidermal junction, hair follicles, and adnexal glands in conjunction with hydropic degeneration and apoptosis in the basal cell layer in DLE; hyperkeratosis and lymphocytic interface dermatitis in ECLE; and a lymphocyte-rich interface dermatitis and folliculitis with vesiculation at the dermal-epidermal junction in VCLE.
- Immunohistochemistry may be required.
- Biopsy for fungal and bacterial culture (DLE)

TREATMENT

TREATMENT OVERVIEW

Control and resolution of existing lesions are the goals of treatment. More than one therapeutic modality may be necessary. Typically, secondary/concurrent infections are treated first if present, and topical immunosuppression is the cornerstone of treatment.

ACUTE GENERAL TREATMENT

DLE:

- Routine antibiotic therapy: cephalexin, 22–30 mg/kg PO q 12 h for 30 days to rule out mucocutaneous pyoderma.
- If no or only partial improvement is noticed, a potent topical glucocorticoid (e.g., betamethasone, 0.1% amcinonide, or fluocinolone in dimethyl sulfoxide [Synotic]) can be used. Switch to a low-potency product (e.g., 1% hydrocortisone cream) once a favorable response is noted. If long-term topical glucocorticoid is not an option, the following treatment can be attempted:
- Topical tacrolimus, 0.1% ointment (ProTopic) q 12 h initially, wean based on a favorable response.
- Vitamin E 400-800 IU/d
- Essential fatty acids (n3 EFA, eicosapentaenoic acid) 30 mg/kg PO q 24 h
- Tetracycline and niacinamide: dogs >10 kg, 500 mg (<10 kg, 250 mg) of each drug PO q 8 h. May take 6–8 weeks to produce improvement. If good response, wean gradually (several weeks). Doxycycline, as an alternative to tetracycline: 5–10 mg/kg PO q 24 h.
- In refractory cases, systemic corticosteroids: prednisone, 1.7–2 mg/kg/d PO initially, then wean based on a favorable response. Concomitant azathioprine, 1–2 mg/kg PO q 24–48 h while administering prednisone.

ECLE and VCLE:

- Oral immunosuppressive doses of prednisone (1.7–2 mg/kg) are the first choice, with appropriate antibiotic therapy (see Canine Pyoderma, p. 951).
- Azathioprine (1–2 mg/kg, q 24-48 h) or cyclosporine (5 mg/kg PO q 12 h) may be added if lesions persist. Some form of combination therapy will likely be required in most cases. In ECLE, pentoxifylline and topical keratolytic/keratoplastic therapy (e.g., salicylic acid/sulfur shampoo) may be added, but in general, therapeutic response is poor.

CHRONIC TREATMENT

- Avoid intense sunlight (e.g., 8 am- 5 pm)
- Topical sunscreens if sunlight exposure is unavoidable
- Bilateral rotational nasal flaps for refractory cases (DLE)

POSSIBLE COMPLICATIONS

- Nasal cartilage erosion and arteriole hemorrhage (DLE)
- Squamous cell carcinoma (DLE)
- Septicemia (VCLE)
- Iatrogenic hyperadrenocorticism with chronic glucocorticoid use

RECOMMENDED MONITORING

- Routine CBC and serum biochemistry profiles if using azathioprine. Initially assessed q 14 days, reducing to q 3 months when condition is stable.
- High-dose corticosteroids are rarely required, but appropriate serum biochemistry profiles and urinalysis should be used in such cases.
- With chronic use of intermediate-or long-acting topical corticosteroid application, adrenal function should be monitored.

PROGNOSIS AND OUTCOME

- DLE: Good, but may require chronic therapy
- VCLE: Guarded
- ECLE: Poor

PEARLS & CONSIDERATIONS

COMMENTS

- Dogs with DLE typically feel and act well; the disorder is usually confined to the nasal planum.
- Depigmentation on the inner surfaces of the nostrils accompanied by nasal discharge suggests an intranasal problem (e.g., nasal aspergillosis) rather than DLE.
- In the past, many cases of mucocutaneous pyoderma and nasal parakeratosis have been wrongly diagnosed as DLE.
- Oral antibiotic trial is required prior to skin biopsies of the nasal planum, particularly in German shepherd dogs.

TECHNICIAN TIP

Dogs may quickly lick topical medications applied to the rostral nose, reducing their efficacy (and causing systemic absorption). Application of a thin film of topical creams or liquids to the nasal planum (using gloves with immunosuppressant drugs like tacrolimus) should be followed by distraction of the patient, feeding of a small treat, or other measures to reduce the likelihood of immediate licking away of the medication.

CLIENT EDUCATION

- Avoid intense ultraviolet light.
- Sunscreen use

SUGGESTED READING

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Cutaneous Cysts

BASIC INFORMATION

DEFINITION

Variably sized nonneoplastic masses within the skin, forming saclike structures with an epithelial lining. Identification of cyst origin depends on epithelial lining or the structure from which the cyst developed. Most common are follicular cysts. Dermoid cysts are congenital and hereditary (see online chapter: Pilonidal Cyst).

SYNONYMS

Infundibular cyst (epidermal inclusion cyst, epidermoid cyst, sebaceous cyst)

EPIDEMIOLOGY

SPECIES, AGE, SEX

Common in dogs, rare in cats. Multiple follicular cysts may be noted in young dogs (congenital). Solitary follicular cysts may occur at any age.

GENETICS & BREED PREDISPOSITION

Follicular cysts: most commonly noted in boxers, Doberman pinschers, shih tzus, and miniature schnauzers

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Follicular cysts, infundibular cysts

HISTORY, CHIEF COMPLAINT

- Patients often present for evaluation of a fluctuant to solid, nonpainful, freely movable mass anywhere within the skin, although may be painful if ruptured or infected.
- Cysts may drain a yellow to brown liquid with caseous material. May refill over time.

PHYSICAL EXAM FINDINGS

- Majority of dogs do not show clinical signs.
- Multiple follicular cysts may be noted over the dorsal midline or pressure points (associated with trauma).
- Solitary follicular cysts are firm to fluctuant dermal or subcutaneous masses, 0.5-5 cm in diameter; often found on the head, neck, sacral area (dogs and cats), and proximal limbs (dogs).
- Ruptured cysts may be painful and pruritic with evidence of inflammation, infection, and self-trauma, especially if cellulitis is present.

ETIOLOGY AND PATHOPHYSIOLOGY

- Majority of cysts are follicular and classified as infundibular, matricial, or of hybrid type, based on whether the cyst develops from the infundibulum of the hair follicle, hair follicle matrix, or a combination of the two, respectively.
- Multiple follicular cysts are thought to be congenital, as are dermoid cysts.
- Solitary follicular cysts may develop secondary to dermal fibrosis, microtrauma, or blockage of follicular ostia.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Chief complaint and physical exam revealing a single or multiple nonpainful cutaneous masses with central fluctuation and/or draining are evocative of cutaneous cysts. Confirmation comes with treatment (excisional biopsy).

DIFFERENTIAL DIAGNOSIS

- Keratoacanthoma (intracutaneous cornifying epithelioma): benign skin tumors, thought to be of follicular origin, that superficially appear very similar to follicular cysts. Usually have a pore with a keratinous plug. May be multiple and generalized.
- Papilloma
- Trichofolliculoma
- Cutaneous horn
- Caseous abscess

INITIAL DATABASE AND ADVANCED OR CONFIRMATORY TESTING

- Excisional biopsy and histopathologic examination to determine specific cyst origin and rule out skin neoplasia
- Fine-needle aspirate with impression smears demonstrates sebaceous or keratinous debris.

TREATMENT

TREATMENT OVERVIEW

Surgical excision is chosen over conservative management (observation) if signs of pain, infection, or rupture are present (or recurrent); if masses are of concern to the owner or interfere with the patient's well-being; or if any uncertainty exists regarding the true nature of the mass. The latter situation is common, such that cutaneous cysts often are only suspected at first, and then are diagnosed postoperatively when histopathologic analysis is complete.

ACUTE GENERAL TREATMENT

Options are:

- Surgical excision
- Observation without treatment

CHRONIC TREATMENT

Retinoids such as isotretinoin (Accutane), 1-2 mg/kg q 12 h PO, or acitretin (Soriatane), 0.5-1 mg/kg PO q 12 h may be helpful as prophylactic therapy for multiple follicular cysts.

POSSIBLE COMPLICATIONS

- Cysts may rupture, leading to inflammation, secondary infection, and a foreign-body reaction.
- Retinoid therapy: keratoconjunctivitis sicca, conjunctivitis, pruritus, hyperactivity, stiffness, mucocutaneous junction, erythema, vomiting, diarrhea, teratogenicity, elevated liver enzymes are possible risks.

RECOMMENDED MONITORING

Retinoids: monitor liver enzymes, tear production.

PROGNOSIS AND OUTCOME

Good to excellent

PEARLS & CONSIDERATIONS

COMMENTS

- Never squeeze a cyst firmly to evacuate it, because this will increase the risk of inward cyst rupture, leading to a foreign-body reaction and secondary infection.

- If the client is concerned enough to present the patient for examination of a skin mass, benign neglect should not be encouraged.

SUGGESTED READING

Medleau L: Small animal dermatology: a color atlas and therapeutic guide, ed 2, 2006, WB Saunders Company.

Scott DW, Miller WH, Griffin CE: In Scott DW, Miller WH, Griffen GE, editors: Muller and Kirk's small animal dermatology, ed 6, Philadelphia, 2001, WB Saunders, pp 1375–1379.

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[+]Deceased

Cryptosporidiosis

BASIC INFORMATION

DEFINITION

A sporadic gastroenterocolitis caused by *Cryptosporidium* sp., a ubiquitous coccidian parasite.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Cats of any age and gender can be affected. Canine cryptosporidiosis is almost entirely seen in puppies <6 months old.

RISK FACTORS

- Immunosuppression due to concurrent viral (feline leukemia virus [FeLV], feline immunodeficiency virus [FIV], canine distemper virus [CDV]) infection
- Overcrowded conditions (humane shelters, catteries, etc.) raises prevalence of infection, since oocysts shed in feces are highly infective.
- Presence of other gastrointestinal parasites (*Giardia* sp., *Toxocara cati*) or in adult cats with severe intestinal disease (e.g., inflammatory bowel disease, lymphoma)
- Feeding home-cooked diets

CONTAGION & ZOONOSIS: Exposure and transmission are from fecally contaminated water or food sources. Zoonosis risk with immunocompromised humans warrants screening of cats/puppies to ensure they are not shedding oocysts.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Chronic small–bowel diarrhea (see p. 305) is the main clinical sign initially. Vomiting is less likely. Tenesmus, hematochezia, and weight loss may occur in long-standing infections.

PHYSICAL EXAM FINDINGS: Many *Cryptosporidium*-infected cats have subclinical infection. In cats with overt clinical signs, gas- and fluid-filled intestinal loops can be identified on abdominal palpation; cats may appear thin, unthrifty, and undernourished with chronic disease. Fever usually does not occur.

ETIOLOGY AND PATHOPHYSIOLOGY

- *Cryptosporidium parvum* and/or *C. felis* (in cats) or *C. canis* (in dogs) are transmitted by the fecal-oral route.
- Oocysts are found in feces. They may be shed at any time—during diarrhea, or in the absence of clinical signs—but the incidence of shedding from carriers (not showing signs) is low.
- Infection occurs without invasion into intestinal epithelium.
- The mechanism of clinical disease is postulated to be an interruption of normal flora by the parasite and later influx of inflammatory cells into the intestinal epithelium, leading to villous atrophy, secretory diarrhea, and malabsorption.
- The terminal ileum usually has the highest parasite load.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Routine screening specifically for *Cryptosporidium* is a low-yield procedure, given current techniques and the low prevalence of shedding, but testing should be considered in animals with compatible clinical signs and/or for immunocompromised pets or owners. More than one method of parasite identification may be necessary to rule out infection in highly suspect animals with clinical disease.

DIFFERENTIAL DIAGNOSIS

- Causes of gastroenterocolitis that prevail in overcrowded conditions: *Giardia* spp., *Cystoisospora* spp., *Tritrichomonas foetus, Toxoplasma gondii, Entamoeba histolytica*
- Other causes of diarrhea and weight loss: inflammatory bowel disease, gastrointestinal lymphoma, hyperthyroidism

INITIAL DATABASE

- Complete fecal examination consisting of direct smear, Sheather's solution flotation, and ZnSO4 analysis (any cat with diarrhea)
  - *Cryptosporidium* oocysts (4 mm; about half the diameter of an erythrocyte) may be identified by light microscopy at 100× power using any of these techniques.
  - Multiple fecal samplings improve the likelihood of finding oocysts.
  - Direct fecal smear stained with crystal violet makes oocysts more visible.
  - Phase microscopy is usually required on unstained preparations from a Sheather's fecal float.
  - In general, microscopic identification of oocysts requires expertise, is challenging even with fluorescent antibody staining and analysis with fluorescent microscopic and direct immunofluorescence, and is inferior to ELISA.
- CBC, serum biochemistry profile, urinalysis, total T4 analysis, abdominal imaging: if diarrhea and weight loss are present (rule out other disorders)
- FeLV and FIV ELISA

ADVANCED OR CONFIRMATORY TESTING

- Specimens shipped to commercial laboratories should be sent in a 38% formaldehyde (100% formalin) solution added to feces in a 1:10 dilution to kill oocysts but still allow detection. The oocysts can be detected using direct immunofluorescence antibody (DFA) staining after centrifugation.
- Feline serum cryptosporidial IgG ELISA: highly correlates with exposure to parasite but not necessarily active infection
- ELISA tests for cryptosporidial antigen in feces of humans and rodents are available. Diagnostic efficacy is unproven in cats and dogs.
- PCR tests for detecting cryptosporidial antigen in feces are available, more sensitive than DFA, and used for molecular typing of species in cats and dogs.
- Intestinal biopsy can differentiate from other intestinal disease but is costly, time consuming, and less effective than fecal examination.
- If necropsy is used for primary diagnosis, intestinal samples should be taken within hours after death; otherwise postmortem autolysis will prevent confirmation.

TREATMENT

TREATMENT OVERVIEW

The overall goals of treatment are to cure the infection, resolve clinical signs, and prevent further oocyst shedding. High numbers of oocysts may still be shed after completion of a course of therapy with resolution of clinical signs. Treatment should persist in an attempt to stop fecal shedding of oocysts.

ACUTE GENERAL TREATMENT

- Parenteral fluid therapy to correct hypovolemia, electrolyte imbalances, and acid-base disturbances if present.
- Antiprotozoal and antibiotic agents have been shown to be effective:
  - Azithromycin, 7-15 mg/kg PO q 12 h for 5-7 days. Current drug of choice for human cryptosporidiosis. Studies in cats have not been performed, but efficacy would be expected.
  - Paromomycin, 125-165 mg/kg PO q 12 h for 5 days, was the traditional drug of choice, but because of side effects, it has fallen from favor.
  - Tylosin, 11 mg/kg PO q 12 h for 28 days, helpful in treatment of diarrhea only
  - Nitazoxanide successfully used in human infections but dose for cats and dogs still under research

CHRONIC TREATMENT

Treatment of concurrent antibiotic-responsive enteritis/small-intestinal bacterial overgrowth (metronidazole, 10-15 mg/kg PO q 12-24 h for 5-7 days) may be beneficial in addition to treatment for *Cryptosporidium*.

NUTRITION/DIET

Feeding of a highly digestible diet is recommended in addition to pharmacotherapy in cats with severe clinical signs of chronic infection.

POSSIBLE COMPLICATIONS

Chronic infection: intestinal intussusception or lymphangiectasia are possible.

RECOMMENDED MONITORING

- Fecal analysis is recommended after treatment to determine if oocyst shedding is still occurring.
- Another fecal analysis may be required if diarrhea persists and/or recurs after treatment.
- Animals with chronic infection should be reevaluated at frequent intervals to assess progress.

PROGNOSIS AND OUTCOME

Prognosis is good with treatment in cats that do not have FeLV/FIV infection.

PEARLS & CONSIDERATIONS

COMMENTS

- This disease occurs in immunocompromised cats.
- Glucocorticoids and other immunosuppressive agents should be avoided until the infection is resolved.

PREVENTION

- This is a disease that is prevalent in overcrowded and unsanitary conditions.
- Reducing environmental contamination with improved sanitation is an important aspect of prevention.
- Although 5% ammonia will kill parasites, it requires 18 hours of contact for effect. Therefore, higher concentrations of ammonia are required if contact time is shortened. Dilute sodium hypochlorite (bleach diluted 1 part bleach to 32 parts water) kills *Cryptosporidium*.

CLIENT EDUCATION

- Potential for zoonosis
- Caution with immunosuppressed individuals and young children (greatest potential for infection)

SUGGESTED READING

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EDITOR: DEBRA L. ZORAN

Cryptorchidism

BASIC INFORMATION

DEFINITION

Failure of one or both testicles to descend into the scrotum. Literally, “hidden testicle.”

SYNONYM

Retained testicle(s)

EPIDEMIOLOGY

SPECIES, AGE, SEX: Intact males, canine and feline. A presumptive diagnosis can be made at 8 weeks, and a definitive diagnosis can be made by 6 months.

GENETICS & BREED PREDISPOSITION

- Considered to be a simple autosomal recessive trait. Incomplete penetrance and failure of Mendelian probability suggest a multifactorial or polygenic mode of inheritance.
- Mixed-breed dogs ~3.9%
- Purebred dogs ~8.7% (toy and miniature breeds show a significantly higher rate of occurrence).
- Cats (mixed and purebred) ~1.3%

RISK FACTORS

- Familial
- Drugs used during pregnancy with antiandrogen effects: diethylstilbestrol, estradiol cypionate, progestagens, cimetidine, flutamide, finasteride

ASSOCIATED CONDITIONS & DISORDERS

- Testicular neoplasia (see p. 1081): a cryptorchid testicle has a 10-fold greater risk of tumorigenesis.
- Intersex: male pseudo-hermaphrodite, Klinefelter's syndrome
- Infertility (see p. 603): only if bilaterally cryptorchid
- Benign prostatic hyperplasia (see p. 919): if left intact, cryptorchid males are as likely to develop prostatic disease as normal intact males.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Unilateral: one testicle retained (the right testicle is twice as likely to be retained as the left).
- Bilateral: both testicles retained (less common than unilateral cryptorchidism)
- Abdominal: testicle(s) retained within the abdomen (usually near the internal inguinal ring; rarely at the caudal pole of the kidney)
- Inguinal: testicle(s) retained within the inguinal canal (most common, ~75%)

HISTORY, CHIEF COMPLAINT

- Absence of one or both testicles in scrotum
- Male breeding behavior in a “neutered” animal

PHYSICAL EXAM FINDINGS

- Only one or no testes are palpable within the scrotum. Testes should be easily palpable and normally descended by 8 weeks of age.
- Penile examination: in cats, presence of penile spines indicates circulating androgens, most likely of testicular origin.

ETIOLOGY AND PATHOPHYSIOLOGY

- Testosterone is responsible for testicular descent in three stages of migration—abdominal, inguinal, and scrotal—through the dissolution of the cranial suspensory ligament and contraction of the gubernaculum.
- Testicular descent in cats is complete at birth, but the testicles can move freely into the inguinal canal for up to 6 months.
- Testicular descent in dogs is not completed until approximately 40 days after birth.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis of cryptorchidism can usually be made by palpation. Under unique circumstances, hormone testing or exploratory surgery may be required to make a definitive diagnosis.

DIFFERENTIAL DIAGNOSIS

- Monorchidism (unilateral testicular aplasia)
- Anorchidism (bilateral testicular aplasia)
- Intersex: male pseudohermaphrodite, Klinefelter's syndrome

INITIAL DATABASE

- Palpation. In tense or nervous animals, the testicle(s) may be drawn proximally toward the inguinal canal and may be palpable under sedation or general anesthesia.
- Examine the feline penis for spines.
- Ultrasonography may be useful in evaluating testicles retained in the abdomen.

ADVANCED OR CONFIRMATORY TESTING

- In animals where it is suspected but castration history is unknown:
  - Exploratory surgery
  - Human chorionic gonadotropin (hCG) stimulation test: measure blood testosterone concentrations before and 24 hours after 750 IU hCG given IV to dogs or cats, regardless of body weight. Presence of testicular tissue should yield a twofold increase in testosterone concentration (>0.1 ng/mL)

TREATMENT

TREATMENT OVERVIEW

- Prevent development of testicular tumors.
- Render the animal sterile to prevent propagation of heritable abnormalities.
- Remove testosterone-producing tissues to eliminate undesirable male behavior.

ACUTE GENERAL TREATMENT

- Castration:
  - Parainguinal approach for inguinally retained testicle(s)
  - Abdominal approach for abdominally retained testicle(s)

CHRONIC TREATMENT

GnRH vaccination: there is a commercially-available canine gonadotropin releasing hormone (GnRH) vaccine (Pfizer Animal Health) labeled for the nonsurgical management of benign prostatic hyperplasia in dogs. Immunization against GnRH elicits a reduction in gonadotropin (follicle-stimulating hormone and luteinizing hormone) and androgen concentrations via the production of serum neutralizing antibodies against GnRH. This immunocastration vaccine has been used by the section editor (Kutzler) for the nonsurgical management of cryptorchid cats and dogs to lower serum testosterone concentrations. The vaccination should be repeated at 6-month intervals to provide continued gonadotropin and androgen suppression. Administration of a nonsteroidal antiinflammatory drug (NSAID) at the time of vaccination will eliminate/minimize temporary injection site tenderness and pyrexia that can occur. The risk of tumorigenesis in the cryptorchid testicle is unknown but likely unchanged.

BEHAVIOR/EXERCISE

Where castration is not an option, cryptorchid males should be isolated from receptive females to prevent unwanted pregnancy. Cryptorchid males have serum testosterone concentrations equivalent to normal intact males, and the propensity to transmit the heritable trait to their offspring.

DRUG INTERACTIONS

Androgen or progestogen administration to pregnant dogs and cats prior to the time of fetal sexual determination may result in masculinization of female fetuses or increased incidence of cryptorchidism in male fetuses. Masculinized female offspring are genetically female with ovaries (no testicular tissue) but possess external genitalia similar to males.

POSSIBLE COMPLICATIONS

- If left untreated, it is considered a matter of time before neoplasia develops in the retained testicle.
- If left untreated, BPH and prostatitis (see p. 919) are potential secondary disease processes that commonly affect intact males.

RECOMMENDED MONITORING

If bilateral testicles cannot be palpated at 8 weeks, it is recommended to recheck the animal at 6 months before definitively diagnosing it as cryptorchid.

PROGNOSIS AND OUTCOME

Prognosis for life is excellent. Surgical castration eliminates the risk of testicular cancer and greatly reduces the risk of prostatic disease.

PEARLS & CONSIDERATIONS

COMMENTS

- Surgical correction or medical treatment (using gonadotropin-releasing hormone [GnRH] or hCG) to induce descent of the aberrant testicle into the scrotum have been reported in dogs (GnRH: two injections 50-100 mcg given SQ or IV with a 7-day interval; hCG: four injections of 100-1000 IU given IM with a 3- to 4-day interval between injections), but efficacy and ethics of such protocols are suspect. In addition, artificially corrected, cryptorchid testicles have the same 10-fold increased potential for neoplasia as retained testicles.
- A luteinizing hormone (LH) test is commercially available and commonly used to diagnose the presence or absence of ovarian tissue in bitches and queens. In spayed females, LH concentrations remain persistently elevated due to the lack of negative feedback from the gonads. This has also been found to be true in castrated male dogs. A positive LH test result (LH level > control [1 ng/mL]) is consistent with a castrated dog and rules out cryptorchidism.

PREVENTION

- Removal of affected animals from the breeding population results in reduced incidence within the breed.
- The dam and female siblings of affected males may be homozygous or heterozygous carriers but will not demonstrate phenotypic signs.
- The sire and some male siblings will be heterozygous carriers not showing any manifestations of cryptorchidism.

CLIENT EDUCATION

Do not breed animals that are cryptorchid or have sired cryptorchid offspring.

SUGGESTED READING

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Klonisch T, et al: Molecular and genetic regulation of testis descent and external genita-lia development. Develop Biol 270:1–18, 2004.

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EDITOR: MICHELLE A. KUTZLER

Cryptococcosis

BASIC INFORMATION

DEFINITION

A systemic mycosis caused by a dimorphic fungus with the yeast phase being infective, unlike other mycoses. Clinically, there is a predilection for the upper respiratory tract, central nervous system (CNS), skin, and eyes. The organisms are called the *Cryptococcus neoformans/Cryptococcus gatti* species complex.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- This is the most common systemic fungal disease in cats.
- Domestic and wild animals and humans may be infected.
- Cats may be more susceptible than dogs.
- No age or sex predilection in cats
- Young adult dogs are more commonly affected.

RISK FACTORS

- Exposure to pigeon droppings and soil in warm, humid climates
- Immunosuppressed states (glucocorticoids) and diseases (feline immunodeficiency virus [FIV] or feline leukemia virus [FeLV] infections in cats, ehrlichiosis/anaplasmosis in dogs) may be risk factors.

CONTAGION & ZOONOSIS

Zoonosis is unlikely, but caution is warranted. The yeast form is infective, and this does not aerosolize from infected tissues or body fluid.

GEOGRAPHY AND SEASONALITY

Worldwide distribution

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Respiratory, cutaneous, CNS, and ocular forms

HISTORY, CHIEF COMPLAINT

- Cats typically present with upper respiratory tract signs (sneezing, nasal discharge), swelling of the nose, skin lesions. Neurologic or ophthalmic signs may also be present.
- Dogs may present with weight loss, anorexia, lethargy, and neurologic or ophthalmic signs.

PHYSICAL EXAM FINDINGS

- Cats: unilateral or bilateral nasal discharge, sneezing, firm swelling over bridge of nose. Submandibular lymphadenomegaly.
- Dogs and cats: Multifocal neurologic signs with cranial nerve involvement. Ocular abnormalities including retinal detachment, chorioretinitis, panophthalmitis, optic neuritis. Cutaneous lesions including papules, nodules, or ulcerated draining lesions. Fever possible.

ETIOLOGY AND PATHOPHYSIOLOGY

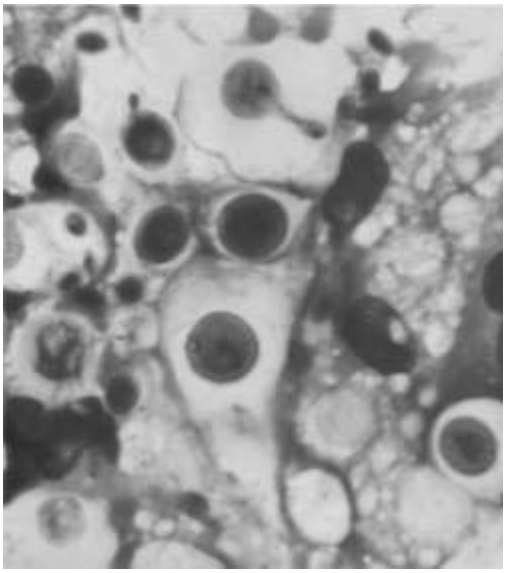
- *Cryptococcus* spp. are a saprophytic, round, yeastlike dimorphic fungus with a large heteropolysaccharide capsule
- Inhalation of yeastlike, nonencapsulated, airborne organisms is the most likely route of infection.
- The organism may then establish itself in the upper respiratory tract or in the alveoli, forming granulomas.

- In tissues, the organism forms a polysaccharide capsule that interferes with the immune response, preventing clearance of the organism.
- Hematogenous dissemination and invasion into the CNS and eyes may follow.
- Establishment of the organism in tissues and dissemination will occur if there is a poor cell-mediated immune response.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Characteristic physical findings raise the suspicion of the diagnosis; confirmation is achieved via serologic titers (most often) or fine-needle aspiration and cytology (less common now).



CRYPTOCOCCOSIS Cytology shows capsulate yeasts with narrow-neck budding and prominent unstained region surrounding each yeast (corresponding to capsule). Diff-Quik-stained smear.

(Courtesy R. Malik, University of Sydney, Sydney, Australia. In Greene CE: Infectious diseases of the dog and cat, ed 3, St Louis, 2006, Saunders, 2006, p 587, with permission.)

DIFFERENTIAL DIAGNOSIS

- Lymphosarcoma
- Respiratory: chronic rhinitis (bacterial or viral), nasal tumors, other systemic fungal diseases, toxoplasmosis, nasal polyps
- CNS:
  - Feline infectious diseases (FeLV, FIV, feline coronavirus/feline infectious peritonitis, toxoplasmosis, rabies)
  - Canine infectious diseases (canine distemper, rabies, ehrlichiosis, Rocky Mountain spotted fever, toxoplasmosis)
  - Noninfectious: granulomatous meningoencephalitis, neoplasia
- Cutaneous: bacterial pyoderma, abscesses, autoimmune skin disease
- Other systemic fungal disease (dogs)

INITIAL DATABASE

- CBC, serum chemistry panel, and urinalysis can be within normal limits.
- May find *Cryptococcus* spp. organisms in urine sediment (uncommon)
  - Stain to help differentiate organisms from fat droplets
- Thoracic radiographs may show an interstitial nodular pattern.
- Nasal radiographs may show bony lysis or proliferative lesions.

ADVANCED OR CONFIRMATORY TESTING

- Cytologic examination of nasal exudates, skin exudates, lymph node aspirate, cerebrospinal fluid (CSF), ocular fluid, tissue biopsy may reveal organisms.
- Latex agglutination test for capsular antigen in serum, urine, or CSF:
  - Diagnostic test of choice: positive test result indicates infection.

- False-negative results possible with localized infection
- Fungal culture from exudates, CSF, urine, ocular or joint fluid, and tissue samples
  - Represent a possible zoonotic hazard (aerosol) and should be performed in a specialized laboratory only. Not clinically recommended.

TREATMENT

TREATMENT OVERVIEW

Most cats can be treated with oral antifungal drugs only. Some cats/dogs may require additional treatment in severe cases. Treatment typically is given for months and can be expensive.

ACUTE AND CHRONIC TREATMENT

- Treatment of choice is fluconazole, 5-15 mg/kg PO q 12-24 h (dogs and cats); should continue at least 1 month past resolution of clinical signs.
- Amphotericin B if oral drugs are impossible or cost of fluconazole is prohibitive (dogs); ensure adequate hydration and renal function.
  - SQ: 0.5-0.8 mg/kg diluted with 400-500 mL 0.45% saline/2.5% dextrose and given 2-3 times weekly to a cumulative dose of 8-26 mg/kg (dogs; caution with fluid overload in small dogs)
  - IV: 0.25 (cats) or 0.5 (dogs) mg/kg IV q 48-72 h; total cumulative target dose of 4-8 mg/kg or 4-10 mg/kg for cats and dogs, respectively
- Lipid-soluble amphotericin B (less nephrotoxic, more expensive): 1 mg/kg IV q 48-72 h for 60 days (target for dogs, cats)
- Itraconazole (less expensive than fluconazole), 5 mg/kg PO with food q 12 h (cats). Formulation may make dosing difficult (100-mg capsules), but oral liquid (10 mg/mL) available.
- Ketoconazole, 5-15 mg/kg PO q 12 h (dogs). Least effective but least expensive.
- Terbinafine, 10 mg/kg PO q 24 h (cats that show resistance to azoles)
- Voriconazole is also effective (and crosses blood-brain barrier) but very expensive.
- CNS infections: fluconazole is preferable (crosses the blood-brain barrier) over amphotericin B or ketoconazole.

DRUG INTERACTIONS

- Itraconazole and ketoconazole should not be administered with other hepatically metabolized drugs.
- Amphotericin B should not be administered with other renally excreted drugs.
- Fluconazole is eliminated through the kidneys, and dose must be decreased in patients with renal failure.

POSSIBLE COMPLICATIONS

- Itraconazole may result in gastrointestinal signs and hepatotoxicity (initially manifested with elevated serum alanine aminotransferase). Rare side effects include vasculitis and cutaneous ulcerations.
- Ketoconazole may cause gastrointestinal signs and elevated serum liver enzymes. Cats have an increased risk for hepatotoxicity, and use of this drug is controversial in this species.
- Amphotericin B is potentially nephrotoxic and can cause phlebitis.

RECOMMENDED MONITORING

- Monitoring of serial titers may help assess response to therapy:
  - A decrease in serum antigen titer implies a favorable prognosis (specifically, better prognosis if titer decreases 10-fold or more after 2 months of treatment).
  - Use of antigen titers to guide duration of treatment: treatment should be continued for 1 month after complete resolution of clinical signs and a decrease in titer by at least two orders of magnitude (e.g., if 1:512 at diagnosis, then 1:128, 1:64, or lower) but ideally when there is an undetectable titer.
  - In some cats it may take 3-5 years to reach a negative titer, if ever, irrespective of treatment.
- Liver enzymes and renal values should be routinely monitored while animal is treated with antifungals.
- Animals treated with amphotericin B should have blood urea nitrogen (BUN), creatinine, urine GGT if possible, and urine sediment examinations performed routinely. A rising BUN and/or casts in the urine sediment may necessitate discontinuing or lowering the dose of amphotericin B.

PROGNOSIS AND OUTCOME

- Infection may be cleared in cats; however, maintenance antifungal therapy may be necessary, especially in FeLV/FIV-positive cats.
- FeLV/FIV seronegative status is significantly associated with treatment success (data for itraconazole) in cats with nasal cryptococcosis. FeLV/FIV-positive cases are associated with severe signs involving the CNS and eyes.
- CNS infections and disseminated infections are more likely to exist in cats with FeLV or FIV and may be more difficult to clear.
- Magnitude of pretreatment antigen titers has no significant effect on prognosis using itraconazole.
- More cats with the cutaneous forms of cryptococcosis (82%) were treated successfully than cats with intranasal (53%) cryptococcosis or cryptococcal infection of other sites (43%).
- Guarded prognosis in dogs

PEARLS & CONSIDERATIONS

TECHNICIAN TIP

The subtle deformation of the muzzle or face of an early lesion of cryptococcosis may first be noticed by a member of the technical staff and is an important observation to bring to the attention of the attending veterinarian.

PREVENTION

- No vaccine available
- Avoid pigeon droppings and damp, shaded soil.

SUGGESTED READING

Sellon RK, Legendre AM: Systemic fungal infections. In Bonagura JD, Twedt DC, editors: Kirk's current veterinary therapy XIV. Philadelphia, 2009, Elsevier, pp 1265–1267.

Jacobs GJ, Medleau L: Cryptococcosis. In Greene CE, editor: Infectious diseases of the dog and cat. Philadelphia, 2006, Elsevier, pp 584–598.

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Cricopharyngeal Achalasia/Dysphagia

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Cricopharyngeal achalasia is a rarely diagnosed condition representing the failure of upper esophageal sphincter (the cricopharyngeus muscle) relaxation and lack of synchrony with pharyngeal muscular activity.

SYNONYMS

Cricopharyngeal dysphagia, cricopharyngeal asynchrony

EPIDEMIOLOGY

SPECIES, AGE, SEX

Spaniel dogs overrepresented (springer, cocker). Often congenital; most cases present at a young age upon weaning. Rarely is diagnosed in older animals or in conjunction with other conditions. Predominantly recognized in the puppy/young dog.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

Signs include gagging, retching, regurgitating food, coughing, and nasal reflux, typically beginning with the introduction of solid food (time of weaning). Repeated attempts to swallow may be seen upon careful evaluation during eating. Dogs are often thin and in poor body condition because of ineffective food intake and may lose weight despite an increased appetite.

PHYSICAL EXAM FINDINGS

- Patients are usually thin and may be smaller in stature compared to littermates.
- Observation of respiratory effort and thoracic auscultation may offer clues of underlying aspiration pneumonia. The dog should be observed while eating; repeated, ineffective attempts to swallow are suggestive of cricopharyngeal achalasia.

ETIOLOGY AND PATHOPHYSIOLOGY

- Cricopharyngeal achalasia results from asynchrony of relaxation of the cricopharyngeus muscle in relation to pharyngeal activity that forms and directs a bolus caudally.
- The cricopharyngeus muscle contracts during normal activity. When a bolus formed by pharyngeal muscular activity is pushed caudally by the base of the tongue, the cricopharyngeus muscle relaxes, allowing passage of the bolus into the upper esophagus.
- Asynchronous cricopharyngeal relaxation results in repeated caudal movement of a bolus against persistent cricopharyngeal contraction. Boluses may eventually reach the upper esophagus, may be regurgitated, or may be aspirated into the trachea.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Characteristic history of prehension of food but inability to swallow is highly suggestive of the diagnosis. Confirmation is obtained with fluoroscopic evaluation of the oropharyngeal and esophageal processing of liquids and solids. Clinical signs and static imaging (even with contrast) may not differentiate oral, pharyngeal, and cricopharyngeal disorders. However, a correct diagnosis is imperative prior to surgical treatment to avoid worsening clinical signs and aspiration pneumonia.

DIFFERENTIAL DIAGNOSIS

- Pharyngeal dysfunction (usually results in the inability to form a bolus)
- Oral dysfunction (interferes with prehension)

- Oropharyngeal/proximal esophageal obstruction (foreign body, mass): apparent radiographically, on sedated pharyngeal exam, or endoscopically

INITIAL DATABASE

- Clinical pathologic abnormalities result from severe malnutrition or aspiration pneumonia.
- Thoracic radiographs should be made to rule out megaesophagus and aspiration pneumonia.

ADVANCED OR CONFIRMATORY TESTING

A definitive diagnosis is made with fluoroscopy of the pharynx and esophagus when the patient is offered food mixed with barium.

- A bolus is formed, but repeated attempts at caudal movement of the bolus beyond the upper esophageal sphincter result in little or no entry of barium into the esophagus. Barium may enter the nasopharynx or the trachea.
- When barium does enter the esophagus, esophageal motility must be evaluated prior to considering surgical correction of the condition. Decreased esophageal motility or megaesophagus are contraindications to surgical therapy.

TREATMENT

TREATMENT OVERVIEW

- The definitive treatment approach of choice is surgical; medical management of complications (e.g., aspiration pneumonia) is imperative for preoperative stabilization.
- The goal of surgical treatment is to allow unimpaired passage of boluses from the pharynx into the esophagus, without tracheal contamination.

ACUTE AND CHRONIC TREATMENT

- Treatment of complications prior to anesthesia (e.g., aspiration pneumonia (p. 885), undernourishment)
- Partial cricopharyngeal myectomy: most common. Partial thyropharyngeal myectomy in conjunction with cricopharyngeal myectomy has also been reported. Referral to a veterinary soft-tissue surgeon is recommended.

NUTRITION/DIET

- Preoperatively, esophagostomy tube (see p. 1267) or gastrostomy tube (see p. 1270) placement may be required to meet nutritional requirements and normalize body condition.
- Postoperatively, the patient is fed canned food in the form of easily swallowed round portions. The diet may be returned to normal over a period of 1 month.

POSSIBLE COMPLICATIONS

Clinical signs can recur due to inadequate muscular excision or fibrosis of the myectomy site. Reoperation may be performed on the contralateral side of the cricopharyngeus muscle if necessary. Surgery with concurrent esophageal dysfunction is relatively contraindicated because it results in recurrent reflux of esophageal contents in the caudal pharynx, and endotracheal aspiration.

PROGNOSIS AND OUTCOME

- The prognosis for cricopharyngeal achalasia is generally good, but poor in cases of concurrent pharyngeal or esophageal dysfunction.
- Recurrence of clinical signs or aspiration pneumonia has been reported in 0 of 6 and 8 of 14 patients in two different studies.

PEARLS & CONSIDERATIONS

- To decrease the risks of anesthesia and surgery, intensively treat undernourishment and/or aspiration pneumonia prior to surgical intervention.
- Seriously consider whether cricopharyngeal myectomy should be done in patients with esophageal motility disorders, as aspiration pneumonia is likely after surgery.
- Closely monitor patients after surgery, and consider reoperation if clinical signs recur.

SUGGESTED READING

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Warnock JJ, Marks SL, Pollard R, Kyles AE, Davidson A: Surgical management of crico-pharyngeal dysphagia in dogs: 14 cases (1989-2001). J Am Vet Med Assoc 223:1462–1468, 2003.

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Cranial Vena Cava Syndrome

BASIC INFORMATION

DEFINITION

Cranial vena cava syndrome is an uncommon sequela to extraluminal compression, invasion, or intraluminal obstruction of the cranial vena cava (CrVC). Obstruction of the CrVC results in pitting edema of the head, neck, and forelimbs.

SYNONYMS

Caval syndrome, precaval syndrome, superior vena caval syndrome

EPIDEMIOLOGY

SPECIES, AGE, SEX

Depends on underlying cause

RISK FACTORS

- Jugular catheters
- Cranial mediastinal neoplasia (e.g., thymoma, lymphoma, carcinoma, aortic body tumors)
- Hypercoagulable conditions (e.g., sepsis, immune-mediated hemolytic anemia, protein-losing nephropathies, corticosteroid excess, neoplasia, pancreatitis)
- Mycoses leading to the formation of granulomas (e.g., blastomycosis, cryptococcosis)
- Transvenous pacemaker implantation

CONTAGION & ZOONOSIS

Fungal granulomas causing CrVC syndrome may be caused by organisms that can also infect humans (*Blastomyces dermatitidis, Cryptococcus neoformans*), but these would be common-source infections, not zoonoses.

GEOGRAPHY AND SEASONALITY

Infectious causes (e.g., blastomycosis) are more prevalent in certain geographic areas.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Head, neck, and forelimb swelling
- Additional clinical signs depend on underlying cause

PHYSICAL EXAM FINDINGS

- Symmetric, nonpainful pitting edema of head, neck, and forelimbs
- Dyspnea, tachypnea, muffled heart/lung sounds (if pleural effusion present)
- Weakness, tachycardia, arrhythmias, muffled heart sounds (if pericardial effusion present)
- ± Jugular venous distension
- ± Engorgement of conjunctival and scleral vessels
- Additional physical exam findings depend on underlying cause.

ETIOLOGY AND PATHOPHYSIOLOGY

- Extraluminal compression, invasion, or intraluminal obstruction of the CrVC causes impaired venous return from the cranial portion of the body. This leads to interstitial fluid accumulation, resulting in edema of the head, neck, and forelimbs.
- The most common causes include mediastinal neoplasia, fungal granulomas, cranial vena caval thrombosis (e.g., secondary to hypercoagulable states, tumor emboli, jugular catheters), and transvenous pacemaker implantation.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The physical exam findings (notably pitting edema of the head and forelimbs) are highly suggestive of the diagnosis. Diagnostic tests such as thoracic radiographs, advanced imaging, cytologic evaluation of masses and effusions, and histopathologic examination of tissue specimens are used in sequential steps to confirm the diagnosis and identify the underlying etiology.

DIFFERENTIAL DIAGNOSIS

For head and neck swelling:

- Angioedema (e.g., vaccine reaction, insect-bite hypersensitivity)
- Generalized peripheral edema (e.g., secondary to hypoalbuminemia, vasculitis, right-sided congestive heart failure)
- Acute blunt trauma to head/neck
- Subcutaneous emphysema
- Lymphangiosarcoma of the head and neck
- Myxedema (e.g., secondary to hypothyroidism)
- Foreign body around neck (e.g., elastic band)
- Salivary mucocele (cervical)
- Jugular vein thrombosis or mass
- Abscessation or cellulitis
- Rattlesnake bite

INITIAL DATABASE

- To help determine underlying cause:
- CBC
- Serum biochemistry profile
- Urinalysis
- Feline leukemia and feline immunodeficiency tests (to help evaluate for the presence of lymphoma in cats)
- Thoracic radiographs (to identify cranial mediastinal masses, pleural and/or pericardial effusion)

ADVANCED OR CONFIRMATORY TESTING

- Thoracic ultrasonography (to visualize emboli or tumor compression/invasion of cranial vena cava)
- Nonselective angiography, venography (to identify CrVC filling defects, localize site of obstruction, highlight collateral circulation)
- CT or MRI
- Echocardiography (to identify pericardial effusion or masses at the level of the terminal CrVC)
- Fine-needle aspiration or biopsy of thoracic masses
- Blastomycosis urine antigen test (for detection and potential monitoring of blastomycosis infections)

TREATMENT

TREATMENT OVERVIEW

Treatment is directed toward removing obstructive lesion from CrVC and treating inciting cause.

ACUTE GENERAL TREATMENT

- Mediastinal masses: depending on tumor type, treatment may include surgery, chemotherapy, or radiation (alone or in combination).
- Fungal granulomas: systemic antifungal drugs (e.g., itraconazole, fluconazole, depending on extent and type of mycosis)
- CrVC thrombosis:
  - Treat underlying cause
  - Remove jugular catheters if present
  - ± Anticoagulants (e.g., heparin): efficacy unproven
  - ± Thrombolytic agents (e.g., streptokinase, tissue plasminogen activator): efficacy controversial; may result in life-threatening hemorrhage
- ± Diuretics (to minimize edema formation): efficacy limited

CHRONIC TREATMENT

Depends on underlying disease

POSSIBLE COMPLICATIONS

Thrombolytic agents may result in life-threatening hemorrhage.

PROGNOSIS AND OUTCOME

- Prognosis depends on severity of underlying illness; presence of CrVC syndrome does not appear to confer a worse prognosis than that of the underlying disorder alone.
- Head, neck, and forelimb edema may abate if CrVC obstruction removed and/or if adequate collateral circulation develops.

PEARLS & CONSIDERATIONS

COMMENTS

- Although the name is similar, heartworm caval syndrome is an entirely different clinical entity involving right-sided heart failure, hemolysis, and hemoglobinuria as a consequence of severe heartworm disease.
- Human medicine offers promising alternatives to the current therapies available in veterinary medicine:
    - Surgical bypass of the CrVC obstruction
    - Endovascular therapy—a combination of:
        - Thrombolytic agents
        - Angioplasty (balloon dilation of obstructed vessel)
        - Stent placement at the level of vascular obstruction
        - ± Anticoagulants

PREVENTION

- Avoid jugular catheters in hypercoagulable patients.
- Consider prophylactic anticoagulant therapy in patients with hypercoagulable disorders.
- If thrombolysis successful, the use of antiplatelet therapy to reduce vascular reocclusion of residual thrombus or endothelial injury is recommended.

SUGGESTED READING

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Cranial Cruciate Ligament Injury

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Partial or complete tearing of the cranial cruciate ligament (CrCL), causing stifle instability; a very common condition in dogs and an uncommon condition in cats.

SYNONYM

Anterior cruciate ligament (ACL) rupture

EPIDEMIOLOGY

SPECIES, AGE, SEX

Seen in dogs, and less frequently in cats, of all ages

GENETICS & BREED PREDISPOSITION

- Dogs: more common in large breeds, especially rottweilers, Labrador retrievers, Newfoundlands, Staffordshire terriers. Genetic predisposition has been demonstrated in Newfoundlands and boxers (so far)
- Cats: not known to be a heritable problem

RISK FACTORS

- Underlying systemic disease: hyperadrenocorticism, autoimmune disease, cutaneous asthenia
- Overweight condition

ASSOCIATED CONDITIONS & DISORDERS

- Patellar instability
- Intercondylar notch stenosis
- Meniscal injury
- Osteoarthritis
- Immune-mediated arthritis

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Partial CrCL rupture
- Complete CrCL rupture
- Avulsion of the insertion of the CrCL: usually occurs in immature dogs
- Injury to the medial meniscus often accompanies CrCL rupture

HISTORY, CHIEF COMPLAINT

- Variable lameness of one or both hind limbs; onset acute or progressive
- Affected hind limb may be held up or off-weighted when animal is standing.
- Lameness may worsen with exercise and improve with rest.

PHYSICAL EXAM FINDINGS

- Unilateral or bilateral hind limb lameness; affected limb may be held up in acute injuries, will be weightbearing with more chronic affliction
- Affected stifles are externally rotated and more flexed than normal when walking.
- Stifle joint effusion and thickening of joint capsule, often most pronounced over medial aspect of proximal tibia (medial

buttress formation)
- Asymmetric sitting position with one stifle abducted
- Cranial drawer sign, cranial tibial thrust (see Initial Database) may or may not be elicited.
- Meniscal clicking may be present during joint manipulation.

ETIOLOGY AND PATHOPHYSIOLOGY

- Biomechanical instability of the stifle joint results from an imbalance of muscular and weight-bearing forces necessary to control the cranial tibial thrust, excessive internal rotation, and hyper-extension of the stifle usually limited by an intact cranial cruciate ligament.
- In dogs, CrCL rupture is usually due to degeneration rather than direct trauma. The cause of this degeneration is unknown: conformation problems, collagen abnormalities, immune disease and low-grade bacterial infection may play a role.
- In cats, direct trauma is usually the cause.

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

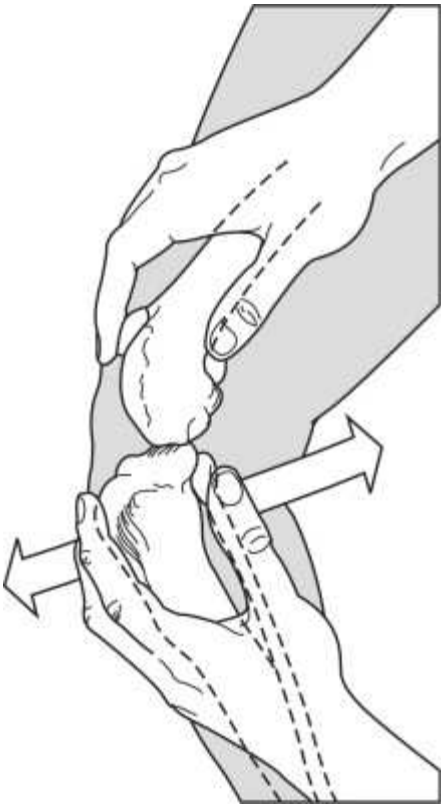
Diagnosis is usually based on presence of the characteristic hindlimb lameness combined with evidence of stifle effusion on physical examination and radiographs. Absence of pain on manipulation, cranial drawer sign, or cranial tibial thrust does *not* rule out cranial cruciate rupture as the source of the lameness.

DIFFERENTIAL DIAGNOSIS

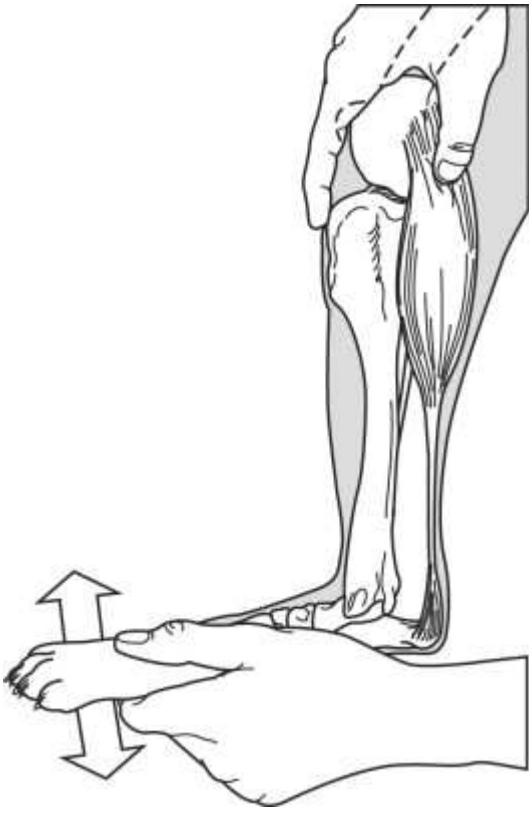
- Patellar luxation
- Lumbosacral disease
- Hip dysplasia or osteoarthritis
- Iliopsoas strain
- Bone/joint neoplasia
- Osteochondrosis of the lateral femoral condyle
- Bacterial, rickettsial, or fungal infection
- Immune-mediated arthritis
- Caudal cruciate or collateral ligament injury (uncommon)
- Long digital extensor tendon avulsion (uncommon)
- Isolated meniscal injury (boxers almost exclusively)

INITIAL DATABASE

- Rickettsial and/or fungal titers (based on geography)
- Palpation of stifle joints for instability; this may require sedation:
    - Cranial drawer sign: manual cranial displacement of tibia relative to femur
    - Cranial tibial translation or thrust: cranial movement of tibial tuberosity as hock is flexed and gastrocnemius muscle contracts.
- Lateral and craniocaudal stifle radiographs
    - Effusion will be evident in almost all patients (except for some small dogs). Degenerative changes are present in cases more chronic than a few weeks. Some animals (especially small dogs and cats) will show cranial displacement of the tibia relative to the femur (static drawer).
    - Measurements such as tibial plateau slope angle are made for planning when an osteotomy technique is chosen for repair.



CRANIAL CRUCIATE LIGAMENT INJURY Palpation of the stifle joint for cranial drawer motion of the tibia relative to the femur with cranial cruciate ligament insufficiency.



CRANIAL CRUCIATE LIGAMENT INJURY Palpation of the stifle joint using tibial compression test for cranial cruciate ligament injury. With cranial cruciate ligament injury, flexion of the hock will cause cranial displacement of the tibia.

ADVANCED OR CONFIRMATORY TESTING

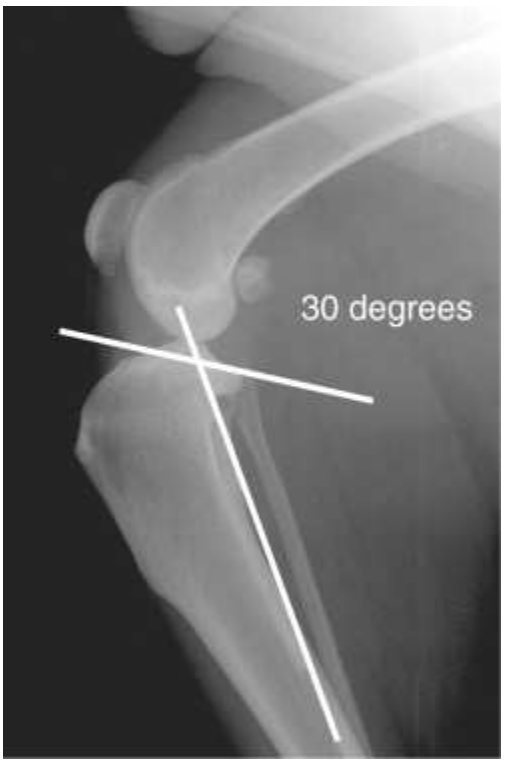
- Arthrocentesis (to eliminate infection, immune-mediated arthropathy as causes)

- Arthroscopy or arthrotomy (the most common way to confirm diagnosis)
- MRI

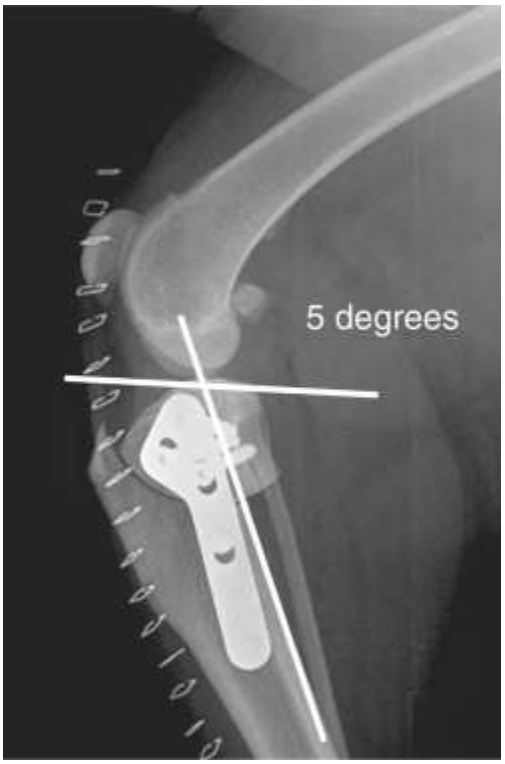
TREATMENT

TREATMENT OVERVIEW

- About 50% of small (<15 kg) dogs and most cats do well with conservative therapy. Only about 20% of larger dogs return to good function with conservative management. By contrast, all of the surgical treatments listed below have a reported success rate of 85% or more for patients of all sizes.
- Surgical management usually involves inspection (and débridement or release if necessary) of menisci, combined with a stabilization technique. Stabilization techniques involve either creation of a structure ("prosthetic ligament") to mimic the function of the CrCL, or osteotomy to change the geometry of the stifle so there is minimal cranial tibial translation when the limb is bearing weight.
- Success rates are similar for prosthetic ligament and osteotomy (TPLO, TTA) repairs. After osteotomy techniques, return to full weightbearing is usually faster and progression of osteoarthritis may be somewhat slower (controversial), however. Cats and small dogs are most commonly treated with prosthetic ligament techniques.



CRANIAL CRUCIATE LIGAMENT INJURY Preoperative radiograph of the stifle of a dog with cranial cruciate ligament rupture. The tibial plateau angle is 30°.



CRANIAL CRUCIATE LIGAMENT INJURY Photograph of the same stifle after tibial plateau leveling osteotomy (TPLO). The tibial plateau angle is satisfactory at 5°.

ACUTE GENERAL TREATMENT

- Medical management:
  - Physical rehabilitation (see Physical Rehabilitation section p. 1329 for details)
    - Controlled leash walks
    - Sit-to-stand exercises
    - Swimming, water treadmill work
  - Nonsteroidal antiinflammatory drugs (NSAIDs):
    - Carprofen, 2 mg/kg PO q 12 h; *or*
    - Etodolac, 10-15 mg/kg PO q 24 h; *or*
    - Deracoxib, 1-2 mg/kg PO q 24 h (may use 3-4 mg/kg PO q 24 h for first 7 days only); *or*
    - Meloxicam, 0.1 mg/kg PO q 24 h; *or*
    - Meclofenamic acid, 1.1 mg/kg PO q 24 h after eating for 5 days maximum; *or*
    - Tepoxalin, 10 mg/kg PO q 24 h (new product, objective data pending)
- Surgical stabilization of the stifle:
  - Intraarticular fascia lata or patellar tendon autogenous graft: limits cranial motion and internal rotation of the tibia.
  - Extracapsular suture stabilization (femoral condyle or fabella to tibia): limits drawer motion and rotation. There are a number of variations on this theme.
  - Fibular head transposition: advances the insertion of the lateral collateral ligament so it can limit cranial drawer and internal rotation.
  - Tibial plateau leveling osteotomy (TPLO): neutralizes cranial tibial thrust by chancing tibial plateau angle from a normal of 20○-26○ to between 5○ and 10○ postoperatively.
  - Tibial tuberocity advancement (TTA): neutralizes cranial tibial thrust by making the pull of the patellar tendon perpendicular to the tibial plateau when the knee is bearing weight.
  - Triple tibial osteotomy (TTO) simultaneously reduces tibial plateau slope and slightly advances the tibial tuberosity, making it something like a hybrid of TPLO and TTA.
  - Pinning or wiring of avulsion injuries to reattach ligament origin or insertion can be done in young dogs with large avulsion fragments.
- Treatment of meniscal injury:
  - Medial meniscectomy (partial or complete)
  - Medial meniscal release (has an effect similar to meniscectomy, sometimes done prophylactically)

CHRONIC TREATMENT

- Management includes the same treatments as in acute cases, but more long-term medical management of osteoarthritis may

be required. Success rates are similar for surgical treatment of acute and chronic cranial cruciate injuries.
    - NSAIDs as listed previously
    - Physical rehabilitation
    - Disease-modifying osteoarthritis agents may be helpful, including:
        - Polysulfated glycosaminoglycan, 5 mg/kg IM once weekly × 4-6 weeks; *or*
        - Pentosan polysulfate, 3 mg/kg SQ once weekly; *or*
        - Oral formulations (glucosamine, chondroitin sulfate, avocado soy unsaponifiables): according to formulation/labeled instructions

NUTRITION/DIET

- Weight control helps alleviate lameness due to osteoarthritis.

POSSIBLE COMPLICATIONS

- Medical management:
    - Gastrointestinal, hepatic, renal, or other systemic reactions from NSAID therapy
    - Continued progression of degenerative joint disease
    - Failure of medical management to control pain
- Surgical management:
    - Failure to stabilize the stifle joint
    - Progression of degenerative joint disease
    - Postoperative meniscal injury:
        - Damage not recognized at surgery
        - Shear forces not neutralized
    - Fracture or implant failure
    - Infection (soft tissue or bone)

RECOMMENDED MONITORING

- Basic laboratory monitoring of patients on NSAID therapy
- Weight loss, exercise levels (rehabilitation), and clinical signs as dictated by the patient
- Radiographic monitoring of healing of osteotomies (usually at 6 and 10 weeks after surgery), and of any repair if clinical signs worsen

PROGNOSIS AND OUTCOME

- Long-term function for patients that have undergone a reconstructive procedure is good. Published assessments of most techniques in the past 25 years describe improvement in 80%-90% of dogs after surgery, regardless of the methodology.
- Postoperative rehabilitation is critical for clinical recovery (see p. 1329).

PEARLS & CONSIDERATIONS

COMMENTS

- Bilateral lameness may be difficult to recognize and is often confused with neurologic disease.
    - A careful orthopedic examination is essential.
- Injury of the contralateral cranial cruciate ligament occurs in 40%-50% of canine patients. No measures have yet been identified to prevent this from occurring.
- Some surgeons recommend surgery for patients (including cats) of any size to ensure optimum function.
- In one arthroscopic study of partial CrCL injury, TPLO stopped the progression of further ligament rupture in six of seven dogs.
- *Editor's note*: Practitioners should consider consultation and referral with an orthopedic surgeon; selection of the “best” procedure continues to be controversial among specialists.

SUGGESTED READING

Dejardin LM: Tibial plateau leveling osteotomy. In Slatter D, editor: Textbook of small animal surgery, ed 3, Philadelphia, 2002, Saunders, pp 2090–2133.

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EDITOR: JOSEPH HARARI

1ST EDITION AUTHORS: JAMES P. BOULET, BARBARA R. GORES

Cough

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

A reflexive, forceful expulsion of air from the lungs and airways

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs and cats of any age and either sex

RISK FACTORS

- Exposure to airborne irritants or allergens
- Contact with other animals (infectious causes)

CONTAGION & ZOONOSIS

- Dogs: infectious tracheobronchitis ("kennel cough"); canine distemper
- Cats: viral rhinotracheitis

ASSOCIATED CONDITIONS & DISORDERS

Vomiting: the "terminal retch" that occurs at the end of a paroxysm of coughing may be misinterpreted as vomiting by clients.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

A useful way to consider the causes of cough, and the way to manage a coughing patient, involves the following categories:

- Purposeful cough. The cough is beneficial in expelling foreign material (e.g., inhaled foreign body) or substances (e.g., pus in pneumonia patients).
- Warning cough. The cough is a respiratory manifestation of a systemic disturbance that may become life threatening (e.g., pulmonary edema from congestive heart failure, pulmonary hemorrhage from anticoagulant rodenticide toxicosis).
- Nuisance cough. The cough is disturbing or distressing to the patient and/or the owner but is not immediately life threatening (e.g., infectious tracheobronchitis/"kennel cough," chronic sterile bronchitis).

HISTORY, CHIEF COMPLAINT

- Character (moist versus dry, soft versus hacking, nocturnal versus diurnal): may offer some insight regarding cause, but much overlap exists between different diseases.
- Dyspnea concurrently: generally indicates a more pressing need for diagnosis and treatment (purposeful and warning categories).
- Exposure to detrimental environment: contagion, inhalation of irritant substances
- Duration of the cough: coughs that have maintained an equal intensity for months or more are commonly associated with disorders in the "nuisance cough" category.

PHYSICAL EXAM FINDINGS

- Dyspnea. See History, Chief Complaint above.
- Inducible cough. A cough that is elicited with application of tracheal pressure may occur with tracheobronchial diseases, with pulmonary parenchymal disease, or in unaffected animals. It does not indicate the anatomic location of the underlying problem. Tracheal pressure may be useful for confirmatory purposes if the owner is unsure whether the clinical sign observed at home is a cough.
- Pulmonary auscultation. Possible abnormalities include crackles/rales (interstitial fibrosing lung disease, pulmonary edema,

others), loud bronchovesicular sounds (pulmonary edema, airway disease, others), wheezes (airway disease), and decreased lung sounds (pleural effusion, pneumothorax, intrathoracic mass).
- Cardiac auscultation. The presence of a heart murmur in a coughing dog raises the possibility of pulmonary edema (see p. 468). However, unrelated cardiac and respiratory diseases often coexist.
- A complete physical examination is indicated because many disorders produce cough as only one manifestation of the underlying disease.

ETIOLOGY AND PATHOPHYSIOLOGY

- Abnormal presence of gases, substances, or material on the respiratory epithelium triggers afferent vagal impulses to the brainstem.
- Efferent impulses cause a sequence of glottis closure, abdominal and thoracic muscle contraction, and sudden glottis opening, causing the burst of air flow that is the cough.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The first step is to confirm if the chief complaint is indeed coughing if the owner is unsure; tracheal pressure to elicit a cough or videotaping at home can help. With a confirmed cough, history, physical exam, and thoracic radiographs are the cornerstones of first-line diagnostic evaluation.

DIFFERENTIAL DIAGNOSIS

Causes of cough:

- Tracheobronchitis
- Collapsing trachea (dogs only)
- Chronic sterile bronchitis
- Asthma/allergic airway disease (cats)
- Bronchiectasis
- Allergic bronchitis
- Tracheal neoplasia
- Tracheal/bronchial foreign body
- Pneumonia (aspiration, bacterial, fungal, protozoal)
- Cardiogenic pulmonary edema (dogs only)
- Noncardiogenic pulmonary edema/acute respiratory distress syndrome
- Eosinophilic bronchopneumopathy
- Pulmonary hemorrhage
- Heartworm disease
- Pulmonary thromboembolism
- Pulmonary neoplasia
- Lungworms
- Tracheobronchial lymphadenopathy
- Left atrial enlargement
- Mediastinal mass

INITIAL DATABASE

- Thoracic radiographs and lateral cervical radiograph:
  - Radiographs are the initial diagnostic test of choice for coughing patients.
  - Indicated in any patient with signs of systemic illness, any patient with a cough of >10 days' duration, and any patient whose owner is concerned and wishes more than an exam-room evaluation
- Fecal analysis (Baermann) if lung-worms are locally endemic
- Heartworm antigen test in endemic areas
- Routine medical evaluation, including CBC, serum biochemistry profile, and urinalysis if patient shows systemic signs
- Prothrombin time, partial thromboplastin time, platelet count if the patient roams outdoors or could otherwise have been exposed to anticoagulant rodenticide

ADVANCED OR CONFIRMATORY TESTING

Based on specifics of case as assessed with history, presenting signs, physical exam findings, and initial database results

TREATMENT

TREATMENT OVERVIEW

- Correction/cure of inciting disorder when possible
- Palliation of cough if underlying cause cannot be eliminated

ACUTE AND CHRONIC TREATMENT

- Dependent on underlying cause:
  - Purposeful cough: primary respiratory lesion requires correction (e.g., pneumonia treatment, foreign body removal, lung lobectomy) and treatments that increase the efficacy of the cough (e.g., nebulization and coupage). Cough suppression is contraindicated.
  - Warning cough: systemic disorder must be identified and addressed promptly. (Cardiogenic pulmonary edema: diuretics. Pulmonary hemorrhage from anticoagulant toxicity: plasma transfusion, vitamin K1 replacement.) Treatments to increase the efficacy of the cough, such as nebulization and coupage, or treatments aimed at decreasing the cough (cough suppressants) are contraindicated.
  - Nuisance cough: avoidance of triggers (e.g., allergens, dusts) and cough suppression. Treatment of complicating factors if they occur (e.g., infection).
- Cough suppressants (e.g., butorphanol, 0.25-1 mg/kg PO q 8-24 has needed; or hydrocodone, 0.25 mg/kg PO q 6-24 h as needed; or codeine 0.5-2 mg/kg PO q 6-12 h as needed):
  - Only used when a sterile, uncomplicated process is responsible for the cough and the patient is systemically well. Examples: collapsing trachea, chronic sterile bronchitis, uncomplicated allergic airway disease.
- Empirical antibiotics or corticosteroids are not recommended in the absence of a diagnosis for the cause of the cough (minimum: completion of the initial database).

RECOMMENDED MONITORING

- Respiratory effort
- Resolution of cough is expected in 7-10 days, with no worsening or new clinical signs of illness, in cases of benign, self-contained processes such as infectious tracheobronchitis. Failure to self-resolve may indicate a more complex cause and warrants further evaluation.

PROGNOSIS AND OUTCOME

Based on cause:

- Purposeful cough: prognosis fair to good if underlying cause can be controlled (eradication of pneumonia, removal of foreign body)
- Warning cough: short-term prognosis guarded. Long-term prognosis variable, based on response to acute treatment and underlying cause.
- Nuisance cough: short-term prognosis generally good, long-term prognosis fair (e.g., with collapsing trachea patients responding well to treatment) to good (e.g., patients with infectious tracheobronchitis)

PEARLS & CONSIDERATIONS

COMMENTS

- Cough is a clinical sign, not a disease. Optimal management must involve an accurate diagnosis of the underlying cause.
- Cigarette smoke inhalation and obesity are common but reversible complicating factors in patients with chronic cough.

SUGGESTED READING

Anderson-Wessberg K: Coughing. In Ettinger SJ, Feldman EC, editors: Textbook of veterinary internal medicine, ed 7, St Louis, 2010, Saunders Elsevier, pp 250–253.

AUTHOR & EDITOR: ETIENNE CÔTÉ

Coronaviral Enteritis

BASIC INFORMATION

DEFINITION

Infectious intestinal disease that causes a generally mild diarrhea in dogs and cats. Coronaviral infections causing feline infectious peritonitis are discussed in greater detail on .

SYNONYMS

CCV (canine coronavirus), FECV (feline enteric coronavirus)

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs: neonatal puppies are more severely affected. Cats: virus virtually ubiquitous in the cat population; however, clinical disease is more common in young kittens in catteries and shelters.

RISK FACTORS

Dogs: infection is prevalent in animal shelters and breeding farms (dense populations and concurrent infections). Cats: multicat households (more than five cats) or catteries.

CONTAGION & ZOONOSIS

Dogs: CCV is highly contagious and spreads rapidly through groups of susceptible dogs (dog to dog). Cats: FECV is highly contagious and spreads rapidly through multicat households (cat to cat). Transmission is by the fecal-oral route. CCV and FECV are not known to infect people.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Dogs:

- Subclinical in adult dogs
- Diarrhea and vomiting (neonatal puppies)

Cats:

- Subclinical in adult cats
- Mild to moderately severe diarrhea in kittens
- Mutation to feline infectious peritonitis virus resulting in multisystemic disease (see p. 383)

HISTORY, CHIEF COMPLAINT

Some or all may be present:

- Mild to moderately severe diarrhea
- Blood in feces (infrequent)
- Vomiting is more common in dogs.
- Lethargy and inappetence
- Weight loss

PHYSICAL EXAM FINDINGS

- Dehydration; degree depends on severity of the diarrhea

- Occasionally concurrent ocular and nasal discharge, or weight loss in chronically infected kittens

ETIOLOGY AND PATHOPHYSIOLOGY

- Member of the virus family Coronaviridae; single-stranded RNA virus
- Dogs and cats: virus infects epithelial cells in the tips of small-intestine villi, causing a malabsorptive diarrhea. The virus remains infective for 2-3 days at room temperature (several days longer at temperatures just above freezing) and may be transmitted to other animals via infected litterboxes or fomites.
- Cats only: RNA mutations of FECV result in the formation of a new virus (feline infectious peritonitis [FIP] variant) that is able to enter and replicate within feline macrophages (see p. 383).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected in dogs or cats with generally mild, self-limiting diarrhea. Most cases require little if any treatment, so diagnostic testing is not necessary for confirming the diagnosis. Rather, tests are indicated to rule out other more serious disorders that initially mimic (or coexist with) coronavirus infection.

DIFFERENTIAL DIAGNOSIS

- Intestinal disease caused by enteric bacteria (*Campylobacter*, salmonellosis), protozoa (coccidiosis), or other viruses (i.e., canine parvoviral enteritis, feline panleukopenia-associated enteritis)
- Dietary indiscretion (dogs)
- Parasites (both dogs and cats)
- Dietary intolerance (cats)

INITIAL DATABASE

- CBC, biochemistry panel, urinalysis: nonspecific changes
  - Severe diarrhea can result in marked dehydration and electrolyte abnormalities.
- Fecal testing for parasites and protozoa

ADVANCED OR CONFIRMATORY TESTING

Generally not performed, since corona-viral enteritis is usually self-limiting (exception: FIP) and even in severe cases, responsive to supportive care. *Dogs:*

- Detection of CCV in fresh feces by electron microscopy (false-negative findings possible)
- Virus isolation (however, CCV does not grow well).
- Reverse transcriptase PCR has been developed to detect CCV in fecal specimens (not commercially available).
- Serologic evaluation: positive titers only confirm exposure to CCV, not necessarily active infection.

Cats:

- Serologic evaluation (indirect immunofluorescent antibody, ELISA)
  - Does not differentiate FECV that causes isolated enteritis from FECV that causes FIP
  - Does not correlate with severity of disease
  - Positive titers only confirm exposure to FECV, not necessarily active infection.
  - In multicat (more than six cats) households, virtually all cats are seropositive.
- Reverse transcriptase PCR has been developed to detect FECV in fecal specimens.
  - Does not reliably differentiate FECV that causes isolated enteritis from FECV that causes FIP

TREATMENT

TREATMENT OVERVIEW

Treatment, if any is required, is primarily supportive during the time needed for the disease to run its natural course.

ACUTE GENERAL TREATMENT

- Parenteral fluids to maintain fluid and electrolyte balance
- Broad-spectrum antimicrobial agents to treat secondary bacterial infections are rarely indicated.
- Good nursing care and hygiene

POSSIBLE COMPLICATIONS

Dogs:

- Clinical course (typically 7-10 days) may be longer and more severe in dogs that develop secondary complications or infection.
- Dehydration, acidosis, shock
- Concurrent canine parvovirus or parasitic infections

Cats:

- In immunocompromised kittens or cats, the virus may persist, resulting in chronic diarrhea or vomiting (months).
- Enteric coronavirus can mutate into feline infectious peritonitis virus. Monitor the affected cat and others in contact with it for signs of FIP (e.g., abdominal distension, fever, weight loss, neurologic signs, and icterus). However, the occurrence of coronaviral enteritis in an individual cat is not predictive of FIP.

RECOMMENDED MONITORING

Response to therapy

PROGNOSIS AND OUTCOME

- Dogs: good; neonatal puppies with concurrent parvovirus and coronavirus infections have a more guarded prognosis.
- Cats: generally good; guarded to poor in cats in whom FECV mutates and causes FIP

PEARLS & CONSIDERATIONS

COMMENTS

- Clinical disease is considered infrequent compared with other viral enteropathies.
- Dogs: CCV vaccines are not considered core vaccines but should be reserved for animals in which the risk of exposure may be higher (dense, stressful environments).
- Cats:
    - Inapparent infection is common in normal cats.
    - FECV-associated enteritis does not predispose a cat to development of FIP.

CLIENT EDUCATION

Reducing the number of cats per household (especially kittens less than 12 months old) and keeping potentially FECV-contaminated surfaces clean (e.g., litterboxes) can reduce population loads of FECV and thus also reduce the risk of FIP.

RECOMMENDED READING

Pederson NC, et al: Common virus infection in cats, before and after being placed in shelters, with emphasis on feline enteric coro-navirus. J Feline Med Surg 6(2):83–88, 2004.

Sanchez-Morgado JM, et al: Molecular characterization of a virulent canine coronavirus BG strain. Virus Res 104(1):27–31, 2004.

AUTHOR: BRANDY PORTERPAN

EDITOR: DEBRA L. ZORAN

Cornification Disorders

Additional Images Available on Website

BASIC INFORMATION

DEFINITION

A well-recognized class of scaling or greasy skin disorders resulting from primary (usually hereditary) or secondary (acquired) defects in epidermal maturation, desquamation, or sebum production. Many disorders were formerly grouped under the heading *seborrhea*, but this term was nonspecific and inaccurate and is now obsolete.

SYNONYMS

- Keratinization defects/disorders
- Keratoseborrheic disorders

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Primary (hereditary) causes: early in life for many conditions
- Secondary (acquired): any age; usually adult animals

GENETICS & BREED PREDISPOSITION

- Primary idiopathic seborrhea: cocker spaniel, West Highland white terrier, basset hound, shar-pei, dachshund, Doberman pinscher, English springer spaniel, German shepherd, Irish setter, Labrador retriever
- Primary hereditary seborrhea oleosa: Persian, Himalayan, and exotic short hair cats
- Vitamin A–responsive dermatosis: cocker spaniel, Labrador retriever, miniature schnauzer
- Zinc-responsive dermatosis: Alaskan malamute, Siberian husky, Samoyed
- Lethal acrodermatitis: bull terrier
- Epidermal dysplasia: West Highland white terrier
- Sebaceous adenitis (see p. 1007): Akita, Samoyed, standard poodle, and many other breeds have been reported to have this condition.
- Ichthyosis: golden retriever, Norfolk terrier

CONTAGION & ZOONOSIS

Most are not contagious, but parasitic and fungal etiologies have contagious and zoonotic potential.

GEOGRAPHY AND SEASONALITY

Scaling (formerly called seborrhea sicca) is more common in the winter (low environmental humidity).

ASSOCIATED CONDITIONS & DISORDERS

Primary cornification disorders may be associated with ceruminous otitis externa.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Primary cornification disorders (usually hereditary and incurable) or secondary (acquired, usually curable)
- Generalized or localized

HISTORY, CHIEF COMPLAINT

Owners generally present pets for evaluation of an unpleasant-appearing hair coat or coat with a foul odor. Specific complaints may include a generalized waxy or scaly coat condition, often associated with a rancid odor. Pruritus is of variable intensity, depending on presence of parasites, dry skin, or secondary bacterial or yeast infection; however, scaling may be an incidental finding in some

animals.

PHYSICAL EXAM FINDINGS

- Primary cornification disorders: varying degrees of alopecia and dry scale that may be focal, multifocal, or generalized over the trunk. Animals may present with large hyperkeratotic patches of adherent scale. Follicular casts (waxy debris surrounding hair shafts), fronds (clumps of hairs stuck together like a paint brush), or severe “dandruff” with large flakes may be noted.
- Localized cornification disorders:
  - Nasal hyperkeratosis of the Labrador retriever: restricted to the nasal planum
  - Nasodigital hyperkeratosis: restricted to nasal planum and digital pads
  - Ear margin dermatosis: alopecia and scaling of distal pinnal margins, possibly associated with fissures
  - Feline acne: comedones on the chin +/− lips; papules, pustules, erosion, crust and pruritus if secondarily infected
- Secondary cornification disorders: general physical findings depend on underlying etiology or vary with underlying etiology. Cutaneous findings include a dull (or waxy) coat with various combinations of alopecia, scaling, crusting, collarettes, and excoriations secondary to self-trauma and pyoderma.

ETIOLOGY AND PATHOPHYSIOLOGY

- Cornification encompasses all the processes that lead to the formation of the stratum corneum. This includes keratinization and formation of the lipid-rich intercellular domain that binds corneocytes to maintain a relatively impermeable barrier.
- Disorders of cornification are due to a defective cornification process or excessive proliferation and/or defective desquamation (retention hyperkeratosis). Therefore, any alteration in epidermal turnover times, maturation processes, and/or desquamation or trans epidermal water loss lead to scaling.
- Other considerations include abnormal apocrine or sebaceous glandular secretions (either in volume or quality).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Scale formation is a common response of the skin to any insult. It is critical to evaluate the patient for underlying causes—in particular, the roles parasite and microbial dermatitis may be playing if any—before pursuing other etiologies.

DIFFERENTIAL DIAGNOSIS

- Secondary cornification disorders; underlying causes include:
  - Microbial: pyoderma, *Malassezia*, dermatophytosis, leishmaniasis
  - Parasitic: flea infestation, cheyletiellosis, sarcoptic mange, pediculosis, and demodicosis (including *Demodex injai*, the long-bodied *Demodex* mite that has been associated with a greasy seborrheic dermatosis, especially in adult terriers)
  - Endocrinopathy: hypothyroidism, hyperadrenocorticism, sex hormone imbalance (e.g., Sertoli cell tumor)
  - Allergic: dermatologic adverse food reaction (food allergy), atopic dermatitis
  - Management deficiencies: low environmental humidity, inappropriate topical therapy or frequency, nutritionally inadequate diet (especially if high in phytates and fiber, low in fatty acids)
  - Metabolic disease (especially liver disease)
  - Immune-mediated disease: pemphigus foliaceus, systemic lupus erythematosus, adverse drug reaction
  - Neoplasia: Cutaneous epitheliotropic lymphoma, exfoliative dermatitis associated with thymoma in cats
- Primary cornification disorders: usually genetically determined; may be multi-focal and generalized or localized:
  - Multifocal and generalized:
    - Idiopathic primary seborrhea (dogs)
    - Hereditary seborrhea oleosa (cats)
    - Vitamin A–responsive dermatosis
    - Zinc-responsive dermatosis
    - Sebaceous adenitis
    - Epidermal dysplasia
    - Schnauzer comedo syndrome
    - Canine ichthyosis
  - Localized:
    - Nasal parakeratosis of the Labrador retriever (autosomal recessive)
    - Footpad hyperkeratosis in dogues de Bordeaux and Irish terrier
    - Feline acne
    - Stud tail
    - Ear margin dermatosis

INITIAL DATABASE

- Comprehensive evaluation for ectoparasites (skin scrapings, flea combing, acetate tape preparations, fecal evaluation, ectoparasiticide response trial)
- Skin cytologic examination (to rule out bacterial and yeast involvement)
- Fungal culture (dermatophytosis)
- CBC, serum biochemical profile, urinalysis (as appropriate, to look for evidence of underlying disease)

ADVANCED OR CONFIRMATORY TESTING

- Skin biopsy: useful for many disorders once infectious and parasitic causes have been ruled out
- Elimination diet trial to rule out food allergy (if pruritic)
- Intradermal and serum allergy testing for atopic dermatitis (if pruritic)
- Response to dietary management (if poor-quality diet)
- Thyroid function testing
- Adrenal function testing

TREATMENT

TREATMENT OVERVIEW

- The goal of treatment is to address the underlying etiology specifically if possible. In primary conditions, it is important to control secondary microbial dermatitis while controlling the amount of scale produced.

ACUTE GENERAL TREATMENT

- Systemic antibiotics, such as cephalexin, 22-30 mg/kg PO q 12 h for at least 2 weeks past resolution of clinical signs or until improvement plateaus (minimum of 4 weeks), if a bacterial component is suspected. Some animals require chronic treatment.
- Essential fatty acid (EFA) oral supplementation (omega-3 and omega-6); rarely provides complete control of scaling but may be beneficial as adjunctive therapy
- Systemic and topical antifungal treatment as needed (see *Malassezia* dermatitis, p. 682; Dermatophytosis,)
- Topical therapy: clipping of hair coat may benefit topical therapy:
    - Antiseborrheic shampoos contain keratolytic and/or keratoplastic compounds and are used initially twice weekly. Good choices of ingredients for dry, scaly coats include sulfur and salicylic acid; decrease frequency as needed.
    - Topical antiseborrheic products containing phytosphingosine may be of benefit.
    - Greasy, scaly skin in dogs can be degreased using products containing benzoyl peroxide, or selenium sulfide. These products should always be followed with a conditioner. Note: Shampoos containing benzoyl peroxide are drying and will bleach fabric.
    - Mild dry scaling may respond to moisturizing or hypoallergenic shampoos. Conditioners containing lipids or humectants (agents that help the skin to retain moisture) are beneficial.

CORNIFICATION DISORDERS Extensive erythroderma and scaling (exfoliative erythroderma) in a dog with epitheliotropic lymphoma.

(Copyright Dr. Manon Paradis.)

CORNIFICATION DISORDERS Primary seborrhea oleosa in a Himalayan cat. Note the greasy haircoat especially apparent across the ventrum.

(Copyright Dr. Manon Paradis.)

CHRONIC TREATMENT

- Generalized disease
  - Primary idiopathic seborrhea: topical therapy as already described; EFA supplementation; antibiotics administered as already described. Consider retinoids; acitretin (Soriatane), 0.5-1 mg/kg PO q 24 h; or cyclosporine, 5-10 mg/kg PO q 12-24 h.
  - Vitamin A–responsive dermatosis: topical therapy and antibiotics as already described; vitamin A 625-800 IU/kg PO q 24 h; usually 10,000 IU PO daily, lifelong, for the average cocker spaniel. Improvement is noted by 3 weeks, with remission in 8-10 weeks.
  - Zinc-responsive dermatosis: zinc supplementation is recommended at 1-3 mg/kg elemental zinc PO q 24 h (see p. 1189).
  - Epidermal dysplasia: address any bacterial, yeast, parasitic, atopic, and hypersensitivity disorders. Bathe the animal frequently with keratolytic and keratoplastic shampoos.

- Schnauzer comedo syndrome: benzoyl peroxide shampoos help the condition via follicular flushing. Systemic antibiotics (as already described) to control bacterial folliculitis. In some cases, retinoids such as isotretinoin (Accutane), 1-2 mg/kg PO q 24 h, may be helpful but can be costly. Wean to alternate day therapy after 4 weeks if a favorable response is noted.
- Canine ichthyosis: Antiseborrheic shampoos and a topical spray conditioner containing propylene glycol and humectants can be useful. Try isotretinoin (Accutane), 1-2 mg/kg PO q 24 h for 8-12 weeks, decreasing to alternate-day therapy if effective) in more severe cases
- Sebaceous adenitis (see p. 1007):

- Localized disease
  - Feline acne (see p. 20)
  - Ear margin dermatosis: local use of an antiseborrheic shampoo. If inflammation is severe, topical glucocorticoid such as 0.5%-1% hydrocortisone may reduce inflammation.
  - Nasal and digital hyperkeratosis: moisturize affected area with water or wet dressings, and then apply petrolatum jelly. More severely affected animals may benefit from topical application of an ointment containing salicylic acid and urea, or 50%-75% propylene glycol, or 0.025 or 0.01% tretinoin gel (Retin-A).

DRUG INTERACTIONS

Cyclosporine: Concurrent use of cyclosporine with other *P*-glycoprotein inhibitors or substrates can increase blood cyclosporine levels. This may be beneficial (e.g., lowers the dose of cyclosporine required by half when administered with standard doses of ketoconazole) but can also increase the potential toxicity.

POSSIBLE COMPLICATIONS

- High fatty acid treatment may increase the potential for gastrointestinal (GI) disturbance or pancreatitis.
- Retinoids: keratoconjunctivitis sicca, conjunctivitis, pruritus, hyperactivity, stiffness, mucocutaneous junction erythema, vomiting, diarrhea, teratogenicity, elevated liver enzymes
- Cyclosporine: diarrhea, vomiting, anorexia, gingival hyperplasia, gingivitis, renal effects, hypertension; monitor animals for tumors.

RECOMMENDED MONITORING

- Vitamin A, retinoids: monitor liver enzymes and tear production.
- Cyclosporine: physical examination (tumor, infection, gingival hyperplasia), urea, creatinine, urinalysis, and liver enzymes; blood pressure. Check trough serum cyclosporine levels if adverse reactions are noted or if there is a poor clinical response (see p. 1471).

PROGNOSIS AND OUTCOME

Primary causes often require lifelong therapy; secondary syndromes usually recover with correction or control of underlying etiology.

PEARLS & CONSIDERATIONS

COMMENTS

- Control secondary microbial dermatitis, and evaluate thoroughly for other underlying secondary etiologies before diagnosing a primary seborrheic syndrome.
- The term *seborrhea* as a diagnosis should be limited to the breed-specific diseases (e.g., idiopathic primary seborrhea of cocker spaniel, primary hereditary seborrhea oleosa of Persian cats). Use other descriptive terms such as *scaling, exfoliation, crusting, greasiness, malodor* to characterize skin changes, rather than the nonspecific term, *seborrhea*.

PREVENTION

Animals affected with primary (genetically determined) cornification disorders should not be used for breeding.

CLIENT EDUCATION

Concept of control versus cure

SUGGESTED READING

Paradis M: Primary hereditary seborrhea oleosa. In August JR, editor: Consultation in feline medicine, ed 4, Philadelphia, 2001, Churchill-Livingstone, pp 202–207.

AUTHOR: STEPHEN WAISGLASS

EDITOR: MANON PARADIS

Corneal/Scleral Trauma

BASIC INFORMATION

DEFINITION

Ocular injury secondary to blunt or sharp trauma. *Penetrating* infers partial-thickness injury; *perforating* infers full-thickness injury. *Simple* wounds involve only cornea or sclera; *complicated* wounds involve multiple ocular structures.

EPIDEMIOLOGY

SPECIES, AGE, SEX

Any species, age, or sex

RISK FACTORS

- Young, active animals
- Hunting animals
- Interanimal fighting
- Dog's head out the window while car is in motion
- Existing visual impairment may predispose

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Running through dense or dry vegetation just before onset of clinical signs
- Owner may or may not observe trauma or causal event.
- Acute onset of any or all of the following:
  - Blepharospasm
  - Ocular discharge
  - Blood or fluid coming from eye
  - Swelling around the eye (e.g., eyelids; conjunctiva)
  - Cloudy eye

PHYSICAL EXAM FINDINGS

- Signs of pain on ophthalmic examination (see p. 1313) manifested by blepharospasm and resistance to ophthalmic examination.
- Linear, V-shaped, or stellate corneal lesion of acute onset accompanied by any or all of the following:
  - Hyphema (see p. 571) and/or sub-conjunctival hemorrhage
  - Corneal edema with or without cellular infiltrate
  - Uveal prolapse: appears as pigmented structure in damaged cornea or sclera; associated with:
    - Dyscoric/misshapen pupil
    - Hyphema (see p. 571)
  - Foreign body embedded in cornea or perforating cornea
  - Signs of uveitis, particularly with perforating trauma (see p. 1151)
  - Fibrin in cornea may fill perforation; light brown in color, may be associated with blood.
  - Yellowish/whitish lens material in anterior chamber and cataract (see p. 181) if lens involved
  - Shallow anterior chamber if wound actively leaking
- Thorough examination of the entire conjunctival sac is necessary to identify any retained foreign material. Sedation, general anesthesia, or referral may be required in difficult cases or if this procedure is unfamiliar to the practitioner.
- Subconjunctival hemorrhage and hyphema should alert clinician to possibility of posterior scleral rupture if no anterior segment lesions are present, particularly if accompanied by very low intraocular pressure (i.e., <10 mm Hg).

ETIOLOGY AND PATHOPHYSIOLOGY

- Variable; usually traumatic (sharp or blunt) in origin

- Foreign body may be retained in laceration.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

History and preliminary examination suggest the diagnosis; an ophthalmic exam helps define whether the cornea and/or sclera has/have been damaged. If so, the exam should also determine whether lesion is partial or full thickness (affects prognosis).

DIFFERENTIAL DIAGNOSIS

If traumatic event not witnessed, consider other causes:

- Corneal ulceration
- Uveitis
- Hyphema

INITIAL DATABASE

- Assess vision: menace response, dazzle reflex, direct and consensual pupillary light reflexes (if deficient, see Blindness, p. 141)
- Cytologic study and aerobic culture and sensitivity of wound
- CBC, serum biochemistry profile, urinalysis for preanesthetic purposes if surgery necessary

ADVANCED OR CONFIRMATORY TESTING

- Consider ocular ultrasound exam to determine extent of intraocular involvement, presence of intraocular foreign body, or posterior globe rupture.
- Orbital radiographs or CT to determine presence or path of foreign body if suspected
- Seidel test to determine if cornea or scleral wound is sealed: apply dry fluorescein strip carefully to surface of wound to cover surface with stain; leaking aqueous will appear as a green rivulet.

TREATMENT

TREATMENT OVERVIEW

Goals of treatment are to:

- Remove foreign bodies if present.
- Repair lacerations that penetrate >50% of the thickness of the corneal stroma or perforate the cornea or sclera.
- Eliminate infection.
- Control intraocular inflammation.

ACUTE GENERAL TREATMENT

- Do not put pressure on the globe until the possibility of rupture is eliminated.
- Elizabethan collar placement to prevent self-trauma
- Small, nonperforating or very small sealed perforating wounds without uveal prolapse, consider conservative therapy:
  - Topical antibiotic solution (e.g., neomycin/polymyxin/gramicidin, gentamicin, or ciprofloxacin) q 6 h
  - Add broad-spectrum systemic antibiotics if perforating (e.g., amoxicillinclavulanate, 13.75 mg/kg PO q 12 h; base long-term choice on culture and sensitivity).
  - Systemic antiinflammatory therapy with either nonsteroidal antiinflammatories (e.g., meloxicam, 0.1 mg/kg PO q 24 h; or carprofen, 2 mg/kg PO q 12 h) or antiinflammatory doses of prednisone (e.g., 0.5-1 mg/kg PO q 24 h)
  - Topical atropine 1% solution q 6-24 h if significant uveitis present (see p. 1151).
- Perforating or deep, large, or gaping penetrating wounds and wounds with uveal prolapse require primary surgical repair (referable procedure) involving:
  - Replacement of viable uveal tissue or resection of nonviable uveal tissue
  - Irrigation and reinflation of anterior chamber
  - Repair of cornea with appropriate-size suture material (8-0 to 10-0)
  - Careful inspection of lens; if lens rupture noted, lens should be removed by phacoemulsification.

CHRONIC TREATMENT

- Monitor and treat for uveitis and wound dehiscence.
- Consider changing antibiotics if indicated by culture and sensitivity results.

DRUG INTERACTIONS

Do not use topical ophthalmic ointments if globe rupture is suspected.

POSSIBLE COMPLICATIONS

- Retinal Detachment, p. 985
- Cataracts, p. 181
- Chronic Uveitis, p. 1151
- Glaucoma, p. 448
- Endophthalmitis (inflammation of the uveal tract and anterior and posterior compartments of the eye)
- Loss of vision and eye
- Cats may develop posttraumatic ocular sarcomas years after original injury, particularly if lens involved (see p. 620).

RECOMMENDED MONITORING

- Reevaluate in 24-48 hours to ensure wounds are sealed, inflammation is improving, and there are no signs of infection.
- Frequency of examination then depends on response to therapy.

PROGNOSIS AND OUTCOME

- Intuitively, small, shallow penetrating wounds of the cornea or lacerations involving only the cornea have a good prognosis, whereas complicated, perforating wounds with uveal and/or lens involvement have a poorer prognosis for vision.
- Posterior wounds involving sclera or sclera and uvea have a grave prognosis for vision.
- Blunt trauma usually has a grave prognosis for vision, particularly if extensive hyphema is present.
- Negative menace response and negative dazzle and pupillary light reflexes at initial examination of a patient with corneal or scleral trauma indicate grave prognosis for vision.

PEARLS & CONSIDERATIONS

COMMENTS

- Consider sedation to keep patient calm and prevent self-trauma.
- Elizabethan collar to prevent self-trauma

PREVENTION

Animals should be monitored when introduced to new environment with other animals.

CLIENT EDUCATION

Discuss the possibility of long-term complications that could lead to loss of vision and loss of an eye.

SUGGESTED READING

Miller PE: Ocular emergencies. In Maggs DJ, Miller PE, Ofri R, editors: Slatter' s fundamentals of veterinary ophthalmology, ed 4, Philadelphia, 2008, WB Saunders, p 419.

AUTHOR: ELLISON BENTLEY

EDITOR: CHERYL L. CULLEN

Corneal Vascularization

BASIC INFORMATION

DEFINITION

The presence of blood vessels in or on the cornea

SYNONYMS

Corneal neovascularization, vascularized keratitis

EPIDEMIOLOGY

SPECIES, AGE, SEX

Varies depending on underlying cause

ASSOCIATED CONDITIONS & DISORDERS

Corneal ulceration, irritation, desiccation, uveitis, episcleritis, or scleritis

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

Some or all may be present:

- History:
  - Ocular trauma
  - Chronic ophthalmic disorder (e.g., keratoconjunctivitis sicca, indolent corneal ulcer, others)
- Chief complaint:
  - Red discoloration of the eye
  - Ocular discharge
  - Signs of ocular pain, manifesting as behavior change, blepharospasm

PHYSICAL EXAM FINDINGS

- Focal to diffuse red discoloration of the corneal surface or stroma
- New corneal vessels enter stroma at the limbus and may be small:
  - May give the affected cornea a reddish haze
  - Are leaky and cause surrounding corneal edema (bluish haze)
  - May be missed altogether owing to a cursory exam
- Other findings will vary depending on the cause.

ETIOLOGY AND PATHOPHYSIOLOGY

Blood vessel ingrowth occurs:

- As a response to injury of the corneal epithelium or stroma as a normal component of healing
  - Neutrophils, which enter the cornea from the tear film and the limbus, are important sources for angioblast and fibroblast growth factors.
  - There is a 3- to 4-day delay before the ingrowth of corneal blood vessels.
  - Ingrowth then occurs at a rate of approximately 1 mm/d.
- As part of an immune-mediated inflammatory response
- Secondary to disease of adjacent ocular tissues, including uveitis, episcleritis, scleritis, glaucoma, and orbital disease

DIAGNOSIS

DIAGNOSTIC OVERVIEW

- The diagnosis is made on careful visual inspection of the corneal surface. Important features for pinpointing the underlying cause and treatment approach include the location and pattern of vascularization, and evaluation for other concurrent ocular disease.

DIFFERENTIAL DIAGNOSIS

- Corneal injury or inflammation:
  - Corneal ulceration
  - Chemical irritation
  - Mechanical irritation:
    - Distichiasis/ectopic cilia/trichiasis
    - Entropion
  - Exposure:
    - Large palpebral fissure
    - Lagophthalmos (incomplete closure of the eyelids)
    - Ectropion
    - Buphthalmos (chronic glaucoma)
    - Exophthalmos
  - Neuroparalytic keratitis (cranial nerve VII lesion)
  - Neurotrophic keratitis (cranial nerve V lesion)
  - Keratoconjunctivitis sicca
  - Qualitative tear film abnormalities
  - Chronic superficial keratitis (CSK/pannus) (dogs)
  - Proliferative keratoconjunctivitis (cats)
  - Corneal degeneration
- Adjacent ocular disease:
  - Uveitis
  - Episcleritis/scleritis
  - Orbital disease
  - Glaucoma

INITIAL DATABASE

- Neuroophthalmic examination, : evaluate palpebral reflexes (cranial nerves V and VII) and completeness of eyelid closure.
- Schirmer tear test: values <10 mm/min and clinical signs consistent with keratoconjunctivitis (KCS)
- Tear film break-up time: values <10 seconds are suggestive of qualitative tear film abnormalities.
- Fluorescein staining: positive in corneal ulceration
- Tonometry: elevated intraocular pressure (>30 mm Hg) in glaucoma, or reduced (<10 mm Hg) in cases of uveitis
- Ophthalmic examination, : evaluate for abnormalities of eyelids and aberrant cilia, sclera, and intraocular structures.

TREATMENT

TREATMENT OVERVIEW

- The goals of treatment are to address the underlying cause, halt progression, and reduce ocular discomfort.

ACUTE GENERAL TREATMENT

Treatment will vary depending on underlying cause.

POSSIBLE COMPLICATIONS

- Corneal vascularization may lead to pigmentation and scarring.
- Vascularization is often part of normal healing and should not be inappropriately suppressed.

PROGNOSIS AND OUTCOME

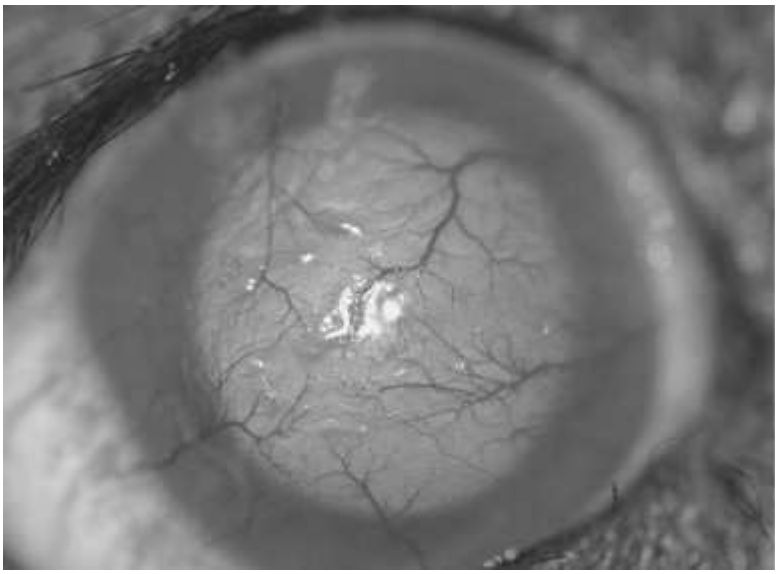
- Prognosis and outcome will vary depending on the underlying cause.
- In corneal injury, corneal vascularization denotes progression toward healing and is therefore a positive sign, provided the underlying problem can be controlled or eliminated.

PEARLS & CONSIDERATIONS

COMMENTS

It may be useful to distinguish between superficial and deep vascularization:

- Superficial vascularization occurs in response to superficial corneal or external ocular disease.
    - Superficial blood vessels arise from the conjunctiva, cross the limbus, are bright red, and branch frequently.
- Deep vascularization occurs in response to deep corneal or intraocular disease.
    - Deep blood vessels arise from the ciliary circulation, disappear at the limbus, and appear darker red and straight.



CORNEAL VASCULARIZATION Superficial corneal vascularization secondary to keratoconjunctivitis sicca in a dog. Note the numerous branching blood vessels located diffusely throughout the cornea.

(Courtesy Dr. Bruce Grahn.)

SUGGESTED READING

Chavkin MJ, et al: Risk factors for development of chronic superficial keratitis in dogs. J Am Vet Med Assoc 204:1630–1634, 1994.

Morgan RV, et al: Feline eosinophilic keratitis: a retrospective study of 54 cases: (1989-1994). Vet Comp Ophthalmol 6:131, 1996.

AUTHOR: LYNNE SANDMEYER

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Corneal Ulceration

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

A common condition of loss of superficial corneal epithelium with or without loss of varying amounts of the underlying corneal stroma. There are three main categories of corneal ulceration:

- *Simple* corneal ulcer: an acute loss of epithelial layers of the cornea due to trauma; usually noninfected
- *Complex* corneal ulcer: an acute or chronic loss of epithelial and stromal layers of the cornea due to trauma and/or infection
- *Indolent/refractory* corneal ulcer: a superficial ulcer resulting from failure of epithelial adhesion to the corneal basement membrane and stroma

SYNONYMS

Corneal abrasion, corneal erosion, keratomalacia, ulcerative keratitis

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Simple/complex ulcers: dogs and cats of any age or sex
- Indolent/refractory ulcers: middle-aged to older dogs

GENETICS & BREED PREDISPOSITION

- Simple/complex ulcers: brachycephalic breeds (dogs and cats) predisposed, but any breed may be affected
- Indolent/refractory ulcers: dogs: boxers predisposed, but any breed may be affected

RISK FACTORS

- Keratoconjunctivitis sicca (KCS, dry eye; see p. 628)
- Brachycephalic conformation
- Eyelid conformational abnormalities (see Entropion/Ectropion, ; Distichiasis/Ectopic Cilia/Trichiasis, p. 319)
- Feline herpesvirus 1 (FHV-1), feline viral rhinotracheitis infection (see p. 524)

CONTAGION & ZOONOSIS

FHV-1 keratoconjunctivitis is contagious among cats.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Three main categories of corneal ulceration:

- Simple corneal ulcer
- Complex corneal ulcer:
  - Stromal ulcer (ulcer with loss of varying amounts of the corneal stroma)
  - Keratomalacia/melting ulcer (softening and necrosis of the cornea, often associated with infection)
  - Descemetocele (loss of all stromal layers down to Descemet's membrane [basement membrane of the corneal endothelium] and endothelium)
  - Ruptured ulcer (perforation of the cornea)
- Indolent/refractory corneal ulcer

HISTORY, CHIEF COMPLAINT

- Variable onset from acute to insidious or chronic

- +/− History of trauma
- Ocular pain (squinting and/or rubbing at eye)
- Cloudiness to surface of eye
- "Red" eye
- Ocular discharge (watery, mucoid or mucopurulent)
- Occasionally, upper respiratory signs in cats (see p. 524)

PHYSICAL EXAM FINDINGS

- Simple and indolent corneal ulcers—any or all of the following may be present:
  - Blepharospasm (squinting)
  - Conjunctival hyperemia (enlarged vessels) +/− swelling
  - Third eyelid elevation
  - Ocular discharge: often serous
  - Corneal edema, usually focal
  - Obvious defect in corneal epithelium
  - Fluorescein dye retention in corneal stroma
  - Miotic (small) pupil (reflex uveitis; see p. 1151)
  - Aqueous flare (see p. 1151)
- Complex corneal ulcer—any or all of the above *and* one or more of the following:
  - Mucopurulent ocular discharge
  - Diffuse corneal edema
  - Corneal blood vessels (see p. 254)
    - Corneal vessels indicate chronicity (vessels migrate at a maximum of 1 mm/d)
  - Corneal white-yellow cellular infiltrate (inflammatory cells +/− microorganisms)
  - Corneal stromal defect (i.e., crater appearance to affected cornea)
  - Keratomalacia/melting (softening and necrosis of the cornea as evidenced by edema, a gelatinous appearance to the affected tissues, and/or stromal loss)
  - Hypopyon (white blood cells in anterior chamber; see p. 583)
- Descemetocele—any or all of the above *and* the following:
  - Fluorescein-negative clear center of a stromal ulcer (Descemet's membrane is hydrophobic and does not retain fluid or fluorescein stain)
- Ruptured corneal ulcer—any or all of the above *and* one or more of the following:
  - Copious ocular discharge with fibrin and/or blood (see Hyphema, p. 571) in the anterior chamber
  - Visible tan-brown-black iris prolapse (iris filling the corneal defect) and/or tan-yellow fibrin clot within ulcer
  - Shallow anterior chamber
  - Dyscoria (abnormal pupil shape)
  - Visible anterior synechia (iris adhesion) to the ulcerated area
- Indolent ulcer—in addition to any or all of the findings of a *simple ulcer*, indolent ulcers are characterized by the following clinical findings:
  - Rim of loose epithelium
  - Halo of fainter fluorescein uptake around stained ulcer
  - Minimal to moderate pain
  - +/− Corneal vascularization (slow to vascularize)
  - Noninfected

ETIOLOGY AND PATHOPHYSIOLOGY

- Trauma
- Ocular foreign body
- Tear film abnormalities:
  - Keratoconjunctivitis sicca (i.e., quantitative tear film deficiency [see p. 628])
  - Mucin and/or lipid deficiency (i.e., qualitative tear film deficiency [see p. 1076])
- Eyelid conformational abnormalities:
  - Entropion/ectropion
  - Distichiasis/ectopic cilia/trichiasis
  - Lagophthalmos (incomplete closure of the eyelids, usually in brachycephalics)
- Neurologic disorders (e.g., facial nerve paralysis [cranial nerve VII lesion]; corneal denervation [cranial nerve V lesion])
- FHV-1 infection
- Corneal sequestration (cats)
- Simple corneal ulcers may progress to complex or ruptured corneal ulcers secondary to bacterial infection or sterile inflammation.
- Indolent ulcers result from a primary defect of corneal epithelial adhesion to the underlying corneal basement membrane and stroma:

- Look for and address any other underlying cause(s) listed previously to promote healing of these refractory corneal ulcers.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Corneal ulceration is suspected based on history and physical exam findings. The cornerstone of diagnosis is a complete ophthalmic examination, including tear testing and fluorescein staining, and assessment of the cornea for edema, vessels, pigment, cellular infiltrate, fibrosis, and defects in the stroma. The goals of the ophthalmic exam are (1) confirm that an ulcer is present (versus healed defects), (2) determine whether the ulcer is acute or chronic (consider history and presence/length of corneal vessels), (3) determine the depth of the ulcer (and thus the risk of perforation), and (4) determine whether the ulcer may be infected (presence of cellular infiltrate, marked pain, uveitis, stromal loss, etc). When infection is suspected, corneal culture and susceptibility and cytologic examination should also be performed to direct appropriate antimicrobial therapy.

DIFFERENTIAL DIAGNOSIS

- Corneal dystrophy or degeneration
- Proliferative/eosinophilic keratoconjunctivitis (cats)
- Anterior uveitis
- Glaucoma
- Horner's syndrome

INITIAL DATABASE

- Cranial nerve examination (see pp. 1311 and p. 1313): menace response, pupillary light reflexes, palpebral and corneal reflexes
- Schirmer tear test (STT): Normal >15 mm/min in dogs, variable in cats
- Fluorescein dye application: Stains exposed stroma to confirm and demarcate ulcer
- Tear film break-up time (TFBUT): see p. 1076
- Corneal culture and sensitivity: ideally performed before STT and topical anesthesia
- Corneal cytologic study: assess for evidence of infection, such as neutrophils, bacteria (gram-positive cocci, gram-negative rods) and/or fungal hyphae. Identification of microorganisms can direct initial choice of therapy.
- Intraocular pressure to rule out glaucoma (recommended for any “red eye”)

ADVANCED OR CONFIRMATORY TESTING

- Keratectomy sample for corneal histopathologic evaluation
- Corneal swab and/or keratectomy sample for PCR (FHV-1, bacterial, fungal)

TREATMENT

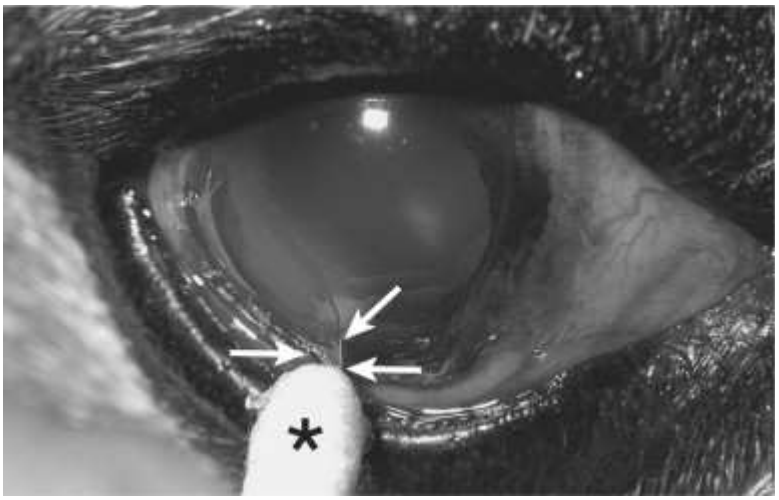
TREATMENT OVERVIEW

- Prevent progressive loss of corneal stroma and corneal rupture.
- Eliminate ocular pain.
- Prevent or eliminate corneal infection.
- Promote corneal epithelialization.
- Minimize corneal scarring.
- Standard treatment of a corneal ulcer consists of topical application of abroad-spectrum antimicrobial agent q4-6 h and atropine q 12-48 hours, +/− systemic administration of a nonsteroidal antiinflammatory medication (NSAID).

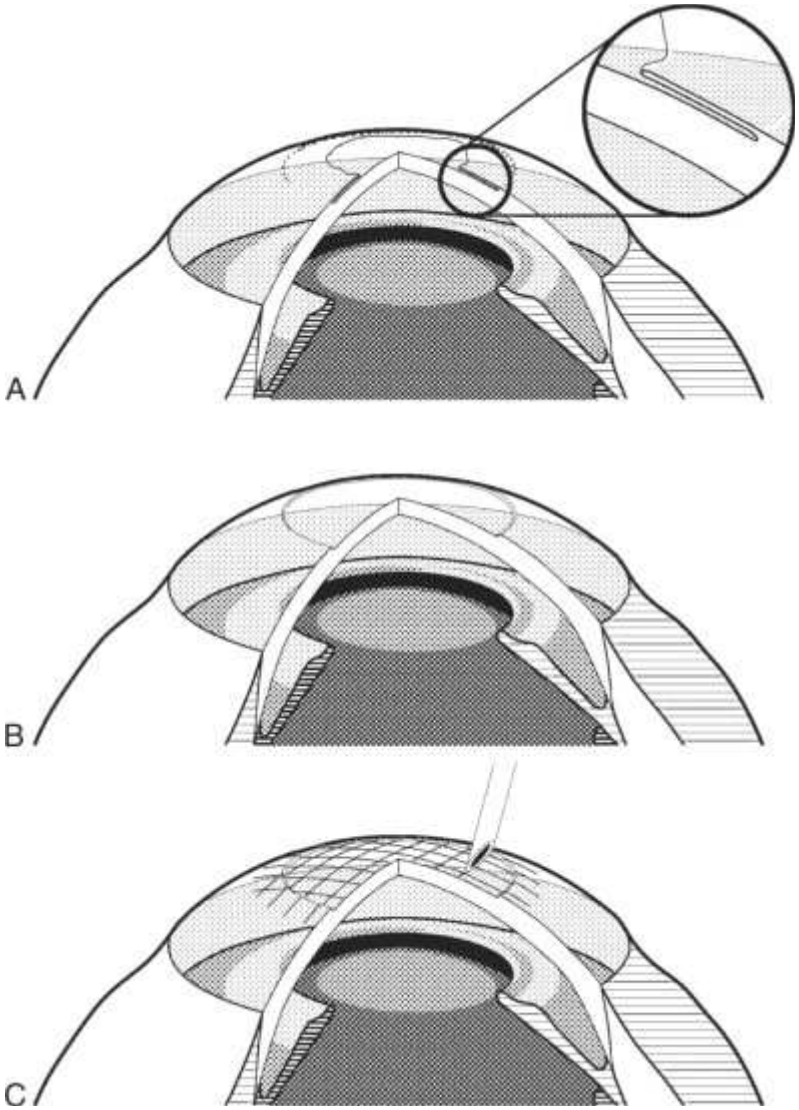
ACUTE GENERAL TREATMENT

- Simple corneal ulcer:
  - Broad-spectrum topical antibiotic solution or ointment (e.g., triple antibiotic or oxytetracycline/polymyxin B) q 6 h
    - Gentamicin is a poor first choice because of its narrow spectrum for only gram-negative bacteria (ocular flora is primarily gram-positive bacteria).
  - Topical atropine 1% ophthalmic solution or ointment q 12-48 h
  - ± Systemic NSAID

- Complex corneal ulcer—any or all of the above *and* one or more of the following:
  - Anticollagenase therapy is indicated if keratomalacia/melting/stromal ulcer detected:
    - Oxytetracycline/polymyxin B ointment topically q 4-6 h *and/or*
    - Autogenous serum q 1-4 h (prepared by obtaining a sample of the patient's own blood, anticoagulating and centrifuging, and using the supernatant [serum] topically for its antiprotease, anticollagenase properties)
  - Topical fluoroquinolone antibiotic (e.g., ciprofloxacin or levofloxacin; q 2-4 h for 24 h, then q 4-6 h) for improved corneal penetration and spectrum of activity. Use at increased frequency (q 2-4 h) for keratomalacia/melting/stromal ulcer.
  - +/− Topical antifungal agent q 4-6 h (e.g., natamycin or those derived from systemically administered agents such as voriconazole or miconazole) if fungal keratitis is implicated by corneal cytologic evaluation and/or culture (fungal keratitis is *rare* in cats and dogs)
  - Hospitalization of animals with deep or rapidly progressive ulcers for frequent medical treatments and monitoring
  - +/− Structural surgical repair (i.e., keratectomy to remove the diseased cornea with placement of a graft: conjunctival, corneal); referral procedure is advisable if:
    - Stromal loss continues despite aggressive appropriate medical management
    - Ulcer exceeds 50% stromal depth or is ruptured
- Indolent/refractory ulcer:
  - Application of topical ophthalmic anesthetic (e.g., proparacaine 0.5% solution) with or without sedation or general anesthesia (depending on the animal)
  - Débridement of all loose corneal epithelium with dry, sterile, cotton-tipped applicators
  - Perform multiple grid keratotomy with the beveled edge of a 25-gauge needle held at a 45-degree angle to the cornea:
    - Gentle vertical and horizontal scratches every 0.5 mm over ulcerated area just through basement membrane into superficial stroma (grid lines should be barely visible)
    - Contraindicated in cats (may predispose to sequestrum formation [see p. 248])
  - Oxytetracycline/polymyxin B ointment (promotes corneal epithelialization) q 6-8 h
- Atropine 1% ophthalmic solution or ointment q 24-72 h
- ± Systemic NSAID (e.g., carprofen)
- ± Application of a bandage soft contact lens to improve comfort and minimize mechanical forces of eyelids on migrating corneal epithelium
- Placement of an Elizabethan collar to prevent dog from rubbing eye



CORNEAL ULCERATION Débridement of an indolent corneal ulcer of the right eye in a dog. Note the lip of nonadherent corneal epithelium *(arrows)* attached to the sterile cotton-tipped applicator *(asterisk).*



CORNEAL ULCERATION Grid keratotomy. **A,** Indolent ulcer with corneal epithelial flaps (at time of presentation). **B,** After topical anesthesia and débridement. **C,** Performing the grid keratotomy.

CHRONIC TREATMENT

- Adjust antimicrobial therapy as directed by culture and susceptibility results and/or lack of improvement.
- Change to a topical antibiotic with expanded spectrum and/or improved corneal penetration (e.g., fluoroquinolone).
- FHV-1 ulcer (see p. 524 for details):
    - Topical antiviral ointment or solution (idoxuridine, vidarabine, trifluridine) q 4-6 h.
    - +/− Famciclovir (systemic antiviral)
    - Oxytetracycline/polymyxin B ointment q 6-8 h (to prevent secondary bacterial infection)
    - Chronic ulceration may lead to formation of corneal sequestrum

POSSIBLE COMPLICATIONS

- Corneal perforation, corneal scarring, corneal pigmentation, corneal stromal permanent defect (i.e., facet), corneal sequestration (cats), vision impairment/loss are possible.

RECOMMENDED MONITORING

- Evaluate for epithelialization (healing) or progressive loss of corneal stromal layers.
- Repeat corneal cytology and/or culture to monitor response to antimicrobial therapy, especially if progressive stromal loss occurs despite current therapies.
- STT: repeat after ulcer is healed to rule out KCS as initiating cause.

PROGNOSIS AND OUTCOME

- Simple/indolent: most heal with minimal scarring within 5-10 days with appropriate treatment.
- Complex: healing may take 2-8 weeks, and substantial corneal scarring is expected.

PEARLS & CONSIDERATIONS

COMMENTS

- Topical corticosteroids are contraindicated with corneal ulceration; they delay healing and promote keratomalacia/melting.
- Referral to a veterinary ophthalmologist is recommended if ulcer progresses despite appropriate medical management and/or if ulcer exceeds 50% stromal depth or is ruptured, because surgical repair is usually required.
- Any simple corneal ulcer that does not heal within 5-10 days should be considered a complex or indolent/refractory ulcer, and underlying causes such as infection, foreign body, ectopic cilia, distichia, and the like must be ruled out.
- Gentamicin is a poor first choice for the treatment of simple corneal ulcers because of its limited spectrum of activity (gram-negative only).

PREVENTION

Avoid or treat underlying cause(s).

CLIENT EDUCATION

- Simple corneal ulcers may become complex; therefore, topical antibiotic treatment and regular follow-up to assess ulcer healing are crucial.
- Indolent corneal ulcers may recur in the same eye or occur in the opposite eye.
- The patient's eye is frequently more uncomfortable for 24-48 hours after epithelial débridement and multiple grid keratotomy have been performed to treat an indolent corneal ulcer.

TECHNICIAN TIPS

- To prevent rupture or expulsion of aqueous humor due to increased intraocular pressure, avoid excessive restraint or jugular pressure in patients diagnosed with a descemetocele or corneal rupture.

SUGGESTED READING

Gilger BC, et al: Diseases and surgery of the canine cornea and sclera. In Gelatt KN, editor: Essentials of veterinary ophthalmology, ed 2, Oxford, 2008, Blackwell Publishing, p 119.

Stiles J, Townsend WM: Feline ophthalmology. In Gelatt KN, Essentials of veterinary ophthalmology, ed 2, Oxford, 2008, Blackwell Publishing, p 293.

AUTHOR: ANNE J. GEMENSKY-METZLER

EDITOR: CHERYL L. CULLEN

Corneal Sequestration, Cat

BASIC INFORMATION

DEFINITION

Corneal sequestration is a disease unique to cats, characterized by an area of necrotic cornea that is variably pigmented.

SYNONYMS

Corneal mummification, corneal necrosis, corneal sequestrum, corneal nigrum, necrotizing keratitis

EPIDEMIOLOGY

SPECIES, AGE, SEX

Cats of any age; average age of 5 years in retrospective studies

GENETICS & BREED PREDISPOSITION

All breeds, but Persian, Himalayan, Burmese appear predisposed.

RISK FACTORS

- Feline herpesvirus type 1 (FHV-1; see p. 524), particularly in domestic short-hairs and longhairs
- Any corneal insult, particularly chronic
- Brachycephalic cats are predisposed.
- Grid keratotomy performed for non-healing/indolent corneal ulcers (see p. 250) in cats may predispose to sequestrum formation.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- “Black spot on eye”
- Blepharospasm
- Ocular discharge
- “Red” eye

PHYSICAL EXAM FINDINGS

- Circular to oval pigmented lesion in central to paracentral cornea is pathognomonic.
- Pigmentation varies from subtle tan discoloration of cornea to a dense black, opaque lesion.
- Lesion may form a slightly raised, irregular corneal plaque.
- Corneal neovascularization with chronicity
- Variable corneal edema and inflammation surrounding sequestrum
- A rim of loose, edematous corneal epithelium may develop around the sequestrum.
- Depth of corneal involvement (i.e., extent of lesion) difficult to ascertain because sequestrum often opaque

ETIOLOGY AND PATHOPHYSIOLOGY

- The fundamental problems generated by corneal sequestration are (1) pain, (2) obstruction of vision, and (3) cosmetic appearance.
- Chronic corneal irritation, such as that found in brachycephalic cats with entropion (see p. 348) and/or lagophthalmos (incomplete closure of the eyelids), is a common feature.
- FHV-1 is linked to sequestrum formation, particularly in nonbrachycephalic cats (see p. 524).
- Tear film deficiencies (e.g., keratoconjunctivitis sicca [see p. 628], qualitative tear film abnormality [e.g., mucin deficiency; see p. 1076]) have been reported in cats with sequestra.
- Source of pigment unknown; cats with sequestra noted to have pigmented tears. Contact lenses placed in cats with

sequestra (see Acute General Treatment below) often become discolored.

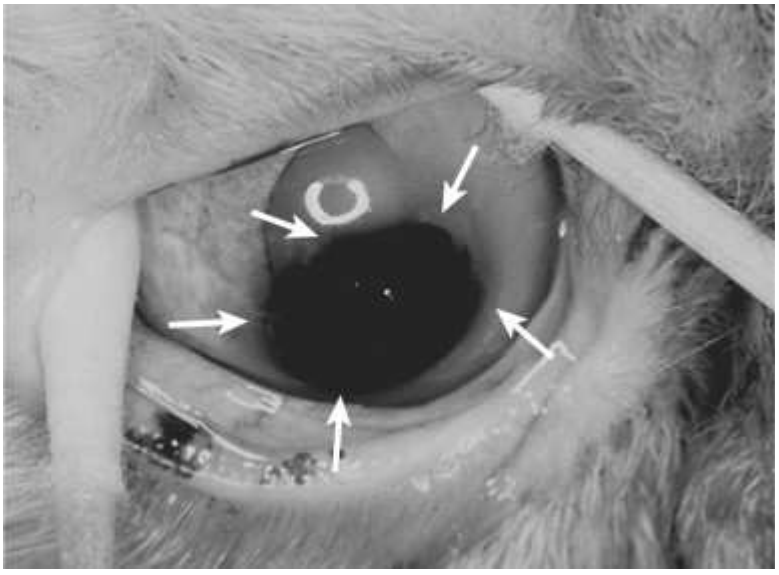
DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is generally based on signalment (species) and physical appearance of the lesion.

DIFFERENTIAL DIAGNOSIS

Corneal rupture with iris prolapse (should have dyscoric/misshapen pupil and uveitis if this has occurred; see p. 249)



CORNEAL SEQUESTRATION Corneal sequestrum in a cat *(arrows).* Note its dark appearance and paracentral location.

INITIAL DATABASE

Complete ophthalmic examination to assess for underlying causes of corneal irritation:

- Schirmer tear test (if <5 mm/min, see Keratoconjunctivitis Sicca,)
- Fluorescein dye application (sequestrum itself often does not retain fluorescein dye; there may be positive fluorescein dye retention around sequestrum).

ADVANCED OR CONFIRMATORY TESTING

- Consider testing for FHV-1 (see p. 524).
- Tear film break-up time (see Corneal Ulceration, p. 250, Tear Film Abnormalities, p. 1076)

TREATMENT

TREATMENT OVERVIEW

Treatment goals are to:

- Completely remove the sequestrum and prevent recurrence.
- Eliminate ocular pain.
- Minimize corneal scarring.

ACUTE GENERAL TREATMENT

- Prophylactic topical antibiotic therapy (can be ointment or solution formulation) such as ciprofloxacin or neomycin/polymyxin /gramicidin q 6-8 h, particularly if fluorescein positive

- If sequestrum appears small and superficial and affected eye is comfortable, observation is a treatment option:
  - Sequestrum may spontaneously slough, resulting in minimal scarring; however, sequestra can take months to years to slough. Rupture of the eye may occur if sequestrum is deep.
- If sequestrum is long-standing, large, or eye is painful, surgical removal is indicated through keratectomy (sequestrum excision using a corneal dissector; generally a referable procedure)
  - No postoperative pigmented corneal tissue should remain; a contact lens may be placed for protection for 2 weeks.
  - Very deep sequestra may require conjunctival or frozen donor corneal grafting.

CHRONIC TREATMENT

Treat underlying contributing factors/causes, such as entropion or lagophthalmos (see p. 348) and FHV-1 (see p. 524)

POSSIBLE COMPLICATIONS

- Recurrence of the sequestrum in the surgical site
- If the sequestrum is allowed to slough, descemetocele (see Corneal Ulceration, p. 250) formation or corneal rupture is a possibility.

RECOMMENDED MONITORING

- If the lesion is not treated surgically, owners should monitor carefully for sequestrum sloughing and return to the veterinarian immediately after the sequestrum sloughs to avoid complications from deep corneal defects. At the time of sequestrum sloughing, initiation of prophylactic topical antibiotic treatment (e.g., neomycin/polymyxin/gramicidin or ciprofloxacin) q 6-8 h is indicated, and referral for further evaluation (with or without surgical treatment) should again be considered.
- Surgical treatment: usually several rechecks at 1- to 2-week intervals until defect is epithelialized.

PROGNOSIS AND OUTCOME

Good, but recurrence is possible

PEARLS & CONSIDERATIONS

COMMENTS

Avoid topical corticosteroid use, because this may induce herpetic stromal keratitis if FHV-1 is an underlying cause.

CLIENT EDUCATION

Recurrence possible, as is involvement of contralateral eye

SUGGESTED READING

Cullen CL, et al: Ultrastructural findings in feline corneal sequestra. Vet Ophthalmol 8:295–303, 2005.

Featherstone HM, Sansom J: Feline corneal sequestra: a review of 64 cases (80 eyes) from 1993 to 2000. Vet Ophthalmol 7:213–227, 2004.

AUTHOR: ELLISON BENTLEY

EDITOR: CHERYL L. CULLEN

Corneal Pigmentation

BASIC INFORMATION

DEFINITION

Brown to black discoloration of the cornea, usually due to the presence of melanin

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs: pigmentary keratitis: brachycephalic breeds; no age or sex predilection; chronic superficial keratitis (CSK; see p. 825)
- Cats: corneal sequestrum (see p. 248)

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Brown discoloration of cornea
- Concurrently: redness of the conjunctiva, ocular discharge, ocular pain, reduced vision

PHYSICAL EXAM FINDINGS

- Brown or black discoloration of the corneal epithelium, stroma, or endothelium
- Extensive pigmentation may cause reduced or absent menace response.
- Other findings will vary depending on underlying cause.

ETIOLOGY AND PATHOPHYSIOLOGY

- Epithelial and stromal pigmentation:
  - Melanin is produced by melanocytes in the epithelium and superficial stroma in response to chronic corneal irritation from desiccation or mechanical trauma.
  - Proliferation and migration of limbal melanocytes into the stroma may also occur secondary to chronic inflammation in response to corneal ulceration, degeneration, or an immune response to corneal antigen.
- Endothelial pigmentation:
  - Adherence of melanin or melanin-containing cells, usually arising from the anterior uvea, to the endothelium.
- Stromal infiltration at the limbus as extension of a melanin-containing neoplasm.
- Protrusion of pigmented tissue through a corneal defect (see Corneal/Scleral Trauma, p. 249).
- Corneal sequestrum (cats; see p. 248):
  - Associated with chronic irritation
  - The central/paracentral corneal stroma becomes necrotic, stained, and the overlying epithelium is usually disrupted.
  - Cause of stromal discoloration is unresolved.

DIAGNOSIS

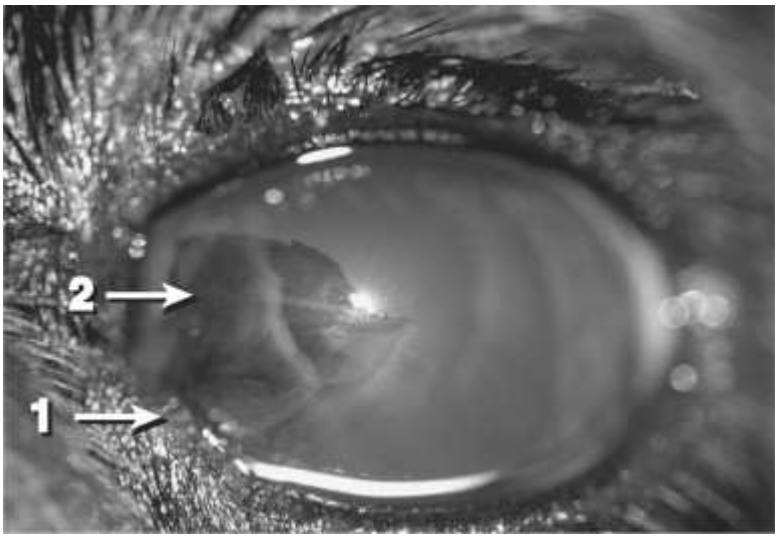
DIAGNOSTIC OVERVIEW

The diagnosis is apparent on physical examination, assisted by determining the location and pattern of the pigmentation as well as evaluating for other concurrent ocular disease. Species and breed are also important considerations.

DIFFERENTIAL DIAGNOSIS

- Epithelial and stromal pigmentation:
  - Pigmentary keratitis: large palpebral fissure, lagophthalmos (incomplete closure of the eyelids), distichiasis/ectopic cilia, trichiasis (entropion, nasal folds, aberrant dermis at medial canthus)
  - Exposure keratitis: buphthalmos (chronic glaucoma), neuroparalytic keratitis (cranial nerve VII lesion)

    - Keratoconjunctivitis sicca
    - Chronic superficial keratitis (CSK/pannus): dogs
    - Limbal melanocytoma (Note: melanomas of the limbus in dogs and cats are almost always benign and therefore are appropriately called melanocytomas, benign tumors of melanocyte origin.)
    - Invasive anterior uveal melanoma/melanocytoma
    - Protrusion of iris tissue through corneal defect (i.e., iris prolapse)
    - Corneal sequestrum (cats)
    - Brown foreign material
- Endothelial pigmentation: persistent pupillary membrane (iris to cornea), anterior synechia, uveal melanoma/melanocytoma, rupture of pigmented uveal cyst



CORNEAL PIGMENTATION Pigmentary keratitis of the left eye in a brachycephalic dog. There is medial entropion *(1)* and a triangular area of corneal pigmentation *(2)* overlying the medial cornea, secondary in part to the entropion.

(Courtesy Dr. Bruce Grahn.)

INITIAL DATABASE

- Neuroophthalmic examination (): evaluate palpebral reflexes and completeness of eyelid closure
- Schirmer tear test (STT): values <10 mm/min and clinical signs consistent with keratoconjunctivitis = KCS
- Fluorescein staining: positive if corneal ulceration is present. Fluorescein uptake usually occurs only around the edge of a corneal sequestrum
- Tonometry: elevated intraocular pressure (>30 mm Hg) in glaucoma (can arise with uveal melanoma/melanocytoma and uveal cysts) and reduced (<10 mm Hg) in cases of uveitis (can cause anterior synechia)
- Ophthalmic examination (see p. 1313): evaluate for abnormalities of eyelids and aberrant cilia

TREATMENT

TREATMENT OVERVIEW

The goals of treatment are to address the underlying cause, halt progression, reduce pigmentation, and reduce ocular discomfort.

ACUTE GENERAL TREATMENT

Treatment will vary depending on underlying cause.

RECOMMENDED MONITORING

- Recheck at regular intervals (every 4-6 months or more frequently depending on the cause).
- Photographs help monitor progression of lesions.

PROGNOSIS AND OUTCOME

Prognosis and outcome will vary depending on the underlying cause.

PEARLS & CONSIDERATIONS

COMMENTS

Ocular examination is an essential part of the routine physical examination, because corneal pigmentation may go unnoticed by owners until it is so extensive it compromises vision.

SUGGESTED READING

Carter R, et al: The causes, diagnosis, and treatment of canine keratoconjunctivitis sicca. Vet Med 97:683–694, 2002.

Swinger RL, et al: Keratoconjunctivitis associated with Toxoplasma gondii in a dog. Vet Ophthalmol 12(1):56–60, 2009.

AUTHOR: LYNNE SANDMEYER

EDITOR: CHERYL L. CULLEN

Corneal Lipid Infiltrates

BASIC INFORMATION

DEFINITION

- *Corneal dystrophy* is a hereditary, noninflammatory, often bilateral infiltration of lipid not associated with systemic disease.
- *Corneal degeneration* is stromal lipid and/or mineral deposition secondary to previous or concurrent corneal disease.
- *Lipid keratopathy* is a typically bilateral, predominantly peripheral corneal stromal lipid infiltrate secondary to dyslipoproteinemias of systemic disease origin.

SYNONYMS

- Arcus lipoides corneae; corneal arcus; corneal limbal lipid infiltrates
- Calcareous (calcium) degeneration; lipid (fatty) degeneration
- Corneal epithelial dystrophy; corneal stromal dystrophy

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs; rare in cats
- Corneal dystrophy: usually develops between 2 and 4 years of age

GENETICS & BREED PREDISPOSITION

Corneal dystrophy: any breed of dog, rare in cats; most commonly diagnosed breeds include the beagle, Cavalier King Charles spaniel, Siberian husky, Alaskan malamute, Samoyed, American cocker spaniel, and Labrador retriever.

ASSOCIATED CONDITIONS & DISORDERS

- Corneal degeneration: ulcerative and nonulcerative keratitides including:
  - Chronic superficial keratitis (see p. 825)
  - Limbal melanocytoma
  - Nodular granulomatous episclero-keratitis (see p. 356)
  - Keratoconjunctivitis sicca,
  - Ocular trauma (see p. 249)
  - Lipid keratopathy: hyperlipoproteinemias/systemic diseases including:
    - Hypothyroidism, p. 562
    - Hyperadrenocorticism, p. 548
    - Diabetes Mellitus,
    - Pancreatitis Dog, p. 820; Pancreatitis, Cat, p. 817
    - Primary hyperlipidemia (see p. 558)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Corneal dystrophy: well-demarcated, oval to round, grey-white or silver opacities in the central or paracentral cornea, often ringlike with a clear central zone
- Corneal degeneration: highly variable appearance, dense white to grayish stromal scars, irregular shape and distribution, often with ulceration and stromal vascularization
- Lipid keratopathy: dense, often arc-shaped, white to yellow crystalline opacities in the peripheral cornea, often separated from the limbus by a clear zone; additional opacity centrally if the cornea is vascularized

HISTORY, CHIEF COMPLAINT

- Corneal opacity
- Visual behavior change (uncommon in corneal dystrophy)

- Blepharospasm, serous ocular discharge/tearing (with ulceration in corneal degeneration)

PHYSICAL EXAM FINDINGS

- See Disease Forms/Subtypes, above
- Corneal abnormalities (corneal dystrophy, corneal degeneration)
- Variable, dependent on systemic disorder involved (lipid keratopathy)

ETIOLOGY AND PATHOPHYSIOLOGY

- Heritable genetic mutation (corneal dystrophy)
- Secondary pathologic changes, including altered lipid metabolism and dystrophic calcification (corneal degeneration)
- Deposition of lipid-laden serum across the limbus from hyperlipidemia (lipid keratopathy)

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Ophthalmic exam is an important first step to differentiate corneal lipid infiltrates from other types of grey to white corneal opacities (see Differential Diagnosis below). Corneal lipid infiltrates tend to be crystalline white in appearance. It is important to then determine the type of corneal lipid deposits (i.e., corneal dystrophy versus corneal degeneration versus lipid keratopathy) to address the underlying cause when possible (e.g., corneal disease with corneal degeneration; systemic disease with lipid keratopathy) and to aid in prognostication.

DIFFERENTIAL DIAGNOSIS

Other types of grey to white corneal opacities (see p. 245) including:

- Scar: dull grey to white; does not retain fluorescein stain
- Edema: bluish to grey; indistinct borders
- Ulcer: retains fluorescein stain (see p. 250)
- Inflammatory cell infiltrate: grey to yellow; indistinct borders and varying degrees of uveitis (see p. 1151)

INITIAL DATABASE

- Complete ophthalmic examination (see p. 1313) including:
  - Assessing corneal appearance (see Disease Forms/Subtypes above)
  - Schirmer tear test (may be low in cases of corneal degeneration, which can occur as a result of keratoconjunctivitis sicca [see p. 628]). Normal >15 mm in 1 minute in dogs, variable in cats.
  - Fluorescein dye application (positive staining of cornea most common with corneal degeneration)
- CBC, serum biochemistry panel (including fasting cholesterol, triglycerides, blood glucose, calcium, phosphorus) to screen for underlying disorders, and urinalysis (typically unremarkable except for systemic disorders)

ADVANCED OR CONFIRMATORY TESTING

- Referral to a veterinary ophthalmologist to confirm/document crystalline nature and depth/distribution (often breed-specific) of presumed lipid infiltrate via slit-lamp biomicroscopic examination (corneal dystrophy)
- Evaluation of thyroid and adrenal function (see pp. 588 and p. 548); serum lipid electrophoresis (lipid keratopathy)

TREATMENT

TREATMENT OVERVIEW

Goals of treatment are to:

- Minimize further deposition of lipid infiltrate if possible
- Surgically remove infiltrate if significant visual impairment and/or chronic corneal ulceration (referral to veterinary ophthalmologist)
- Manage any underlying systemic disease

ACUTE GENERAL TREATMENT

- Corneal dystrophy:
  - Treatment typically not required
  - Poor response to medical management
  - If advanced epithelial or stromal disease with vision impairment and/or corneal ulceration, may require surgical removal (lamellar keratectomy); may or may not recur
- Corneal degeneration:
  - Therapy aimed at underlying corneal disease
  - Lamellar keratectomy if degeneration is progressive and interfering with functional vision or creating ocular discomfort (chronic ulceration)
  - Topical application of disodium EDTA in an ophthalmic preparation (0.4%-1.38% q 6-8 h) if calcium component suspected.
- Lipid keratopathy:
  - Therapy aimed at underlying systemic disease (dogs); treat anterior segment inflammation/uveitis (often seen concurrently in cats; see p. 1151).

CHRONIC TREATMENT

Management/resolution of systemic disorder if present

NUTRITION/DIET

Corneal degeneration: anecdotal evidence of improvement subsequent to dietary restriction of lipid/cholesterol or following use of dietary additives to reduce cholesterol (flaxseed oil, oat bran, niacin)

RECOMMENDED MONITORING

Dictated by concurrent corneal disease management (corneal degeneration) or systemic disease management (lipid keratopathy)

PROGNOSIS AND OUTCOME

- Corneal dystrophy: favorable prognosis because opacities are focal and lesion typically nonprogressive; may resolve spontaneously
- Corneal degeneration: prognosis dependent on underlying corneal disease; may progress with chronic inflammatory or neoplastic disease; typically static after trauma
- Lipid keratopathy: may improve post resolution or control of underlying systemic abnormality

PEARLS & CONSIDERATIONS

COMMENTS

- The most common cause of corneal lipid infiltrate is corneal dystrophy; it is often discovered as an incidental finding and rarely causes appreciable vision impairment.
- At this time, there are serious questions about the safety and efficacy of systemically administered “lipid-lowering” medications for small-animal ocular disease.

CLIENT EDUCATION

Corneal dystrophy: suspected cases should be evaluated by a veterinary ophthalmologist, because the disease has genetic implications.

SUGGESTED READING

Crispin S: Ocular lipid deposition and hyperli-poproteinaemia. Prog Retin Eye Res 21:169, 2002.

AUTHOR: RICHARD F. QUINN

EDITOR: CHERYL L. CULLEN

Corneal Discoloration

BASIC INFORMATION

DEFINITION

Any alteration of corneal clarity

SYNONYMS

Corneal opacification, corneal opacity

EPIDEMIOLOGY

SPECIES, AGE, SEX

Varies depending on the underlying cause

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Brown, white, white/yellow, white/pink, blue/grey, or red spot(s) on or within the cornea
- Vision may be reduced, depending on the location and size of discoloration.
- Discomfort and ocular discharge may be present, depending on the cause.

PHYSICAL EXAM FINDINGS

- Focal to diffuse brown, white, white/yellow, white/pink, blue/grey, or red discoloration of the corneal surface, stroma, or endothelium
- Reduced or absent menace response if lesion covers significant portion of axial cornea

ETIOLOGY AND PATHOPHYSIOLOGY

- Brown discolorations:
  - Epithelial and stromal pigmentation occurs secondary to chronic irritation or inflammation:
    - Melanin is produced by melanocytes in the epithelium and superficial stroma in response to chronic corneal irritation from desiccation or mechanical trauma.
    - Proliferation and migration of limbal melanocytes into the stroma may also occur secondary to chronic inflammation in response to ulceration, degeneration, or an immune response to corneal antigen.
  - Endothelial pigmentation:
    - Adherence of melanin or melanin-containing cells, usually arising from the anterior uvea, to the endothelium
    - Stromal infiltration at the limbus as extension of a melanin-containing neoplasm
    - Protrusion of pigmented tissue through a corneal defect (i.e., iris prolapse)
  - Corneal sequestrum (cats):
    - Associated with chronic irritation: the central/paracentral stroma becomes necrotic, stained, and overlying epithelium is usually disrupted.
    - Cause of stromal discoloration is unresolved.
    - See p. 248.
- White discolorations:
  - Fibrosis/scarring:
    - During the healing of stromal injury, such as ulceration, trauma, or inflammation, fibroplasia occurs, and newly produced collagen is laid down in a disorganized fashion.
  - Lipid (see p. 245):
    - Lipid deposition is associated with a primary defect of corneal lipid metabolism in inherited corneal dystrophy in some breeds.
    - Lipid deposition may be associated with a secondary defect of corneal metabolism such as in corneal degeneration caused by trauma, ulceration, chronic irritation, uveitis, or glaucoma.
    - Lipid infiltration in the cornea may occur in systemic disorders of lipid metabolism as a result of leakage of

lipid-laden serum at the limbus (arc-shaped) or in association with corneal vascularization.
    - Calcium:
        - Calcium deposition may be associated with a secondary defect of corneal metabolism such as in corneal degeneration caused by trauma, ulceration, chronic irritation, uveitis, or glaucoma.
        - Calcium deposition in the cornea may occur secondary to derangements in systemic calcium and phosphorus metabolism.
- White/yellow or white/pink discolorations:
    - Epithelial or stromal infiltration of inflammatory cells occurs in association with sterile inflammation or secondary to infection.
    - Endothelial deposition of inflammatory cells occurs in association with chronic uveitis (keratic precipitates).
    - Epithelial inclusion cysts usually form when mitotically active basal epithelial cells become displaced into the corneal stroma as a result of trauma or surgery and continue to grow.
- Grey/blue discolorations:
    - Corneal edema:
        - Fluid from the tear film may enter the corneal stroma secondary to loss of corneal epithelium (i.e., corneal erosion, ulcer, or other trauma).
        - Aqueous humor may enter corneal stroma owing to loss or damage of corneal endothelium or endothelial pump function.
        - Fluid from vascular leakage secondary to newly formed blood vessels may enter the cornea.
    - Florida spots:
        - Slowly to nonprogressive corneal disease that does not cause other overt clinical signs
        - Typically characterized by bilateral multifocal, grey-white opacities within the cornea
        - Recognized in dogs and cats in the southeastern United States
        - Etiology unknown, possibly mycobacterial organism
- Red discolorations:
    - Corneal vascularization:
        - Vascularization occurs as a response to injury of the corneal epithelium or stroma as a normal component of healing.
        - Vascularization may occur as part of an immune-mediated inflammatory response.
        - Vascularization may occur secondary to disease of adjacent ocular tissues including episcleritis, uveitis, and glaucoma.
    - Hemorrhage into the cornea may be due to trauma to blood vessels invading the cornea or as an extension of conjunctival hemorrhage.

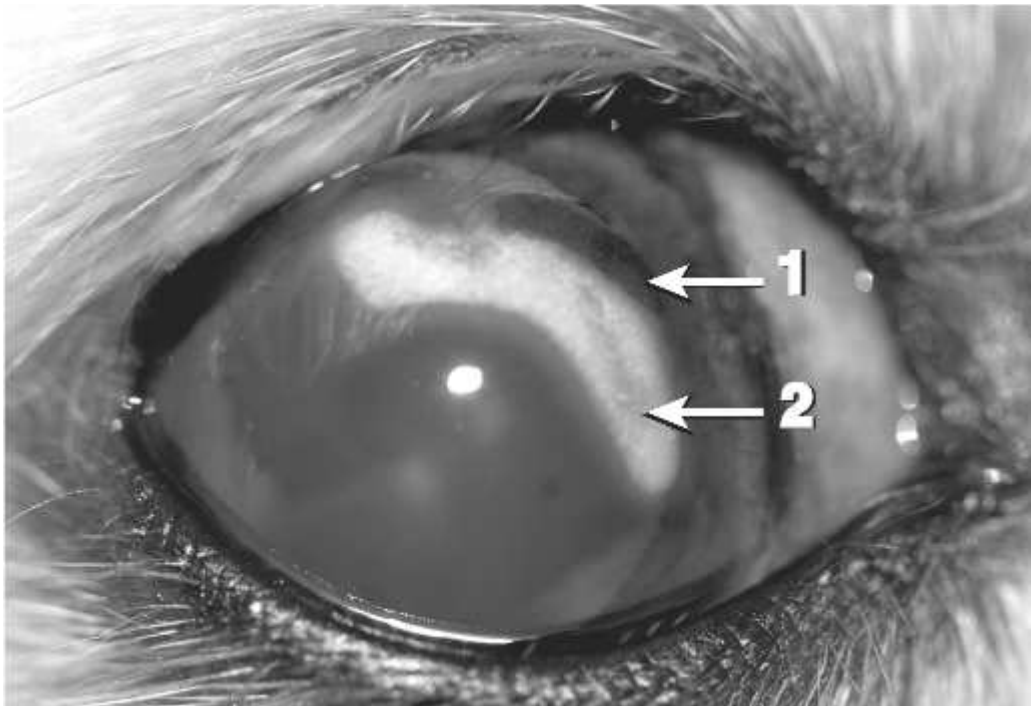
DIAGNOSIS

DIAGNOSTIC OVERVIEW

- The diagnosis is broad, and evaluation should begin with determining qualities such as color, location, pattern, and size of discoloration as well as evaluation for other concurrent ocular disease.

DIFFERENTIAL DIAGNOSIS

- Brown discolorations:
    - Corneal Pigmentation, p. 246:
        - Chronic irritation/inflammation:
            - Pigmentary keratitis (in brachycephalic dogs primarily): large palpebral fissure, lagophthalmos (incomplete closure of the eyelids), ectopic cilia, trichiasis (entropion, nasal folds, aberrant dermis at medial canthus)
            - Exposure keratitis: buphthalmos (chronic glaucoma), neuroparalytic keratitis (cranial nerve VII lesion)



CORNEAL DISCOLORATION Corneal degeneration in a dog. There is a horizontally ovoid area of corneal pigmentation *(1)* and a white arc of corneal lipid deposit *(2)*.

- Keratoconjunctivitis sicca (KCS)
- Chronic superficial keratitis (CSK/pannus): dogs
- Protrusion of iris tissue through corneal defect
- Persistent pupillary membrane (iris to cornea)
- Anterior synechia
- Rupture of pigmented uveal cyst
- Neoplasia (see p. 620): limbal melanocytoma, invasive anterior uveal melanoma
- Corneal sequestrum: cats (see p. 248)
- Brown foreign material

- White discolorations:
  - Corneal fibrosis/scarring (hazy grey-white) (see p. 249)
  - Corneal lipid infiltrate or deposition (bright white, crystalline; see p. 245):
    - Corneal dystrophy
    - Corneal degeneration
    - Lipid keratopathy (systemic lipid abnormalities): diabetes mellitus, pancreatitis, hypothyroidism, hyperadrenocorticism, thyroid carcinoma, hepatic disease, primary hyperlipoproteinemia, postprandial hyperlipoproteinemia
  - Corneal calcium deposition (dense, chalky-white)
    - Corneal degeneration
    - Systemic disease: hypercalcemia, hyperphosphatemia, hyperadrenocorticism, renal disease, hyperparathyroidism, hypervitaminosis D
- White/yellow or white/pink discolorations:
  - Inflammatory cell infiltration:
    - Infected corneal ulcer
    - Corneal abscess (infectious or sterile)
  - Feline proliferative keratoconjunctivitis (plaques and infiltrates)
  - Corneal epithelial inclusion cyst
- Grey-blue discolorations:
  - Corneal edema:
    - Corneal endothelial loss or damage: endothelial dystrophy, uveitis, glaucoma, trauma (anterior lens luxation with endothelial contact, intraocular surgery)
    - Corneal edema due to epithelial loss: corneal ulceration
    - Corneal edema associated with corneal vascularization
  - Florida spots (see Etiology and Pathophysiology above)
- Red/pink discolorations:
  - Corneal vascularization
    - Corneal injury or inflammation:

- Corneal ulceration
- Chemical irritation
- Mechanical irritation: (trichiasis, ectopic cilia, entropion)
- Exposure: large palpebral fissure, lagophthalmos (incomplete closure of the eyelids), ectropion, buphthalmos (chronic glaucoma), exophthalmos, neuroparalytic keratitis (cranial nerve VII lesion)
- Neurotrophic keratitis (cranial nerve V lesion)
- Keratoconjunctivitis sicca
- Qualitative tear film abnormalities (see p. 1076)
- Chronic superficial keratitis (CSK/pannus): dogs
- Proliferative keratoconjunctivitis: cats
- Corneal degeneration (see figure)

- Adjacent ocular disease: uveitis, episcleritis, scleritis, orbital disease, glaucoma

INITIAL DATABASE

Complete ophthalmic examination (see p. 1313) is essential, including the following:

- Schirmer tear test: values <10 mm/min are consistent with KCS; values of 10 to 15 mm/min suggestive of KCS and should be interpreted in light of other clinical signs
- Tear film break-up time: values <10 seconds are suggestive of a qualitative tear film abnormality (see p. 1076)
- Fluorescein staining: positive in corneal ulceration
- Tonometry: elevated intraocular pressure (>30 mm Hg) in glaucoma, and reduced (<10 mm Hg) in cases of uveitis

ADVANCED OR CONFIRMATORY TESTING

- CBC, serum biochemistry profile, urinalysis, serum lipid profile (total serum lipids, cholesterol, triglycerides, lipoprotein electrophoresis, ± cholesterol esters and phospholipids), thyroid ± adrenal gland testing are recommended if lipid or calcium infiltration is suspected in association with systemic disease.
- Cytologic evaluation of conjunctival scraping or conjunctival biopsy is useful in diseases associated with conjunctival inflammation or proliferation.
- Cytologic evaluation of corneal scrapings is useful in proliferative disease of the cornea or inflammatory cell infiltration of a corneal ulcer.

TREATMENT

TREATMENT OVERVIEW

- The goals of treatment are to halt progression of the lesion, treat the underlying cause, and reduce ocular discomfort.

ACUTE AND CHRONIC TREATMENT

Treatment will vary depending on the underlying cause.

PROGNOSIS AND OUTCOME

Prognosis and outcome vary depending on the underlying cause.

PEARLS & CONSIDERATIONS

COMMENTS

In determining the underlying cause, documentation of location, color, shape, and pattern of corneal discoloration and presence of other concurrent ocular disease are extremely helpful.

SUGGESTED READING

Chavkin MJ, et al: Risk factors for development of chronic superficial keratitis in dogs. J Am Vet Med Assoc 204:1630–1634, 1994.

Crispin SM, et al: Dystrophy, degeneration and infiltration of the canine cornea. J Small Anim Pract 24:63–83, 1983.

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AUTHOR: LYNNE SANDMEYER

EDITOR: CHERYL L. CULLEN

Cor Triatriatum Sinister and Supravalvular Mitral Stenosis

BASIC INFORMATION

DEFINITION

- Congenital cardiac malformations involving membranous division of the left atrium into a proximal high-pressure chamber and a distal low-pressure chamber
- Cor triatriatum sinister (CTS) can be distinguished from supravalvular mitral stenosis (SVMS) by the location of the membrane relative to the left auricle.
    - Cor triatriatum ("three atria") sinister ("left"): the auricle is distal to the dividing membrane and connected with the distal low-pressure left atrial chamber.
    - Supravalvular mitral stenosis: the left auricle is proximal to the dividing membrane and is connected with the proximal high-pressure left atrial chamber.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Feline; most often diagnosed in cats younger than 1 year of age but has been reported in older cats; males reported more frequently
- Canine: no cases reported (see cor triatriatum dexter)

GENETICS & BREED PREDISPOSITION

Uncommon; no known breed predisposition or genetic defect defined

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Respiratory distress
- Anorexia
- Lethargy

PHYSICAL EXAM FINDINGS

Not all signs will be present in every patient:

- Tachypnea
- Dyspnea
- Tachycardia
- Gallop
- Diastolic murmur
- Arrhythmias with pulse deficits
- Crackles and/or wheezes
- Muffled lung sounds (pleural effusion)

ETIOLOGY AND PATHOPHYSIOLOGY

- CTS results from incomplete incorporation of the embryologic pulmonary venous chamber into the developing left atrium.
- SVMS results from embryologic malformation of the mitral valve apparatus.
- Both CTS and SVMS cause left atrial inflow obstruction, which may result in signs of left-sided congestive heart failure, including pulmonary edema, pleural effusion, and pericardial effusion. Therefore, clinical signs of CTS and SVMS are identical.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Clinical presentation of left-sided congestive heart failure should generally lead to the suspicion of other, more common cardiac disorders. However, the diagnosis is established during the echocardiographic examination (generally an unexpected finding).

DIFFERENTIAL DIAGNOSIS

- Mitral valve stenosis
- Hypertrophic cardiomyopathy
- Dilated cardiomyopathy
- Thyrotoxic heart disease
- Left atrial tumor

INITIAL DATABASE

- Thoracic radiographs demonstrate marked left atrial enlargement, ± left ventricular enlargement. Signs of congestive heart failure may also be present: pulmonary venous distension, interstitial to alveolar infiltrate, and/or pleural effusion.
- Electrocardiogram may show wide P waves consistent with left atrial enlargement, and tall R waves consistent with left ventricular enlargement.
- CBC may show a stress leukogram. Biochemistry panel and urinalysis are likely to be unremarkable.

ADVANCED OR CONFIRMATORY TESTING

- Echocardiography:
  - Two-dimensional echocardiography will display a membrane dividing the atrium and indicating the position of the membrane relative to the auricle.
  - Doppler echocardiography can be used for determining the degree of obstruction by measuring the velocity of blood flow across orifice.
    - The modified Bernoulli equation can be used for calculating the pressure gradient across the membrane (Pressure change = 4 × velocity^2).
- Angiography is an alternate imaging technique to define the location of the obstruction and determine if other concurrent cardiac defects are present, but invasiveness of angiography makes echocardiography a superior first choice.

TREATMENT

TREATMENT OVERVIEW

Alleviate clinical signs of left heart failure. The lesion does not lend itself to catheter-based correction; open-heart surgery is the definitive method of correction of the defect.

ACUTE GENERAL TREATMENT

If patient is in acute heart failure, then treat with furosemide, oxygen, and nitroglycerin (see p. 468).

CHRONIC TREATMENT

- Furosemide and an angiotensin-converting enzyme inhibitor to control fluid accumulation (see p. 470)
- Periodic thoracocenteses may be necessary to treat pleural effusion (see p. 1338).
- Successful surgical correction of CTS has been reported.

DRUG INTERACTIONS

Electrolyte depletion and dehydration may result from overzealous diuretic administration.

POSSIBLE COMPLICATIONS

Surgery is highly invasive, and therefore the risk of mortality is increased with an inexperienced surgeon.

RECOMMENDED MONITORING

- Pulmonary edema/pleural effusion should resolve with successful reduction/removal of the membranous obstruction.

- Renal function should be periodically monitored if medical therapy is chosen.

PROGNOSIS AND OUTCOME

- Excellent with successful reduction/removal of the obstruction
- Medical management alone is unlikely to be satisfactory on a long-term basis if signs of congestive heart failure have already occurred, but the small number of recorded veterinary cases of CTS/SVMS limits the extent of this conclusion.

PEARLS & CONSIDERATIONS

COMMENTS

These defects are rare but represent potentially curable abnormalities. Any cat presenting with signs of heart failure should have an echocardiogram performed to rule out CTS or SVMS.

CLIENT EDUCATION

Owner should monitor for recurrence of heart failure: increased respiratory rate or effort, lethargy, or anorexia. Owner should monitor patient's resting respiratory rate and call clinician if rate exceeds 40 breaths/min when the patient is asleep.

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Coprophagia

BASIC INFORMATION

DEFINITION

Ingestion of feces, common in dogs

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Common and generally normal behavior in all types of dogs
- Normal expression of maternal behavior during pregnancy and nursing in both cats and dogs; very rare in cats

RISK FACTORS

- Dietary preference
- Access to feces
- Lack of other outlets for exploratory behavior
- Inadequate diet, hunger
- Inadequate utilization of food (e.g., severe intestinal malabsorption, exocrine pancreatic insufficiency [EPI], severe parasitism)

GEOGRAPHY AND SEASONALITY

- Ubiquitous behavior of domestic dogs
- May increase in winter when feces are frozen or when less access to organic material in environment

ASSOCIATED CONDITIONS & DISORDERS

- Polyphagia
- Poor body condition associated with malnutrition
- Anxiety
- Compulsive behavior which may include pica (ingestion of nonfood items other than feces)

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Acute or chronic behavior, often an incidental finding
- Ingestion of own feces, those of other dogs, or of any other herbivore or carnivore species, especially of cats
- May occur daily or intermittently
- With EPI, owners may report weight loss, ravenous appetite, steatorrhea, borborygmus, flatulence, and diarrhea with voluminous stools

PHYSICAL EXAM FINDINGS

- Typically no abnormal findings on physical exam
- In an older dog may indicate abnormality in endocrine function (e.g., hyperadrenocorticism, hypothyroidism) or cognitive dysfunction

ETIOLOGY AND PATHOPHYSIOLOGY

- Typically normal behavior in domestic dogs, likely evolved from scavenging and nest-cleaning behaviors
- Onset may be associated with change in diet or environment, but behavior will often persist after return to previous management

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A common and normal behavior in many dogs, coprophagia alone should not ordinarily arouse suspicion of a dietary, physical, or behavioral abnormality.

DIFFERENTIAL DIAGNOSIS

- Hunger
- Separation anxiety
- Compulsive disorder
- Pica
- Polyphagia (e.g., diabetes mellitus, hyperadrenocorticism, drug-induced)
- EPI
- Thiamine deficiency (rare)

INITIAL DATABASE

- Generally no additional diagnostic testing required beyond regular wellness recommendations
- If abnormality suspected based on history and physical exam, basic laboratory diagnostic tests may be indicated, including CBC, serum chemistry, urinalysis, and fecal analysis for parasites.

ADVANCED OR CONFIRMATORY TESTING

Thyroid profile, trypsin-like immunore-activity, serum cobalamin, serum folate, fecal fat, and fecal trypsin may be considered for cases where a primary medical disturbance is suspected (rarely the case).

TREATMENT

TREATMENT OVERVIEW

Many dogs are highly motivated to engage in this self-rewarding behavior, and it should therefore be expected that behavior modification will be difficult and not completely successful in the long term.

ACUTE AND CHRONIC TREATMENT

- No additives to the dog's food or products applied to the feces have been consistently effective in preventing coprophagia.
- The most effective methods for prevention include:
    - Attention to yard hygiene
    - Removing access to cat litterboxes
    - Training the dog to defecate on command and then return immediately to the owner
    - Use of a remote-activated spray collar to interrupt the behavior
    - Use of a head collar on walks to redirect the behavior
    - Addressing any issues related to separation anxiety and poor environments
    - Client education

NUTRITION/DIET

In dogs already receiving a nutritionally adequate diet, a change in diet is unlikely to influence the frequency of this behavior.

PROGNOSIS AND OUTCOME

Prognosis is guarded for complete cessation of this unwanted behavior, although it is possible to reduce the frequency of coprophagia through behavior modification and environmental management.

PEARLS & CONSIDERATIONS

COMMENTS

- Coprophagia and pica (ingestion of nonfood items) may both be found in patients with polyphagia. Therapeutic success depends on properly identifying the primary disorder.
- Many owners find coprophagia by dogs to be extremely offensive and are not aware that it is normal for the species.
- Owner counseling is important to reduce the likelihood of inhumane treatment or abandonment of dogs due to coprophagia.

PREVENTION

- Reducing access to feces by young dogs may prevent the initial ingestion of feces as part of exploratory behavior.
- Providing dogs with an adequate diet, exercise, and socialization may reduce the likelihood of coprophagia but is unlikely to completely prevent it from occurring.

CLIENT EDUCATION

Clients should be reassured that coprophagia is normal and generally harmless to their dog, and be provided with strategies to reduce the likelihood of it occurring if it adversely affects the way they interact with their dog.

SUGGESTED READING

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EDITOR: ETIENNE CÔTÉ

Contact Dermatitis

BASIC INFORMATION

DEFINITION

Cutaneous inflammation which occurs after contact with an irritant or antigenic substance

SYNONYMS

Allergic contact dermatitis, contact hypersensitivity, irritant contact dermatitis

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Uncommon in dogs and rare in cats
- Allergic contact dermatitis typically occurs in animals older than 1 year; irritant contact dermatitis may occur at any age.

GENETICS & BREED PREDISPOSITION

Terrier breeds, French poodles, and golden retrievers may be at increased risk.

RISK FACTORS

Concurrent inflammatory dermatoses

ASSOCIATED CONDITIONS & DISORDERS

- Atopic dermatitis
- Secondary bacterial or *Malassezia* dermatitis is common.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Allergic contact dermatitis
- Irritant contact dermatitis

HISTORY, CHIEF COMPLAINT

- Allergic contact dermatitis:
  - The chief complaint is typically chronic pruritus that may be seasonal or nonseasonal, depending on the allergen.
  - A recent change in environment or housing is typically not noted, because signs may take longer than 2 years to develop from the time of initial exposure.
  - The animal is typically the only one in the household affected.
- Irritant contact dermatitis:
  - The chief complaint may be acute cutaneous pain rather than pruritus.
  - Onset of the condition often correlates with the introduction of a new substance.
  - There may be more than one individual affected (including the owner).

PHYSICAL EXAM FINDINGS

Lesion distribution reflects the area of the body in contact with the offending substance.

- Sparsely haired areas and those areas in contact with the environment are more frequently affected (ventral surfaces of the feet, chest, and abdomen, perineum, and scrotum).
- Regional dermatitis of the muzzle and chin may occur with reactions to substances such as rubber chew toys or plastic food dishes (rare).

- A generalized distribution may be present with contact reactions to shampoos.
- The ears may be the only area affected if the offending substance is a topical otic medication
- The primary lesion is an erythematous papular and macular eruption.
- Vesicles are occasionally present.
- With chronic exposure, alopecia, lichenification, and hyperpigmentation develop.

ETIOLOGY AND PATHOPHYSIOLOGY

- Allergic contact dermatitis is a type IV hypersensitivity disorder. The development of clinical disease requires two stages: induction and elicitation. The induction phase is the time from allergen exposure until the time lymphocytes become programmed to recognize the allergen (lasts months to years; no evidence of clinical disease). Elicitation is the time from reexposure to the allergen to the development of cutaneous inflammation. This phase may take several days. Reported causes include shampoos, insecticides, topical/otic medications, plastic, detergents, wool, synthetic rugs, fertilizers, cement, perfumed cat litter, and several species of plants.
- Irritant contact dermatitis is an antigen-independent process that is the result of direct keratinocyte damage by the offending compound. No induction phase is necessary. Acids, alkalis, surfactants, solvents, enzymes, and oxidants may cause irritant contact dermatitis.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Contact dermatitis is difficult to definitively diagnose with commonly available clinical tools. Its diagnosis often relies upon ruling out other potential causes of inflammation in conjunction with a suggestive history. More common causes of the apparent clinical signs need to be ruled out first.

DIFFERENTIAL DIAGNOSIS

- Parasitic: fleas, contagious acarioses *(Sarcoptes, Cheyletiella, Otodectes, Notoedres), Demodex, Pelodera,* chiggers, and hookworm dermatitis
- Allergic: flea-bite hypersensitivity, atopic dermatitis, food hypersensitivity
- Bacterial pyoderma
- Fungal: dermatophytosis, *Malassezia* dermatitis
- Erythema multiforme
- Drug eruptions
- Lupus erythematosus

INITIAL DATABASE

- Skin scrapings and cytologic examination should be performed to detect microbial or parasitic infections.
- A fungal culture should be considered, especially in cats, to detect dermatophytosis.
- An elimination food trial may be performed to rule out dermatologic adverse food reactions/food allergy.
- Intradermal skin testing or in vitro serum allergy testing may be performed to investigate atopic dermatitis.

ADVANCED OR CONFIRMATORY TESTING

- Histopathologic evaluation may provide supportive evidence and help differentiate between allergic and irritant contact dermatitis if biopsies are taken early in the disease process. Results from biopsies of chronically diseased skin are usually nonspecific.
- Patch testing is a specific test for investigating allergic contact dermatitis. A series of compounds is applied to the skin for 48 hours, and the degree of erythema, induration, and papular eruptions caused by each agent is evaluated. Standardized kits for veterinary medicine are not available, but human standardized kits have been used successfully in dogs.
- Restriction and provocative exposure is the most reliable test. Ideally the animal should be bathed to remove all possible allergens and removed completely from the home environment for 2 to 4 weeks. After resolution, the animal is reintroduced to the environment. A return of clinical signs will typically occur within 24 to 72 hours in cases of contact dermatitis.

TREATMENT

TREATMENT OVERVIEW

The ideal treatment involves identification and removal of the offending substance. Unfortunately, patch testing and restriction/provocation testing are either not widely available are logistically difficult to perform, often leaving history as the only clue to the potential contact allergen/irritant. In cases where the offending substance cannot be identified, nonspecific palliative therapy may be necessary.

ACUTE GENERAL TREATMENT

- Treat any secondary microbial infections.
- Identify and remove the offending substance.
- Palliative therapy with glucocorticoids (prednisone, 0.5-1 mg/kg PO q 24 h initially, before weaning down based on response), pentoxifylline (15-20 mg/kg PO q 8-12 h), or topical tacrolimus (0.1% ointment) may provide relief in cases of allergic contact dermatitis.

CHRONIC TREATMENT

- Long-term palliative therapy may be necessary if clinical signs persist and the offending substance cannot be identified and removed. The treatment plan for each patient should be chosen based upon efficacy in that patient as well as long-term safety. For example, pentoxifylline is typically well tolerated and should be chosen over glucocorticoids for long-term treatment if effective.

PROGNOSIS AND OUTCOME

Excellent if the offending substance is identified and removed

PEARLS & CONSIDERATIONS

COMMENTS

Some substances may cause both irritation and allergic contact dermatitis.

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EDITOR: MANON PARADIS

Constipation/Obstipation and Megacolon

BASIC INFORMATION

DEFINITION

- Constipation: infrequent or difficult evacuation of feces; does not imply loss of function
- Obstipation: intractable constipation
- Megacolon: persistent dilation of the large intestine associated with chronic constipation or obstipation, or occurring secondary to idiopathic loss of colon function. Dilated megacolon implies permanent loss of colonic structure and function.

EPIDEMIOLOGY

SPECIES, AGE, SEX

Constipation: both dogs and cats. Megacolon is rarely reported in dogs. Obstipation/megacolon is reported to be more common in middle-aged, male cats of the domestic shorthair, domestic long hair, or Siamese breeds.

GENETICS & BREED PREDISPOSITION

Manx cats may be predisposed to neurogenic megacolon.

RISK FACTORS

- Intrinsic dysfunction preventing passage of feces: spinal cord/spinal nerve disease or trauma, dysautonomia
- Mechanical obstruction preventing passage of feces: pelvic fracture, colonic stricture or neoplasia, extraluminal mass or stricture compressing colon, anal stricture, colonic foreign body
- A predominantly bony diet and low levels of exercise may predispose dogs to megacolon.

ASSOCIATED CONDITIONS & DISORDERS

Perineal hernia may be either the cause or result of constipation and megacolon.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Hypertrophic megacolon: develops as a consequence of obstructive lesions and thus may be reversible with early therapy,
- Dilated megacolon: end stage of colonic dysfunction (both idiopathic or untreated hypertrophic megacolon); may be poorly responsive to treatment

HISTORY, CHIEF COMPLAINT

- Reduced, absent, or painful defecation is typical presentation.
- Fecal balls are often very hard if passed, and occasionally watery diarrhea may be passed around fecal concretion.
- Prolonged constipation will result in anorexia, lethargy, weight loss, or vomiting (may be projectile).

PHYSICAL EXAM FINDINGS

- Poor body condition
- Dehydration
- Colon distended with hard feces on abdominal palpation; signs of abdominal pain may be present.
- Perineal irritation/ulceration
- Rectal exam (usually requires sedation in cats): hard feces, possible pelvic narrowing, stricture or mass palpated, perineal hernia

ETIOLOGY AND PATHOPHYSIOLOGY

- Prolonged retention of feces in colon due to functional (neurogenic) or mechanical obstruction (e.g., pelvic fractures, intraluminal or extraluminal masses)
- Inflammation can also be associated with constipation (perianal fistula, proctitis, anal sac abscess, or perianal bite wounds).
- Water absorption from feces in colon results in concretion that is difficult or impossible to pass (common in cats with chronic progressive renal disease or diabetes mellitus).
- Neurogenic dysfunction from dysautonomia (autonomic system failure), trauma to pelvic or hypogastric nerves (pelvic fracture), neoplasia of spinal cord, or caudal spinal cord diseases (e.g., lumbosacral disease, lumbosacral stenosis/cauda equina syndrome, Manx cat sacral deformities)
- Prolonged distension of colon causes irreversible changes in colonic smooth muscles and nerves.
- Retained bacterial toxins may be absorbed, resulting in endotoxemia and signs of illness (anorexia, lethargy, vomiting).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis of constipation is based on a history of difficult, reduced, or absent defecation and finding firm feces in the colon on abdominal palpation. The underlying cause can usually be determined by physical examination and abdominal radiography.

DIFFERENTIAL DIAGNOSIS

- Reversible causes of constipation:
  - Dehydration, electrolyte disorders, inflammatory diseases of the anorectum
  - Drug administration (opioids, anticholinergics)
  - Environmental changes (inactivity, litter box changes)
- Any of the risk factors causing mechanical obstruction

INITIAL DATABASE

- CBC: leukocytosis (mature neutrophilia/stress leukogram), occasionally anemia
- Serum biochemistry profile: azotemia (associated with dehydration or concurrent chronic renal failure), hypokalemia, hypercalcemia
- Urinalysis: no specific changes. Isosthenuria in azotemic patients if chronic kidney disease.
- Abdominal radiographs: feces-distended colon. Underlying cause of initial colonic distension/fecal retention may be evident: pelvic fractures, evidence of spinal trauma (vertebral fracture/luxation), extraluminal compressive masses, foreign material in colon.

ADVANCED OR CONFIRMATORY TESTING

- Ultrasonography: identifies suspected extraluminal masses. Poor utility for intraluminal visualization because even minute amounts of colonic gas block ultrasound waves.
- Barium enema: defines strictures or intraluminal masses (see p. 1204)
- Endoscopy: identifies colorectal neoplasia, stricture, inflammatory lesions, sacculations and diverticula, etc.
- Evaluation of animals with suspected neurologic impairment may include cerebrospinal fluid analysis, CT/MRI scanning of distal spinal cord and cauda equina region, myelogram, and electrophysiologic studies (electromyography).
- Diagnosis of dysautonomia is based on finding other systemic evidence of the disease (megaesophagus, mydriasis, decreased lacrimation, prolapsed nictitans, and bradycardia) but is considered a rare cause of megacolon (see).

TREATMENT

TREATMENT OVERVIEW

Mild to moderate constipation is usually successfully treated with a combination of enemas, laxatives, colonic prokinetic agents, and diet modification. Patients with severe constipation often also require intravenous fluid therapy and manual extraction of feces under anesthesia. Subtotal colectomy is necessary for patients with end-stage megacolon.

ACUTE GENERAL TREATMENT

- Fluid therapy for dehydration, with supplementation to correct hypokalemia if present. Intravenous fluid therapy (60-90 mL/kg/d) is often needed for most severely affected cats. Correction of dehydration assists in constipation relief through rehydration of the colonic mucosa.

- Enemas and careful manual extraction of feces if obstipated. In most cats, sedation or anesthesia will be required. Multiple procedures over a day or two may be needed in the most severely obstipated/impacted cats to prevent additional injury or rupture of the diseased colon.
- Warm water enemas (5-10 mL/kg water) using a 12-14 Fr, well-lubricated, red rubber catheter for insertion are well tolerated. See for procedure description. Higher volumes of water must be used with caution because they may cause vomiting (and aspiration). If multiple enemas are administered in a short period of time, saline is preferred instead of tap water to avoid an excessive osmotic shift of sodium and other electrolytes into the colon, and resultant hyponatremia.
- Enemas should not contain soaps or other irritants; lactulose or mineral oil can be used.
- Enemas containing sodium phosphate (e.g., Fleet) are contraindicated in cats and small dogs because of the severe hyperphosphatemia and subsequent hypocalcemia they can cause.
- Broad-spectrum antibiotics (e.g., ampicillin, 22 mg/kg IV q 8 h, and enrofloxacin, 5 mg/kg diluted 1:1 in saline and given slowly IV q 12 h [q 24 h in cats]) are indicated if signs of endotoxemia or fever are noted.

CHRONIC TREATMENT

- Medical therapy includes stool softeners or laxatives (e.g., lactulose, 0.25-0.5 mL/kg PO q 8-12 h; or docusate sodium/dioctyl sulfosuccinate, 50 mg/cat PO q 12-24 h; or mineral oil) and prokinetics (cisapride, 0.1-1 mg/kg POq 8-12 h or 2.5-5 mg/cat PO q 8-12 h). Lactulose is the most effective stool softener and is given to effect daily to maintain a soft to semiformed stool (usual dose after titration: 1-4 mL/cat PO q 8-12 h).
- Bulk-forming laxatives (cellulose, psyllium) will not be effective in cats prone to dehydration or in cats with poor colonic muscle function, because their mechanism of action is similar to high-fiber diets.
- Stimulant laxatives (e.g., bisacodyl, castor oil, cascara) should not be used for relieving constipation but are best used as a preventive in cats that still have normal colonic function.
- Prokinetic therapy may assist smooth-muscle function in cats with recurrent constipation or obstipation. The most effective drugs are the serotonergic agonists (cisapride, prucalamide) and histamine H2 receptor antagonists (ranitidine, 1-2 mg/kg PO q 8-12 h, or nizatidine [dogs only] 5 mg/kg PO q 24 h; famotidine does not have this effect).
- Correct underlying cause: remove masses or strictures causing obstruction to outflow, or correct pelvic fractures obstructing outflow with pelvic osteotomy.
- Subtotal colectomy (with or without preservation of the ileocolic valve) may be indicated if lack of response to medical treatment or pelvic fracture malunion >6 months from onset of obstipation.

NUTRITION/DIET

- Control recurrent constipation with high-fiber or low-residue diet.
- High-fiber diets induce colonic contraction and are useful in management of constipation when the patient still has a functional colon and is well hydrated. Avoid high-fiber diets in patients that are prone to dehydration (can exacerbate it).
- Low-residue diets are often best inpatients with chronic recurrent episodes of obstipation or true megacolon, because they reduce the amount of material reaching the colon and make it easier to keep a soft stool.

POSSIBLE COMPLICATIONS

- Medical treatment: perforation secondary to trauma from enemas and evacuation of feces; gentle manipulation and being patient (don't be in a hurry to remove the concretion) are essential.
- Subtotal colectomy: leakage, dehiscence, and peritonitis; chronic diarrhea (may be associated with bacterial overgrowth from loss of ileocolic sphincter); recurrent constipation; stricture.

RECOMMENDED MONITORING

- For cats undergoing medical management, close observation of fecal passage by the owner is essential for prevention of severe recurrent constipation.
- After subtotal colectomy, monitor:
    - Hydration
    - Appetite
    - Temperature, blood glucose, abdominal pain (signs of leakage or dehiscence of anastomosis)

PROGNOSIS AND OUTCOME 

- Fair prognosis with medical management. Recurrent constipation requiring repeated enemas and manual evacuation is common.
- Good to excellent prognosis with subtotal colectomy. Owner needs to be aware that stools are usually soft, and the frequency of defecation is increased, for 2 to 3 months after surgery. Occasionally diarrhea is a persistent long-term problem.
- Guarded prognosis with pelvic osteotomy for pelvic fracture malunion. Correction of obstruction may not resolve megacolon

and constipation.

PEARLS & CONSIDERATIONS

COMMENTS

- Do not attempt correction of pelvic malunion by pelvic osteotomy if >6 months from onset of signs of obstipation. Perform subtotal colectomy instead.
- Do not perform enema immediately before surgery for megacolon. It is more difficult to control contamination of the abdomen with liquid feces during surgery.

PREVENTION

Early repair of pelvic fractures that cause obstruction of pelvic canal

CLIENT EDUCATION

Warn owners that diarrhea can be severe after subtotal colectomy but that it usually resolves within 8 weeks. If the cecum is removed during surgery, consider treatment for bacterial overgrowth if diarrhea persists >8 weeks.

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Conjunctivitis, Dogs

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Inflammation of the conjunctiva, a thin mucous membrane lining the inner surface of the upper and lower eyelids (palpebral conjunctiva) and both sides of the third eyelid. In the conjunctival fornix ("cul-de-sac"), the conjunctiva reflects onto the globe (bulbar conjunctiva) and becomes continuous with the corneal epithelium. The conjunctiva is an immunologically active structure with an abundance of immune cells, blood vessels, and lymphatics. Conjunctivitis is one of the most commonly diagnosed ocular disorders in dogs.

SYNONYMS

Canine adenovirus 1: infectious canine hepatitis

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Typically no age predisposition, although allergic conjunctivitis and follicular conjunctivitis typically occur in younger dogs
- No sex predisposition

GENETICS & BREED PREDISPOSITION

Breeds predisposed to:

- Pannus (Chronic Superficial Keratitis), see p. 825
- Plasmacellular conjunctivitis: German shepherd, collie
- Keratoconjunctivitis sicca, see p. 628
- Abnormal eyelid conformation (e.g., Entropion/Ectropion, p. 348)
- Deep orbits, narrow skull conformation, and inadequate tear drainage (i.e., medial canthal pocket syndrome): dolichocephalic breeds including Afghan hound, Doberman pinscher, standard poodle
- Ligneous conjunctivitis (rare): Doberman pinscher

RISK FACTORS

- Outdoor activities (e.g., hunting: allergic conjunctivitis, follicular conjunctivitis)
- Unvaccinated animals, dog shelters, dog shows (see Distemper, Canine, p. 317; canine adenovirus [CAV-1, CAV-2] conjunctivitis)

CONTAGION & ZOONOSIS

Canine distemper virus and CAV-1, CAV-2: contagious dog-to-dog

ASSOCIATED CONDITIONS & DISORDERS

Allergic dermatitis/skin lesions, otitis externa (allergic conjunctivitis)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Unilateral or bilateral:

- Primary: allergic, follicular, immune-mediated, bacterial, parasitic
- Secondary: underlying ocular and/or systemic (infectious or noninfectious) disease, environmental, neoplasia, idiopathic (e.g., ligneous conjunctivitis)

HISTORY, CHIEF COMPLAINT

- Painful, red eye (unilateral or bilateral)
- Ocular discharge

PHYSICAL EXAM FINDINGS

- Conjunctival hyperemia
- Conjunctival edema (chemosis)
- Lymphoid follicles on conjunctiva
- Thick, opaque palpebral conjunctival membrane formation (ligneous conjunctivitis)
- Ocular discharge (see p. 777)
- Blepharospasm (squinting)
- Protrusion of the third eyelid

ETIOLOGY AND PATHOPHYSIOLOGY

- Primary:
  - Allergic conjunctivitis
  - Follicular conjunctivitis (chronic antigenic stimulation)
  - Immune-mediated conjunctivitis (clinical signs together with plasmacellular infiltration on cytologic/histologic evaluation suggestive of immune-mediated condition)
  - Bacterial conjunctivitis (*Staphylococcus* spp. and other gram-positive organisms uncommon; more often secondary to keratoconjunctivitis sicca or eyelid abnormalities)
  - Parasitic conjunctivitis (*Thelazia* spp.)
- Secondary:
  - Other ocular causes of red eye (see p. 967) including:
    - Keratoconjunctivitis sicca (see p. 628)
    - Mechanical ocular irritation (e.g., entropion, ectropion, trichiasis, distichiasis, ectopic cilia, eyelid mass, exophthalmos [cranial displacement of the globe], lagophthalmos [incomplete closure of the eyelids], foreign body)
    - Corneal ulceration (see p. 250)
    - Anterior uveitis (see p. 1151)
    - Ocular trauma
    - Glaucoma (see p. 448)
    - Blepharitis
    - Dacryocystitis (see p. 280)
    - Scrolled cartilage of the third eyelid and/or prolapsed gland of the third eyelid (see p. 1089)
  - Environmental:
    - Irritation from dust, smoke, or chemicals
    - Actinic-related/solar conjunctivitis in dogs lacking pigment along margin of third eyelid
  - Systemic infectious diseases:
    - Viral (canine distemper, CAV-1, CAV-2)
    - Systemic mycoses (see Blastomycosis, p. 138; Coccidioidomycosis, p. 222; Cryptococcosis, p. 266; Histoplasmosis, p. 538)
    - Leishmaniasis (see p. 643)
  - Systemic noninfectious diseases (e.g., systemic histiocytosis, polycythemia vera)
  - Neoplasia (e.g., lymphosarcoma, multiple myeloma, mast cell tumor, squamous cell carcinoma, melanoma)
  - Idiopathic:
    - Ligneous conjunctivitis
      - Conjunctival injury and exaggerated, inflammatory immune response implicated in human form of disease
      - May be associated with membrane formation involving the oral mucosa, upper respiratory tract, or urinary tract

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Conjunctivitis in dogs arises most commonly as a result of other causes of red eye (i.e., secondary), including KCS, mechanical ocular irritation, and systemic disease. Determining whether the conjunctivitis is primary versus secondary in nature requires physical examination and ophthalmic examination (), and is crucial to direct the appropriate treatment.

DIFFERENTIAL DIAGNOSIS

Primary conjunctivitis must be differentiated from secondary conjunctivitis (i.e., other causes of red eye; see Etiology and Pathophysiology).

INITIAL DATABASE

Complete ophthalmic examination, including:

- Examination of all conjunctival surfaces, including lacrimal puncta, with diffuse light and magnification
- Conjunctival swabs for bacterial ± fungal culture(s) and sensitivity (done before other diagnostic tests)
- Conjunctival scrapings for cytologic evaluation: diagnosis of bacterial or fungal infection, intracytoplasmic inclusions in conjunctival epithelial cells in distemper infection
- Schirmer tear test (normal is >15 mm/min)
- Fluorescein dye application (monitor nares for exit of dye to determine if nasolacrimal system patent)
- Tear film break-up time (TFBUT; mean TFBUT = 19.7 seconds; <10 seconds is considered accelerated)
- Intraocular pressures (normal is 15-25 mm Hg)

ADVANCED OR CONFIRMATORY TESTING

- Conjunctival samples may be submitted for PCR testing for infectious diseases (e.g., distemper virus).
- Conjunctival samples for indirect fluorescent antibody staining (distemper virus, adenovirus)
- Flush nasolacrimal system if occlusion suspected (see online chapter: Dacryocystitis).
- Conjunctival biopsy and histopathologic examination (neoplasia; ligneous conjunctivitis)

TREATMENT

TREATMENT OVERVIEW

Determining the underlying cause of canine conjunctivitis (primary versus secondary) is critical to direct the appropriate therapy. Many causes of secondary conjunctivitis can be vision threatening (e.g., chronic KCS) and/or have an association with life-threatening systemic disease (e.g., systemic mycoses). Therapeutic goals are to treat underlying cause, eliminate infection if present, and eliminate ocular pain.

ACUTE AND CHRONIC TREATMENT

- Primary:
  - Allergic or follicular or immune-mediated/plasmacellular:
    - Topical corticosteroid or corticosteroid/antibiotic combination (e.g., 0.1% dexamethasone ± neomycin/polymyxin B solution or ointment) q 6-8 h, tapered slowly based on response to treatment; may recur; address contributing factors (e.g., atopy, food allergy). Corneal ulceration contraindicates this treatment (p. 250).
    - Topical cyclosporine A (CsA; 0.2%-2%) q 12 h (plasmacellular conjunctivitis); usually required long term
  - Bacterial:
    - Topical broad-spectrum antibiotics (e.g., bacitracin/neomycin/polymyxin B; or based on culture and sensitivity results) q 6-8 h for 7-10 days
  - Parasitic:
    - *Thelazia* spp.: flushing the conjunctival sac with tetramisole (0.5% solution)
- Secondary–treat underlying cause:
  - Ligneous:
    - Topical cyclosporine A (0.2%-2%) q 12 h
    - Azathioprine, 1.5-2 mg/kg PO q 24 h until clinical improvement; then gradually tapered to as low a dose as possible (e.g., 1 mg/kg PO q 24 h, then every other day, then weekly for maintenance)
    - ±Prednisone orally 1-2 mg/kg PO q 24 h until clinical improvement; then gradually tapered over 3 to 4 weeks until maintenance dose reached

Indefinite maintenance therapy usually required for immune-mediated causes of conjunctivitis (i.e., plasmacellular conjunctivitis [see Pannus (Chronic Superficial Keratitis), p. 825]) and ligneous conjunctivitis.

PROGNOSIS AND OUTCOME

- Variable depending on cause
- Usually good if underlying cause addressed
- Some breeds with medial canthal pocket syndrome develop chronic conjunctivitis and may need indefinite topical treatment.
- Immune-mediated causes of conjunctivitis typically require lifelong treatment.

PEARLS & CONSIDERATIONS

COMMENTS

Do not use topical corticosteroids if corneal ulceration is noted.

PREVENTION

Conjunctivitis due to breed predisposition: avoid breeding affected or closely related dogs.

SUGGESTED READING

Peña MA, Leiva M: Canine conjunctivitis and blepharitis. Vet Clin North Am Small Anim Pract 38:233–249, 2008.

AUTHOR: URSULA M. DIETRICH

EDITOR: CHERYL L. CULLEN

Conjunctivitis, Cats

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

An inflammation of the conjunctiva, a thin mucous membrane that lines the inner surface of the upper and lower eyelids (palpebral conjunctiva) and both sides of the third eyelid. In the conjunctival fornix ("cul-de-sac"), the conjunctiva reflects onto the globe (bulbar conjunctiva) and becomes continuous with the corneal epithelium. Conjunctivitis is one of the most common feline ocular diseases.

SYNONYMS

Red eye, *Chlamydophila felis* (formerly *Chlamydia psittaci*), feline herpesvirus (FHV-1), feline viral rhinotracheitis, eosinophilic conjunctivitis

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Younger cats: FHV-1, *C. felis, Mycoplasma* spp., eosinophilic conjunctivitis
- Older cats: lipogranulomatous conjunctivitis, neoplasia

GENETICS & BREED PREDISPOSITION

Lightly colored (white cats) predisposed to actinic-related conjunctivitis, lipogranulomatous conjunctivitis, squamous cell carcinoma

RISK FACTORS

- Multicat household, catteries, boarding kennels, veterinary hospitals, cat shows, free-roaming cats (infectious conjunctivitis)
- Underlying systemic viral infection (feline leukemia virus [FeLV], feline immunodeficiency virus [FIV]) may predispose to FHV-1 infection.
- Stress and immunosuppression may reactivate FHV-1 and *Chlamydophila felis* infection.

CONTAGION & ZOONOSIS

- FHV-1, *C. felis, Mycoplasma* spp.: contagious cat-to-cat
- *C. felis*: identified in humans with conjunctivitis

ASSOCIATED CONDITIONS & DISORDERS

Most cats with upper respiratory syndrome (see p. 1127) present with conjunctivitis.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Unilateral (e.g., trauma, topical irritants, intraocular neoplasm, uveitis) versus bilateral (e.g., infectious conjunctivitis, systemic illness)
- Primary (infectious causes common in cats; see above) versus secondary (underlying ocular and/or systemic disease [e.g., uveitis, lymphosarcoma])

HISTORY, CHIEF COMPLAINT

- Painful, red eye (unilateral or bilateral)
- Ocular discharge
- Signs of upper respiratory tract infection (FHV-1), including sneezing, nasal discharge, inappetence
- Recurrent signs of red, painful eye and/or ocular discharge (FHV-1)

PHYSICAL EXAM FINDINGS

- Conjunctival hyperemia
- Conjunctival edema (chemosis)
- Lymphoid follicles on conjunctiva
- Smooth, cream or white conjunctival nodules (lipogranulomatous)
- Ocular discharge (see p. 777 ; sometimes dark brown to black, waxy discharge in Persian, Himalayan, Siamese cats)
- Blepharospasm
- Protrusion of the third eyelid

ETIOLOGY AND PATHOPHYSIOLOGY

- Primary:
  - Viral: FHV-1 (see p. 524) is one of the most important causative agents of feline conjunctivitis; has high affinity for conjunctival and respiratory epithelia and causes epithelial necrosis. Other viruses involved in feline upper respiratory syndrome, but less likely to cause conjunctivitis, include calicivirus and reovirus.
  - Bacterial: *C. felis, Mycoplasma* spp., other bacterial infections *(e.g. Staphylococcus* spp., *Bacillus* spp., *Corynebacterium* spp.); uncommon in cats
  - Immune-mediated: eosinophilic conjunctivitis, allergic conjunctivitis (rare in cats)
- Secondary:
  - Other ocular causes of red eye (see p. 967), including: mechanical ocular irritation (e.g., entropion, trichiasis, distichiasis, exophthalmos, cranial displacement of the globe), lagophthalmos (incomplete closure of the eyelids), foreign body, corneal ulceration (see p. 250), anterior uveitis (see p. 1151), ocular trauma, glaucoma (see p. 448), blepharitis
  - Obliteration of lacrimal puncta/ducts secondary to symblepharon (adhesions of conjunctiva to surrounding tissues)
  - Actinic-related conjunctivitis
  - Lipogranulomatous conjunctivitis:
    - Likely a reaction to sebaceous secretions from damaged meibomian glands
    - May be a form of chalazion (see Eyelid Defects: Trauma, Masses, p. 373)
    - Possible role of actinic radiation
  - Systemic infectious diseases:
    - Viral (FeLV, FIV)
    - Systemic mycoses
  - Neoplasia (e.g., squamous cell carcinoma, lymphosarcoma)

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis of conjunctivitis is made on physical exam. A complete ophthalmic examination (see p. 1313) identifies the cause in many instances and is indicated in every case. In cats where examination alone does not provide a conclusive diagnosis, options (with attendant advantages and drawbacks) include referral to a veterinary ophthalmologist, pursuing diagnostic testing in-house, and monitoring response to treatment.

DIFFERENTIAL DIAGNOSIS

Primary conjunctivitis must be differentiated from secondary conjunctivitis (i.e., other causes of red eye; see Etiology and Pathophysiology above).

INITIAL DATABASE

Complete ophthalmic examination (see p. 1313), including:

- Examination of all conjunctival surfaces, including lacrimal puncta, with diffuse light and magnification
- Conjunctival swabs for bacterial ± fungal culture(s) and sensitivity (done before other diagnostic tests)
- Conjunctival scrapings for cytology; diagnosis of bacterial or fungal infection, *C. felis* and *Mycoplasma* spp. inclusions; eosinophils (eosinophilic conjunctivitis)
- Schirmer tear test (normal is >15 mm/min but can be variable in cats)
- Tear film break-up time (TFBUT): 16.7 (±4.5) seconds is normal in cats; decreased in cats with conjunctivitis.
- Fluorescein dye application (monitor nares for exit of dye to determine if nasolacrimal system patent).
- Intraocular pressures (normal is 15-25 mm Hg)

ADVANCED OR CONFIRMATORY TESTING

- Conjunctival samples may be submitted for PCR testing for infectious diseases (FHV-1, *C. felis, Mycoplasma* spp., FeLV).
- Conjunctival samples for indirect fluorescent antibody staining (FHV-1)
- Flush nasolacrimal system if suspect occlusion (see online chapter: Dacryocystitis).
- Conjunctival biopsy and histopathology (neoplasia)

TREATMENT

TREATMENT OVERVIEW

The treatment of feline conjunctivitis should be directed at the underlying etiology(ies). Depending on the underlying cause(s), conjunctivitis in cats may become chronic (e.g., *C. felis*) and/or recurrent (e.g., FHV-1) and require prolonged therapy. Lysine may help limit recurrences in some FHV-1-infected cats (see p. 524). Therapeutic goals are to treat the underlying cause, eliminate infection if possible, and eliminate ocular pain.

ACUTE GENERAL TREATMENT

- Primary:
  - FHV-1 or bacterial:
    - Topical broad-spectrum antibiotics (e.g., tobramycin) q 6-8 h for 7-10 days (to prevent secondary bacterial conjunctivitis if FHV-1-induced)
    - Consider oral administration of lysine (500 mg PO q 12 h: lifelong treatment) to reduce herpesviral replication in cats with frequent recurrences and/or associated herpesviral keratitis (see p.524).
  - *C. felis* and/or *Mycoplasma* spp.:
    - Topical tetracycline ointment, q 6-8 h; continued for 10-14 days after clinical signs have resolved
  - Eosinophilic:
    - Topical corticosteroids (e.g., prednisolone acetate 1% suspension or 0.1% dexamethasone solution or ointment) q 6-8 h, tapered to indefinite maintenance dose
    - Topical cyclosporine A (CsA; 0.2%-2%) q 8-12 h as indefinite treatment
- Secondary—treat underlying cause:
  - Lipogranulomatous:
    - Surgical excision typically curative

CHRONIC TREATMENT

- FHV-1: see p. 524
- *C. felis* and/or *Mycoplasma* spp.:
  - Prolonged topical tetracycline if concurrent infection with FIV is confirmed
  - Oral antibiotics (e.g., doxycycline, 5 mg/kg PO q 12 h for 3-4 weeks for difficult cases)

POSSIBLE COMPLICATIONS

FHV-1 may cause:

- Corneal Sequestration, Cats, p. 248
- Symblepharon
- Keratoconjunctivitis sicca,

PROGNOSIS AND OUTCOME

- Variable depending on cause
- Usually good
- Conjunctivitis caused by *C. felis* may become chronic.
- Recurrent conjunctivitis is observed with FHV-1 infection.

PEARLS & CONSIDERATIONS

COMMENTS

- FHV-1 infection may not only cause conjunctivitis but may also cause keratitis in cats.
- Topical corticosteroids should be avoided in cats with conjunctivitis, unless eosinophilic or lipogranulomatous conjunctivitis is confirmed cytologically and/or histologically.

TECHNICIAN TIP

Some ophthalmic drugs have virtually identical names for their formulations with and without corticosteroids. This similarity presents a risk of using the wrong drug. It is extremely useful for technicians to carefully read the label of the tube/vial and identify whether it contains corticosteroids *prior* to topical application (read label of tube/bottle), and to check the medical record for consistency. Substitution error (especially administering corticosteroids when they are contraindicated) can be devastating and has been made by veterinarians, technicians, and clients.

PREVENTION

Reduction of known stresses is useful (FHV-1).

CLIENT EDUCATION

- Monitor for recurrent signs of conjunctivitis (FHV-1).
- Stress factors (e.g., concurrent systemic disease [FeLV, FIV], systemic or topical corticosteroids, general anesthesia, multicat household, moving) can trigger flare-up of FHV-1-induced conjunctivitis.

SUGGESTED READING

Read RA, Lucas J: Lipogranulomatous conjunctivitis: clinical findings from 21 eyes in 13 cats. Vet Ophthalmol 4:93–98, 2001.

Spiess AK, Sapienza JS, Mayordomo A: Treatment of proliferative feline eosino-philic keratitis with topical 1.5% cyclospo-rine: 35 cases. Vet Ophthalmol 12:132–137, 2009.

AUTHOR: URSULA M. DIETRICH

EDITOR: CHERYL L. CULLEN

Coma

BASIC INFORMATION

DEFINITION

A state of unconsciousness unresponsive to all stimuli; a well-recognized neurologic emergency

EPIDEMIOLOGY

RISK FACTORS

- Any condition that increases intracranial pressure (ICP)
- Older animals: neoplasia
- Younger animals: trauma and toxins

CONTAGION & ZOONOSIS

Consider rabies.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Obtunded: conscious state with mild to moderate reduction in alertness
- Stupor: unconscious state that requires strong stimuli (usually noxious; toe pinch) to evoke a response (often reduced)

HISTORY, CHIEF COMPLAINT

- Acute onset or rapid deterioration: consider toxin, trauma, rapidly bleeding tumor, or embolism/infarction
- Chronic slow progression: consider tumor, metabolic disease, or encephalitis

PHYSICAL EXAM FINDINGS

- Recumbent with no response
- Patient may present in shock
- Neurologic exam: focus on level of consciousness (response to toe pinch and loud noise), pupillary size and light reflexes, ability to elicit physiologic nystagmus, limb rigidity, and respiratory patterns to determine prognosis

ETIOLOGY AND PATHOPHYSIOLOGY

- There are two general causes of unconsciousness:
  - Diffuse cerebral cortical injury
  - Interruption of the ascending reticular activating system located in the brainstem
- Diffuse cortical injury generally carries a better prognosis than brainstem injury.
- Brainstem (midbrain, medulla) injury may be suspected based on:
  - Deficits in pupillary light response or pupil size: midbrain (assuming exam reveals no evidence of ocular or optic nerve lesion)
  - Inability to elicit normal physiologic nystagmus: medulla (assuming no evidence of middle/inner ear abnormality on exam)
  - Limb rigidity: medulla (assuming no spinal cord or neuromuscular signs)
  - Respiration abnormalities: medulla or midbrain (barring primary airway/lung lesion)
    - Kussmaul (rapid, deep, labored breathing, associated with diabetic coma)
    - Cheyne-Stokes (abnormal breathing pattern with alternating periods of apnea and deep, rapid breathing; the cycle begins with slow, shallow breaths that gradually increase in depth and rate and is then followed by a period of apnea).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

- The diagnosis should be suspected in any recumbent animal that does not show a response to initial physical examination and stimulation, and then established following a neurologic examination that confirms the patient is recumbent and unresponsive to all stimuli (including noxious stimuli).

DIFFERENTIAL DIAGNOSIS

- Intracranial:
  - Trauma, tumor, hemorrhage, status epilepticus, embolism/ischemic encephalopathy, granuloma, abscess, developmental disorders (hydrocephalus, storage diseases), and infections (rabies, feline infectious peritonitis, canine distemper, fungal, parasitic)
- Systemic:
  - Toxins: lead, barbiturates, antidepressants, tranquilizers, alcohol, ethylene glycol
  - Metabolic: hypoglycemia, diabetic ketoacidosis, hepatic encephalopathy, uremic encephalopathy, hypoadrenocorticism, myxedema coma
  - Hyperosmolar syndromes: hyperosmolar nonketotic diabetes mellitus, ethylene glycol, hypernatremia
  - Hyperviscosity: polycythemia, hyperglobulinemia
  - Miscellaneous: severe hypovolemia/shock, post arrest, heat stroke, hyponatremia

INITIAL DATABASE

Laboratory tests:

- CBC (infection or thrombocytopenia)
- Serum biochemistry panel (metabolic disorders)
- Urinalysis:
  - Glucose, ketones (diabetes mellitus/ketoacidosis)
  - Calcium oxalate monohydrate crystals (ethylene glycol intoxication)
  - Ammonium biurate crystals (portosystemic shunt)
  - Low urine specific gravity (USG)/ casts (renal disease [consider other causes of low USG])
- Prothrombin time/partial thromboplastin time or activated clotting time (coagulopathies)
- Serum bile acids (liver failure) Imaging:
- Thoracic radiographs (metastatic lesions, trauma, or infections)
- Skull radiographs (trauma/skull fractures)

ADVANCED OR CONFIRMATORY TESTING

MRI or CT followed by cerebrospinal fluid analysis after systemic disease is eliminated

TREATMENT

TREATMENT OVERVIEW

- Coma can result from a number of underlying conditions; therefore, the initial therapy should focus on stabilization of the cardiovascular (perfusion), respiratory (oxygenation and ventilation), and neurologic (cerebral oxygen delivery and ICP) systems, followed by specific therapy tailored to the underlying cause.

ACUTE GENERAL TREATMENT

Airway and breathing:

- Endotracheal intubation assists ventilation and protects the airways (comatose patients cannot swallow; salivary secretions, regurgitation, and vomiting may cause airway obstruction and aspiration pneumonia). Avoid cough reflexes, which increase ICP.
- Provide supplemental oxygen (maintain Pao2 > 60 mm Hg, SaO2 > 90%).
- Caution: nasal oxygen lines can induce sneezing, which increases ICP.
- Ensure ventilation (maintain Pco2 between 35-45 mm Hg).

Circulation:

- Place intravenous catheter (avoid jugular veins if ICP elevated).
- Correct hypovolemia.
  - Fluid choice is controversial.
    - Crystalloids usually sufficient. Administer ¼ shock dose (15 mL/kg, dogs; 10 mL/kg, cats) repeatedly in rapid IV increments until cardiovascularly stable.
  - Avoid overhydration.
- Provide maintenance fluids, and replace ongoing fluid losses.
- With cardiac disease or hyperosmolar syndromes, administer fluids cautiously.

Decrease ICP:

- In comatose patient, assume ICP elevated until proven otherwise.
- Elevate head 20-30 degrees.
- Avoid pressure on jugular veins.
- Give mannitol (0.5-2 mg/kg IV over 20-30 minutes) if diagnosis is unconfirmed or patient shows neurologic deterioration.
- Avoid mannitol in dehydrated, hypovolemic patients and when underlying cardiac disease or hyperosmolar states are present.

Supportive care:

- Control seizures:
  - Diazepam (0.5-1 mg/kg IV; can repeat twice in 15 minutes. If ineffective, then use constant rate infusion or different drug); *or*
  - Phenobarbital (2-15 mg/kg slow IV bolus [monitor respiration]); *or*
  - Propofol (if severe hepatopathy/hepatic coma) (1-6 mg/kg IV bolus; can repeat or switch to constant rate infusion [monitor respiration]).
- Treat hypoglycemia with IV dextrose:
  - Dose: 0.5 g/kg slow IV. Dilute 50% dextrose, 1 mL/kg, into 0.9% NaCl, 3 mL/kg, and administer IV slowly.
  - Avoid hyperglycemia.
- Glucocorticoids (e.g., methylprednisolone sodium succinate, 30 mg/kg IV initial dose, then according to standard protocols, or dexamethasone, 0.1 mg/kg IV) may be beneficial (neoplasia) or harmful (trauma).
- Try to confirm diagnosis before giving glucocorticoids.
- If life-threatening deterioration occurs before the diagnosis is confirmed, rapid-acting intravenous glucocorticoids can be administered for suspected neoplasia or encephalitis.

Specific therapy:

See specific diseases.

POSSIBLE COMPLICATIONS

- Hypotension
- Hypothermia
- Brain herniation
- Cardiac arrhythmias
- Hypoventilation
- Aspiration pneumonia
- Seizures

RECOMMENDED MONITORING

- Rapid deterioration possible: monitor until stable and deterioration unlikely.
- Neurologic examination every 30-60 minutes
- Continuous electrocardiogram
- Blood pressure every 30-60 minutes (systolic: > 90 mm Hg but < 180 mm Hg; mean: > 60 mm Hg but < 140 mm Hg)
- Blood gases (PaCO2 and Pao2) every 60 minutes or capnography and pulse oximetry continuously
- Blood glucose and electrolytes as needed

PROGNOSIS AND OUTCOME

- Varies with underlying disease

- Generally guarded until diagnosis confirmed
- Declines as level of consciousness decreases
- Worse with systemic complications
- Unresponsive pupils, decerebrate rigidity, abnormal respiratory patterns, and loss of physiologic nystagmus carry a grave prognosis.
- Miotic responsive pupils suggest cortical lesions and a better prognosis.
- Can use modified Glasgow Coma Scale for prognosis in dogs with head trauma (see p. 464).
- Failure to improve over 5-7 days warrants poor prognosis.

PEARLS & CONSIDERATIONS

COMMENTS

- Animals that display decerebrate rigidity are also comatose.
- Cranial nerve reflexes (depending on location of the lesion) and spinal reflexes are often present.
- Bradycardia with concurrent hypertension suggests elevated ICP.
- Can use caloric test to evaluate nystagmus (infusion of warm or cold water into the ear canal normally results in nystagmus).
- Administration of lidocaine during intubation (0.75 mg/kg IV) may suppress gag and cough reflexes, which would otherwise increase ICP.

TECHNICIAN TIPS

- Physical therapy, turning to change recumbencies, lubrication of the eyes, and moistening the mouth every 4 hours are important elements of support for comatose patients.
- A urinary catheter assists with monitoring urine output and preventing urine scald.

CLIENT EDUCATION

- Full neurologic recovery can take weeks to months.
- Long-term neurologic deficits and seizures can occur.

SUGGESTED READING

Kline KL: Altered states of consciousness: coma and stupor. In Ettinger SJ, Feldman EC, editors: Textbook of veterinary internal medicine, ed 7, St Louis, 2010, Saunders Elsevier, pp 225–228.

AUTHOR: SΦREN R. BOYSEN

EDITOR: ETIENNE CÔTÉ

Color Disorders of the Skin and Haircoat

BASIC INFORMATION

DEFINITION

Very common spectrum of innate or acquired pigmentary abnormalities of the skin or hair

SYNONYMS

- Hyperpigmentation: melanoderma, melanotrichia
- Hypopigmentation: depigmentation, leukoderma, leukotrichia, poliosis

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Some conditions present at birth (e.g., albinism).
- Most are acquired at any age in dogs and cats.

GENETICS & BREED PREDISPOSITION

- Hyperpigmentation:
  - Acanthosis nigricans: dachshund
  - Recurrent flank alopecia: boxer, English bulldog, Airedale terrier
  - Papillomavirus-associated plaques: pug, miniature schnauzer, shar-pei
- Hypopigmentation:
  - Vitiligo: rottweiler, Belgian sheepdog, Siamese cat, others
  - Waardenburg-Klein syndrome: dalmatian, bull terrier, others
  - Premature graying: golden retriever, Labrador retriever, Irish setter
  - Dermatomyositis: Shetland sheepdog, collie
  - Color dilution alopecia: blue or fawn Doberman pinschers and other dogs
  - Canine cyclic hematopoiesis: collie (rare)
  - Chédiak-Higashi syndrome: Persian cat (rare)

RISK FACTORS

Depends on underlying cause

CONTAGION & ZOONOSIS

Dermatophytosis and *Sarcoptes scabiei* (may exhibit hyperpigmentation)

GEOGRAPHY AND SEASONALITY

- “Snow nose”: decreased nasal pigmentation during winter months
- Recurrent flank alopecia: often seasonal

ASSOCIATED CONDITIONS& DISORDERS

- Postinflammatory hyperpigmentation or hypopigmentation: see Differential Diagnosis
- Waardenburg-Klein syndrome: blue eyes, deafness
- Uveodermatologic syndrome: uveitis, blindness
- Dermatomyositis: may exhibit myositis
- Chédiak-Higashi syndrome: immunologic deficiency
- Canine cyclic hematopoiesis: usually lethal before age 6 months

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Acquired change in skin or coat color tends to be gradual.
- Question owners about sun exposure, changes in overall health, any evidence of inflammation (e.g., pruritus).

PHYSICAL EXAM FINDINGS

- Note distribution of color change, and examine skin for lesions, particularly for evidence of inflammation (e.g., erythema, lichenification).
- Certain physical abnormalities are associated with specific pigmentation disorders (e.g., uveitis, myositis, deafness, enlarged lymph nodes).

ETIOLOGY AND PATHOPHYSIOLOGY

Normal pigmentation of the skin and hair is a highly complex process under the influence of numerous genetic and acquired factors. Both depigmentation and hyperpigmentation can be seen as a result of inflammatory dermatoses.

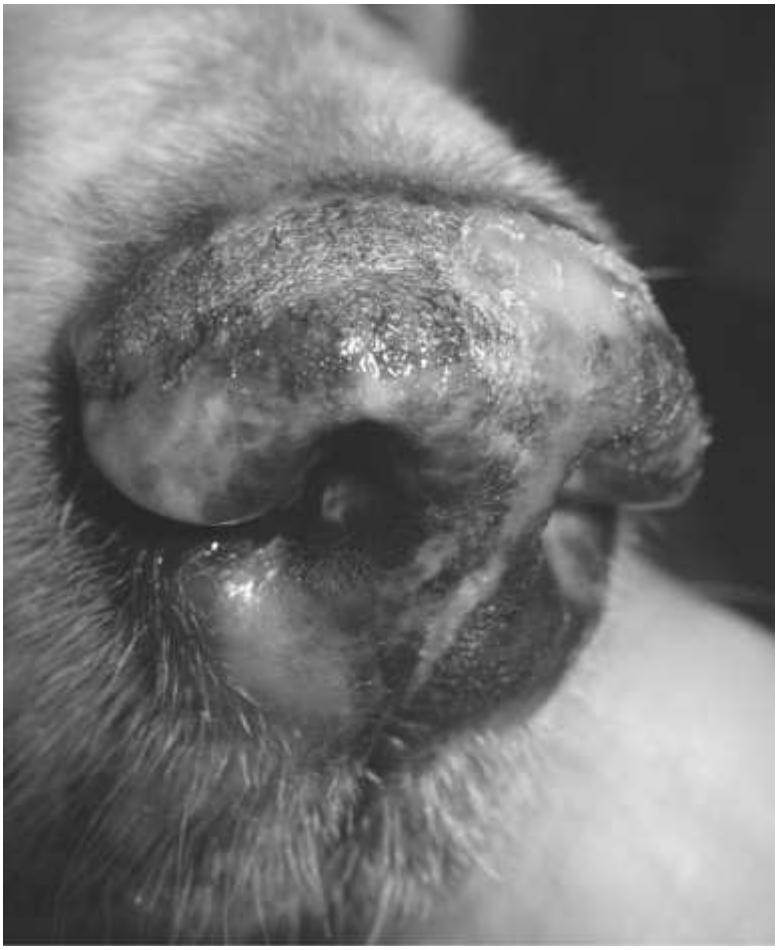
DIAGNOSIS

DIAGNOSTIC OVERVIEW

Causes of color disorders of dogs and cats are myriad but often visually distinctive.

DIFFERENTIAL DIAGNOSIS

- Acquired hyperpigmentation:
  - Postinflammatory: common in dogs; can occur with any chronic inflammatory process, but particularly common with hypersensitivity disorders, *Malassezia,* demodicosis, pyoderma. In cats, it is almost exclusively seen with dermatophytosis. Inflammation also sometimes affects hair color (melanotrichia) in dogs and in Siamese and Himalayan cats.
  - Endocrinopathy: hyperadrenocorticism, hypothyroidism, alopecia X, sex hormone dermatoses
  - Neoplasia: feline Bowen's disease, other pigmented tumors
  - Acanthosis nigricans in dachshunds: localized to axillae. A reaction pattern with multiple causes (friction, infection, hypersensitivity) is more likely than a primary genetic form.
  - Lentigenes: macular melanosis (orange cats)
  - Other: recurrent flank alopecia, sun exposure, drug therapy–induced, papillomavirus-associated plaques
- Acquired hypopigmentation:
  - Postinflammatory: common. On the nasal planum, consider discoid lupus erythematosus, as well as pemphigus erythematosus or foliaceus, uveodermatologic syndrome, other immune-mediated diseases. Pyoderma, dermatomyositis, and other inflammatory conditions also may cause depigmentation in affected areas.
  - Neoplasia: particularly epitheliotropic lymphoma, which may cause striking leukotrichia
  - Vitiligo: multifactorial genetic cause likely. Symmetric patchy loss of pigment from hair, skin, and mucosa, most often on the face (including nose and lips).
  - Nasal hypopigmentation: noninflammatory conditions include “snow nose,” in which partial depigmentation of the nasal planum occurs in winter.
  - Nutrition (e.g., reddish-brown coat in black cats due to tyrosine deficiency)
  - Lightening of the coat can occur with excessive exposure to chlorinated water, sunlight, or in hair cycle arrest (e.g., endocrine disease).
  - Others: drug-induced, periocular leukotrichia/depigmentation in Siamese cats
- Congenital hyperpigmentation or hypopigmentation:
  - Color dilution alopecia, albinism, Waardenburg-Klein syndrome, canine cyclic hematopoiesis, Chédiak-Higashi syndrome, Dudley nose



COLOR DISORDERS OF THE SKIN AND HAIRCOAT Depigmentation of the nasal planum and leukotrichia in a golden retriever with cutaneous lymphoma.

INITIAL DATABASE

May include:

- Skin scrapings
- Skin cytologic examination
- Skin biopsies
- Trichograms (microscopic examination of plucked hairs, useful for assessing color dilution alopecia)
- CBC, serum biochemistry profile, urinalysis

ADVANCED OR CONFIRMATORY TESTING

For specific diseases, additional testing may include:

- Screening tests for endocrinopathy (hyperadrenocorticism, hypothyroidism)
- Ocular examination (uveodermatologic syndrome)
- Fungal examination: Wood's light, fungal culture
- Muscle evaluation (dermatomyositis)
- Auditory evaluation (Waardenburg-Klein syndrome)
- Serologic testing for deep fungal infections, leishmaniasis

TREATMENT

TREATMENT OVERVIEW

The goal is to restore normal pigmentation to skin and hair.

CHRONIC TREATMENT

Depends on underlying cause:

- Many conditions do not require or respond to treatment.
- Inflammation, endocrinopathy, or neoplasia may be treatable.
- Uveodermatologic syndrome requires aggressive therapy to save vision.
- Reduce sun exposure in alopecic dogs.

PROGNOSIS AND OUTCOME

- Good prognosis for acquired hyperpigmentation, providing the underlying condition can be controlled; variable for other conditions.
- Improvement may be very slow for all conditions.

PEARLS & CONSIDERATIONS

COMMENTS

- When examining a nasal planum exhibiting hypopigmentation or depigmentation, inflammatory or infiltrative processes (e.g., discoid lupus erythematosus) typically cause loss of the normal cobblestone architecture. Skin biopsies are usually indicated. Conversely, processes with little or no inflammation (e.g., vitiligo, “snow nose”) spare the normal surface pattern.
- The best sites to biopsy the nasal planum (or other mucocutaneous junction) exhibiting depigmentation are gray, rather than completely depigmented. These areas are most likely to show active inflammation or pigment loss.
- Abundant melanosomes can be seen on surface cytologic examination from hyperpigmented skin. Although these small oval structures are easy to mistake for bacteria, they are distinctly brown rather than blue/purple on a Diff-Quik preparation.

SUGGESTED READING

Paradis M: Pigmentary disorders of the skin. In Morgan RV, editor: Handbook of small animal practice, ed 5, St Louis, 2006, Saunders Elsevier, pp 901–905.

Schmutz S, Berryere TG: Genes affecting coat colour and pattern in domestic dogs: a review. Anim Genet 38:539–549, 2007.

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EDITOR: MANON PARADIS

Collapsing Trachea

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

A common condition in small- and toy-breed dogs, characterized by a weakening of tracheal cartilage support for large airways, resulting in cough and impaired conduction of air

SYNONYMS

Collapsed trachea, tracheal collapse

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Primarily a disease of middle-aged, small-breed dogs; rarely reported in large-breed dogs
- No known sex predilection

GENETICS & BREED PREDISPOSITION

Breeds commonly affected include the Yorkshire terrier, toy and miniature poodle, and Pomeranian.

RISK FACTORS

Obesity may exacerbate frequency and severity of signs.

ASSOCIATED CONDITIONS & DISORDERS

Small-breed dogs with collapsing trachea often have concurrent noninfectious chronic tracheitis and bronchitis.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Grades of tracheal collapse:

- I: minor protrusion of dorsal membrane into airway lumen, <25% reduction in diameter; generally not associated with clinical signs
- II: 50% reduction in airway lumen, tracheal rings elongated and mildly flattened
- III: 75% reduction in airway lumen, tracheal rings markedly flattened
- IV: >90% reduction in airway lumen, severely flattened tracheal rings, possibly with dorsal deviation of ventral tracheal surface; generally associated with frequent, constant, or severe clinical signs

HISTORY, CHIEF COMPLAINT

- Owners often complain of a recurrent loud, honking cough, with gagging or retching commonly observed at the end of a series of coughs.
  - Signs may worsen with excitement, heat, eating or drinking, or exercise.
- Milder clinical signs may have been present since early in life.
- Severely affected animals may exhibit cyanosis or syncope in addition to frequent coughing.

PHYSICAL EXAM FINDINGS

- Dry cough elicited with tracheal palpation
  - This finding is nonspecific, however, since many other respiratory disorders, including pulmonary parenchymal disorders (e.g., pulmonary edema), may cause a cough to be elicited easily with tracheal palpation.
- With cervical collapsing trachea, wheezes may be ausculted over the cervical tracheal region.

- With thoracic collapsing trachea, loud snapping noises may be ausculted due to the dynamic opening and collapse of large airways (sound is due to airway opening during inspiration).
- Increased expiratory effort may be seen.

ETIOLOGY AND PATHOPHYSIOLOGY

- Decreased rigidity of tracheal cartilage rings results in dynamic collapse during inspiration with cervical involvement, and during expiration with thoracic involvement.
- The etiology is unknown, but suggested mechanisms include:
  - Failure of chondrogenesis
  - Acquired secondary to chronic small airway disease
  - Cartilage degeneration
  - Trauma
  - Loss of innervation of the trachealis dorsalis muscle

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

The diagnosis is suspected in at-risk breeds based on the presence of a recurrent cough and/or wheezing; confirmation requires advanced diagnostics such as radiographs, fluoroscopy, or bronchoscopy.

DIFFERENTIAL DIAGNOSIS

- Sterile chronic bronchitis
- Congestive heart failure
- Infectious tracheobronchitis
- Bronchial compression due to left atrial enlargement or lymphadenopathy
- Pneumonia
- Tracheal or laryngeal obstruction
- Other causes of syncope (see p. 1065)

INITIAL DATABASE

- Routine laboratory testing is usually unremarkable.
- Thoracic and lateral cervical radiographs may reveal collapse.
  - Ideally, obtain images during inspiration for cervical collapse and expiration for thoracic collapse.
  - Can underestimate the degree of collapse

ADVANCED OR CONFIRMATORY TESTING

- Fluoroscopy is usually helpful in identifying dynamic collapse, with an elicited cough.
- Bronchoscopy can identify severity, characterize the collapse location, and facilitate collection of airway wash samples to rule out concurrent infectious and inflammatory conditions.

TREATMENT 

TREATMENT OVERVIEW

Treatment consists of cough suppressants, anti-inflammatory medication, bronchodilators, and in severe cases, surgically or fluoroscopically/endoscopically placed stents to help decrease the severity and frequency of cough and associated clinical signs.

ACUTE GENERAL TREATMENT

- Oxygen and judicious use of sedatives and cough suppressants may be necessary in an acute crisis.
- Butorphanol (0.02-0.1 mg/kg SQ q 4-6 h) can lessen acute severe cough and respiratory distress.
- Low-dose acepromazine (0.05-0.1 mg/kg IM) can provide sedation that breaks the cycle of airway irritation and coughing when a bout of extremely severe, collapsing trachea-related coughing occurs.

CHRONIC TREATMENT

- Obesity leads to decreased lung expansion and increased breathing effort. Therefore, weight loss is important in any obese dog diagnosed with collapsing trachea.
- Antitussives help reduce irritation or damage to the tracheal epithelium from chronic cough:
  - Hydrocodone, 0.22 mg/kg PO q 6-12 h; *or*
  - Butorphanol, 0.55-1.1 mg/kg PO q 8-12 h; *or*
  - Diphenoxylate hydrochloride and atropine, 0.2-0.5 mg/kg PO q 12 h
- Antiinflammatory therapy may be needed to decrease laryngeal or tracheal inflammation:
  - Prednisone 0.5-1 mg/kg PO q 12-24 h tapered and discontinued after 5-7 days of use
  - Only short-term use is recommended.
- Bronchodilators may benefit dogs with intrathoracic collapse or expiratory effort that do not improve with initial therapy:
  - β2 Agonists
    - Terbutaline (total amount per dose): small dogs, 0.625-1.25 mg PO q 12 h; medium dogs, 1.25-2.5 mg PO q 12 h; large dogs, 2.5-5 mg PO q 12 h; *or*
    - Albuterol: 0.05 mg/kg PO q 8 h
  - Methylxanthines
    - Not all long-acting theophylline products are equivalent in bioavailability in dogs. Implications are that failure to respond to a certain product should prompt the consideration of switching bronchodilators (to a different brand of theophylline or a different class of bronchodilator altogether [e.g., a ^{2} agonist]), and that certain animals may develop signs of toxicosis when receiving doses that are well tolerated by others.
      - Extended-release theophylline is recommended at 10 mg/kg PO q 12 h; *or*
      - Aminophylline or theophylline, 10 mg/kg PO q 8 h
- Surgical implantation of external prosthetic rings can be considered inpatients with grade II-IV collapse that fail medical management.
  - Rings are more practical for cervical collapse but can be attempted for thoracic collapse through cranial retraction of the trachea. Several potential drawbacks exist, including implant failure and extension of the collapsing process beyond the length of the implant over time.
- Intraluminal stents placed under fluoroscopic guidance can be considered in patients that fail medical management. Such stents can be used for cervical or thoracic collapse. Stents are typically placed with endoscopic or fluoroscopic guidance (see p. 1342).

POSSIBLE COMPLICATIONS

- Cough suppressants: somnolence, sluggishness at higher doses
- Stents: stent migration, stent fracture, exuberant granulation tissue, tracheitis

RECOMMENDED MONITORING

Clinical signs

PROGNOSIS AND OUTCOME

- The prognosis for survival is good. With appropriate treatment, most dogs show improvement but varying degrees of persistent clinical signs. The prognosis for cure is poor because collapsing trachea is irreversible and progressive.
- Dogs with severe clinical signs (cyanosis, syncope) have a guarded prognosis for comfortable survival if not effectively treated with medical therapy. Prognosis for these dogs is often improved with stents.

PEARLS & CONSIDERATIONS

COMMENTS

- Hydrocodone cough suppressants may be more difficult to obtain. Of those available, many are combined with other medications (acetaminophen, guaifenesin, and various antihistamines) that may not be safe or routinely recommended.
- By reducing bronchial smooth-muscle contraction during cough (lessens dynamic component of cough) and slowing the velocity of air flow during coughing (by increasing bronchial diameter), bronchodilators may help patients with collapsing trachea even though the drugs do not act directly at the site of the lesion.

PREVENTION

Affected dogs should probably not be bred.

TECHNICIAN TIPS

When performing radiographs to evaluate for collapsing trachea, taking inspiratory films of the neck and expiratory films of the chest may help better demonstrate a dynamic collapse.

CLIENT EDUCATION

For most dogs, the tracheal collapse is managed with weight control, antitussives, and periodic administration of anti-inflammatory drugs.

SUGGESTED READING

Herrtage M: Medical management of tracheal collapse. In Bonagura JD, Twedt DC, editors: Kirk's current veterinary therapy XIV. St Louis, 2009, Saunders, p 630.

Johnson L: Tracheal collapse. Vet Clin North Am Small Anim Pract 30:1253–1266, 2000.

Sura PA, Krahwinkel DJ: Self-expanding niti-nol stents for the treatment of tracheal collapse in dogs: 12 cases (2001-2004). J Am Vet Med Assoc 232:2, 2008.

AUTHOR: LAURA RIDGE COUSINS

EDITOR: RANCE K. SELLON

Collapse

BASIC INFORMATION

DEFINITION

Loss of the ability to support weight and ambulate without assistance; may include the loss of consciousness

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs, cats
- Age and sex depend on underlying disease.

GENETICS & BREED PREDISPOSITION

Exercise-induced collapse in Labrador retrievers; intervertebral disk extrusion in chondrodystrophic breeds

RISK FACTORS

Increased ambient temperature, obesity

CONTAGION & ZOONOSIS

Common-source infections:

- Agents causing polyarthritis, such as *Borrelia burgdorferi*
- Agents affecting the neuromuscular junction, such as *Clostridium botulinum*

GEOGRAPHY AND SEASONALITY

Areas with a high incidence of infectious agents that can cause collapse

RISK FACTORS

Diabetes mellitus, cardiomyopathies, hypoadrenocorticism, immune-mediated hemolytic anemia, hemangiosarcoma, cervical vertebral instability (wobbler's syndrome)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Neuromuscular: paresis/paralysis but mentation normal
- Neurologic: alterations in intracranial (mentation, cranial nerves) and/or spinal (reflexes, reactions) function, without an underlying systemic cause
- Orthopedic: signs of joint or bone pain, reduced range of motion, or fracture
- Metabolic/endocrine: characteristic systemic signs
- Cardiovascular: characteristic signs of heart disease and/or vascular disturbances
- Respiratory: overt respiratory signs (usually dyspnea) in the absence of systemic, neuromuscular, or cardiovascular causes

HISTORY, CHIEF COMPLAINT

Dependent on underlying cause. Often includes one or more of the following: weakness, inability to rise, incontinence (urine or feces), anxiety/distress, abdominal distension, vomiting, diarrhea, respiratory distress, unconsciousness.

PHYSICAL EXAM FINDINGS

- Dependent on underlying cause:

- Nonspecific signs commonly include recumbency, alterations in mentation (disorientation, unconsciousness), vomiting, variable heart rate (normal, bradycardic or tachycardic), variable pulse quality (absent, weak to hyperdynamic), and pale to hyperemic mucous membranes.

- Some underlying causes may be more likely in the presence of certain physical findings:
  - Asynchronous pulse quality (cardiac arrhythmias), muffled heart sounds (pericardial effusion/cardiac tamponade, pleural effusion if muffled lung sounds also), stertorous upper airway noises (upper airway obstruction), abdominal fluid wave (hemoabdomen, right-sided congestive heart failure, or pyoabdomen/sepsis), moist lung sounds (respiratory, cardiovascular, or pulmonary hemorrhage), flaccid to fasciculating muscles (neuromuscular), decreased to increased spinal reflexes (neuromuscular or neurologic), neck or back pain (orthopedic, neurologic), joint effusion (orthopedic).

ETIOLOGY AND PATHOPHYSIOLOGY

Collapse is caused by loss of normal, coordinated function of muscles that support the body.

- Neuromuscular: reduced nerve conduction, disturbance of neuromuscular junction, or primary myopathy (rare)
- Neurologic: intracranial or spinal failure to generate or communicate impulses for normal mentation and/or limb function
- Orthopedic: failure of the skeleton and/or joints to support weight
- Metabolic/endocrine: limitation of metabolic fuel for muscles, nerves, or central nervous system (e.g., hypoglycemia, hypocalcemia, hypokalemia)
- Cardiovascular: inadequate perfusion of muscles and/or central nervous system
- Respiratory: inadequate oxygenation of blood and therefore of tissues

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

The majority of conditions causing collapse can be identified with a good history, physical examination (including checking stool for toxins), and complete but basic diagnostic tests such as blood work and thoracic and abdominal radiographs.

DIFFERENTIAL DIAGNOSIS

- Neuromuscular/Musculoskeletal: myasthenia gravis, polyradiculoneuritis, tick paralysis, botulism, polyarthritis, toxins (metaldehyde, strychnine, marijuana)
- Neurologic: intervertebral disk extrusion, fibrocartilaginous emboli, spinal fracture, spinal tumor, meningitis, intracranial neoplasia, narcolepsy (rare)
- Metabolic/endocrine: anemia, shock (hemorrhagic, anaphylactic), sepsis, insulin overdose, insulinoma, eclampsia, hypoparathyroidism, renal disease, hepatic dysfunction, hypoadrenocorticism, heat stroke, toxins that affect oxygen binding to hemoglobin such as carbon monoxide and acetaminophen toxicity, additional toxins such as xylitol, paintball ingestion
- Cardiovascular: arrhythmias, arterial thromboembolism, cardiac tamponade
- Respiratory: pneumonia, laryngeal paralysis, brachycephalic upper airway syndrome, laryngeal masses, pharyngeal swelling/foreign body, tracheal collapse, tracheal foreign body, nasopharyngeal polyp

INITIAL DATABASE

- CBC, biochemical profile, electrolytes
- Electrocardiogram, blood pressure (multiple limbs if thromboembolism suspected)
- Thoracic and abdominal radiographs
- Remove any ectoparasites (ticks) Results variable depending on underlying cause

ADVANCED OR CONFIRMATORY TESTING

As dictated by history, physical findings, and initial test results:

- Arterial blood gas, saline agglutination testing, tickborne disease titers, arthrocentesis, adrenocorticotropic hormone stimulation, abdominal ultrasound, echocardiography, MRI or myelogram, cerebrospinal fluid analysis, pharyngeal examination, laryngeal function assessment, abdomino/thoraco/pericardiocentesis, acetylcholine receptor antibody titers, Holter monitor/event recorder, insulin/glucose ratio, parathormone and ionized calcium, edrophonium (Tensilon) response test.

TREATMENT

TREATMENT OVERVIEW

Correct acute/life-threatening disturbances (severe biochemical or electrolyte abnormalities, severe anemia, hypotension, body temperature abnormalities). Address underlying problem.

ACUTE GENERAL TREATMENT

- Intravenous fluids, oxygen supplementation, and/or intubation if needed, blood transfusion, dextrose supplementation (hypoglycemia), electrolyte supplementation, insulin (combined with dextrose) for hyperkalemia, analgesia/sedation if indicated
- Antibiotics, antiinflammatories, diuretics, and antiarrhythmic medications may be indicated depending on underlying problem.
- Dexamethasone (0.2-1 mg/kg IV) may be given if a hypoadrenocortical crisis is suspected; it will not interfere with diagnostic testing.

CHRONIC TREATMENT

Dependent on underlying disease process

NUTRITION/DIET

Hypoglycemic patients benefit from nutritional support in the form of frequent meals, hand feeding, or feeding tube placement (see p. 1270)

POSSIBLE COMPLICATIONS

Edrophonium can cause acute cholinergic crisis.

RECOMMENDED MONITORING

Blood glucose, electrolytes, ECG, blood pressure

PROGNOSIS AND OUTCOME

In general, prognosis is guarded but varies from good to poor depending on underlying disease process.

PEARLS & CONSIDERATIONS

COMMENTS

- Many of the pathologic processes that cause collapse are not common, and establishing the diagnosis can be difficult.
- Common diseases, such as hemoabdomen secondary to mass rupture and intervertebral disk disease, should be considered first, and the diagnostic evaluation can proceed to less common etiologies afterwards.
- Two diseases leading to collapse that are commonly overlooked in general practice are pericardial effusion and hypoadrenocorticism.

TECHNICIAN TIP

A good history is essential for identifying (or ruling out) important possible causes of collapse. Useful points to discuss with owners include travel history, exposure to medications/sugar free products/other potential toxins, inquiring whether the individual animal is curious by nature and prone to chewing or ingesting foreign material, and encouraging owners to investigate the animal's home environment looking for toxins.

SUGGESTED READING

Rudloff E, Kirby R: Fluid resuscitation and the trauma patient. Vet Clin North Am Small Anim Pract 38(3):645–652, 2008.

Platt SR, Garosi LS: Neuromuscular weakness and collapse. Vet Clin North Am Small Anim Pract 34(6):1281–1230, 2004.

AUTHOR: ADAM J. REISS

EDITOR: ETIENNE CÔTÉ

Colitis, Chronic

BASIC INFORMATION

DEFINITION

A common cause for persistent (>3 weeks' duration) signs of colonic inflammation, characterized by large-bowel diarrhea with tenesmus/dyschezia, urgency, and increased frequency of defecation. Feces often contain mucus and/or fresh blood. Systemic signs attributable to nutrient malabsorption (e.g., anorexia, weight loss) are uncommon.

EPIDEMIOLOGY

SPECIES, AGE, SEX

More common in middle-aged and older dogs and cats as a consequence of infiltrative mucosal disorders (e.g., inflammatory bowel disease [IBD] and neoplasia). Infectious disorders (e.g., *Trichuris vulpis*, gastrointestinal [GI] histoplasmosis, *Tritrichomonas foetus*) may be seen in younger dogs and cats (less common).

GENETICS & BREED PREDISPOSITION

Boxers are predisposed to histiocytic ulcerative colitis (HUC). German shepherds and purebred cats are at increased risk for lymphocytic-plasmacytic IBD.

CONTAGION & ZOONOSIS

Some bacterial enteropathogens (e.g., *Clostridium perfringens,* potentially contagious) may cause chronic colitis if not detected early. Also, some helminth parasites (*Trichuris* spp., potentially contagious) and protozoa *(Giardia* spp., potentially zoonotic; *Tritrichomonas* spp., potentially contagious and zoonotic) may cause persistent signs of colitis in pets.

GEOGRAPHY AND SEASONALITY

Midwestern United States for GI histoplasmosis

ASSOCIATED CONDITIONS & DISORDERS

Colonic motility disorders (e.g., irritable bowel syndrome in dogs and colonic constipation/obstipation in cats) may mimic mucosal inflammation and cause signs of large-bowel diarrhea with tenesmus. Note that these diseases are due to functional defects in colonic motility and have no mucosal/structural disease.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Dietary responsive disorders: includes both food intolerance (nonimmunologically mediated) and dietary sensitivity (immunologically-mediated; see p. 402). Food-responsive causes for GI signs, including large-bowel diarrhea, are common in both dogs and cats.
- Infectious disorders: includes select nematode/protozoal parasites, bacteria, and fungal organisms (especially GI histoplasmosis). *Tritrichomonas foetus* is being recognized with increased frequency as a cause for chronic intermittent colitis in young cats.
- Infiltrative mucosal diseases: includes fungal, benign (e.g., IBD), and malignant (e.g., mucosal neoplasia) diseases

HISTORY, CHIEF COMPLAINT

Persistent large-bowel diarrhea, which is characterized by tenesmus (straining to defecate), increased frequency of defecation, mucoid feces, and fresh (red) blood. Note that some disorders (e.g., IBD, GI histoplasmosis, GI lymphoma) may affect the small intestines as well, causing mixed large/small-bowel signs.

PHYSICAL EXAM FINDINGS

- The animal is often well fleshed without systemic signs (e.g., unthriftiness, weight loss) of illness. Fungal disease, severe IBD, and neoplasia may selectively cause fever, alterations in appetite, and peripheral/mesenteric lymphadenopathy.
- Rectal examination: evaluate the character of the feces, obtain fecal samples for parasitic examination, procure exfoliative cytologic specimens, and evaluate the rectum for possible mass lesions.

ETIOLOGY AND PATHOPHYSIOLOGY

- Large-bowel diarrhea is characterized by increased amounts of mucus, owing to the large numbers of mucus-secreting goblet cells in the colon.
- Hematochezia indicates severe mucosal disruption of the distal colon and rectum.
- Parasites, both helminth and protozoa: *Trichuris vulpis* (dogs), *Tritrichomonas foetus* (cats), *Giardia lamblia* (dogs, cats)
- Dietary causes: incriminating antigens or dietary ingredients (nonimmunologic)
- Specific bacterial pathogens: cause colonic inflammation via invasion or enterotoxin production. Adherent/invasive *E. coli* is a newly recognized bacterial enteropathogen associated with HUC in boxers.
- Infiltrative mucosal disorders: benign, malignant, or infectious (e.g., fungal)

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis of many causes for chronic colitis will require histologic evaluation of mucosal biopsy specimens.

DIFFERENTIAL DIAGNOSIS

- Specific causes: see Etiology and Pathophysiology above.
- Occasionally patients with rectal diseases (e.g., perineal hernia, perineal fistula, diverticula, or rectal polyps or masses) will present with signs of large-bowel disease. These are generally distinguished by digital examination and careful inspection; normal pelvic and rectal structure on examination more strongly suggests large-bowel disease in such cases.

INITIAL DATABASE

- Physical examination: perform abdominal palpation and digital examination, with collection of feces.
- Fecal examination for nematode and protozoal parasites. Both fecal flotations and fecal smears should be performed. Note that multiple (three) zinc sulfate flotation tests using fresh feces may be required for identification of *Giardia* spp. trophozoites.
    - Commercial ELISA kits are also sensitive for the detection of *Giardia* antigen.
- Rectal cytology may indicate evidence of bacterial pathogens (e.g., vegetative spores of *Clostridia* or increased numbers of fecal leukocytes indicative of acute mucosal inflammation). Exfoliative cytology (e.g., rectal scrape using a uterine curette or a curette of the same type used for bone graft harvesting) is also a useful tool for confirming the presence of *Histoplasma* organisms contained within colonic macrophages.
- PCR for detection of *Tritrichomonas foetus* infection
- Abdominal imaging (survey radiographs, pneumocolonography, and/or ultrasonography) may identify fecal impaction, mass lesions, or evidence of significant mesenteric lymphadenopathy. Generally, ultrasonography is a poor screening tool for colonic disease, owing to the obstructive effect of air in the colonic lumen on the ultrasound beam, and because intestinal wall thickness is difficult to standardize.

ADVANCED OR CONFIRMATORY TESTING

- Colonoscopy with procurement of multiple mucosal biopsy specimens is required to diagnose most infiltrative diseases. Exfoliative cytology at the time of GI endoscopy is a useful adjunct to mucosal biopsy.
- Proctoscopy can also be used to examine and obtain biopsy specimens of the distal colon and rectum when the disease is confined to distal aspects or when colonoscopy is unavailable.
- Colonic biopsies should not be obtained routinely by laparotomy, since the bacterial content of the colon and attendant risk of bacterial peritonitis after biopsy of a diseased colon is markedly greater than in the small intestine.

TREATMENT

TREATMENT OVERVIEW

Treatment of chronic colitis is based on the specific definitive diagnosis, because empirical therapies are often inadequate or deleterious (e.g., use of corticosteroids in animals with GI histoplasmosis).

CHRONIC TREATMENT

- Treat for suspect nematode and protozoan parasites (even if fecal exams are negative for parasites) using appropriate broad-spectrum anthelmintics or antiprotozoal (fenbendazole, 50 mg/kg PO q 24 h for 3-5 days) medications. Confirm efficacy of therapy with repeat follow-up fecal examinations.
- Feed a hypoallergenic diet to animals with dietary-responsive disorders and IBD. Reduction in the quantity of dietary antigens will assist in reducing mucosal inflammation with these disorders. Other animals with colitis but not requiring a specific antigen-restricted diet will benefit from being fed a low-fat, fiber-enriched, and highly digestible commercial ration.
- Choose diets (or supplement the diet) with increased n-3: n-6 fatty acids to reduce mucosal inflammation.
- Avoid all treats and supplements containing protein or flavors during the dietary trial period.
- Use diets with added soluble or mixed fiber or add small to moderate amounts of soluble fiber to the diet to reduce tenesmus and facilitate colonic epithelial repair.
- Only use antibiotics in animals with confirmed bacterial causes (e.g., colonization with enteropathogenic bacteria) for their signs. Antimicrobials used in this fashion are best chosen based on susceptibility testing to the incriminating pathogen. Exceptions to this caveat are animals with HUC (which may respond to oral fluoroquinolone therapy, enrofloxacin 10 mg/kg PO q 24 h) and lymphocytic-plasmacytic colitis (IBD), which may respond to metronidazole (10 mg/kg PO q 12 h, used as an immunomodulator) alone or in combination with other immunosuppressive drugs.
- Sulfasalazine (20-30 mg/kg PO q 8 h, typically for 3-6 weeks in dogs) or newer mesalamine drugs, and glucocorticoids (e.g., prednisone or prednisolone, 1 mg/kg PO q 12 h for dogs; 1-2 mg/kg PO q 12 h for cats) are first-choice immunosuppressive drugs for therapy of colonic IBD.
- Drugs effective against GI histoplasmosis: see p. 538
- Treatment for colonic neoplasia: see p. 37

NUTRITION/DIET

- Appropriate dietary management may include elimination, fiber-supplemented, or low-residue diets. The remission of signs due to food-responsive causes for chronic colitis will require feeding an elimination (intact protein or hydrolysate) diet.
- Fiber supplementation is an important component of therapy because these dietary additives bind colonic irritants, normalize dysmotility, and promote colonic epithelial repair and renewal.

POSSIBLE COMPLICATIONS

- Cure is not possible with colonic IBD, but the prognosis for control of signs is good with effective therapy.
- Animals treated with amphotericin B for GI histoplasmosis are at risk for drug-induced renal disease.
- Myelosuppression may occur with use of multidrug chemotherapy for malignant colonic neoplasia.

RECOMMENDED MONITORING

Ideally, animals responsive to elimination diets (e.g., those having dietary responsive causes for chronic colitis) should be returned to their normal (incriminating) diet to see if large-bowel signs recrudesce. This is impractical in most instances.

PROGNOSIS AND OUTCOME

The prognosis varies according to the underlying cause, from good (dietary-responsive disorders when the inciting dietary constituent is removed) to poor (metastatic colonic neoplasia).

PEARLS & CONSIDERATIONS

COMMENTS

- Major causes of chronic colitis include dietary, infectious, and infiltrative disorders.
- Most animals with chronic signs of large intestinal disease will require a thorough diagnostic evaluation to rule out the varied causes for colonic inflammation. Prophylactic deworming and dietary trials with an elimination diet and/or soluble fiber supplementation are easy and cost-effective empirical therapies to offer clients prior to more extensive diagnostic testing.
- Colonoscopy with mucosal biopsy is imperative for diagnosis of most forms of chronic colitis that fail rational empirical therapies.

PREVENTION

- Prophylactic deworming

- Avoid dietary indiscretion.
- Perform dietary trials.

CLIENT EDUCATION

Dietary modification to a diet suitable for colonic disease may be required for the life of the pet.

SUGGESTED READING

Washabau RJ, et al: Diseases of the large intestines. In Ettinger SJ, Feldman EC, editors: Textbook of veterinary internal medicine, ed 6, Philadelphia, 2005, WB Saunders, pp 1378–1408.

AUTHOR: ALBERT E. JERGENS

EDITOR: DEBRA L. ZORAN

Colitis, Acute

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

A common disorder characterized by sudden onset (<72 hours) of colonic inflammation (large-bowel diarrhea and straining to defecate), manifesting with diarrhea that is typically mild, of small volume, and contains mucus and/or fresh blood (also see Diarrhea, Acute,). Systemic signs of illness are generally absent.

SYNONYM

“Stress” colitis

EPIDEMIOLOGY

SPECIES, AGE, SEX

Predominantly seen in young dogs and cats (<1 year old) as a consequence of parasitism, bacterial enteropathogens, or dietary indiscretion

RISK FACTORS

Age (predominantly young animals), recently kenneled animals, dietary factors, free-roaming pets, gastrointestinal tract parasitism

CONTAGION & ZOONOSIS

Helminth parasites (*Trichuris* spp.), protozoa (*Giardia* spp., *Tritrichomonas* spp.), and bacteria (*Campylobacter* spp., *Clostridium* spp., enterotoxigenic *Escherichia coli, Salmonella* spp.) have potential for contagion, common-source infection, and/or zoonosis.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

Large-bowel diarrhea, which is characterized by tenesmus (straining), increased frequency of defecation, mucoid feces, and fresh (red) blood

PHYSICAL EXAM FINDINGS

Generally well fleshed without systemic signs (e.g., unthriftiness or weight loss) of illness. Rectal examination fails to reveal significant abnormalities except the character of feces.

ETIOLOGY AND PATHOPHYSIOLOGY

- Parasites: both helminth and protozoa
- Dietary causes: gluttony, spoiled food, dietary indiscretion with ingestion of foreign or abrasive materials (e.g., cat litter, rocks, indigestible materials such as hair in long-haired cats)
- Specific bacterial pathogens may cause colonic inflammation via invasion or enterotoxin production.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Acute colitis rarely requires extensive diagnostic evaluation. A thorough history, physical examination, routine feces examination for nematode or protozoal parasites, and fecal/rectal smears for cytologic evaluation generally suffice.

DIFFERENTIAL DIAGNOSIS

Specific causes: see Etiology and Pathophysiology above.

INITIAL DATABASE

- Physical examination: abdominal palpation and digital rectal examination with collection of feces
- Fecal examination for nematode and protozoal parasites. Both fecal flotations and direct fecal smears should be performed. Note that multiple (three) zinc sulfate flotation tests using fresh feces may be required for identification of *Giardia* spp. trophozoites (see p. 447).
- Commercial ELISA kits are also sensitive for the detection of *Giardia* antigen.
- Rectal cytologic evaluation may indicate evidence of bacterial pathogens (e.g., vegetative spores of *Clostridia*) or increased numbers of fecal leukocytes indicative of acute mucosal inflammation.

ADVANCED OR CONFIRMATORY TESTING

Generally not indicated. Animals that fail to respond to empirical therapy (see below) will require confirmatory testing (e.g., fecal cultures, PCR, or other assays) for suspect bacterial pathogens.

TREATMENT

TREATMENT OVERVIEW

Initial management of animals with acute colitis is nonspecific and supportive. In most instances, signs are self-limiting and/or respond readily to empirical therapy.

ACUTE GENERAL TREATMENT

- Treat for suspect nematode and protozoan parasites using appropriate broad-spectrum anthelmintics or antiprotozoal medications (e.g., fenbendazole, 50 mg/kg PO q 24 h for 3 days).
- Avoid the use of antibiotics in animals, except those with confirmed bacterial causes for their gastrointestinal signs. Empirical use of commercial probiotics (FortiFlora, Purina) for 3-5 days may facilitate clinical recovery, although clinical trial data supporting its use are lacking.

NUTRITION/DIET

- Feed a bland or mixed-fiber diet (either commercial or homemade), giving small volumes at increasingly frequent interval for 3-5 days.
- Avoid all treats and dietary supplements during the dietary trial period.
- If using a bland diet, add fiber (small amounts of soluble fiber such as psyllium mucilloid, 1 teaspoon/10 kg at each feeding) to the diet to reduce tenesmus and facilitate colonic epithelial repair.

RECOMMENDED MONITORING

Have clients communicate their pet's progress after 48-72 hours of therapy.

PROGNOSIS AND OUTCOME

Generally excellent for full recovery

PEARLS & CONSIDERATIONS

COMMENTS

In general practice, acute colitis is a common complaint that is very responsive to supportive therapy. Elimination of infectious and parasitic causes is the key to treating acute colitis.

PREVENTION

- Prophylactic deworming
- Avoid dietary indiscretion.

- Avoid allowing pets to roam freely.
- In cats with recurrent colitis due to hair, frequent brushing, administration of hairball laxatives, or removing excess hair (shaving) may be indicated to control signs.

TECHNICIAN TIPS

Always perform multiple fecal examinations to exclude parasitism as a cause for colitis.

CLIENT EDUCATION

Monitor for failure to respond to empirical treatments.

SUGGESTED READING

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Cognitive Dysfunction

BASIC INFORMATION

DEFINITION

The decline in behavioral condition with advanced age, in the absence of causative physical or medical conditions

SYNONYMS

Senility, cognitive dysfunction syndrome (CDS)

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Cats: typically >10 years old
- Dogs: typically >6 years old (large breeds), >12 years (small breeds)

GENETICS & BREED PREDISPOSITION

Dogs and cats, like humans, may have “susceptibility genes” for the development of lesions associated with clinical cognitive syndromes. The understanding of taupathies that exists for human medicine does not currently exist for veterinary medicine.

ASSOCIATED CONDITIONS & DISORDERS

Concurrent anxiety-related conditions are common.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Disorientation, changes in social and interactive behavior (becoming “needier” or, conversely, more aloof), changes in locomotor and sleep cycle behaviors, and loss of “housetraining”
- In early-onset cognitive dysfunction, animals may have only slightly altered sleep cycles and appear more anxious.

PHYSICAL EXAM FINDINGS

- May be unremarkable
- Possible abnormalities include worn claws or scraped nose if “trapped” in corners or if exhibiting ritualistic locomotor behavior.
- Weight loss (from excessive locomotion and/or inappetence due to anxiety)
- When examined on video, the behaviors exhibited by an animal with CDS often seem without purpose; in extreme cases, animals appear to be moving without purpose, as if they cannot stop.

ETIOLOGY AND PATHOPHYSIOLOGY

- Dogs, like humans, develop lesions of amyloid plaques, the density of which appears to roughly correlate with the level of impairment in some patients.
- Unlike humans, dogs do not appear to develop neurofibrillary tangles that are associated with the tauopathy, Alzheimer's disease.
- Both cats and dogs experience a decrease in brain cortical mass and a relative increase in ventricular volume with aging. These changes may be more extreme in patients with cognitive dysfunction.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Cognitive dysfunction is an insidious-onset, slowly progressive disorder that is almost always suspected based on history and signalment (geriatric patient). Routine tests are indicated to identify confounding systemic metabolic abnormalities, if any. Confirmation using brain imaging and cerebrospinal fluid (CSF) analysis is only undertaken if the clinical picture suggests a different disorder is possible (e.g., cranial nerve or other deficits are more consistent with a disorder other than cognitive dysfunction).

DIFFERENTIAL DIAGNOSIS

- Generalized anxiety disorder
- Anxiety: usually transient; associated with changes in physical capabilities (e.g., diminished or changing sensory or locomotor capabilities)
- Separation anxiety: old-age onset
- Panic disorder
- Attention-seeking behavior
- Meningoencephalitis
- Hepatic encephalopathy
- Brain neoplasia
- Hyperthyroidism (cat), hypothyroidism (dog)

INITIAL DATABASE

- CBC, serum biochemistry profile, and urinalysis: generally unremarkable
- Neurologic examination: generally unremarkable
- Thyroid profile: rule out hyperthyroidism (cats) or hypothyroidism (dogs)

ADVANCED OR CONFIRMATORY TESTING

If neurologic signs are present or develop, a full neurologic evaluation, including clinical neurologic exam (see p. 1311), CSF analysis (p. 1228), and brain CT or MRI (pp. 1233 and 1302, respectively) may be indicated. If MRI indicates only increased ventricle size and all other laboratory and physical findings are unremarkable, a presumptive diagnosis of cognitive dysfunction may be made.

TREATMENT 

TREATMENT OVERVIEW

Goals of treatment are a decrease in the rate at which the animal appears to mentally fail, while relieving pain and distress associated with changes in physical and mental status,

ACUTE GENERAL TREATMENT

- Avoid exposure stimuli known to distress the animal.
- Early rewarding of any normal, preferred, or good interactive or elimination behaviors and encouraging normal locomotion
- There should be absolutely no punishment—physical, verbal, deprivational, or mental—for any undesirable behavior that occurs as a result of this condition. Such actions will render the patient more anxious.
- Protect the patient from attendant wanderings or odd behaviors while keeping it comfortable. The latter may involve containing it in an area with an absorbent surface when left alone.
- Mental stimulation in the early stages is important and may delay clinical progression. Treat balls, food toys, games involving puzzle solving, safe exercise, interactive tasks (“get the mouse,” “bring the ball,” etc.), and olfactory stimulation are useful.

CHRONIC TREATMENT

- As stated, plus physically and mentally stimulating exercises, such as swimming, massage, range of motion exercises.
- Encourage relaxation.
- If “loss of housetraining” occurs, ensure that the animal is taken out frequently to minimize the cost of “mistakes;” reward frequently as for a young pup and if needed diaper dog to decrease both client and dog distress.
- Encourage reestablishment of daily cycles by feeding at regular hours and at least a few hours before bedtime, and administer a benzodiazepine (alprazolam, clonazepam) before bed if needed.
- Protect the pet from accidents (e.g., falling into the swimming pool, falling down stairs).
- Specialized diets rich in antioxidants decrease the rate of cognitive dysfunction progression, improve behavioral function, and may have a protective effect (e.g., Hill's B/D [Brain Diet]; Purina Veterinary Diets EN).
- In the United Kingdom, nutraceutical food additives are available and have been shown to improve function in dogs with cognitive changes (e.g., Aktivait, Vet Plus UK).
- Newer additives also are recommended as preventative agents (e.g., Senilife, CEVA; Novifit [SAM-e; Virbac]; omega-3 fatty

acids [Nordic Naturals])
- The monoamine oxidase inhibitor, selegiline (Anipryl), 0.5 mg/kg PO q 24 h (may double dose after 1 month if ineffective) is the drug of choice and is licensed for use for the treatment of canine cognitive dysfunction in the United States.

POSSIBLE COMPLICATIONS

Any concurrent untreated anxiety-related or behavioral conditions generally worsen with age and will render the signs of cognitive dysfunction worse.

RECOMMENDED MONITORING

Examination, CBC, serum chemistry profile, urinalysis, ± thyroid profile as needed, and at least q 6-12 months if medications. Any ongoing medical condition could worsen any older animal's anxiety and make the signs of cognitive dysfunction worsen or appear to worsen.

PROGNOSIS AND OUTCOME

- The course is inexorable, but with diet, exercise, and appropriate stimulation, patients in the early stages can have years of quality life.
- Prognosis is improved by early diagnosis, comprehensive treatment, including preventative treatment with antioxidants and cognitive stimulation in middle age, and client compliance.

PEARLS & CONSIDERATIONS

COMMENTS

- If the clients videotape the animal early in the development of the condition, they will be better able to monitor changes, assess treatment, and make quality-of-life decisions.
- Clients often are made the saddest by the feeling that they are losing their emotional and intellectual connection with their pet. Treatment must acknowledge this concern and address it when possible.
- Other cats or dogs in the household can often help calm these patients and help them with activities they may now find challenging.

TECHNICIAN TIP

- When their cognitive functions decline, these patients may require extra care and handling, especially when known to the hospital staff for many years. It is a common mistake of veterinarians and technicians alike to assume a pet can behave the same as always when he/she ages, and being aware of such potential changes can help prevent injury.

PREVENTION

- Diets rich in antioxidants may decrease risk.
- Mental and physical activity is essential and may have a much larger role to play than originally thought. For cats and dogs, olfactory stimulation is likely coupled with cognition, and some mental stimulation should involve work for food, food puzzles, food games, or some mental exercise that involves olfaction.

CLIENT EDUCATION

- Clients must understand that problematic behaviors attendant with cognitive dysfunction are not willful acts of disobedience by a vengeful pet.
- Treatment of this condition is an ongoing process and will continue for the life of the pet. Relapses may occur with treatment discontinuation or added stressors.

SUGGESTED READING

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Coccidiosis, Intestinal

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

A diarrheal disease caused by infection of the intestinal tract with Apicomplexan parasites in the genus *Cystoisospora*

SYNONYM

Isospora

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs and cats
- Young animals or animals that are stressed are more likely to have clinical signs than are older animals.

RISK FACTORS

Recent weaning or overcrowded conditions

CONTAGION & ZOONOSIS

Oocysts of *Cystoisospora* species can infect and cause latent infections in a number of paratenic hosts. There is no risk of zoonotic infection with dog or cat *Cystoisospora* species.

GEOGRAPHY AND SEASONALITY

Cystoisospora species have a worldwide distribution and are present year round.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

Diarrhea with or without vomiting are the most common complaints. Diarrhea is not bloody but is often foul smelling, pasty, and semiformed to liquid.

PHYSICAL EXAM FINDINGS

Weight loss (or poor growth), dull haircoat, dehydration, and slightly elevated temperature may be present.

ETIOLOGY AND PATHOPHYSIOLOGY

- Intestinal coccidiosis in cats is caused by *Cystoisospora felis* and *Cystoisospora rivolta.* Intestinal coccidiosis in dogs is caused by *Cystoisospora canis* and *Cystoisospora ohioensis* complex *(C ohioensis, C neorivolta, C. burrowsi).*
- Intestinal damage is caused by rupture of host cells lining the intestinal villi of the small intestines. Villous atrophy and villous erosions occur secondary to parasite multiplication.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Nonspecific diarrhea is confirmed to be caused by *Cystoisospora* by simple microscopic fecal examination.

DIFFERENTIAL DIAGNOSIS

Giardiasis or other protozoal enteric infections, viral- or bacterial-induced diarrhea, dietary indiscretion, other parasitic (helminths) diseases of the intestines

INITIAL DATABASE

- Fecal examination and demonstration of characteristic oocysts.
- Parvovirus ELISA may be indicated in affected puppies with severe diarrhea to rule out concurrent parvoviral enteritis.
- Kittens should be tested for feline leukemia virus or feline immunodeficiency virus (older than 4 months).

ADVANCED OR CONFIRMATORY TESTING

None needed

TREATMENT

TREATMENT OVERVIEW

Goals of treatment are remission of diarrhea and cessation of oocyst production.

ACUTE GENERAL TREATMENT

- Sulfadimethoxine (Albon oral suspension 5%):
  - 55 mg/kg PO once, followed 24 h later by 27.5 mg/kg PO q 24 h in dogs.
  - Treatment is continued until clinical signs have resolved for 48 hours.
  - To prevent dehydration, adequate water intake must be maintained during treatment.
  - Supportive care includes fluids; providing a warm, dry environment; and an appropriate diet.
- Off-label:
  - Toltrazuril (Baycox) 30 mg/kg PO as a single treatment
  - Ponazuril (Marquis) 30 mg/kg PO as a single treatment
  - A combination of sulfadimethoxine with ormetoprim (Primor) 55 mg/kg PO q 24 h (for up to 21 days) is also effective.
  - Amprolium (Corid) 300-400 mg/kg PO q 24 h for 5 days or 110-220 mg/kg for 7-12 days. Amprolium is bitter, and care should be taken that the appropriate dose is ingested and not spit out.

CHRONIC TREATMENT

Same as for acute

DRUG INTERACTIONS

See sulfonamides (p. 1665).

RECOMMENDED MONITORING

Adult animals with documented coccidiosis should be evaluated for other causes of intestinal disease (e.g., inflammatory bowel disease, lymphoma) or immunocompromise (e.g., Cushing's disease).

PROGNOSIS AND OUTCOME

Good; most animals will respond readily to anticoccidial treatment.

PEARLS & CONSIDERATIONS

COMMENTS

- It is virtually impossible to prevent exposure to coccidia in dogs and cats. Clinical disease often develops around weaning or after other stressful events like shipping or moving locations.
- The strategic use of newer anticoccidials (ponazuril or toltrazuril) at times when animals are likely to develop coccidiosis may become common practice in the future. An example of a strategic treatment would be administration of ponazuril a few days prior to or at weaning to prevent development of coccidiosis in recently weaned puppies.

PREVENTION

Reduce environmental contamination as much as possible (control populations, keep the environment clean, and remove fecal contamination of all litter boxes and living areas).

CLIENT EDUCATION

Coccidian parasites of dogs and cats are not infectious for humans.

SUGGESTED READING

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Coccidioidomycosis

BASIC INFORMATION

DEFINITION

A respiratory or systemic fungal infection caused by *Coccidioides immitis* or *Coccidioides posadasii;* occurs predominantly in the southwestern United States

SYNONYMS

San Joaquin Valley fever, valley fever

EPIDEMIOLOGY

SPECIES, AGE, SEX

Young adult, male, medium- to large-breed dogs that have access to the outdoors are more commonly infected. Cats are infrequently diagnosed with coccidioidomycosis but often develop severe clinical illness.

RISK FACTORS

- Being predominantly outdoors during the day
- Amount of roaming space >1 acre
- Walking in the desert
- ± Immunosuppression

In endemic areas, a decreased risk has been associated with walking preferentially on sidewalks.

CONTAGION & ZOONOSIS

- Coccidioidomycosis occurs in humans, who may become infected from the same environmental source as dogs and other animals.
- Direct transmission from infected animals to humans is extremely unlikely, because the yeast phase (present at body temperature) is not transmitted by aerosol. Transmission of *Coccidioides* to a human following a cat bite has been reported.
- Conversion of the yeast phase to the mycelial phase, which produces infectious spores (arthroconidia) that may be inhaled, could occur on bandages, necropsy specimens, tissue samples, or instruments; such material should be dealt with safely and immediately (e.g., disinfected or autoclaved).
- The mycelial/hyphal form of *Coccidioides,* which grows in vitro and in nature, is highly infectious by the aerosol route; in-house culture of possibly infected specimens is contraindicated.

GEOGRAPHY AND SEASONALITY

- Coccidioidomycosis occurs mainly in the southwestern United States, including the central valley of California *(Coccidioides immitis);* southern regions of Arizona, Nevada, Utah, and New Mexico; and western Texas *(Coccidioides posadasii).* To a lesser extent, it occurs in regions of Mexico and Central and South America (particularly Venezuela). Having lived in or traveled through these regions up to several years prior to the onset of illness is almost always a component of the history.
- Because the disease is acquired through inhalation of airborne spores, the incidence increases following soil disturbance (dust storms, earthquakes).
- Latent infection may be present for years before causing overt signs.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Chronic cough (pulmonary or hilar lymph node involvement); may be dry and harsh or moist and productive. Severe pulmonary involvement may be associated with respiratory distress.
- Other presenting complaints include inappetence, weight loss, lethargy, lameness, cutaneous masses with or without draining tracts, signs of head or neck pain, signs of vision loss, or neurologic signs such as seizures and ataxia. Dogs with pericardial

involvement may present with signs of right-sided heart failure.
- Cats are more likely to present with skin lesions than dogs.

PHYSICAL EXAM FINDINGS

Harsh lung sounds, dyspnea, and tachypnea are common. Systemic signs may include fever, depression, and weakness. Lameness may be noted +/− firm swellings over long bones. Cutaneous masses with or without draining tracts may be present. Other findings include lymphadenopathy, cranial and cervical hyperesthesia, ascites, and signs of uveitis, focal chorioretinitis, or panophthalmitis.

ETIOLOGY AND PATHOPHYSIOLOGY

- *Coccidioides* spp. are dimorphic fungi; they have both yeast and mycelial (hyphal) forms:
  - The mycelial form exists in soil and produces arthroconidia that are dispersed by wind and easily inhaled.
  - Inhalation of 10 or fewer arthroconidia is sufficient to cause infection that produces clinical signs.
  - After inhalation, arthroconidia enter the pulmonary alveoli and cause subpleural lesions.
  - In this location, the fungus changes morphology to the yeast form, which grows as spherules containing endospores in tissue. The spherule releases endospores which can disseminate following phagocytosis and form new spherules. This, together with the pyogranulomatous inflammatory response, results in clinical illness.
  - The incubation period from the time of inhalation to the appearance of respiratory signs is typically 1-3 weeks, sometimes months.
- Disease may remain localized to the respiratory tract or become systemic with dissemination to lymph nodes, bones, eyes, skin, pericardium, and central nervous system (CNS).
- The course of illness may be protracted over several months to years.
- Many animals develop transient, subclinical infections, and some may recover from localized respiratory illness without therapy.
  - Approximately 28% of dogs living in an endemic region develop antibodies to *Coccidioides* spp. by the age of 2 years, and approximately 6% develop clinical infection.

COCCIDIOIDOMYCOSIS Geographic area in which coccidioidomycosis is endemic. Areas of highest prevalence are cross-hatched.

(From Rippon JW: Medical mycology, ed 3, Philadelphia, 1988, Saunders, p 436. Reprinted with permission.)

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A definitive diagnosis of coccidioidomycosis is made by cytologic or histologic visualization of the organism. If the organism cannot be identified, the diagnosis is based on history, clinical signs, physical examination findings, and results of serologic tests.

DIFFERENTIAL DIAGNOSIS

- Cough:
  - Initially, a dry hacking cough may be mistaken for infectious tracheobronchitis.
  - Other differentials include collapsing trachea, chronic bronchitis, pulmonary eosinophilic diseases, bacterial pneumonia, mycobacteriosis, nocardiosis, other mycotic or parasitic causes of pneumonia, neoplasia, and congestive heart failure.
- Bone lesions: bacterial osteomyelitis, other fungal infections, bone neoplasia
- Skin lesions: draining tracts due to other systemic mycoses, bony lesions such as infected sequestra, abscesses due to bite wounds or other penetrating injuries, or neoplasia
- Ocular lesions: other systemic infectious illnesses and immune-mediated diseases

INITIAL DATABASE

- CBC may reveal an inflammatory leukogram and a mild nonregenerative anemia.
- Hypoalbuminemia (almost all cases) and hyperglobulinemia (approximately 50% of cases) are common. Hypercalcemia has not been described with this form of fungal infection.
- Urinalysis is usually unremarkable.
- Thoracic radiographs are frequently abnormal and are indicated in any patient suspected of having coccidioidomycosis:
  - Common findings include a diffuse interstitial or nodular interstitial pulmonary pattern and hilar lymphadenopathy, which may be profound.
  - Alveolar infiltrates, miliary interstitial patterns, or nodules with or without pleural effusion or evidence of pericardial effusion may also be seen.
- Radiographs of long bones may reveal mixed proliferative and lytic lesions, typically located distally (distal diaphysis, metaphysis, epiphysis).

ADVANCED OR CONFIRMATORY TESTING

- Coccidioidomycosis can be definitively diagnosed via cytologic examination of exudates, sputum or aspirates, or histopathologic examination of tissue:
  - Spherules are large (1-10 times the diameter of a red blood cell), round structures typically surrounded by neutrophils and macrophages.
  - Transtracheal washes and lymph node aspirates are often falsely negative. Cytologic evaluation of fluid from draining tracts or of pleural effusion is more likely to yield organisms, which appear on Romanowsky stains as sometimes crinkled, deeply basophilic structures.
  - Organisms can be difficult to find histopathologically on bone biopsies but are readily identified within bony microabscesses. Silver stains and periodic acid-Schiff stains may assist with organism identification.
- Serologic testing is available for dogs and cats. Several serologic tests are available for both immunoglobulin M (IgM) and IgG. Serologic tests may be positive in subclinically infected dogs. The agar gel immunodiffusion assay (AGID) is commonly used, which detects IgM and IgG.
  - As with other forms of serology, IgM reflects the acute antibody response. A positive titer can be noted within 2 weeks of exposure (i.e., during or just after the incubation period) and may last 4-6 weeks. Tests for IgM use tube precipitin (TP) antigens.
  - IgG indicates exposure or infection. Tests for IgG use complement fixation (CF) antigens. The magnitude of the titer is considered important, with higher titers (=1:64) suggesting disseminated or severe pulmonary infections. Titers < 4 may be consistent with previous exposure and recovery.
  - IgG titer is expected to decrease slowly but may not reach zero with successful treatment.
  - Positive IgG titers from dogs living in endemic areas are more likely due to exposure than from active infection.
  - Negative serologic tests in dogs infected with *Coccidioides* spp. are uncommon to rare.

TREATMENT

TREATMENT OVERVIEW

Antifungal therapy with ketoconazole, itraconazole, or fluconazole is most commonly employed. Itraconazole and fluconazole have fewer adverse effects than ketoconazole. Fluconazole is the treatment of choice for CNS or ocular involvement.

ACUTE GENERAL TREATMENT

- Supportive care for systemic illness and respiratory distress as warranted:
  - See Oxygen Supplementation,p. 1318.
  - See Hypotension, Systemic, p. 1068.
- Mild respiratory cases may resolve without medications, but antifungal therapy is often instituted to avoid dissemination. Broad-spectrum antibiotics and immunosuppressive medications should be avoided.
- Azole antifungal drugs. Care should be taken to obtain generic azole preparations from a reliable source. Liver parameters +/− serum drug levels should be monitored periodically during therapy.
  - Ketoconazole (5-10 mg/kg PO q 12 h). Effective, least costly; may produce adverse hepatic effects or vomiting/inappetence.
  - Itraconazole (5 mg/kg PO q 12 h). More effective than ketoconazole in some cases, less so in others (not predictable). Costly. May have fewer adverse effects. Unless significant inflammation is present, may not penetrate the eye and CNS.
  - Fluconazole (5 mg/kg PO q 12 h). Highly lipid soluble, best penetration of eye and CNS tissues.
- Cats generally receive 25-50 mg total of the antifungal azole agent q 12-24 h.
- Amphotericin B can be used in patients that do not tolerate (e.g., anorexia, vomiting, hepatic dysfunction) or are not responding to azole drugs. The dose for dogs is 0.5 mg/kg IV q 48-72 h, given over 4-6 h in 5% dextrose, for 1 month. Side effects include nephrotoxicity and perivascular irritation/sloughing. Renal parameters should be assessed prior to each dose. Lipid forms of amphotericin B are less nephrotoxic but more expensive. Amphotericin B does not penetrate the CNS.
- Surgical treatment via subtotal pericardectomy and epicardial excision has been used successfully for relief of right-sided heart failure in dogs with effusive-constrictive pericarditis.

CHRONIC TREATMENT

The decision to stop antifungal therapy should be based on resolution of clinical signs, radiographic lesions, and serologic titers. Therapy must persist at least 2 months beyond resolution of clinical signs and radiographic abnormalities, which may be >12 months with disseminated disease, especially if there is bone involvement. Titers can be monitored to assess response to therapy; rising titers suggest an inadequate response to therapy.

DRUG INTERACTIONS

- Some patients receiving azole drugs can develop liver dysfunction, vomiting or diarrhea, thrombocytopenia, and skin reactions.
- Compatibility of other medications with antifungal agents should be investigated before use.
- Caution should be taken in patients receiving o,p'DDD, warfarin, digoxin, phenobarbital, phenytoin, methylprednisolone, and cyclosporine, because azole drugs may raise serum levels of these medications substantially.

POSSIBLE COMPLICATIONS

If clinically significant respiratory signs are left untreated, systemic spread of illness is likely.

PROGNOSIS AND OUTCOME

- Prognosis for patients with disease limited to the respiratory tract is fair to good.
- Patients with disseminated disease have a guarded to poor prognosis for full recovery, depending on the severity of disease and degree of dissemination. Patients with CNS involvement have a poor prognosis.

PREVENTION

To minimize the risk of infection in endemic areas, keep animals away from desert soil and locations where soil is disrupted (e.g., construction sites), and discourage digging.

PEARLS & CONSIDERATIONS

COMMENTS

Fungal culture of *Coccidioides* should not be attempted within a veterinary practice, because the hyphae are the infectious form of the fungus and are highly infectious to humans as well as domestic animals.

TECHNICIAN TIPS

Bandages used for covering cutaneous draining tracts may be infectious to humans if the lesion is due to *Coccidioides* infection; therefore, bandages should be avoided in such situations, or if indispensable, should be changed on a daily basis and disinfected or destroyed (autoclaved) immediately when removed.

SUGGESTED READING

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Cobalamin Deficiency

BASIC INFORMATION

DEFINITION

A reduced cellular concentration of the B vitamin, cobalamin, usually secondary to insufficient intestinal uptake due to malnutrition/malabsorption.

SYNONYM

Vitamin B12 deficiency

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Acquired form: dogs and cats (mean age for cats: 7.1 years)
- Hereditary form: young kittens and puppies (6-12 weeks old)

GENETICS & BREED PREDISPOSITION

Chinese shar-pei, giant schnauzer, beagle, border collie, Australian shepherd

RISK FACTORS

- In theory, a pure vegetarian diet may cause cobalamin deficiency (reported in humans); unlikely in dogs and cats eating commercial pet food.
- Surgical resection of the ileum (site of cobalamin absorption)
- Exocrine pancreatic insufficiency (EPI): in dogs and cats, the pancreas is a major source of intrinsic factor, which is necessary for ileal absorption of cobalamin.
- Severe and chronic small-intestinal disease may damage ileal cobalamin receptors.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Hereditary (rare); defect in receptors for uptake
- Secondary (most common): caused by EPI, small-intestinal bacterial overgrowth and antibiotic-responsive diarrhea (SIBO/ARD), chronic enteropathies (e.g., inflammatory bowel disease [IBD], lymphosarcoma, histoplasmosis), any form of chronic malabsorption/malnutrition; interference with ileal cobalamin uptake

HISTORY, CHIEF COMPLAINT

- Hereditary form: gastrointestinal (GI) disorders, failure to thrive, hematologic and biochemical abnormalities (normocytic nonregenerative anemia/"pernicious anemia," leukopenia), proteinuria, seizures
- Acquired form: clinical signs of GI disease most common; hematologic and biochemical abnormalities rare

PHYSICAL EXAM FINDINGS

- Most dogs and cats with cobalamin deficiency only show clinical signs of GI disease dependent on the underlying cause (chronic diarrhea, vomiting, weight loss, poor body condition).
- Neurologic signs have been reported occasionally in dogs and cats with selective cobalamin deficiency (i.e., hyperammonemic encephalopathy, organic acidemia).
- Neutropenia and anemia (usually normocytic) are usually features of the hereditary form and occur very rarely in acquired disease.

ETIOLOGY AND PATHOPHYSIOLOGY

- Cobalamin (Vitamin B12) is a water-soluble vitamin produced exclusively by microorganisms. Animals are unable to synthesize cobalamin and are dependent on nutritional sources. Cobalamin (Cbl) is an important cofactor for a variety of biochemical reactions (e.g., amino acid metabolism and DNA synthesis).
- Dietary cobalamin binds to intrinsic factor (pancreatic), which in dogs and especially cats is mainly produced in the pancreas, serving as a transporter for absorption at the distal small intestine.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Cobalamin deficiency is usually suspected as a possible secondary complication with GI or pancreatic disease. Measurement of serum cobalamin levels is the clinical diagnostic test of choice.

DIFFERENTIAL DIAGNOSIS

- Chronic GI disease
- EPI, IBD, SIBO/ARD, intestinal lymphoma, histoplasmosis

INITIAL DATABASE

- CBC, serum biochemistry profile: to rule out other systemic disease

ADVANCED OR CONFIRMATORY TESTING

- Measurement of serum cobalamin
  - Reference range established at the GI Laboratory at Texas A&M University:
    - Dogs: 251-908 ng/L, Cats: 290-1500 ng/L
    - Other laboratories may have different reference ranges.
- Measurement of methylmalonic acid (MMA) in serum or urine: not commercially available
  - Increased serum or urinary MMA indicate cobalamin deficiency at the cellular level
- Serum trypsin-like immunoreactivity to rule out EPI
- Serum folate to rule out SIBO/ARD

TREATMENT

TREATMENT OVERVIEW

The goal of treatment is to correct cobalamin deficiency at the cellular level and correct clinical signs/symptoms (i.e., GI, hematologic, immunologic, and neurologic)

CHRONIC TREATMENT

- Repeated high doses by parenteral administration are necessary.
  - Cyanocobalamin is the primary choice, but hydroxycobalamin can also be used.
  - Multivitamin preparations contain an insufficient amount of cobalamin and are not recommended.
- Recommended empirical dosing schedule of cyanocobalamin:
  - 150-250 mcg per injection in cats; 250-1200 mcg per injection in dogs
  - SQ q 7 days for 6 weeks, then q 14 days for 6 weeks, then q 30 days for 1 injection, then reevaluate serum cobalamin concentration 1 month later
  - If the underlying disease process has resolved and cobalamin body stores have been replenished, serum cobalamin concentration should be supra-normal at the time of reevaluation.
  - If serum cobalamin concentration is in the normal range, treatment should be continued at least in monthly intervals.
  - If serum cobalamin concentration at the time of recheck is subnormal, further workup is required to definitively diagnose the underlying disease process; cobalamin supplementation should be continued weekly or biweekly.

POSSIBLE COMPLICATIONS

Cobalamin is nontoxic and can be parenterally administered in large doses with minimal risk of side effects.

RECOMMENDED MONITORING

- Depending on the underlying cause of cobalamin deficiency and the clinical signs, every few months
- In animals with the congenital form, a more frequent check may be necessary until an optimal dose regimen has been established.

PROGNOSIS AND OUTCOME

- In the congenital form, the response to parenteral cyanocobalamin is usually excellent, leading to reversal of clinical abnormalities.
- In the acquired form, prognosis depends on the underlying disease:
  - Usually excellent in animals with EPI in combination with pancreatic enzyme replacement therapy
  - Hypocobalaminemia has been associated with a poor outcome in dogs with severe chronic enteropathies.

PEARLS & CONSIDERATIONS

- Animals with GI disease and cobalamin deficiency have a diminished capacity of oral cobalamin absorption and recycling via enterohepatic circulation. This leads to a more rapid depletion of body stores, and those animals require frequent parenteral administration of cobalamin.
- Patients with severe cobalamin deficiency often do not respond to therapy of the underlying GI disorder until cobalamin is supplemented.
- A recent study has shown that cats with chronic GI disease and cobalamin deficiency that were unresponsive to previous therapy responded with weight gain quickly after initiation of cobalamin supplementation.
- Cobalamin deficiency on a cellular level may even occur when serum cobalamin concentration is at the low end of the normal range (<350 ng/L), and parenteral cobalamin supplementation should also be considered in these patients.

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http://www.cvm.tamu.edu/gilab

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Clostridial Enterocolitis

BASIC INFORMATION

DEFINITION

Clostridial enterocolitis or enterotoxicosis is a form of intestinal disease that causes diarrhea in dogs and cats and is suspected to be caused by *Clostridium perfringens*. It typically causes large intestinal diarrhea that may be acute and self-limiting or may be chronic in nature.

SYNONYMS

Acute nosocomial colitis, canine nosocomial diarrhea

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs are more commonly affected than cats. Acute disease can occur in any age animal, whereas chronic disease can occur in middle-aged to older animals.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

Some or all may be present.

- Large-intestinal diarrhea. Small volumes of feces, increased frequency of defecation, and straining are common, and mucus and/or fresh blood may be visualized in the feces. Vomiting and flatulence may also be present in some patients. Many patients show no clinical signs other than the diarrhea.
- A small number of patients may also have small-bowel diarrhea marked by large volumes of watery feces and abdominal discomfort.

PHYSICAL EXAM FINDINGS

- Findings are nonspecific and relate to large-intestinal diarrhea. There may be abdominal discomfort during palpation. There may also be signs of pain during digital rectal examination.
- Acute nosocomial diarrhea associated with *C. perfringens* is often seen 1 to 5 days after boarding or kenneling. This syndrome appears to be self-limiting and responds well to supportive care.

ETIOLOGY AND PATHOPHYSIOLOGY

- *C. perfringens* is an anaerobic, spore-forming, gram-positive bacillus that is also found in normal dogs and cats.
- Sporulation of toxigenic strains causes release of enterotoxin A. This enterotoxin can cause mucosal damage and fluid secretion in the colon.
- Other factors must also be involved. Enterotoxin-related damage cannot be the sole explanation for this disorder, because enterotoxin has been identified in the feces of normal animals.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is conclusively established with fecal bacterial cultures, but in most cases the transient nature of the illness means that a definitive diagnosis is neither achieved nor clinically necessary.

DIFFERENTIAL DIAGNOSIS

- All causes of large-intestinal diarrhea, both primary gastrointestinal and systemic/nonprimary gastrointestinal, need to be considered (see p. 303).
- Primary gastrointestinal disease includes parasites, inflammatory bowel disease, neoplasia, fungal disease, idiopathic colitis, and histiocytic ulcerative colitis.
- Systemic/extraintestinal causes of acute diarrhea include anxiety/nervousness, other intraabdominal disorders, and intoxications (e.g., organophosphates).

INITIAL DATABASE

- CBC, biochemical profile, urinalysis, fecal flotation: generally unremarkable
- Fecal ELISA for *Giardia* or other pathogens
- Fecal smear with Gram stain
- Rectal scraping for cytologic evaluation (to rule out histoplasmosis, lymphoma); see p. 1334
- Fecal analysis is very important in all cases of large-bowel diarrhea, because this test is noninvasive and may yield important clues to the problem, even if the diagnosis is elusive.

ADVANCED OR CONFIRMATORY TESTING

- Advanced diagnostic evaluation may include fecal culture and evaluation for the presence of enterotoxin in feces.
- Abdominal imaging with radiographs or ultrasound is often normal but can be warranted to rule out extragastrointestinal diseases.
- Colonoscopy is rarely indicated to diagnose this condition, but in severe cases may be necessary to rule out other causes of colitis:
  - Mucosal hyperemia or ulceration are typical.
  - Histopathologic analysis of biopsies may indicate neutrophilic colitis, the presence of other inflammatory bowel disease, or may be normal.
- Fecal cytologic evaluation may indicate the presence of sporulating clostridial organisms, which have the appearance of safety pins. However, the presence of these organisms does not confirm that a *Clostridium* is the cause of the clinical disease.
- Anaerobic fecal cultures will typically identify high concentrations of *C. perfringens* (>3-5 organisms/field on oil immersion).
- Other available diagnostic tests include ELISA enterotoxin assays and PCR enterotoxin genotyping.

TREATMENT

TREATMENT OVERVIEW

Therapeutic goals are to provide supportive care and eliminate large-bowel diarrhea. These patients may be dehydrated, anorexic, and lethargic. Supportive care should be directed toward correcting volume deficits, correcting electrolyte disturbances, and reducing intestinal discomfort (including vomiting) so the patient will eat and be more comfortable.

ACUTE GENERAL TREATMENT

- Treatment with intravenous crystalloid solutions to correct volume deficits is very important.
- The use of antimicrobials, including amoxicillin (20 mg/kg PO q 8 h), clindamycin (10-20 mg/kg PO q 12 h), tylosin (5-10 mg/kg PO q 12 h), or metronidazole (15-20 mg/kg PO q 12 h) for 5-7 days is generally beneficial. Parenteral antibiotics with anaerobic bactericidal activity (e.g., ampicillin, 20 mg/kg IV q 6-8 h) are indicated if the patient is systemically ill.

CHRONIC TREATMENT

- Long-term antimicrobial therapy may be required along with dietary management.
- In some cases, the antibiotic therapy may be discontinued so long as the high-fiber diet is maintained.

NUTRITION/DIET

Dietary management with high-fiber diets has been shown to reduce clinical signs and speed recovery.

RECOMMENDED MONITORING

Based on the presence or absence of diarrhea

PROGNOSIS AND OUTCOME

The prognosis depends on the presenting condition of the patient. In most cases, the prognosis is excellent.

PEARLS & CONSIDERATIONS

- There is no gold standard on how to treat this disease; treatment is adapted based on specific abnormalities identified on physical exam and diagnostic testing.
- There is still some question as to whether Koch's postulates have been fulfilled regarding causality of *C. perfringens* and this form of enteritis.

CLIENT EDUCATION

In most cases, the signs associated with this disease subside with supportive care, but some patients may be chronically affected.

SUGGESTED READING

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Cleft Palate

BASIC INFORMATION

DEFINITION

Congenital, physical defect of the lips, hard and/or soft palate

SYNONYMS

Primary cleft palate: harelip, cleft lip. Secondary cleft palate: cleft of the soft palate or cleft of the soft and hard palate.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs and cats of either sex
- Incidence higher in brachycephalic dog breeds and Siamese cats
- Nursing difficulties noted in puppies and kittens soon after birth

GENETICS & BREED PREDISPOSITION

- Inherited as either autosomal recessive or irregularly dominant genes
- Mating of parents with cleft palate results in 41% incidence in offspring.

RISK FACTORS

See Etiology and Pathophysiology.

ASSOCIATED CONDITIONS & DISORDERS

- Aspiration pneumonia
- Sneezing, nasal discharge, chronic rhinitis

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

The upper lip and most rostral hard palate supported by the palatine processes of the incisive bones constitute the *primary palate.* The hard palate that is supported by the palatine processes of the maxillary bones and the horizontal laminae of the palatine bones and the soft palate constitute the *secondary palate.*

- Primary palate defects: unilateral, midline, or bilateral; unilateral defects are more often found on left side.
- Secondary palate defects:
  - Midline cleft of hard and soft palate or soft palate only
  - Unilateral cleft of soft palate
  - Hypoplasia of soft palate

HISTORY, CHIEF COMPLAINT

- Primary palate defects:
  - Lip defects only: owner may note physical appearance
  - Most rostral hard palate defects: mild nasal congestion, sneezing, and discharge
- Secondary palate defects (depends on extent of defect): failure to create negative pressure for nursing, nasal discharge (drainage of milk from the nares during or after nursing), coughing, gagging, sneezing, nasal reflux, rhinitis, tonsillitis, laryngotracheitis, aspiration pneumonia, poor weight gain, and general unthriftiness

PHYSICAL EXAM FINDINGS

- Small stature
- Nasal discharge, sneezing
- Auscultation: dyspnea, increased lung sounds, wheezing, or crackles (aspiration pneumonia)
- Oral examination:
    - Primary palate defects: “harelip” only (unilateral, midline, or bilateral lip defect); rostral hard palate defect only (uni- or bilateral); or defects of both the lip and most rostral hard palate; can also be associated with abnormalities of the secondary palate.
    - Secondary palate defects: midline hard palate cleft can usually be visualized, but soft palate defect may be difficult to evaluate without chemical restraint.

ETIOLOGY AND PATHOPHYSIOLOGY

Etiology:

- Hormonal: gestational corticosteroid administration
- Infectious: viral-induced
- Mechanical: intrauterine trauma
- Metabolic
- Nutritional
- Toxic: secondary to drug, viral toxins
- Hereditary:
    - Autosomal recessive or irregularly dominant genes
    - Growth of palatine bones in the fetus may compete with growth of the skull, especially in broad-skulled (brachycephalic) dogs, to achieve normal closure of the palatine plates.

Pathophysiology:

- Defects of the primary and secondary palate result from a *failure of fusion* of paired (and one unpaired) structures during development.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis occurs in one of two contexts: clinical signs are suggestive of the disorder (classically, milk discharge from nostrils in a nursing puppy or kitten), or the defect is identified as an incidental finding during routine examination. In either situation, complete assessment of the defect is done under sedation or anesthesia, generally followed immediately by surgical correction (consider referral).

DIFFERENTIAL DIAGNOSIS

Acquired palate defects (traumatic, infectious)

INITIAL DATABASE

- CBC, serum biochemistry panel, urinalysis: assessment of unthrifty patients
- Thoracic radiographs: evaluation of possible aspiration pneumonia

ADVANCED OR CONFIRMATORY TESTING

Oral examination under general anesthesia: define extent of secondary palate defects

TREATMENT

TREATMENT OVERVIEW

Essential elements are:

- Treat and resolve aspiration pneumonia prior to surgery.
- Nutritional support (tube feeding) until the patient is of adequate age and health for surgery

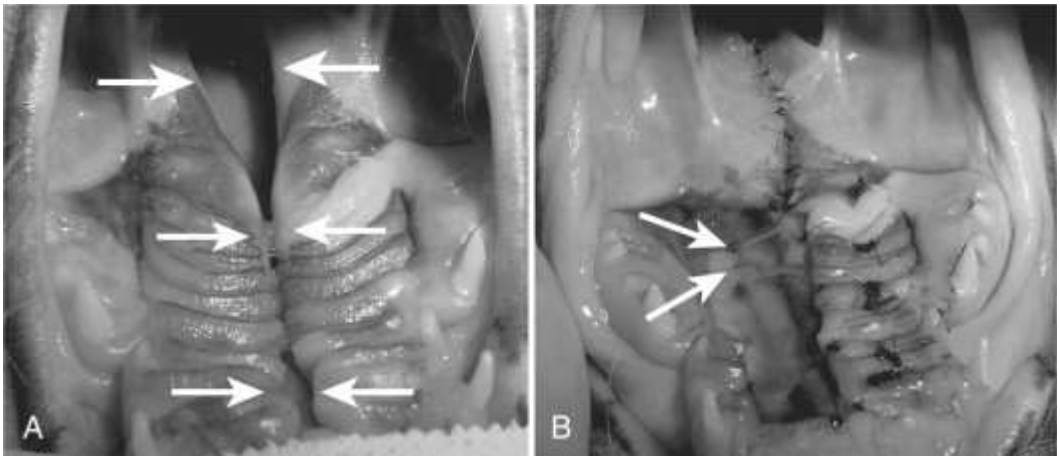
- Complete closure of palate defects

ACUTE GENERAL TREATMENT

Treat aspiration pneumonia (see p. 885)

CHRONIC TREATMENT

- Repair of primary palate defects:
  - Most rostral hard palate defect: reconstructed by creating overlapping flaps of oral (and nasal) tissue or advancement, rotation and transposition flaps harvested from oral tissue only; removal of one or more incisors and canine tooth on the affected side will facilitate flap management.
  - Lip defect: reconstructive cutaneous surgery to provide symmetry (elective)
- Repair of secondary palate defects:
  - Midline hard palate defect: overlapping flaps (preferred technique); medially positioned flaps or unilateral rotation (single pedicle) flaps may be used; the harvested mucoperiosteal flaps must be supplied by major palatine arteries; exposed bone is left to granulate and epithelialize.
  - Midline soft palate defect: medially positioned flaps (with at least a two-layer closure) or overlapping flaps
  - Unilateral soft palate defect: tonsillectomy at affected side, followed by creation and suturing of two nasopharyngeal and two oropharyngeal flaps
  - Soft palate hypoplasia: bilateral tonsillectomy, followed by bilateral creation and suturing of two nasopharyngeal and two oropharyngeal flaps
- Pain control: maxillary nerve block (0.5% bupivacaine hydrochloride) intraoperatively followed by opioids (e.g., hydromorphone, 0.1-0.2 mg/kg IV or IM as needed up to q 2-4 h) and postoperative opioid medication (butorphanol, 0.2-0.4 mg/kg PO q 4-6 h) or nonsteroidal antiinflammatories (e.g., carprofen, 2 mg/kg PO q 12 h) for 4-7 days
- Antibiotics: usually not required unless risk of aspiration or existing aspiration pneumonia
- Wound management: oral application of dilute chlorhexidine solution or gel for 4 weeks; Elizabethan collar to prevent pawing at surgical site



CLEFT PALATE A, Congenital cleft palate. This 14-week-old dog is under general anesthesia and in dorsal recumbency; rostral is towards the bottom of the image. A congenital defect of the secondary palate (midline cleft of the hard and soft palate) is seen *(arrows)*. **B**, Congenital cleft palate, repaired. The hard palate defect was repaired utilizing the overlapping flap technique (note the exposed major and accessory palatine arteries *[arrows]*); the donor area is left to granulate and epithelialize. The soft palate defect was repaired utilizing the medially positioned flap technique.

NUTRITION/DIET

Preoperatively in juvenile patients:

- Tube feeding (oroesophageal) with milk replacer or other suitable diet (e.g., Hill's a/d) until surgical candidate (best at 3-4 months of age):
  - Supplies nutritional needs
  - Minimizes rhinitis
  - Allows patient to mature: anesthetic purposes, greater strength of palatal tissue, more working room in the oropharynx to effect repair

Postoperatively:

- Soft food, no chewing toys/treats for 4 weeks; esophagostomy or gastrostomy tubes to bypass the oral cavity are rarely needed.

POSSIBLE COMPLICATIONS

Dehiscence due to:

- Excess tension if inadequate mobilization of tissue for closure
- Palatal flap necrosis if major palatine artery is compromised during surgery
- Tongue movements, chewing on hard material, self-trauma (consider E-collar, postoperative tube feeding)

RECOMMENDED MONITORING

Reexamination in 2 weeks for removal of skin sutures at lips

PROGNOSIS AND OUTCOME

- Multiple procedures may be required to close a palate defect. Follow-up surgeries should not be attempted before healing (granulation and epithelialization) of all tissues involved (6-8 weeks).
- Poor prognosis for congenital soft palate hypoplasia (restoration of a pharyngeal sphincteric ring and normal swallowing function may not be achieved).
- Guarded prognosis for secondary palate defects without surgical repair (risk of aspiration)

PEARLS & CONSIDERATIONS

COMMENTS

The best chance of success is with the first surgical procedure; avoid electrocoagulation for hemostasis, handle flaps as carefully as possible, and avoid creating closure that is under tension; referral to an experienced oral surgeon is recommended.

PREVENTION

- Selective breeding
- Avoid gestational corticosteroid administration and other insult during pregnancy (see Etiology and Pathophysiology).

TECHNICIAN TIPS

Technicians caring for these patients pre-and postoperatively should be skilled in correct tube-feeding technique.

CLIENT EDUCATION

Management of patients with cleft palate requires intensive nursing care at home for 2-4 months until surgery can be performed.

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Cleaning Products Toxicosis

BASIC INFORMATION

DEFINITION

Accidental exposure (dermal, oral, or ocular) of pets to household cleaning products, including soaps, detergents, bleaches, and disinfectants. Bleaches are discussed in greater detail in Acid or Alkali (Corrosives) Toxicosis, p. 19.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs more commonly involved than cats
- Cats more sensitive to cationic detergents, phenol, and pine oil–containing products

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Observed or suspected exposure to a household cleaning product
- Rapid onset of clinical signs (minutes to a few hours)

PHYSICAL EXAM FINDINGS

- Hypersalivation, vomiting, diarrhea, lethargy (soaps; anionic, nonionic, and Zwitter detergents)
- Oral ulcers (phenol, cationic detergents)
- Corneal ulcer, conjunctivitis/blepharitis (phenol, cationic detergents)
- Central nervous system depression, aspiration (pine oil)
- Distinct smells: bleach, pine oil
- Salivation, vomiting (bleach, pine oil)

ETIOLOGY AND PATHOPHYSIOLOGY

Source:

- Soaps are salts of fatty acids made by the reaction of alkali with fatty acids.
- Detergents are nonsoap surfactants in combination with inorganic ingredients such as phosphates, silicates, or carbonates.
- Detergents are classified into nonionic, anionic, cationic, or Zwitter agents according to charge present in solution. The classification depends on the active substance in the product (listed on label on product container).
    - Nonionic detergents: most heavy-duty laundry liquids, nonphosphate granular products, and many low-sudsing laundry products; alkyl ethoxylate, alkyl phenoxy polyethoxy ethanol, polyethylene glycol stearates
    - Anionic detergents: soap, emulsifiers for ointments and creams, dishwashing liquids, solvent/detergent degreasers; alkyl sodium sulfonates, alkyl sodium sulfates, dioctyl sodium sulfosuccinates, sodium lauryl sulfates, tetrapropylene benzene sulfonate
    - Cationic detergents (quaternary ammonium compounds): benzethonium chloride, benzalkonium chloride, alkyl dimethyl 3,4-dichlorobenzene, cetyl pyridinium chloride
    - Zwitter detergents: most shampoos, bath products, and nonirritant toiletries
- Disinfectants: chemicals applied on inanimate objects to inhibit or kill microorganisms (e.g., quaternary ammonium compounds [cationic detergents], phenols, pine oils, bleaches).
- Most household bleach products contain sodium hypochlorite 3%-6%. Nonchlorine/colorfast bleaches contain sodium peroxide, or sodium perborates.

Mechanism of Toxicosis:

- Depending on dosage and concentration, soaps, anionic, nonionic, and Zwitter detergents, and chlorine bleaches are mildly irritating to the mucous membranes. Oral or cutaneous burns are rare.
- Inhalation of chlorine fumes can cause pulmonary irritation, coughing, and if severe, dyspnea and noncardiogenic pulmonary edema.

- Quaternary ammonium compounds are structurally similar to dexamethonium (neuromuscular blocking agent) and hexamethonium (ganglionic blocking agent). Therefore, systemic effects may resemble organophosphate insecticide toxicosis (see p. 792). They also cause corrosive damage to skin and oral mucosa.
- Phenol (1%-5%) can cause oral or dermal burns. Phenol (or other phenolic derivatives) can also cause respiratory stimulation and alkalosis followed by metabolic acidosis.
- Pine oil disinfectants are irritating to the mucous membranes.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis relies principally on history: suspicion or direct knowledge of exposure to a cleaning product (chewed up container, chemical smell in the breath or on the skin); it is further supported by presence of oral/dermal ulcers, hypersalivation, vomiting, excessive licking motions, and diarrhea.

DIFFERENTIAL DIAGNOSIS

- Corrosives toxicosis (alkali, acids)
- Uremia (oral ulcers)
- Acute vomiting: foreign body obstruction, viral or bacterial gastroenteritis, garbage toxicosis, pancreatitis

INITIAL DATABASE

- CBC: leukocytosis with cationic detergents, phenol; within normal limits for others
- Serum biochemistry profile: electrolyte changes (from severe vomiting or dehydration; cationic detergents, phenols) may be present.
- Urinalysis: results should be unremarkable.
- Fluorescein staining for corneal ulcers (cationic detergents, phenol)

ADVANCED OR CONFIRMATORY TESTING

- Thoracic radiographs: indicated if coughing, dyspnea, or fever of unknown origin. May show evidence of aspiration pneumonia and/or noncardiogenic pulmonary edema
- Abdominal imaging (radiographs, ultrasound): to rule out other causes of acute severe vomiting
- Endoscopic examination of esophagus to rule out perforation within 12-24 hours (cationic detergents, phenol)

TREATMENT

TREATMENT OVERVIEW

Unlike many intoxications, induction of vomiting is contraindicated (or unnecessary, as many patients vomit spontaneously) in several types of cleaning fluid intoxications. Rather, treatment involves dilution via administration of oral liquid, such as milk, and prophylactic protection of gastrointestinal mucosa. Therapeutic goals are:

- Decontamination of patient
- Protect gastrointestinal (GI) mucosa
- Supportive therapy

ACUTE GENERAL TREATMENT

- Decontamination of patient:
  - Oral dilution: *Best option.* Immediately administer milk or water (approximately, 0.25 to 0.5 cups [125-250 mL] for a 30-lb [14-kg] dog and 1 to 2 tablespoons [5-10 mL] for a 10-lb [4.5-kg] cat). Follow with milk of magnesia (0.2-0.3 mL/kg PO).
  - Emesis induction (see p. 1364) in cases of toxicosis with soaps, detergents (other than cationic); *rarely needed.* Use within 2-4 hours only if very large amounts have been ingested. *Do not induce vomiting for cationic detergents, phenol, or pine oils.*
  - Activated charcoal: rarely needed; 1-3 g/kg PO with a cathartic such as 70% sorbitol (3 mL/kg). Not needed for cationic detergents, phenol, or pine oils.
  - Dermal: wash exposed area (cationic detergents, phenol) with water for 20-30 minutes.

    - Ocular: flush eyes with tepid tap water (or saline) for 20-30 minutes. Repeat fluorescein stain to assess for corneal ulcers.
- Protect GI mucosa (cationic detergents, phenol):
    - H2 receptor antagonists:
        - Famotidine: dogs/cats, 0.5 mg/kg PO, SQ, IM, IV q 12 h
    - Control vomiting. Maropitant 1 mg/kg SQ or 2 mg/kg PO q 24 h for 5 days
    - Sucralfate: dog, 0.5-1 g PO q 8-12 h; cat, 0.25-0.5 g PO q 8-12 h
- Supportive care:
    - Intravenous fluids for rehydration (e.g., lactated Ringer's solution) or maintenance
    - Broad-spectrum antibiotics (e.g., ampicillin, 22 mg/kg IV q 8 h, plus enrofloxacin, 5 mg/kg IM or diluted 1:1 with sterile saline and given slowly IV q 12 h [q 24 h in cats]) if caustic burns and/or secondary infection
    - Manage pain (caustic burns): opiates (e.g., fentanyl patch or butorphanol 0.1-1 mg/kg IM, IV, or SQ).
- Nutrition: feed watery slurry or soft mashed food while visible mucosal erosions are present.

RECOMMENDED MONITORING

- CBC, serum chemistry profile: electrolyte changes and other effects of vomiting
- Monitor oral cavity, perioral skin for caustic burns (cationic detergents, phenol) to determine when to introduce solid food.
- Pulse oximetry, thoracic radiography if aspiration (pine oils)

PROGNOSIS AND OUTCOME

- Excellent with soaps, detergents (other than cationic), and household bleaches
- Good to guarded if pulmonary edema develops (bleaches) or if caustic burns are present (cationic detergents, phenols in cats)

PEARLS & CONSIDERATIONS

COMMENTS

Soaps, detergents (other than cationic), and household bleaches have a low order of toxicity and can be treated by immediate dilution (oral administration of milk or water). Exposure to cationic detergents can lead to oral ulcers/burns and systemic effects (ataxia, weakness, seizures).

PREVENTION

Keep household cleaning products out of reach of pets.

SUGGESTED READING

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Claw Disorders

BASIC INFORMATION

DEFINITION

- Onychodystrophy: claw deformity caused by abnormal growth
- Onychomadesis: sloughing of the claw
- Onychomycosis: fungal infection of the claw
- Onychorrhexis: brittle claws that tend to split or break
- Paronychia: inflammation of soft tissue around the claw
- Symmetric lupoid onychodystrophy (SLO): a lupus-like condition that causes sloughing (onychomadesis) of multiple claws

In dogs and cats, the term *claw* is more appropriate than *nail.* Strictly speaking, the term *nail* should be restricted to human and other primates.

EPIDEMIOLOGY

SPECIES, AGE, SEX

Most claw conditions have no specific age or sex predilections other than those listed here:

- SLO: in dogs aged from 3 to 8 years, rare in cats
- Subungual squamous cell carcinoma (SCC): in older dogs
- Subungual melanomas: common in older dogs, rare in older cats
- Onychomycosis: *Malassezia* common but dermatophytosis rare in both dogs and cats

GENETICS & BREED PREDISPOSITION

- SLO: often noted in German shepherds
- Subungual SCC: seen in large breeds (75%) and in breeds with a black coat (66%, such as in the black Labrador retriever and black poodle)

RISK FACTORS

Nonneoplastic claw disorders: immuno-suppression, feline leukemia virus (FeLV) infection, vascular insult, trauma, improper trimming/care of claws, diabetes mellitus

ASSOCIATED CONDITIONS & DISORDERS

- In cats and dogs: hyperadrenocorticism, diabetes mellitus, hypothyroidism, dermatomyositis, arteriovenous fistula, cold-agglutinin disease, drug reaction, vaccine reaction, vasculitis, trauma, leishmaniasis
- In cats only: hyperthyroidism, primary pulmonary bronchiolar adenocarcinoma, pulmonary SCC, cutaneous SCC with metastasis

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

Owners can observe licking at affected digit(s), signs of pain, lameness, claw sloughing, or may have noted a swollen toe or a mass during claw trim. A single foot or multiple feet can be involved. The claw disorder can be part of a more generalized skin condition.

PHYSICAL EXAM FINDINGS

- Bacterial claw infections
  - One or many affected digits
  - Paronychia, toe swelling, purulent discharge, and possible separation and purulent discharge from the claw
  - Regional lymphadenopathy, with fever and possible osteomyelitis
  - Other clinical signs of immunocompromising conditions

- Onychomycosis
  - Dermatophytic claw infections result in paronychia with minimal pain, irritation, and pruritus. Typically only one or two affected digits with friable and misshapen claws. Usually accompanied with focal or multifocal skin lesions.
  - A notable "brown line" on the claws (consisting of a waxy discharge) is a clue for *Malassezia* overgrowth and is typically associated with inter-digital dermatitis, paronychia, and pruritus, as well as other possible evident areas of cutaneous involvement (see p. 682 and 891).
- SLO
  - Onychomadesis starting with a single abnormal claw on two or more paws; within 2-9 weeks, all claws on all four paws are affected.
  - Regrowth of short, misshapen, dry, soft, brittle, and crumbling claws
  - Paronychia is uncommon unless a secondary bacterial infection is present.
- Subungual SCC
  - Single, swollen, painful toe with paronychia and associated erosive/ulcerative dermatitis and often loss of the claw
  - Multiple digits can be affected over time in black Labradors, black standard poodles, and giant schnauzers.
- Subungual melanoma
  - Solitary, well-circumscribed, dome-shaped, firm, wart-like growth
  - Varies in size from 0.5-10 cm in diameter
  - Possibly pigmented or nonpigmented and ulcerated

ETIOLOGY AND PATHOPHYSIOLOGY

- Bacterial claw infection
  - Infection is secondary (e.g., trauma if one or two claws are infected; if many claws are infected, consider hypothyroidism, hyperadrenocorticism, immune-mediated condition [pemphigus], or SLO).
  - *Staphylococcus pseudintermedius* is the most common bacterium isolated.
  - Concurrent demodicosis occurs in both single- and multiple-digit involvement.
  - Leishmaniasis should be considered in endemic areas (the Mediterranean, limited areas in the United States).
- Onychomycosis
  - *Microsporum canis* in cats
  - *Trichophyton mentagrophytes* in dogs
  - *Malassezia* spp. in dogs and cats
  - *Microsporum gypseum* and candidiasis (yeast) less common
- Symmetric lupoid onychodystrophy: currently regarded as an idiopathic condition. SLO may either be a clinical manifestation of many different diseases or an immune-mediated condition itself. Current emphasis is to look for potential underlying conditions, including hypersensitivity disorders (drug, food, environmental allergens) and hormonal and metabolic abnormalities before committing a pet to lifelong therapy.
- Subungual SCC
  - Neoplasm generally originating from the germinal epithelium of the claw
  - Reverse also possible (metastasis from a primary pulmonary neoplasm/carcinoma to toe), a sequence that is more common in cats than in dogs
- Subungual melanoma: malignant proliferation of melanocytes involving the claw beds in older dogs

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis originates with observation of claw abnormalities on physical exam. Complementary testing is selected based on history, remainder of exam (especially whether one or several claws is/are affected), and results of the initial database.

DIFFERENTIAL DIAGNOSIS

- Single claw affected
  - Trauma-induced condition
  - Neoplasia (subungual SCC, subungual melanoma high-grade mast cell tumors, fibrosarcoma, neurofibrosarcoma, eccrine carcinoma, osteosarcoma, subungual keratoacanthoma)
  - Primary pulmonary bronchiolar adenocarcinoma, pulmonary SCC, and cutaneous SCC with metastasis to digits in cats
- Multiple claw involvement
  - SLO
  - Immune-mediated diseases (pemphigus complex, bullous pemphigoid, drug eruption, vasculitis, cold-agglutinin disease)
  - Metabolic disease (hypothyroidism, hyperadrenocorticism, feline hyperthyroidism); rare

INITIAL DATABASE

- Cytologic examination of claw exudates
  - Suppurative or pyogranulomatous inflammation with engulfed bacteria: consistent with bacterial claw infection
  - Broad-based budding yeast consistent with *Malassezia* infection (see p. 682)
  - Evidence of acantholytic cells: indicative of pemphigus
  - Round cell tumor cells: consistent with melanoma
- Fungal culture (Dermatophyte Test Medium):
  - Indicated if a single claw/claw bed is involved (see p. 292 and p. 1248)
- CBC, serum biochemistry profile, urinalysis:
  - Evidence of systemic conditions (diabetes mellitus, hyperadrenocorticism, systemic lupus erythematosus [SLE])
- Thyroid profile:
  - Indicated if multiple claws are affected and other consistent clinical signs are present. Hypothyroidism (in dogs) and hyperthyroidism (in cats) are rare concurrent/causative conditions.

ADVANCED OR CONFIRMATORY TESTING

- Bacterial culture and sensitivity: often *Staphylococcus pseudintermedius*
- Biopsy for histopathologic exam and special stains
  - Usually via toe amputation; longitudinal claw and ungula bed excision may be complex and painful.
  - SLO: hydropic and lichenoid interface dermatitis
  - Rule out other immune-mediated conditions (pemphigus, bullous pemphigoid).
  - Identify fungal hyphae and arthrospores or bacterial organisms.
  - About 10% of melanomas (identified by histologic examination) behave malignantly.
- Antinuclear antibody (ANA) test to rule-in the possibility of SLE
- FeLV/feline immunodeficiency virus (FIV) serology
- Radiographs:
  - Rule out osteomyelitis with bacterial claw disease.
  - Bony lysis of third phalanx (P3) and tissue swelling due to neoplasia, particularly subungual SCC
  - Thoracic radiographs: metastasis check
- Fine-needle lymph node aspirates, abdominal ultrasound
  - If SCC or melanoma is confirmed histologically

TREATMENT

TREATMENT OVERVIEW

The goal of treatment is to achieve permanent cure or control of the disease. Sometimes palliative treatment is the only option (e.g., SLO).

ACUTE AND CHRONIC TREATMENT

- Claw fracture or avulsion: The clinician should trim or file (using a Dremel tool) any fractured claws, using sedation, analgesia, local/general anesthesia as necessary; remove loose claws and bandage foot. In severe conditions or patients with neoplasia, P3 amputation may be necessary.
- Bacterial claw infections
  - Antibiotic therapy for 2 weeks beyond clinical resolution: cephalosporin (e.g., cephalexin, 22 mg/kg PO q 8 h, or 30 mg/kg PO q 12 h), amoxicillin-clavulanate (22 mg/kg PO q 12 h), or potentiated sulfonamide (e.g., trimethoprim-sulfa, 15-30 mg/kg PO q 12 h).
  - Topical creams/ointments: silver sulfadiazine
  - Foot scrubs: 2%-4% chlorhexidine topical soaks q 12-24 h for 7 days beyond clinical resolution
- Onychomycosis (dermatophytic)
  - Long-term antifungal/anti-yeast treatment on a daily or pulse basis (6 months or longer); e.g., 3 days on and 4 days off (ketoconazole) or 1 week on and 1 week off (itraconazole)
  - Ketoconazole (10 mg/kg PO q 24 h), itraconazole (5-10 mg/kg PO q 24 h), fluconazole (5 mg/kg PO q 24 h), or terbinafine (10-40 mg/kg PO q 24 h) given with food for maximal absorption unless using liquid azoles
  - Treatment is continued 1-3 months beyond complete claw regrowth and a negative repeat fungal culture from claw trimmings.
  - Topical antifungal products include chlorhexidine, miconazole, clotrimazole, terbinafine, enilconazole, or lime sulfur.
- Symmetric lupoid onychodystrophy:
  - Varying combinations of these treatments are used based on individual response and tolerance.
  - Omega-3 fatty acids (36 mg/kg PO q 24 h) and omega-6 fatty acids (500-1000 mg PO q 24 h) for a minimum of 3

months, then as maintenance therapy
    - Vitamin E (10-20 IU/kg PO q 12 h to q 8 h) for a minimum of 3 months or longer if improved
    - Elimination diet for 8 to 12 weeks to rule out adverse food reaction as a trigger.
    - Tetracycline and niacinamide (500 mg of each for dogs >10 kg; 250 mg of each for dogs <10 kg) PO q 8 h, until improvement (about 2 to 3 months); then taper the medication monthly. Doxycycline (5-10 mg/kg q 12 h) may be substituted for tetracycline.
    - Prednisolone (2-4 mg/kg PO q 24 h induction, weaning based on a favorable response) alone or with azathioprine (2.2 mg/kg PO q 24-48 h; dogs only) as corticosteroid-sparing agents; monitor for myelosuppression, hepatotoxicity, opportunistic infection.
    - Pentoxifylline (10-30 mg/kg PO q 8-12 h) until resolution of lesions, then taper the medication monthly.
    - Cyclosporine (5 mg/kg PO q 12 h microemulsion [Atopica, Neoral]) until resolved, then taper to lowest frequency that controls relapse of clinical signs.
    - Onychectomy (P3 amputation) as a last resort
- Subungual SCC
    - Post-staging amputation of the affected digit to the proximal inter-phalangeal level
    - SCC is locally invasive and metastasis rate is low; no need for chemotherapy or radiation therapy.
- Subungual melanoma
    - Radical surgical excision of both malignant and benign areas
    - Follow-up chemotherapy or radiation therapy

PROGNOSIS AND OUTCOME

- Bacterial claw infections
    - Generally good for complete resolution
    - Protracted therapy (about 3 to 6 months) may be necessary.
    - Response may be influenced by underlying immunosuppressive factors.
- Onychomycosis
    - Prognosis is good to guarded, owing to incomplete resolution in dermatophytic onychomycosis.
    - May require either P3 amputation or pulse antifungal therapy for life
    - Prognosis for *Malassezia* is good if underlying etiology is addressed.
    - Response may be influenced by underlying etiologies or immunosuppressive factors.
- SLO
    - Chronic and recurrent problem if not treated
    - Clinical improvement is usually seen within 3 to 4 months; if not, change therapies.
    - Claw regrowth is good, although claws may be slightly deformed or friable.
    - Refractory cases may require P3 amputation.
- Subungual SCC
    - Locally invasive with low metastatic potential: regional node or distant metastasis in <30% of cases
    - The 1- and 2-year survival rates are 95% and 75%, respectively, if subungual. Rates are 60% and 40%, respectively, if not specifically from the subungual region, as determined via dermatohistopathologic exam.
- Subungual melanomas
    - Good if benign; poor if malignant. About 50% of dogs die because of distant metastasis.

PEARLS & CONSIDERATIONS

COMMENTS

- When reevaluating the claws, look for normalization of growth patterns at the base of the claw.
- In SLO, taper immunomodulatory medications gradually, and treat for several months beyond clinical resolution.

TECHNICIAN TIP

Shortening claws using a claw file or Dremel tool tends to be more readily accepted by pets affected with fragile claws.

PREVENTION

Routine claw care will result in early detection of claw and claw bed disorders.

CLIENT EDUCATION

Patience is required, as claws grow slowly.

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Citrus Oil Extract Toxicosis

BASIC INFORMATION

DEFINITION

Adverse effects typically caused by excessive dermal exposure of D-limonene. Typical signs of intoxication are excessive salivation, weakness, ataxia, hypothermia, tremors, and erythema. Clinical signs are usually temporary, and an affected animal generally recovers fully within a few hours to a couple of days. Toxicosis usually occurs when concentrated products are not diluted properly.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs and cats of all ages, breeds, and both sexes are vulnerable.
- Cats are more sensitive than dogs.

RISK FACTORS

- Inappropriate dilution or excessive use (i.e., more than 5 to 10 times the manufacturer's recommended use)
- Risk of D-limonene or linalool toxicity increases when formulated with other solvents or essential oils

GEOGRAPHY AND SEASONALITY

Toxicosis more prevalent in summer months during flea season

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- History of exposure (use of spray, shampoo, or dip containing citrus oil extracts)
- Hypersalivation, hypothermia, muscle weakness
- Ataxia and tremors

PHYSICAL EXAM FINDINGS

- A distinct citrus smell virtually always is present on the animal and is an important diagnostic finding.
- Hypersalivation
- Muscle weakness
- Tremors, shivering, or ataxia
- Body temperature: mild to severe hypothermia
- Irritation of eyes and skin. Cutaneous erythema, especially in the scrotal and perineal areas, is a common finding.

ETIOLOGY AND PATHOPHYSIOLOGY

- Crude citrus oil extracts including D-limonene and linalool have some insecticidal properties and are used in shampoos, sprays, or dips for control of fleas on dogs and cats.
- Concentration of D-limonene and linalool in most sprays is less than 1%. Shampoos usually contain D-limonene 5%. Some dips contain 78.2% D-limonene and must be diluted before use on animals.
- Limonene (occurs in D or L form) is a monoterpene that occurs naturally in some fruits (citrus), trees, and bushes. It is commonly used as a flavoring agent, fragrance, feed additive, and in many household cleaning products.
- Linalool is found in nature as a monoterpene in volatile oils, various herbs, leaves, flowers, wood, and citrus products. It is used as a fragrance in soaps, detergents, and perfumes and as a flavoring agent in beverages, chewing gum, and candy.
- The exact mechanism of action of these products in mammals is not clear. Linalool has been ruled out to be a cholinesterase inhibitor.
- It has been suggested that these products cause centrally and peripherally acting vasodilation, resulting in hypothermia and muscle weakness.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Suspect toxicosis based on history and exam: history/evidence of exposure, presence of citrus-like smell on the skin, and any combination of hypersalivation, erythema, hypothermia, hypotension, and weakness.

DIFFERENTIAL DIAGNOSIS

- Intracranial disease
- Toxicosis from pyrethrins/pyrethroids
- Portosystemic shunt

INITIAL DATABASE

- The diagnosis is generally established based on history and physical exam alone. Additional diagnostic testing may be used for ruling out other disorders with similar presenting signs.
- CBC, serum biochemistry profile, urinalysis: typically unremarkable

TREATMENT

TREATMENT OVERVIEW

Treatment consists of providing supportive care (intravenous fluids, maintaining body temperature and blood pressure within the normal range) as needed and dermal decontamination. Hospitalization may be necessary only for very severe cases.

ACUTE GENERAL TREATMENT

- Dermal decontamination:
  - In case of dermal exposure, it is recommended to bathe the patient with an unmedicated detergent or soap and warm water. Drying the patient thoroughly is essential to minimize the risk of hypothermia. Bathing can be repeated until the citrus smell is gone.
- Thermoregulation:
  - Keeping the patient warm and monitoring the body temperature frequently are essential to minimize hypothermia while not overcompensating and causing hyperthermia.
  - Use of heating pads as needed and warm water enema if hypothermia is severe should be considered. However, warm water enema usage will eliminate rectal temperature as a reliable way of measuring core body temperature.
  - Avoid overcompensation (risk of iatrogenic hyperthermia). Active rewarming of the patient should be terminated and switched to passive warmth retention with ongoing monitoring, once the body temperature >98° F (36.7° C).
- Supportive care:
  - Intravenous fluids if necessary (e.g., dehydration, hypotension, electrolyte deficits)

PROGNOSIS AND OUTCOME

- Usually good to excellent; recovery within hours to a couple of days
- Deaths have been reported in cats.

PEARLS & CONSIDERATIONS

COMMENTS

- Animals treated with citrus oil extracts have a distinct smell.
- Hypersalivation is an immediate sign of D-limonene toxicosis in cats; it may last from 15 minutes to 1 hour. Severely affected cats show hypothermia and tremors.
- Linalool exposure produces signs that are more severe and last for longer duration than D-limonene.
- D-limonene and linalool are well absorbed orally.
- When dips are used in higher concentration than recommended, limonene may be absorbed in significant quantities through

the skin, causing systemic effects.

PREVENTION

Follow manufacturer's instructions for dilutions.

SUGGESTED READING

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Cirrhotic/Fibrosing Liver Disease

BASIC INFORMATION

DEFINITION

- Fibrosis: replacement of hepatic parenchyma with extracellular matrix (ECM), collagen, and connective tissue
- Cirrhosis: diffuse hepatic fibrosis with concurrent formation of regenerative nodules that results in irreversible loss of normal hepatic architecture
- Sometimes referred to as *primary hepatitis,* this disorder is being recognized with increasing frequency in a variety of breeds.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Incidence is highest in middle-aged to older dogs (>7 years) with chronic liver disease.
- Middle-aged cats with chronic cholangiohepatitis may suffer from biliary cirrhosis.
- Copper storage hepatopathy (~1-5 years) and idiopathic fibrosis are seen in younger dogs (<2 years).
- Male cocker spaniels, female Doberman pinschers, and Labrador retrievers appear more susceptible.

GENETICS & BREED PREDISPOSITION

- Doberman pinschers, cocker spaniels, Scottish terriers, and Labrador retrievers have a familial predisposition for chronic active (idiopathic) hepatitis (see online chapters: Hepatitis [Chronic] of Doberman Pinscher Dogs and Hepatitis [Chronic] of Cocker Spaniel Dogs).
- Copper storage disease is inherited in Bedlington terriers, West Highland white terriers, Skye terriers, and dalmatians.
- German shepherds and standard poodles develop juvenile idiopathic hepatic fibrosis.

RISK FACTORS

Idiopathic chronic hepatitis (chronic active hepatitis) in dogs, excess hepatic copper or iron storage, extrahepatic biliary obstruction, drug administration (phenobarbital, others)

ASSOCIATED CONDITIONS & DISORDERS

- Portal hypertension, ascites, hepatic encephalopathy, coagulopathies, urolithiasis, acquired portosystemic shunts, gastric ulceration, fat malabsorption and steatorrhea, hypoglycemia, and hypoalbuminemia may result from fibrosing liver disease.
- Rare occurrence of pulmonary edema (hypoalbuminemia), renal failure (hepatorenal syndrome), or transient erythropoietic protoporphyria

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Chronic condition of variable intensity that usually includes lethargy, anorexia, and weight loss
- Vomiting, diarrhea, melena, and polyuria/polydipsia also frequently are part of the history.
- Icterus or signs of coagulopathy uncommonly are reported by owners.
- Owners may report abdominal distension from ascites as “weight gain,” even as the patient loses muscle mass.

PHYSICAL EXAM FINDINGS

- May be unremarkable except for weight loss and muscle wasting
- Icterus occurs commonly.
- Ascites and evidence of coagulopathy in advanced cases
- Microhepatia may be present (dogs), although cats with biliary cirrhosis may have large livers.
- Manifestations of cerebral dysfunction (depression, stupor, others) due to hepatic encephalopathy (see p. 501)

ETIOLOGY AND PATHOPHYSIOLOGY

- ECM deposition (fibrosis) is stimulated by inflammatory mediators (or congenital or idiopathic).
- Chronic fibrosis and regenerative nodule formation results in cirrhosis. Chronic progressive collagen deposition irreversibly destroys normal hepatic architecture.
- Normal hepatic blood flow and bile flow are disrupted, perpetuating hepatocellular injury.
- Any chronic inflammatory hepatic condition may be responsible, although a specific cause is not often identified (i.e., idiopathic).
- Possible underlying etiologies include cholangitis/cholangiohepatitis (cats), copper storage disease (dogs), drugs and/or toxins (aflatoxin, anticonvulsants, azole antifungals, trimethoprim-sulfa), immune-mediated, leptospirosis, canine infectious hepatitis, hypoxia, extrahepatic biliary obstruction, or a single episode of massive hepatic necrosis (i.e., postnecrotic cirrhosis).
- Hepatic vascular resistance may increase, resulting in portal hypertension, ascites, acquired shunts, and encephalopathy.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Although plasma markers of this condition are being developed (transforming growth factor beta-1), histopathologic analysis of a liver biopsy specimen remains central to the diagnosis of this disorder. It is particularly important to look for excess copper accumulation as a treatable cause of progressive hepatic lesions.

DIFFERENTIAL DIAGNOSIS

- Chronic active/idiopathic hepatitis (dogs)
- Cholangitis/cholangiohepatitis (cats)
- Noncirrhotic portal hypertension
- Biliary obstruction
- Pancreatitis
- Hepatic neoplasia (primary or metastatic)
- Feline infectious peritonitis, toxoplasmosis
- Chronic fibrosing pancreatitis
- Congenital portosystemic shunt
- Hepatic lipidosis (cats)

INITIAL DATABASE

- CBC:
  - Nonregenerative anemia (normocytic, normochromic, or microcytic)
  - Acanthocytes (cats)
- Serum biochemistry panel:
  - Elevated hepatic enzyme activities (alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, γ-glutamyl transferase)
  - Hyperbilirubinemia
  - Low blood urea nitrogen (BUN) (variable)
  - Hypoalbuminemia and hyperglobulinemia (variable)
  - Hypocholesterolemia (variable)
  - Hypoglycemia (variable)
  - Electrolyte abnormalities (hypokalemia, hyponatremia)
- Urinalysis:
  - Isosthenuria
  - Ammonium biurate crystalluria (variable)

ADVANCED OR CONFIRMATORY TESTING

- Abdominocentesis and fluid analysis of ascites: pure transudate (hypoalbuminemia) or modified transudate (portal hypertension)
- Coagulation studies: prolonged activated clotting time, partial thromboplastin time (PT), activated partial thromboplastin time (APTT), proteins induced by vitamin K antagonism or absence (PIVKA), buccal mucosal bleeding time. Of these, the PIVKA test is most sensitive, although PT and APTT are acceptable and more readily available. It has not been shown that any of these studies will help predict bleeding following hepatic biopsy.
- Serum bile acids: elevated (fasting and postprandial). Bile acids will be abnormal (and therefore an unnecessary test) in cases where the total bilirubin concentration is elevated.
- Radiographs: small liver (dogs), large liver (cats), loss of abdominal detail

- Abdominal ultrasound:
  - Nodular hyperechoic/mixed echogenicity of hepatic parenchyma with abdominal effusion
  - Acquired portosystemic shunt(s)
  - Possible ascites
- Ultrasound-guided percutaneous gallbladder aspirate
- Laparoscopy or laparotomy:
  - Small, firm, irregular liver
- Liver biopsy for histopathologic analysis: confirmatory
  - Fibrosis: inflammatory (bridging) or noninflammatory (sinusoidal, triads)
  - Cirrhosis, nodular regeneration, loss of normal hepatic architecture
  - Note: suspicion of cirrhotic/fibrosing liver disease should prompt the consideration of wedge biopsy of the liver rather than ultrasound-guided core biopsy, because a firm, severely fibrotic liver may be difficult to penetrate safely with core biopsy instruments, especially if ascites is present. Additionally, needle core biopsies are often inaccurate in cirrhotic livers.

TREATMENT

TREATMENT OVERVIEW

Very few treatment options are proven to directly impact the progression of this condition unless a specific etiology (e.g., copper accumulation, drug-induced) can be targeted. Fortunately, very few of the myriad of potentially beneficial nonspecific treatments (e.g., antioxidants, liver protectants) are thought to have significant adverse effects.

ACUTE GENERAL TREATMENT

- Intravenous fluids (balanced electrolyte solution) as needed:
  - Avoid 0.9% NaCl with ascites and hypoalbuminemia.
  - Avoid lactate with hepatic failure.
  - Potassium (20-40 mEq/L or more, based on serum potassium concentration) and dextrose (2.5%-5%) supplementation may be necessary.
  - Dextrans, hetastarch, or plasma transfusion for oncotic pressure support
    - Plasma advantages include presence of albumin (contributes positively to protein balance), presence of clotting factors, and persistence in circulation (versus protein-losing enteropathy or nephropathy, in which the transfused proteins may be lost quickly); drawbacks include cost and short shelf life (fresh) or need to freeze (fresh frozen).
- Therapeutic abdominocentesis when necessary (i.e., respiratory compromise, significant abdominal discomfort); (see p. 1192)

CHRONIC TREATMENT

See also Hepatic Encephalopathy, p. 501.

- Antibiotics:
  - Specific to infectious agent if identified as underlying etiology (rarely in dogs)
  - For signs of hepatic encephalopathy, consider:
    - Metronidazole (7.5 mg/kg PO q 12 h), *or*
    - Amoxicillin-clavulanate (15 mg/kg PO q 12 h), *or*
    - Ampicillin (20 mg/kg PO q 8 h), *or*
    - Neomycin (20 mg/kg PO q 8 h)
- Antiinflammatory: with histopathologic confirmation of chronic noninfectious inflammation, consider prednisolone (1-4 mg/kg PO q 24-48 h, taper if possible) and/or azathioprine (1 mg/kg PO q 24-48 h).
- Antifibrotic: Colchicine (0.03 mg/kg PO q 24 h), although no published data support its use or clearly demonstrate a beneficial effect; veterinary data regarding safety and efficacy are lacking at present. Prednisone (antiinflammatory) and D-penicillamine (copper chelator; 10-15 mg/kg PO q 12 h) also have antifibrotic properties.
- Lactulose (0.25-0.5 mL/kg PO q 8 h, titrated to achieve loose fecal consistency) with cleansing and/or retention enemas (povidone-iodine diluted 1:10 with tap water or lactulose diluted 1:3 with tap water) to decrease ammonia production/absorption in cases of hepatic encephalopathy. Generally, patients with advanced disease requiring this level of therapy have a grave prognosis.
- Ursodiol (10-15 mg/kg PO q 24 h) as a choleretic in cases of cholestasis
- Alpha-tocopherol (200-600 IU PO q 24 h), *S*-adenosylmethionine (20 mg/kg PO q 24 h), and milk thistle/silymarin (optimal dose unknown) may act as hepatoprotective antioxidants.
- Spironolactone (1-2 mg/kg PO q 12 h) or furosemide (1-2 mg/kg PO q 12 h) in cases of ascites
- Vitamin K1 (1-2 mg/kg SQ or IM) if overt clinical bleeding is identified or if PT or APTT are prolonged greater than twice

normal
- Sucralfate (1 g/25 kg PO q 8-12 h) and/or famotidine (Pepcid 0.5 mg/kg q 24 h) as gastrointestinal ulcer therapy

NUTRITION/DIET

- Most commercial geriatric, liver, or renal diets are appropriate.
- Adjust protein consumption in the face of hepatic encephalopathy (decreased/optimal quantity, replace meat proteins with dairy and/or vegetable protein).
- Fermentable fiber in cases of hepatic encephalopathy
- Water-soluble vitamin supplementation
- Avoid mineral supplements containing copper.

DRUG INTERACTIONS

- Animals with hepatic failure are anesthetic risks. Barbiturates should be avoided, and benzodiazepines should be used with care. Isoflurane or sevoflurane are the gas anesthetics of choice. Propofol, although hepatically metabolized, may be administered to effect (usually requiring a small fraction of normal doses) for controlling seizures due to hepatic encephalopathy.
- Lidocaine, theophylline, propranolol, captopril, and tetracyclines should be avoided.
- Diuretics may worsen hepatic encephalopathy, promote dehydration or metabolic alkalosis, and should be used only in otherwise stable patients for the long-term delay of return of ascites.
- Corticosteroids should be avoided in animals with active infection, may precipitate hepatic failure and/or gastric ulceration, and cause sodium retention (may use dexamethasone [no mineralocorticoid activity] as an alternative to prednisone).
- Nonsteroidal antiinflammatory drugs may exacerbate gastrointestinal ulceration.
- Avoid medications that rely solely or predominantly on hepatic metabolism for effectiveness or clearance.

POSSIBLE COMPLICATIONS

Hepatic encephalopathy, septicemia, hemorrhage/coagulopathy, disseminated intravascular coagulation

RECOMMENDED MONITORING

Body weight, abdominal girth, liver enzymes, albumin, BUN, and bile acids should be monitored on a monthly basis.

PROGNOSIS AND OUTCOME

- In one report, 94% of dogs with hepatic fibrosis/cirrhosis were dead within 1 week of diagnosis.
- Dogs with idiopathic hepatic fibrosis/cirrhosis have been reported to survive for up to 6 years, and intensive therapy may extend the survival of cirrhotic patients, although the prognosis is usually very poor with advanced disease.
- Histopathologic findings may be helpful as a prognostic indicator.
- Patients that are anorectic, patients with hepatic fibrosis/cirrhosis causing clinical signs of hepatic encephalopathy, the presence of a coagulopathy (prolonged PT, APTT, or thrombocytopenia), ascites, hypoglobulinemia, or with histologically severe changes (cirrhosis, advanced fibrosis) usually have a poor prognosis.

PEARLS & CONSIDERATIONS

COMMENTS

- Hepatic fibrosis and cirrhotic changes indicate a progressive, terminal condition that is unfortunately often not recognized or appreciated until the patient is in an advanced state of the disease. An underlying etiology is not often identified, making specific therapy impossible. A histopathologic diagnosis is essential in cases of suspected hepatic fibrosis/cirrhosis.
- Even with severe cirrhotic/fibrosing liver disease, patients may have little active liver inflammation and therefore can have normal or near-normal serum liver enzyme activities.
    - Bile acids (especially postprandial) are much more sensitive for detection.

PREVENTION

- Being aware of breed predispositions and early testing of appropriate animals (i.e., Bedlington terriers) may lead to early intervention.
- Avoid oversupplementation with copper-containing products.

CLIENT EDUCATION

Encephalopathic patients that can be clinically stabilized need attention to nutrition: even extremely small amounts of meat protein (e.g., one small meat-based treat) may precipitate severe signs of hepatic encephalopathy.

SUGGESTED READING

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Chylothorax

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Accumulation of fluid with a high triglyceride concentration (chyle) within the pleural space

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Cats and dogs of any age can develop chylothorax.
- Some diseases associated with chylothorax are more common in middle-aged to older patients.

GENETICS & BREED PREDISPOSITION

Possible breed predispositions include Afghan hounds and Shiba Inu dogs, and purebred cats, especially Asian breed cats.

RISK FACTORS

- Trauma
- Intestinal or generalized lymphangiectasia
- Congestive heart failure (CHF); cats more commonly develop chylothorax as part of CHF than dogs do.
- Thoracic neoplasia
- Thoracic surgery if there is damage to the left brachiocephalic vein

ASSOCIATED CONDITIONS & DISORDERS

Fibrosing pleuritis

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Typical clinical signs include:
  - Tachypnea
  - Increased inspiratory effort
  - Shallow respiration
  - Restrictive breathing pattern
  - Open-mouth breathing
  - Lethargy or exercise intolerance
  - Coughing
  - Possibly cyanosis
- Some animals, especially cats, may show minimal clinical signs until effusion volume is quite large.

PHYSICAL EXAM FINDINGS

- Respiratory distress
- Thoracic auscultation:
  - Muffled heart and lung sounds ventrally
    - Careful auscultation for cardiac murmurs or arrhythmias is warranted, or for displacement of heart sounds to one side or caudally that may suggest a mass effect.
  - Increased bronchovesicular lung sounds dorsally
  - Abnormalities of thoracic auscultation can be very subtle in cats.
- Thoracic percussion: hyporesonance ventrally
- Jugular vein distension or pulsation may be present in animals with heart failure or pericardial disease.
  - Large-volume pleural effusions can contribute to increased central venous pressure and possibly jugular venous distention (i.e., appearance is identical to that seen when the jugular vein is raised manually for blood sampling) or

jugular pulsation.
    - Radiation of a normal carotid pulse to the overlying jugular vein should not be misinterpreted as jugular pulsation.
- Peripheral lymphadenomegaly may be noted with some causes of thoracic neoplasia.
- Peritoneal effusion
- Decreased cranial thoracic compressibility (cats) if associated with mediastinal mass

ETIOLOGY AND PATHOPHYSIOLOGY

- Chyle is the fluid formed from lymphatic drainage of the gastrointestinal tract (composed of lymph and chylomicrons), which is collected in a small abdominal reservoir, the cisterna chyli. The sole outflow of the cisterna chyli is the thoracic duct, a single or paired structure that courses dorsally though the thorax and empties into the cranial vena cava.
- Impaired or disrupted lymphatic drainage:
    - Trauma and subsequent rupture of the thoracic duct
    - Neoplasia, including mediastinal, thoracic wall, or affecting thoracic duct
    - Thoracic lymphangiectasia
        - May be associated with intestinal lymphangiectasia
    - Infectious causes such as fungal granulomas
- Increased central venous hydrostatic pressure (thoracic duct empties into cranial vena cava):
    - CHF (right-sided in dogs, left or right-sided in cats)
    - Pericardial disease:
        - Pericardial effusion
        - Restrictive pericardial disease
    - Pulmonary thromboembolism
    - Heartworm disease
- Chylothorax has been reported in a small number of dogs post lung-lobe torsion correction.
- In many cases, the cause of chylothorax cannot be determined (classification as idiopathic).
- Pleural effusion causes hypoxemia through a combination of hypoventilation and ventilation/perfusion mismatching.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Patients with chylothorax will typically present with clinical signs of pleural effusion, and the presence of the effusion can be confirmed by imaging (radiographs, ultrasonography) or thoracocentesis. The confirmation of chylous fluid is achieved via fluid analysis and the comparison of serum and fluid triglyceride levels.

DIFFERENTIAL DIAGNOSIS

- Other causes of pleural effusion:
    - Hypoalbuminemia
    - CHF
    - Intrathoracic neoplasia
    - Lung-lobe torsion
    - Pyothorax
    - Pseudochylothorax
    - Hemothorax
- Pneumothorax
- Pulmonary parenchymal disease

INITIAL DATABASE

- Thoracic radiographs:
    - Interlobar fissure lines
    - Reduced visualization of the heart, especially on dorsoventral views
    - Retraction of lung margins from the thoracic wall, with an interposed fluid opacity
    - Blunting of the lung margins at the costophrenic angles
    - Increased opacity dorsal to the sternum on lateral views, with rounding of the lung margins ventrally
    - The diaphragm is often obscured.
    - Widened mediastinum
    - Avoid ventrodorsal views, as this increases the risk of respiratory distress.
- Thoracocentesis: chyle is often grossly white or pink and opaque and remains so after centrifugation.
    - Chyle may be classified as a modified transudate (<3000-5000 nucleated cells/mcL) or a nonseptic exudate (>5000

nucleated cells/mcL).
    - Early chylothorax usually has a predominance of lymphocytes.
    - With chronicity, increased numbers of nondegenerate neutrophils and some macrophages may appear.
- Postdrainage thoracic films are advised to check for radiographic signs of pulmonary parenchymal, mediastinal, or cardiac disease.
    - Atelectatic lung lobes may give a false impression of lung masses.
    - Fibrosing/constrictive pleuritis secondary to chronic chylothorax may prevent complete reexpansion post drainage and can cause many of the radiographic abnormalities seen with pleural fluid.
- Thoracic ultrasonography can detect pulmonary or mediastinal masses/lesions, lymphadenomegaly, pulmonary consolidation, lung-lobe torsion, or confirm presence of effusion if in doubt.
    - If the patient is stable, ultrasound is ideally performed before effusion is completely drained to provide an acoustic window.
    - Thoracic ultrasound can detect small volume effusions, guide thoracocentesis if fluid is compartmentalized, or guide fine-needle aspiration of masses or other pathology.

ADVANCED OR CONFIRMATORY TESTING

- CBC:
    - Lymphopenia is possible.
    - Leukogram changes are rarely specific.
- Serum biochemistry profile:
    - Hypocalcemia and hypoalbuminemia/hypoproteinemia are possible if chylothorax is secondary to intestinal lymphangiectasia.
- Urinalysis: generally unremarkable
- Echocardiography can help rule in or rule out myocardial, valvular, or pericardial disease as the cause.
- Biochemical analysis of pleural fluid:
    - Compared to serum concentrations, increased pleural fluid triglyceride and decreased pleural fluid cholesterol levels are consistent with chylous effusion.
- Pseudochylous effusions (rare) have a pleural-fluid cholesterol concentration greater than the serum cholesterol concentration, and pleural-fluid triglyceride concentration lower than the serum triglyceride concentration.
- Occasionally in fasted or anorexic animals, pleural fluid is not milky and can have a reduced triglyceride concentration; consider checking the pleural fluid and serum triglyceride levels postprandially.
- CT or MRI may aid assessment of structural abnormalities in the thoracic cavity.

TREATMENT

TREATMENT OVERVIEW

Treatment of chylothorax is directed at two principal goals: alleviation of signs of respiratory distress when present, and identification and treatment of an underlying cause when one exists.

ACUTE GENERAL TREATMENT

- Oxygen if respiratory distress
- Thoracocentesis is the initial therapy of choice.
    - Complete drainage is not necessary to relieve/improve clinical signs and may be hazardous if fibrosing pleuritis is present, limiting the degree of lung expansion.

CHRONIC TREATMENT

- Specific treatment of the underlying disease, when identified, may be enough to resolve chylothorax.
- Intermittent thoracocentesis during the treatment period may be needed as respiratory signs dictate.
    - If regular thoracocentesis is performed, monitor electrolytes; hyponatremia (secondary to loss in pleural fluid) and hyperkalemia (secondary to reduced renal excretion) can develop.
- If fluid accumulation is rapid, thoracostomy tubes may be required.
- If the underlying disease cannot be determined, medical therapy may be attempted initially.
    - A low-fat diet, either commercial or homemade, helps reduce the flow of chyle.
    - Rutin (50 mg/kg PO q 8 h) has been used for treating lymphedema in humans and has been used in canine and feline chylothorax with some apparent success and no documented adverse effects.
- If medical therapy is unsuccessful, surgical intervention is indicated.
    - Some clinicians advocate surgical intervention as the initial treatment of choice to reduce the risk of fibrosing pleuritis.
    - The optimal timing for surgery in chylothorax is controversial and remains undetermined. Delaying surgery increases

the risk of development of fibrosing/restrictive pleuritis.
    - The most common procedure is ligation of the thoracic duct and its branches, often in combination with lymphangiography.
        - Thoracic duct rupture is rarely detected by lymphangiography.
        - Ligation is accomplished via an intercostal or transdiaphragmatic approach.
        - Lymphangiography is often repeated after ligation to ensure all branches have been ligated.
        - Success rates reported for cats vary from 20%-53% (complete resolution).
        - For dogs, resolution rate is reported at 53%.
        - En bloc ligation of the thoracic duct without lymphangiography has been described in dogs, with similar success rates (50%).
    - After ligation, abdominal lymphaticovenous anastomoses form to transport chyle to the venous system, bypassing the thoracic duct.
    - Thoracoscopic thoracic duct ligation combined with mesenteric lymphangiography has been described.
- A number of other techniques have been suggested in combination with thoracic duct ligation.
    - Pleurodesis promotes development of diffuse adhesions between the parietal and visceral pleura but is not recommended.
    - Passive pleuroperitoneal drainage techniques have been described, but success rates are low, owing to drain obstruction.
    - Active pleuroperitoneal or pleurovenous drainage techniques have been used, but disadvantages include cost, thrombosis, catheter obstruction, air embolism, venous occlusion, sepsis, abdominal distension (if pleuroperitoneal), and potential lack of owner compliance.
    - Omentalization of the pleural space exploits the large surface area and lymph-draining capability of the omentum.
    - Thoracic duct ligation with pericardectomy has been recently reported.
        - A thickened pericardium may increase right-sided venous pressures, impeding drainage of chyle after thoracic duct ligation.
        - Reported success rates approach 100% for dogs and 80% for cats.

POSSIBLE COMPLICATIONS

- Incomplete resolution of chylothorax can occur with any treatment technique.
- Surgical and anesthetic risks for invasive procedures
- Fibrosing pleuritis, pleural thickening by fibrous tissue that restricts normal lung expansion, is a consequence of chronic chylothorax.

RECOMMENDED MONITORING

- Clinical signs
- Thoracic radiographs to assess pleural fluid accumulation/resolution
- Postoperative patients should also be monitored for reaccumulation of fluid.

PROGNOSIS AND OUTCOME

- Some patients will have resolution of chylothorax if the underlying disease can be corrected.
- For patients with idiopathic chylothorax or thoracic lymphangiectasia, the described approach of combining pericardectomy with thoracic duct ligation appears to show the best results.
- If the underlying disease cannot be managed successfully, the prognosis is poorer.

PEARLS & CONSIDERATIONS

COMMENTS

- Cats with pleural effusion can be clinically fragile and must be handled carefully if dyspneic (e.g., during restraint).
- Long-standing chylous pleural effusion can lead to fibrotic pleural disease, an irreversible cause of respiratory impairment.

PREVENTION

There is no reliable means of preventing the development of chylothorax.

TECHNICIAN TIPS

- Animals with large-volume pleural effusions can be very fragile and susceptible to stress with handling. Therefore minimal handling is important.
- Supplemental oxygen can be very helpful in a dyspneic patient with pleural effusion.
- Avoid dorsal recumbency for radiographs in animals with pleural effusions.
- The basics for an emergency thoracocentesis include clippers, skin preparation materials, a butterfly needle or needle with an extension set, three-way stopcock, and syringes.
- The complications of thoracocentesis include pneumothorax and hemothorax. If the patient suddenly develops a high respiratory rate or effort after pleural drainage, alert your clinician as soon as possible.

CLIENT EDUCATION

Chylothorax can be a frustrating disease and requires diagnostic assessment to identify treatable underlying causes.

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Chronic Kidney Disease, Overt (“Symptomatic”)

BASIC INFORMATION

DEFINITION

- Chronic kidney disease (CKD): kidney damage present for over 3 months. Azotemia and/or inadequately concentrated urine (specific gravity <1.035 in cats; <1.030 in dogs) is not necessary for CKD to be present.
- IRIS Staging System for CKD: classification scheme for CKD in dogs and cats is based on serum creatinine, with substages for proteinuria and blood pressure. Developed by International Renal Interest Society:
  - Stage I: creatinine <1.4 mg/dL, dogs; <1.6 mg/dL, cats. Nonazotemic. Some other renal abnormality present (e.g., inadequate concentrating ability without identifiable nonrenal cause; abnormal renal palpation and/or abnormal renal imaging findings; proteinuria of renal origin; abnormal renal biopsy results).
  - Stage II: creatinine 1.4-2 mg/dL, dogs; 1.6-2.8 mg/dL, cats. Mild renal azotemia (lower end of the range lies within the reference range for many labs, but the insensitivity of creatinine as a screening test means that animals with creatinine values close to the upper reference range often have excretory failure). Clinical signs usually mild or absent.
  - Stage III: creatinine 2.1-5 mg/dL, dogs; 2.9-5 mg/dL, cats. Moderate renal azotemia. Systemic clinical signs may be present.
  - Stage IV: creatinine >5 mg/dL dogs and cats. Severe renal azotemia. Many extrarenal clinical signs present.
- Overt CKD: CKD that is responsible for clinical signs in a patient. This generally corresponds to IRIS stage III or IV.
- Azotemia: elevated blood urea nitrogen and/or creatinine. Uremia is the constellation of clinical signs associated with renal failure (i.e., not all azotemic animals are uremic).
- CKD is one of the most common diseases of older cats and is very common in dogs.
- For information on incidentally discovered CKD (not producing overt signs), see p. 205.

SYNONYMS

Clinical CKD; decompensated CKD; symptomatic CKD; CKD: chronic interstitial nephritis, tubulointerstitial nephritis, nephrosclerosis, kidney failure; chronic renal failure (CRF; no longer a preferred term)

EPIDEMIOLOGY

SPECIES, AGE, SEX

- More common in cats than in dogs
- Common in older animals but can occur in animals of any age

GENETICS & BREED PREDISPOSITION

- Increased frequency in Maine coon, Abyssinian, Siamese, Russian blue, and Burmese cats
- Familial nephropathies may lead to early-onset CKD. Familial nephropathies reported in Abyssinian cats, Persian cats, basenjis, beagles, Bedlington terriers, Bernese mountain dogs, boxer dogs, bull terriers, Cairn terriers, chow chows, cocker spaniels, Doberman pinschers, golden retrievers, keeshonds, Lhasa apsos, Newfoundlands, Norwegian elkhounds, Pembroke Welsh corgis, rottweilers, Samoyeds, shar-peis, shih tzus, soft-coated Wheaten terriers, standard poodles

RISK FACTORS

Advanced age, prior episode of acute renal failure, prior nephrotoxic exposure, pyelonephritis, nephrolith/ureterolith, glomerulonephritis, amyloidosis

ASSOCIATED CONDITIONS & DISORDERS

Anemia, dehydration, urinary tract infection, renal secondary hyperparathyroidism, systemic hypertension, hypokalemia, metabolic acidosis, ulcers (gastric or oral), vomiting, weight loss

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Incidentally diagnosed in apparently healthy animals (see p. 205)
- Overtly ill (“symptomatic”) but stable patients (managed as outpatients)
- Decompensated patients (require hospitalization until stabilized)

HISTORY, CHIEF COMPLAINT

(Some or all may be present.)

- Polyuria/polydipsia is common.
- Anorexia +/−
- Weight loss +/−
- Vomiting occurs in decompensated (uremic) animals.
- Lethargy +/−
- Halitosis +/−
- Altered consciousness (general dullness) often found in decompensated (uremic) animals
- Seizures (rarely seen in end-stage uremia)
- Bleeding problems (rarely spontaneous bleeding; increased risk of bleeding with invasive procedures)

PHYSICAL EXAM FINDINGS

(Some or all may be present.)

- Dehydration +/−
- Frequently: small, irregular kidneys; rarely large kidneys; in cats, renal asymmetry common with former obstructive nephropathy or chronic ascending pyelonephritis
- Signs of renal pain unusual
- Uremic halitosis +/−
- Oral ulceration with severe azotemia
- Poor haircoat +/−
- Poor body condition +/− mild pallor if anemic

ETIOLOGY AND PATHOPHYSIOLOGY

- CKD can be the end result of a variety of insults to the kidney, which may start as tubular, glomerular, or interstitial.
- Even if an inciting cause can be cured, after a certain amount of damage has been sustained, renal failure may be progressive (generally when creatinine >3.5 mg/dL).
- The specific etiology of CKD is frequently undetermined:
    - Tubulointerstitial nephritis most common cause (70% of cats, 60% of dogs)
    - Glomerulonephritis also a common cause (30% of dogs, 15% of cats)
    - Other demonstrable causes: amyloidosis, renal dysplasia, polycystic kidney disease, tubulonephrosis, lymphoma, chronic pyelonephritis, nephroliths or ureteroliths resulting in partial obstruction, vasculitis, infarction, and sequelae to acute renal failure with incomplete resolution
    - Obstructive nephropathy from ureterolithiasis is increasingly recognized in cats.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

CKD may be diagnosed based on structural (e.g., renal size/shape changes, polycystic disease) or functional (e.g., proteinuria, azotemia, inadequately concentrated urine) abnormalities. Azotemia is usually present in symptomatic patients.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis of azotemia:

- Prerenal azotemia (dehydration, hypoadrenocorticism, gastrointestinal bleeding)
    - Urine specific gravity is usually > 1.030 (dogs) or > 1.035 (cats)
- Renal azotemia (acute renal failure, chronic kidney disease)
- Postrenal azotemia (urinary tract obstruction, rupture)
    - Dysuria and/or additional clinical pathologic abnormalities (e.g., hyperkalemia)

INITIAL DATABASE

- Assess hydration: azotemia may be caused or worsened by dehydration.
- Serum biochemical profile: azotemia, variable hyperphosphatemia, hypokalemia, hypercalcemia or hypocalcemia, metabolic acidosis are all common in overt CKD.
- CBC: anemia due to lack of erythropoietin (EPO), gastrointestinal (GI) bleeding, anemia of chronic disease common. EPO deficiency results in nonregenerative anemia with normal to increased total protein, whereas GI blood loss results in low total protein.
- Urinalysis: isosthenuric urine specific gravity typical. Active sediment may suggest urinary tract infection (UTI).
- Urine culture: incidental, clinically silent UTI may occur with CKD; pyelonephritis may be the cause of CKD.
- Thyroid level (elderly cats): rule out hyperthyroidism as concurrent disorder.
    - Correction of hyperthyroidism can worsen renal function in cats with CKD.
    - In cats that have both hyperthyroidism and CKD concurrently, treatment emphasis is placed on the disease most responsible for clinical signs.
- Blood pressure (BP): hypertension (systolic BP >160-180 mm Hg, diastolic BP >95 mm Hg) present in 20% of cats with CKD; may cause end-organ damage (especially heart, eyes, central nervous system, kidneys)
- Abdominal imaging: abdominal radiography or ultrasonography may further elucidate cause of CKD (i.e., obstructing or partially obstructing nephroliths or ureteroliths, renal neoplasia, cystic disease, perinephric pseudocysts). Alterations of shape, size, and echogenicity of kidneys are common.

ADVANCED OR CONFIRMATORY TESTING

- Urine protein/creatinine ratio. In dogs and cats with CKD, pathologic proteinuria (urine protein/creatinine [UPC] ratio >0.5 in dogs, >0.4 in cats; urinary sediment is inactive, and culture is negative) may indicate potential benefit from angiotensin-converting enzyme inhibition.
- Glomerular filtration rate (GFR) measurement: rarely measured when azotemia is present.
- Renal biopsy: indicated primarily with renomegaly (rule out lymphoma, feline infectious peritonitis, amyloidosis)

TREATMENT

TREATMENT OVERVIEW

The goals of treatment are to alleviate uremic signs and delay progression of kidney disease.

ACUTE GENERAL TREATMENT

- Compensated state: see Chronic Treatment below.
- Decompensated state (e.g., dehydrated, anorexic, vomiting):
    - Hospitalization is ideal, since oral therapies often are poorly tolerated
    - Rehydration over 24-36 hours usually appropriate
        - Intravenous crystalloid fluid therapy (e.g., lactated Ringer's solution, Plasmalyte, 0.9% saline).
        - Fluid rate: maintenance (66 mL/kg/d) plus replacement of dehydration (percent dehydration [as a decimal, e.g., 10% = 0.1] × kg body weight = liters deficit) plus ongoing losses (estimated volume of polyuria, vomiting).
    - Maintenance:
        - Maintenance rate plus 5%-6% body weight per 24 hours to promote diuresis
        - Practically, twice the calculated maintenance rate is sufficient for most after rehydration.
        - Potassium supplementation of fluids based on electrolyte measurement (not to exceed 0.5 mEq/kg/h; see p. 577).
    - Other treatments described for chronic therapy may be applicable (e.g., H2 blockers, antiemetics; see Chronic Treatment below), but injectable forms are used until oral medications are tolerated.

CHRONIC TREATMENT

- Delay of progression: see p. 205
- Additional therapies may be used, depending on presence of particular uremic signs.
    - Anorexia or vomiting: decrease gastric acidity. Histamine blockers (famotidine, 0.5 mg/kg IV, SQ, PO q 24 h; ranitidine, 0.5-2.5 mg/kg SQ, PO q 24 h [avoid rapid IV administration, which may cause nausea] q 12-24 h); or proton pump inhibitors (e.g., omeprazole, 0.7 mg/kg PO q 24 h).
    - Persistent vomiting: antiemetics (maropitant, 2 mg/kg PO q 24 h for 5 days approved for dogs only [often used off label for cats]; or metoclopramide, 0.2-0.4 mg/kg SQ q 6 h or 0.01-0.02 mg/kg/h as constant rate infusion; phenothiazines). 5HT serotonin antagonists for intractable vomiting (ondansetron, 0.22 mg/kg IV q 8-12 h, or dolasetron). GI ulceration (e.g., hematemesis, melena, anemia, elevated blood urea nitrogen/creatinine ratio): sucralfate, 0.25-1 g PO q 8 h until signs resolve.
    - Hyperphosphatemia: diet ± medications.

        - Phosphate binders to prevent absorption of phosphorus from ingested food
            - Aluminum hydroxide or aluminum carbonate, 30-90 mg/kg/d, divided and administered with meals; dose titrated based on serum phosphorus concentration).
            - Calcium acetate, 60-90 mg/kg/d; hypercalcemia possible side effect
            - Chitosan (Epakitin) 1 gram/5 kg twice daily with food
            - Lanthanum carbonate is a newer phosphate binder that is occasionally used in veterinary medicine (100 mg/kg/d PO).
    - Hypokalemia (more likely in cats than dogs): potassium gluconate (2 mEq per 4.5 kg per day) or potassium citrate (75 mg/kg PO q 12 h).
    - Acidosis (more likely in cats than dogs): consider treatment if total CO2 < 16 mEq/L or pH < 7.2. Potassium citrate, 75 mg/kg PO q 12 h (also addresses hypokalemia), sodium bicarbonate, 10 mg/kg PO q 12 h.
    - Anemia: transfusion based on clinical need. Darbepoetin (Aranesp 0.45-1 mcg/kg SQ q 7 days until hematocrit rises; then q 14-21 days to maintain low-normal hematocrit) plus iron supplementation can be used for stimulating red blood cell production. Risk of pure red cell aplasia from cross-reactive antibodies appears lower with darbepoetin, compared to human recombinant erythropoietin (Epogen, Procrit).
    - Hypertension: calcium channel blockers recommended. If proteinuria is present or calcium channel blocker is insufficient, add ACE inhibitor (see p. 1068).
    - Chronic dehydration or persistent signs of uremia: subcutaneous fluid administration. Dose is empirical, based on subjective assessment of the patient's well-being, hydration status, and presence of other disorders (e.g., heart disease). Typically for cats without heart problems, 100 to 150 mL daily to every other day.
    - Renal secondary hyperparathyroidism (see p. 976)
- Renal transplantation may be appropriate for some animals/owners. Maybe preceded by hemodialysis (see p.1286). Greatest chance of success in mildly to moderately azotemic cats without concurrent illness or infection.

NUTRITION/DIET

- Appropriate high-quality restricted protein and restricted phosphorus diets (“renal diet”) slow progression and decrease clinical uremia.
    - Acceptance of diet changes can be problematic, particularly in severely affected patients.
    - Maintaining adequate caloric intake to avoid weight loss takes precedence over nutrient composition of the diet (see p. 1377).
    - Renal diets should be introduced when uremia (illness) is minimized.
    - Nutritional support occasionally requires appetite stimulation (cats: cyproheptadine, 1 to 2 mg PO q 12 h; mirtazapine, 3.75 mg PO q 72-96 h) or tube feeding.

DRUG INTERACTIONS

- Phosphate binders can interfere with absorption of orally administered medications, especially antibiotics.
- Sucralfate works best in an acid environment and should be given at least 30 minutes before antacid therapy.
- Nephrotoxic drugs (e.g., aminoglycosides) or drug combinations (e.g., NSAIDs plus ACE inhibitors) should be avoided whenever possible.
- Drugs which undergo renal elimination may need adjustment in dose strength or frequency in animals with CKD.

POSSIBLE COMPLICATIONS

- Anorexia, vomiting, GI ulceration, hyperphosphatemia, hypokalemia, acidosis, anemia, and hypertension are common sequelae of CKD.
- Volume overload (pleural effusion, pulmonary edema, dyspnea, or peripheral fluid accumulation) is a concern at high rates of fluid administration, particularly in anemic animals or those with concurrent heart disease.
- Platelet dysfunction in CKD increases risks of bleeding (gingival, GI, bruising, bleeding after invasive procedures).

RECOMMENDED MONITORING

- Routine recheck, including physical exam, weight, chemistry panel, CBC, or packed cell volume. Frequency depends on disease severity.
    - Stage I-II: recheck every 6 months.
    - Stage III: recheck every 2-3 months.
    - Stage IV: recheck monthly.
- Urinalysis and urine culture should be performed at least twice a year.
- Blood pressure measurement should be performed at least every 3 months, or 1-week after antihypertensive drug dose adjustments.
- Changes in clinical signs warrant recheck as well.

PROGNOSIS AND OUTCOME

- Longevity is difficult to predict in an individual patient, with a range of days to years.
- Median survival times are 2 years in cats with stage III CKD and 1 month in cats with stage IV CKD.

PEARLS & CONSIDERATIONS

COMMENTS

- At an early stage of decompensation, renal transplant can be considered for otherwise healthy cats.
- Renal biopsy is rarely informative in cats with chronic kidney disease and small kidneys (the inciting cause is rarely identified).
- Urine culture and sensitivity in patients with CKD is essential at the time of diagnosis and periodically thereafter.
    - UTIs commonly occur without an active urine sediment on urinalysis in CKD patients.
    - Correction of the UTI may improve renal function if subclinical pyelonephritis is present; few other complicating factors can be treated so easily and effectively.

TECHNICIAN TIPS

Technicians can be invaluable in teaching owners how to administer subcutaneous fluids. They can also help emphasize the importance of allowing the animal a constant source of fresh water.

CLIENT EDUCATION

- CKD is in incurable condition in which treatments are aimed primarily at improving the quality of life.
- Renal transplantation is expensive and limited in availability. With successful renal transplant, intensive lifelong medication and frequent rechecks are required, but quality of life can be excellent.

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Chronic Kidney Disease, Occult (“Asymptomatic”)

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

- Chronic kidney disease (CKD): kidney damage present for over 3 months. Azotemia and/or inadequately concentrated urine (specific gravity < 1.035 in cats; < 1.030 in dogs) is not necessary for CKD to be present.
- IRIS Staging System for CKD: classification scheme for CKD in dogs and cats is based on serum creatinine, with substages for proteinuria and blood pressure. Developed by International Renal Interest Society:
  - Stage I: creatinine < 1.4 mg/dL, dogs; < 1.6 mg/dL, cats. Nonazotemic. Some other renal abnormality present (e.g., inadequate concentrating ability without identifiable nonrenal cause; abnormal renal palpation and/or abnormal renal imaging findings; proteinuria of renal origin; abnormal renal biopsy results).
  - Stage II: creatinine 1.4-2 mg/dL, dogs; 1.6-2.8 mg/dL, cats. Mild renal azotemia (lower end of the range lies within the reference range for many labs, but the insensitivity of creatinine as a screening test means that animals with creatinine values close to the upper end of the reference range often have excretory failure). Clinical signs usually absent.
  - Stage III: creatinine 2.1-5 mg/dL, dogs; 2.9-5 mg/dL, cats. Moderate renal azotemia. Systemic clinical signs usually present.
  - Stage IV: creatinine > 5 mg/dL dogs and cats. Severe renal azotemia. Many extrarenal clinical signs present.
- Occult CKD: CKD in which no clinical signs are present. This generally corresponds to IRIS stage I or II.
- CKD is one of the most common diseases of older cats and is very common in dogs
- For information on CKD causing overt clinical signs, see p. 207.

SYNONYMS

Latent CKD, preclinical CKD, asymptomatic CKD, compensated CKD, incidentally discovered CKD, stage I or II CKD, chronic renal failure (CRF; this term is no longer preferred for use)

EPIDEMIOLOGY

SPECIES, AGE, SEX

- More common in cats than dogs
- Any age, but more common in older animals

GENETICS & BREED PREDISPOSITION

Familial nephropathies are reported in a number of dog and cat breeds (see p. 207). These nephropathies may lead to an early onset of renal failure.

RISK FACTORS

Advanced age, prior episode of acute renal failure, prior nephrotoxic exposure, pyelonephritis, nephrolith/ureterolith.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

Incidental CKD is usually detected via routine geriatric or preanesthetic screening, or during investigation of unrelated illness.

PHYSICAL EXAM FINDINGS

Frequently no abnormal physical exam findings. The patient may have small or irregular kidneys.

ETIOLOGY AND PATHOPHYSIOLOGY

- CKD can be the end result of a variety of insults to the kidney, which may start as tubular, glomerular, or interstitial, because each nephron works as a unit. If the glomerulus is irreversibly damaged, the associated tubule will degenerate, and vice

versa.
- As nephrons are lost, the remaining nephrons hypertrophy. Although initially adaptive, glomerular hypertension damages the nephron, leading to further nephron loss. After a certain amount of damage has been sustained (generally when creatinine > 3.5 mg/dL), kidney disease may be progressive despite resolution of initiating cause.
- The specific etiology of CKD is frequently undetermined:
  - Tubulointerstitial nephritis most common cause (70% of cats, 60% of dogs)
  - Glomerulonephritis also a common cause (30% of dogs, 15% of cats)
  - Other demonstrable causes: amyloidosis, renal dysplasia, polycystic kidney disease, tubulonephrosis, lymphoma, chronic pyelonephritis, nephroliths or ureteroliths resulting in partial obstruction, vasculitis, infarction, and sequelae to acute renal failure with incomplete resolution
  - Obstructive nephropathy from previous or current ureterolithiasis is increasingly recognized in cats.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

CKD may be diagnosed based on structural (e.g., renal size/shape changes, polycystic disease) or functional (e.g., proteinuria, azotemia, inadequately concentrated urine) abnormalities.

DIFFERENTIAL DIAGNOSIS

Azotemia:

- Prerenal azotemia (e.g., dehydration, high-protein diet, gastrointestinal bleeding), typically characterized by concentrated urine specific gravity
- Azotemia with inadequately concentrated urine may be due either to kidney disease or to dehydration (i.e., prerenal azotemia) combined with extrarenal impairment of urine concentration:
  - Drug therapy (e.g., diuretics, glucocorticoids)
  - Osmotic diuresis (e.g., diabetes mellitus)
  - Impaired medullary concentration gradient (e.g., hypoadrenocorticism, portosystemic shunting)
  - Central diabetes insipidus
  - Nephrogenic diabetes insipidus (e.g., hypercalcemia, pyometra, pyelonephritis)
- Postrenal azotemia (urinary obstruction, rupture) is generally easily differentiated from kidney disease by dysuria.

INITIAL DATABASE

- CBC: usually unremarkable; occasionally mild anemia
- Serum biochemistry profile: azotemia may or may not be present; sometimes hyperphosphatemia, hypokalemia.
- Urinalysis: frequently isosthenuric or minimally concentrated specific gravity (dogs <1.030; cats < 1.035). Active sediment may indicate urinary tract infection. Proteinuria can be quantified by urine protein/creatinine ratio
- Urine culture is indicated to rule out infection
- Abdominal radiographs or ultrasound: kidneys may be small and irregular or show other structural changes.
- Blood pressure: hypertension present in 20% of cats with stage I-II CKD and up to 75% of dogs with protein-losing nephropathy.

ADVANCED OR CONFIRMATORY TESTING

- Glomerular filtration rate (GFR) measurement: can confirm inadequate GFR, particularly when azotemia is mild and cause of impaired urine concentration unclear. Iohexol clearance, creatinine clearance, and nuclear scintigraphy are most commonly used.
- Urine protein/creatinine ratio; if increased when urine sediment exam is inactive, suggests glomerular disease
- CKD in cats may complicate the diagnosis of concurrent hyperthyroidism by suppressing total thyroxine. Combined measurement of free thyroxine with total thyroxine or thyroid-stimulating hormone are indicated to increase sensitivity of diagnosis for hyperthyroidism.

TREATMENT

TREATMENT OVERVIEW

The treatment goal is to slow progression of kidney disease.

ACUTE GENERAL TREATMENT

As patients are asymptomatic, acute treatment is not needed.

CHRONIC TREATMENT

- For dogs and cats with protein-losing nephropathy, angiotensin-converting enzyme inhibition (ACEi) may slow progression of renal failure (enalapril or benazepril, 0.25-0.5 mg/kg PO q 12-24 h).
- ACEi is not proven to slow progression of kidney disease in cats with UPC <0.4. It may play a beneficial role when proteinuria is present.
- As kidney disease progresses, animals may decompensate (show overt signs caused by CKD). See p. 207 for specific therapeutic recommendations.

NUTRITION/DIET

Restricted-quantity (but high-quality) protein and restricted-phosphorus diet (“renal diet”) slows progression in dogs with CKD:

- Although cats are obligate carnivores, and diet recommendations cannot be generalized, renal diets are recommended.
- There are many different brands of renal diet, and palatability varies with the individual patient.
- Homemade renal diets may also be used but should be formulated carefully.
- It is important to maintain adequate caloric intake.

DRUG INTERACTIONS

- Avoid nephrotoxic drugs (e.g., aminoglycosides) or drug combinations (e.g., nonsteroidal antiinflammatory drugs with ACEi).
- Dosage adjustment of most drugs is unnecessary.

RECOMMENDED MONITORING

- Stable patients with incidental CKD should be monitored every 6 months.
- Recheck should include body weight, CBC (or minimally packed cell volume), biochemical profile with electrolytes, and blood pressure measurement.
- Clinical signs of hypokalemia, hyperphosphatemia, anemia, and hypertension may not occur until devastating; early interventions can be based on detection by routine screening.
- Urinalysis and urine culture twice a year, owing to increased risk of clinically silent urinary tract infection.

PROGNOSIS AND OUTCOME

- Some animals with incidental CKD may remain stable and free of clinical signs for years, while others progress more rapidly.
- The rate of progression to overt CKD is unpredictable.
- Median survival time of cats with stage II CKD is 3 years (range: 1 month to 8 years)

PEARLS & CONSIDERATIONS

COMMENTS

Occult CKD may progress very slowly or more rapidly; the course of progression cannot be predicted. Advanced age, plasma creatinine, and proteinuria are generally associated with more rapid progression. If potentially nephrotoxic drugs are used (e.g., ACE inhibitors), ensure adequate hydration and monitor carefully for deterioration in renal function.

TECHNICIAN TIP

It is often best to find a renal diet palatable to the pet when renal disease is inapparent or mild, rather than waiting until the animal is overtly sick as a result of renal disease. The technician can help clients identify and try various renal diets.

CLIENT EDUCATION

Animals should be promptly presented for care for signs of clinical illness. Progression of renal failure may lead to decompensation, and patients with CKD are less able to cope with extrarenal illness. Vomiting from any cause may lead to dehydration, which may worsen renal function, leading to exacerbation of vomiting, anorexia, and dehydration. Prompt fluid therapy (either IV or SQ,

depending on severity and underlying illness) may be needed to stop the cycle.

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Chondrosarcoma

BASIC INFORMATION

DEFINITION

Chondrosarcoma (CSA) is a malignant mesenchymal tumor that produces chon-droid and fibrillar matrix, but never osteoid.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- In dogs, CSA is the second most common primary bone tumor, accounting for 5%-10% of all primary bone tumors:
  - Median age is around 8 years, but CSA has been reported at ages ranging from 1 to 15 years.
  - There is no gender predilection.
- In cats, primary bone tumors are uncommon, and CSA is third in incidence behind osteosarcoma and fibro-sarcoma. CSA also can occur in the soft tissues at sites of previous vaccinations (see p. 610).

GENETICS & BREED PREDISPOSITION

- CSA is most common in medium- to large-breed dogs weighing between 20 and 40 kg.
- Mixed-breed dogs, golden retrievers, boxers, and German shepherd dogs are overrepresented.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- The majority of CSAs arise from flat bones. Approximately 30% occur in the nasal cavity, accounting for 15% of all nasal tumors; 20% of CSAs arise from the ribs, accounting for 30%-40% of all primary rib tumors.
- A total of 20% of CSAs arise from the appendicular skeleton, often but not always at sites where osteosarcoma typically occurs. CSA accounts for only 3%-5% of all primary bone tumors in the appendicular skeleton.
- Other reported sites include facial bones, skull, vertebrae, pelvis, digits, and os penis.
- Rarely, CSA can arise in soft tissue (extraskeletal) sites.

HISTORY, CHIEF COMPLAINT

- Patients often present with a visible mass at the affected site. Additional clinical signs vary with the site of skeletal involvement.
- Nasal CSA usually is associated with unilateral or bilateral epistaxis. Other clinical signs include sneezing, dyspnea, and swelling over the nasal cavity.
- Appendicular CSA usually is associated with lameness.

PHYSICAL EXAM FINDINGS

- Findings for CSA will depend on the anatomic location. Often, but not always, a firm to hard mass will be palpable.
- Patients with nasal CSA often have reduced airflow through the nares, and hemorrhagic discharge may be present. More advanced tumors may be associated with a visible mass effect (externally or orally). The ipsilateral eye may not retropulse or may be exophthalmic.
- Rib CSA most commonly arises near the costochondral junction. Any rib may be affected.
- Patients with appendicular and digitalCSA are variably lame, ranging from minimal to non–weight-bearing.

ETIOLOGY AND PATHOPHYSIOLOGY

Etiology is largely unknown. Osteochondromatosis (multiple cartilaginous exostoses) lesions can undergo malignant transformation into CSA or, less commonly, osteosarcoma.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

CSA is not the most common primary bone tumor, but it still should be considered as a differential whenever an aggressive bone lesion is identified and especially when the lesion involves the rib or nasal cavity. Histopathology is required to confirm the diagnosis.

DIFFERENTIAL DIAGNOSIS

- General differential diagnoses for aggressive bone lesions:
  - Other primary bone tumors (osteosarcoma, fibrosarcoma, hemangiosarcoma)
  - Metastatic bone tumors (transitional cell, prostatic, mammary, thyroid, anal sac apocrine gland carcinomas)
  - Tumors that locally invade adjacent bone (nasal carcinoma; oral squamous cell carcinoma, melanoma, fibrosarcoma, ameloblastoma; synovial cell sarcoma; histiocytic sarcoma; digital squamous cell carcinoma, melanoma)
  - Hematopoietic tumors (myeloma, lymphoma). Radiographic lesions typically are purely lytic.
  - Bacterial or fungal osteomyelitis
- Additional differentials for epistaxis:
  - Thrombocytopenia or coagulopathy
  - Fungal rhinitis (usually *Aspergillus*)
  - Systemic hypertension
  - Foreign body

INITIAL DATABASE

- Radiographic imaging of the primary tumor:
  - The aggressive bone changes associated with CSA are the same as those seen with osteosarcoma (see p. 801).
  - Nasal neoplasia is most often associated with soft-tissue opacity in the nasal cavity and/or frontal sinuses, as well as destruction of the turbinates, nasal septum, vomer, or surrounding palatine, maxillary, and/or frontal bones.
  - Primary rib tumors often can be distinguished from tumors originating from the lung by the presence of an extrapleural sign, characterized by a smoothly marginated indentation of the lung that tapers gradually at the junction of the thoracic wall.
- After a radiographic or histologic diagnosis, patients should be completely staged with a CBC, chemistry panel, urinalysis, and three-view thoracic radiographs.

ADVANCED OR CONFIRMATORY TESTING

- For axial tumors, CT imaging is recommended to more accurately stage local disease and help with planning surgery and/or radiation therapy. CT imaging can be done in place of radiographic studies.
  - For nasal tumors, CT is superior to radiographs for detecting soft-tissue opacity within the nasal cavity and surrounding sinuses, bony destruction, and extension through the cribriform plate into the brain.
  - If a patient is undergoing CT, concurrent imaging of the lungs is recommended as a more sensitive way to screen for pulmonary metastasis.
- Histopathologic evaluation is required to confirm the diagnosis of CSA.
  - For nasal tumors and large, nonresectable tumors, an incisional biopsy is recommended. For resectable tumors, an incisional biopsy is not contraindicated, but it is reasonable to surgically remove the local disease, with biopsy submission after surgery.

TREATMENT

TREATMENT OVERVIEW

Nasal CSA, like most other nasal tumors, is most effectively treated with radiation therapy. For CSAs arising in other locations, surgery is indicated whenever possible. Palliative therapy, which focuses on controlling pain and other clinical signs associated with the tumor, is recommended for advanced-stage tumors or when definitive therapy is declined.

ACUTE GENERAL TREATMENT

- Treatment of nasal CSA (see also Nasal Tumors):
  - Radiation therapy is the treatment of choice. Definitive treatment schemes typically use total doses of 48-57 Gy administered in 16-19 fractions of 3 Gy each.
  - Surgery is not an effective treatment modality for nasal tumors. It was used prior to the advent of orthovoltage radiation therapy, but it is no longer routinely recommended, because most radiation treatment facilities currently use megavoltage units (cobalt-60 or linear accelerator).
- The treatment of choice for rib CSA is wide surgical resection. Multiple ribs and/or underlying lung may need to be removed.

Prosthetic mesh may be needed to obtain thoracic wall closure, and diaphragmatic advancement techniques may be necessary for caudal thoracic tumors.
    - Adjuvant radiation therapy is recommended if excision is incomplete, but there is little information regarding efficacy.
- The treatment of choice for appendicular CSA is amputation. Limb salvage techniques may be considered for tumors arising from the distal radius or ulna.
- For CSA arising from other sites, wide surgical excision is recommended whenever possible. When excision is incomplete, adjuvant radiation therapy may help improve local control, but there is limited information regarding efficacy.
- There is no information regarding the efficacy of chemotherapy for the treatment of CSA in veterinary patients.
    - In humans with CSA, the use of adjuvant chemotherapy remains controversial, but there is preliminary evidence that chemotherapy might benefit patients with very aggressive variants (dedifferentiated and mesenchymal CSA). Protocols typically include doxorubicin with or without cisplatin, ifosfamide, and/or methotrexate.
- Palliative care is indicated for patients with advanced local disease or visible metastasis, and when owners decline definitive therapy.
    - Nonsteroidal antiinflammatory (NSAID) choices include: aspirin (10-25 mg/kg PO q 8-24 h), carprofen (2 mg/kg PO q 12 h), deracoxib (1-2 mg/kg PO q 24 h; may use 3-4 mg/kg PO q 24 h for first 7 days only), meloxicam (0.1 mg/kg PO q 24 h), firocoxib (5 mg/kg PO q 24 h).
    - Other oral analgesic drugs include acetaminophen with codeine (Tylenol #4 [300 mg acetaminophen, 60 mg codeine]) 0.5-2 mg/kg PO q 6-8 h, with dosing based on codeine, tramadol (2-5 mg/kg PO q 6-12 h), gabapentin (10-15 mg/kg PO q 8-12 h).
    - Pamidronate decreases bone resorption, increases bone mineral density, and can reduce the pain associated with bone tumors. It has been studied most thoroughly for the treatment of osteosarcoma (see p. 801).
    - Palliative radiation therapy very effectively controls the pain associated with bony tumors. Most information regarding efficacy is from the treatment of osteosarcoma, but similar benefits are seen in patients with chondrosarcoma.
    - Patients with pulmonary metastasis or nasal congestion often benefit from antiinflammatory doses of oral corticosteroids such as prednisone, 0.5-1 mg/kg PO q 24 h (do not combine corticosteroids with NSAIDs).

RECOMMENDED MONITORING

Patients should be evaluated every 2-3 months for evidence of local recurrence and metastatic disease. At a minimum, this includes a thorough physical examination and three-view thoracic radiographs. Imaging of the site of the primary tumor may be indicated as well, depending on location, completeness of excision, and clinical signs.

PROGNOSIS AND OUTCOME

- Prognosis for dogs with nasal CSA:
    - Distant metastasis is uncommon.
    - With definitive radiation therapy (megavoltage), 1-year progression-free survival rate is around 50%, and 2-year progression-free survival rate is around 30%.
        - Patients with nasal CSA are three times less likely to have local recurrence than patients with nasal adenocarcinoma.
        - For patients with nasal tumors in general, extension into the frontal sinuses and/or erosion through the bones of the nasal passage is associated with a threefold increase in risk of local recurrence. Unilateral versus bilateral involvement is not a significant prognostic factor.
    - With palliative care alone, survival times are around 3 months.
- For dogs with nonnasal CSA:
    - Some 15%-30% will develop metastatic disease, with the lungs being the most commonly affected site.
    - With aggressive surgery, median survival is >3 years, and many dogs will enjoy long-term local control. However, depending on tumor location and completeness of excision, up to 40% will develop local recurrence.
    - With palliative care alone, survival times of > 1 year are still possible.

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Cholecystitis

BASIC INFORMATION

DEFINITION

Inflammation of the gallbladder wall; can be acute, chronic, necrotizing and/or emphysematous

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Necrotizing and emphysematous cholecystitis occur infrequently in dogs and are extremely rare in cats.
- Acute cholecystitis may occur in cats secondary to bacterial cholangitis/cholangiohepatitis.
- Mean age: 9.5 years
- Male dogs are at increased risk.

GENETICS & BREED PREDISPOSITION

Older, female, small-breed dogs appear to be at increased risk for cholelithiasis. Shetland sheepdogs appear to be predisposed.

RISK FACTORS: Age (increased risk with age), history of previous cholecystitis, and concurrent systemic disease are associated with increased risk of cholecystitis.

ASSOCIATED CONDITIONS & DISORDERS

- Cholangitis (inflammation of the bile ducts), choledochitis (inflammation of the common bile duct), and cholangiohepatitis (inflammation of the biliary tree and periportal hepatic parenchyma)
- Cholelithiasis, gallbladder rupture/perforation, and subsequent bile peritonitis (septic or sterile) can be sequelae to cholecystitis.
- Can occur as the result of gallbladder mucocele
- Diabetes mellitus and cystic duct obstruction: emphysematous cholecystitis (weak association)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Chronic and emphysematous forms may be incidental findings noted on abdominal ultrasound or abdominal radiographs (emphysematous—gas within gallbladder).
- Acute and necrotizing forms generally result in systemic illness.

HISTORY, CHIEF COMPLAINT

- Presenting complaints are generally vague. May include vomiting, diarrhea, depression, lethargy, weight loss, abdominal pain.
- Profound weakness or collapse can occur with gallbladder perforation and peritonitis.

PHYSICAL EXAM FINDINGS

- Nonspecific findings may include tachycardia, tachypnea, fever, dehydration, and cranial abdominal pain.
- Icterus often is present when there is concurrent extrahepatic biliary obstruction.

ETIOLOGY AND PATHOPHYSIOLOGY

- Necrotizing cholecystitis (type I):
  - Secondary to infection with subsequent loss of viability of the gallbladder wall
  - Gallbladder perforation does not occur despite wall necrosis.
- Acute (type II) and chronic (type III) cholecystitis:
  - Etiology is poorly defined.

- Bacterial infection (ascending from the common bile duct or via hematogenous spread) suspected
- Type II cholecystitis results in gallbladder perforation and peritonitis.
- Type III cholecystitis results in cholecystic adhesions (omental and hepatic adhesions) and/or fistulation.

- Emphysematous cholecystitis:
  - Invasion of the wall with gas-forming bacteria
  - Tympanic cholecystitis is the result of gas distension of the lumen of the gallbladder by gas-forming bacteria.
  - Severe tympanic cholecystitis can be associated with emphysematous cholecystitis (gas dissection into the gallbladder wall).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Cholecystitis should be a differential for any patient with cranial abdominal pain and elevated serum hepatic enzyme activities or total bilirubin concentration. Cholecystitis should be the primary differential in a patient with bile peritonitis without a history of trauma. A definitive diagnosis is based on surgical findings and histopathologic analysis.

DIFFERENTIAL DIAGNOSIS

- Other hepatobiliary disease
- Pancreatitis
- Proximal small bowel disease

INITIAL DATABASE

- CBC results are variable depending upon severity and suddenness in onset of cholecystitis.
- Increased serum liver enzyme activities and bilirubin concentration are possible.
- Hypoglycemia possible in cases involving septic peritonitis
- Hyperglycemia may be seen in cases with concurrent diabetes mellitus and emphysematous cholecystitis.
- Abdominal radiographs may show air or calculi in gallbladder. Loss of cranial abdominal detail may be apparent (peritonitis).
- Abdominal ultrasound is highly reliable for the identification of gallbladder rupture (86% sensitivity).
  - Loss of gallbladder wall continuity, hyperechoic fat in the cranial portion of the abdomen, and free abdominal fluid are possible findings. Choleliths may be seen.

ADVANCED OR CONFIRMATORY TESTING

- Definitive diagnosis requires surgical biopsy and histopathologic evaluation of a specimen of the gallbladder wall.
  - Cultures of bile and/or gallbladder mucosa should be performed (*Escherichia coli* and *Klebsiella* spp. most common, but aerobic and anaerobic culture and sensitivity are warranted).
- Laparoscopic evaluation and liver biopsy may prove useful. Conversion to an open procedure and cholecystectomy should be anticipated.
- Ultrasonographic-guided, percutaneous cholecystocentesis: bile cytology and bacterial culture and sensitivity.
- Cholangiography: radiographic imaging of the biliary system; rarely performed.
- Abdominal paracentesis (p. 1192) or diagnostic peritoneal lavage (see online chapter: Diagnostic Peritoneal Lavage) should be performed if ultrasound is not available.
- Scintigraphy is an accurate indicator of canine extrahepatic biliary obstruction (EHBO).

TREATMENT

TREATMENT OVERVIEW

Surgical removal of a severely compromised or perforated GB and relief of EHBO are essential. Nonsurgical management may be appropriate in select cases without compromise of the GB wall's integrity.

ACUTE GENERAL TREATMENT

- Immediate surgical intervention in cases with gallbladder wall rupture and/or concurrent bile peritonitis
- Patients that are systemically ill must be aggressively supported before surgical management (fluids, antibiotics, colloids).

CHRONIC TREATMENT

Select cases of cholecystitis can be managed without surgical intervention, provided (1) there are no signs of systemic illness such as severe lethargy, vomiting, or anorexia; (2) there is no evidence of EHBO or compromise of the gallbladder's integrity; and (3) serum biochemical values (liver enzymes and bilirubin) are decreasing over time or have normalized. Treatments that may be used in conservative (nonsurgical) management of these select cases include long-term antibiotic therapy (e.g., ampicillin, 10-20 mg/kg IV q 8 h; or amoxicillin-clavulanic acid, 10-20 mg/kg PO q 12 h until culture and sensitivity results are available), choleretics (ursodiol, 15 mg/kg PO q 24 h), and treatment of any underlying disease (e.g., pancreatitis, diabetes mellitus).

POSSIBLE COMPLICATIONS

- Gallbladder rupture and bile peritonitis (septic versus nonseptic)
- Recurrence of cholecystitis with inappropriate treatment
- EHBO

RECOMMENDED MONITORING

- Intensive monitoring in a critical care setting is indicated in markedly compromised patients (e.g., necrotizing cholecystitis, bile peritonitis).
- Serial serum biochemistry profiles and serial abdominal ultrasounds as indicated
- Monitoring coagulation profiles and vitamin K supplementation (0.5 mg/kg IM q 12 h until relief of obstruction) is indicated in patients with complete EHBO.

PROGNOSIS AND OUTCOME

- Mortality rates of 25%-39% with canine necrotizing cholecystitis
- Overall mortality rates of 50% with canine bile peritonitis (0% with nonseptic effusions and 73% with septic effusions)
- Septic peritonitis, preoperative elevated creatinine concentration, and immediate postoperative hypotension are associated with a poor clinical outcome.

PEARLS & CONSIDERATIONS

COMMENTS

- Select cases can be managed medically.
- Surgical management is indicated in all cases involving gallbladder compromise, bile peritonitis, or EHBO (excluding select cases of pancreatitis).

TECHNICIAN TIP

Early enteral nutrition is very important to a positive outcome. In severely debilitated patients, esophagostomy and nasogastric feeding should be implemented postoperatively.

CLIENT EDUCATION

- Recurrence is possible if cholecystectomy is not performed.
- Early intervention likely improves outcome.

SUGGESTED READING

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Cholecalciferol Toxicosis

BASIC INFORMATION

DEFINITION

Cholecalciferol (vitamin D3) is used as both a dietary supplement and a rodenticide. Toxicity is characterized by clinical manifestations of hypercalcemia and hyperphosphatemia: anorexia and lethargy due to renal failure, cardiac arrhythmias, and seizures.

SYNONYM

Vitamin D3

EPIDEMIOLOGY

SPECIES, AGE, SEX

- All species susceptible; dogs more likely to be involved
- Young animals may be more sensitive

RISK FACTORS

Preexisting disease such as chronic kidney disease can increase severity of adverse effects.

CONTAGION & ZOONOSIS

Relay toxicosis (intoxication via consumption of prey that has itself consumed cholecalciferol) has not been reported.

GEOGRAPHY AND SEASONALITY

More cases in the fall and the winter months when more rodenticides are used

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- History or evidence of consuming bait
- Lethargy, anorexia, vomiting, diarrhea, polyuria, and polydipsia 12-72 hours post ingestion
- Renal failure 24-72 hours post ingestion

PHYSICAL EXAM FINDINGS

- Anorexia, lethargy
- Dehydration
- Signs of abdominal pain
- Hematemesis, melena
- Dyspnea, cardiac arrhythmias (especially bradycardia)
- Seizures (uncommon)

ETIOLOGY AND PATHOPHYSIOLOGY

Source:

- Cholecalciferol rodenticides
- Dietary supplements (over-the-counter and prescription)
- Common trade names are: Mouse-B-Gon, Rat-B-Gon, Quintox, Rampage, and True Grit. Most baits contain 0.075% cholecalciferol (0.75 mg cholecalciferol/gram bait).
- One IU of cholecalciferol (e.g., in dietary supplements) is equivalent to 0.025 mg of cholecalciferol.

Mechanism of Toxicosis:

- Cholecalciferol is metabolized to calcitriol (1,25 dihydroxyvitamin D).
  - Calcitriol increases intestinal absorption of calcium, stimulates resorption of calcium from bone, and increases renal tubular resorption of calcium.
- Toxic effects are due to hypercalcemia and hyperphosphatemia, resulting in metastatic mineralization of soft tissues, particularly kidney, myocardium, intima of large vessels, and gastrointestinal tract.
- Parathyroid hormone synthesis is suppressed.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is based on history of exposure to bait and evidence of hypercalcemia and hyperphosphatemia. Other causes of hypercalcemia need to be ruled out in cases where exposure history is not available; many possible causes (e.g., neoplasia, primary hyperparathyroidism) can be identified as unlikely on the basis of serum phosphorus level.

DIFFERENTIAL DIAGNOSIS

- Hypercalcemia:
  - Toxicologic:
    - Synthetic vitamin D3 ointment ingestion containing calcipotriene (Dovonex) or tacalcitol (Curatoderm) used for treating psoriasis in humans
    - Chronic overdose of vitamin D3 supplements
  - Spontaneous, nontoxicologic:
    - Hypercalcemia of malignancy(lymphoma, perianal adenocarcinoma, multiple myeloma, others)
- Primary renal failure
- Primary hyperparathyroidism
- Feline idiopathic hypercalcemia
- Addison's disease (hypoadrenocorticism)
- Granulomatous diseases (e.g., blastomycosis, schistosomiasis)

INITIAL DATABASE

- CBC, serum biochemistry profile:
  - Baseline if possible (<8 hour post exposure)
  - Calcium, phosphorus, blood urea nitrogen (BUN), creatinine should be included
  - Monitor daily for 4 days
  - Ca (mg/dL) P (mg/dL) product; if >60, an increased risk of soft-tissue mineralization exists
  - Note that immature animals that are actively remodeling bone may normally have Ca P that exceeds 60 but it is not associated with soft tissue mineralization.
- Urinalysis:
  - Isosthenuria (specific gravity 1.008-1.012) or hyposthenuria (specific gravity of 1.002-1.007) are common; isosthenuria indicates renal failure if concurrent azotemia
- Radiographs for soft-tissue calcification
- Ultrasound may suggest soft-tissue mineralization

ADVANCED OR CONFIRMATORY TESTING

- Serum 25-hydroxycholecalciferol level is elevated with cholecalciferol toxicosis. This assay will not detect calcipotriene found in psoriasis ointments (see p. 169).
- Serum parathyroid hormone levels are low with cholecalciferol toxicosis and hypercalcemia of malignancy but are normal with primary hyperparathyroidism, feline idiopathic hypercalcemia, and chronic kidney disease.
- Plasma parathyroid hormone–related protein may be detectable with hypercalcemia of malignancy but will be absent with other causes of hypercalcemia.
- Necropsy: fresh or frozen kidney. Total wet weight kidney calcium is typically elevated (300-1000 ppm [normal ranges, 100-150 ppm]).
- Histopathologic evaluation of lungs, kidney, aorta, myocardium, and gastric mucosa can reveal soft-tissue mineralization and necrosis.

TREATMENT

TREATMENT OVERVIEW

- For recent exposures prior to elevations in serum calcium and phosphorus, treatment consists of decontamination (induction of emesis and administration of activated charcoal) and measures to minimize effects of the toxicant.
- For animals with elevated serum calcium and phosphorus levels, treatment is aimed at lowering serum calcium and phosphorus promptly and preventing or managing acute renal failure.
- Complicated cases may involve days of intravenous fluid therapy and associated care. Referral to a specialty clinic that can provide 24-hour care should be considered.

ACUTE GENERAL TREATMENT

- Confirmed cholecalciferol ingestions >0.1 mg/kg require decontamination of the patient and monitoring.
- Decontamination of patient: induction of vomiting within 4 hours of ingestion (hydrogen peroxide 3%, 0.25-0.5 mL/kg PO once [dogs], or xylazine hydro-chloride, 0.44 mg/kg IM [cats])
- Repeated doses of activated charcoal (dose according to packaging label of product; e.g., 10 mL/kg of activated charcoal suspension PO made from 2 g activated charcoal suspended in 10 mL tap-water) and a cathartic, given q 8 h 24 hours
- Monitor serum electrolytes for development of hypernatremia 2-4 hours following repeated activated charcoal dosing.
- Treat hypercalcemia in animals showing overt clinical signs:
    - Saline diuresis 0.9% saline at 90 (cats) to 130 (dogs) mL/kg/d
        - Avoid calcium-containing fluids.
        - Adjust dose if cardiac disease or other vascular volume-limiting condition.
    - Furosemide 2.5-4.5 mg/kg PO, SQ, IM, or IV q 6-8 h
        - Do not use thiazide diuretics (calcium-retaining). Example: hydrochlorothiazide.
    - Prednisolone 1-3 mg/kg PO q 8-12 h
    - High doses of dexamethasone at 1-2 mg/kg IV or SQ q 24 h have been recommended.
    - Because dexamethasone has 10 times the glucocorticoid potency of prednisone, these high doses can cause substantial gastrointestinal ulceration and hemorrhage and should only be used as a last resort.
    - Specific antagonists (must choose one or the other; do not combine):
        - Pamidronate (preferred): 1.3-2 mg/kg as a slow IV infusion. Repeat in 5-7 days if needed. May cause a transient increase in BUN or creatinine.
        - Calcitonin (use if supportive treatments are not effective): 4-6 IU/kg-SQ q 8-12 h. Some animals become refractory to salmon calcitonin.

CHRONIC TREATMENT

- Continue treatment until serum calcium stabilizes or Ca × P < than 60 (days to weeks of treatment).
- Treat other signs (renal failure, seizures, arrhythmias).
- Gradually wean off prednisolone/dexamethasone and furosemide when calcium levels reach normal range.
- Avoid sunlight.

NUTRITION

- Phosphate binders: aluminium hydroxide 10-30 mg/kg PO q 8 h. Discontinue phosphate binders when serum phosphorus level stabilizes.
- Low-calcium diet

POSSIBLE COMPLICATIONS

- Soft-tissue mineralization (irreversible)
- Pulmonary edema (mineralization and leakage of pulmonary vessels), hemorrhage, or aspiration pneumonia
- Sudden death associated with myocardial or aortic mineralization
- Gastric ulceration, hematemesis, shock, and collapse
- Hypocalcemia if animals are not weaned from treatment after calcium levels are normalized

RECOMMENDED MONITORING

Monitor serum calcium and phosphorus for 5 to 7 days after values are normalized, then 2-3 times a week for 2 weeks, and then once at 1 month post exposure.

PROGNOSIS AND OUTCOME

- Prognosis good if animal receives prompt treatment, and if soft-tissue mineralization has not occurred

- Prognosis poor to guarded with prolonged elevations in calcium and phosphorus, causing soft-tissue mineralization

PEARLS & CONSIDERATIONS

COMMENTS

- Dietary supplements generally list cholecalciferol, or vitamin D, in IU. One IU of cholecalciferol is equivalent to 0.025 mcg of cholecalciferol.
- Practitioners should be aware that products with the same brand name may contain various active ingredients. For example, Rampage may contain bromethalin or cholecalciferol. It is imperative that active ingredients be verified on the package.
- In nonsurvivors, total wet kidney calcium concentrations can be used for differentiating between ethylene glycol toxicosis (3000-12,000 ppm) and cholecalciferol toxicosis (300-1000 ppm).

TECHNICIAN TIPS

- In dogs, hypercalcemia frequently causes anorexia, so monitoring a dog's appetite may provide an early indication of increasing serum calcium levels.

CLIENT EDUCATION

- Provide information about pet proofing homes.
- Remind clients that rodenticides may be appealing to pets.

SUGGESTED READING

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AUTHOR: SHARON GWALTNEY-BRANT

EDITOR: SAFDAR A. KHAN

1ST EDITION AUTHOR: CHARLOTTE MEANS

Chole(cysto)lithiasis

BASIC INFORMATION

DEFINITION

Formation of stones in the extrahepatic bile duct system (choleliths) and/or specifically in the gallbladder (cholecystoliths)

SYNONYM

Gallstones

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs: older, small-breed, spayed females appear to be predisposed.

Cats: middle-aged to older adults

ASSOCIATED CONDITIONS & DISORDERS

Cats:

- In some cats, possible association with cholangitis, pancreatitis, inflammatory bowel disease

Dogs:

- Cholecystitis
- Gallbladder perforation
- Bile peritonitis due to gallbladder rupture
- Rarely biliary adenocarcinoma

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Cholelithiasis without specific clinical signs:
  - Incidental finding on abdominal radiographs or ultrasound performed for another reason
- Cholelithiasis associated with clinical signs of:
  - Gastrointestinal disease
  - Biliary obstruction
  - Peritonitis when cholelithiasis is associated with biliary disruption/rupture

HISTORY, CHIEF COMPLAINT

- Generally nonspecific: malaise and gastrointestinal signs predominate.
- Dogs: vomiting, anorexia, lethargy, weakness, polydipsia, polyuria, weight loss
- Cats: vomiting, dehydration, anorexia, lethargy
- Note: choleliths may be an incidental finding in both dogs and cats and may not be associated with any clinical signs.

PHYSICAL EXAM FINDINGS

- Icterus is commonly apparent when cholelithiasis is associated with cholangitis, cholecystitis, and/or gallbladder obstruction.
- Fever may be noted in dogs, in association with infection and/or bile peritonitis.
- Signs of abdominal pain are not consistently noted, even when biliary obstruction is present.

ETIOLOGY AND PATHOPHYSIOLOGY

- Etiology unknown
- In dogs and cats, most choleliths contain mainly calcium rather than cholesterol, as seen in humans.
- Choleliths may obstruct the extrahepatic biliary system (see p. 135).
- Decreased absorption of fat and fat-soluble vitamins, notably vitamin K, and subsequent coagulopathy
    - Decreased bile secretion into the intestine may result in decreased binding of endotoxin, predisposing to endotoxemia.
- Cholelithiasis has been associated with concurrent cholecystitis and gallbladder rupture, resulting in bile peritonitis.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Inasmuch as presenting history and physical examination findings are frequently nonspecific, the diagnosis of this problem generally requires diagnostic imaging. Abdominal ultrasonography is the modality of choice.

DIFFERENTIAL DIAGNOSIS

- Cholelithiasis with extrahepatic biliary obstruction and jaundice:
    - Hyperbilirubinemia due to hemolysis:
        - Immune-mediated hemolytic anemia or other diseases causing severe intravascular hemolysis
    - Hepatic disease: cholangiohepatitis (cats), idiopathic chronic hepatitis (dogs), cirrhotic/fibrosing liver disease, neoplasia, copper/other toxins (dogs), acetaminophen toxicosis (cats)
    - Extrahepatic biliary obstruction: pancreatitis, cholangitis, neoplasia, stricture, foreign body obstruction, diaphragmatic hernia
- Cholelithiasis without biliary obstruction:
    - Other causes of vomiting and anorexia, because choleliths are an incidental finding:
        - Viral enteritis
        - Pancreatitis
        - Foreign body obstruction
        - Gastric, intestinal, or pancreatic neoplasia
        - Inflammatory bowel disease
        - Ingested toxins
        - Hepatic and renal diseases

INITIAL DATABASE

- CBC:
    - Possible anemia, though usually mild
    - Inflammatory leukogram
- Serum biochemistry profile:
    - Elevated bilirubin concentration
    - Elevated liver enzyme concentration
    - Possible elevations of amylase and lipase concentrations
    - Hypokalemia
- Survey abdominal radiographs:
    - May delineate radiopaque choleliths
- Survey thoracic radiographs:
    - Rule out metastatic disease if neoplasia is suspected

ADVANCED OR CONFIRMATORY TESTING

- Abdominal ultrasound examination:
    - Common bile duct dilation:
        - Further delineate choleliths
        - >5 mm diameter is diagnostic of bile duct obstruction in the cat
    - Evaluate gallbladder in dogs with concurrent cholecystitis:
        - Wall thickness
        - Contents: choleliths, mucocele
        - Presence of attached omentum
        - Surrounding fluid
            - Evaluate intestine for increased wall thickness and loss of layering associated with neoplasia or inflammatory bowel disease

- Peritoneal fluid analysis (obtained during abdominal ultrasound examination):
  - Bilirubin concentration (elevated: bile peritonitis)
  - Cytologic examination and microbiologic culture and sensitivity testing: septic peritonitis
- Coagulation profile

TREATMENT

TREATMENT OVERVIEW

- If the choleliths are an incidental finding, no treatment is required. The patient should be monitored for development of clinical signs associated with cholelithiasis.
- If signs of biliary stasis, disruption, or obstruction are noted, then patient stabilization and surgical intervention will be necessary.

ACUTE GENERAL TREATMENT

- Rehydration by intravenous administration of balanced electrolyte solution
- Normalization of serum electrolyte concentrations
- Parenteral antibiotics effective against gram-negative bacteria and anaerobes:
  - Empirical therapy:
    - Cefoxitin, 30 mg/kg IV q 4-6 h perioperatively, then q 6 h; or
    - Metronidazole, 7.5-15 mg/kg IV q 12 h with
    - Enrofloxacin, 5-15 mg/kg q 24 h for dogs, 5 mg/kg q 24 h for cats
  - Specific long-term therapy based on culture and sensitivity test results
- Possible administration of fresh frozen plasma (if hypoproteinemia, coagulopathy)
- Vitamin K administration
- Removal of choleliths/relief of extrahepatic biliary obstruction
- Duodenotomy and retrograde flushing of the biliary system
- Choledochotomy for removal of one or two large choleliths
  - Cholecystectomy:
    - Results in the best long-term prognosis if all stones are removed and biliary system is patent
  - Common bile duct stenting
  - Cholecystoduodenostomy/jejunostomy
  - Tube cholecystostomy
- Treatment of bile peritonitis if biliary disruption has occurred (see p. 865)

CHRONIC TREATMENT

Maintenance of bile flow: ursodeoxycholic acid 10-15 mg/kg PO q 24 h; contraindicated while gallbladder obstruction is present.

NUTRITION/DIET

Provide access for enteral feeding if patient is anorexic (see p. 1267 ,p. 1270, and p. 1322).

POSSIBLE COMPLICATIONS

Recurrence of cholelithiasis, bile leakage, pancreatitis, peritonitis, endotoxemia, sepsis, death

RECOMMENDED MONITORING

- If clinical signs were/are present:
  - Clinical and laboratory parameters assessing perfusion, including capillary refill time, pulse rate and quality, blood pressure, urine output, arterial pH, and lactate concentrations
  - Respiratory function
  - Serum liver enzymes and bilirubin concentrations
  - Coagulation profile
- If incidental finding:
  - Physical exam and serum biochemistry profile every 6 months

PROGNOSIS AND OUTCOME

- Fair in clinically ill animals if all choleliths removed and a cholecystectomy is performed
- Guarded if cholelithiasis is associated with biliary leakage and aseptic bile peritonitis
- Poor in patients with septic bile peritonitis
- Open prognosis in patients without clinical signs (incidental finding)

PEARLS & CONSIDERATIONS

COMMENTS

Given the association of biliary obstructive disease (cholelithiasis) in cats with cholangitis/cholangiohepatitis and inflammatory bowel disease, a liver biopsy and culture, bile culture, and small intestinal biopsies should be obtained at the time of surgery in this species.

SUGGESTED READING

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EDITOR: RICHARD WALSHAW

Cholangitis/Cholangiohepatitis Complex of Cats

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

- Inflammation of the biliary tree and surrounding hepatocellular parenchyma. May occur as a primary process, a coexisting condition, or secondary to a variety of other feline diseases.
- Cholangitis: inflammation is centered around the bile ducts.
- Cholangiohepatitis: extension of cholangitis into the surrounding hepatic parenchyma
- Cholangitis/cholangiohepatitis (CCH) has been referred to as both a "complex" (CCHC) and a "syndrome" (CCHS).
    - In either case, this designation emphasizes the fact that a variety of distinct forms of disease is included within a single umbrella term (see disease forms/subtype, below).
- The CCHC of cats is one of the most common feline hepatobiliary disorders.

SYNONYMS

- Acute neutrophilic CCH: suppurative CCH
- Chronic, lymphoplasmacytic CCH: nonsuppurative, lymphoplasmacytic, or lymphoproliferative CCH

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Himalayan, Persian, and Siamese cats may be predisposed.
- Patients with this disease range in age from <1 to >16 years old, but most are middle-aged.
- Cats presenting with acute (suppurative) disease tend to be several years younger than those with chronic (nonsuppurative) disease.
- Male cats appear to be overrepresented.

RISK FACTORS

Extrahepatic biliary obstruction, inflammatory bowel disease (IBD), pancreatitis, cholestatic disease, cholelithiasis, bacterial infection or splenic abscess, feline infectious peritonitis (FIP), toxoplasmosis, immunodeficiencies, choledochal stent placement, drugs (diazepam, tetracyclines, others).

CONTAGION & ZOONOSIS

Not considered either a contagious or zoonotic disease. There is a single report of *H. pylori* isolation from samples of feline bile.

ASSOCIATED CONDITIONS & DISORDERS

Triaditis is the term used for describing the combination of CCH with IBD and pancreatitis. IBD or pancreatitis is seen in 50%–85% of the cases of CCHC, with both present in up to 40% of CCHC patients. Cholangitis/cholangiohepatitis can also be associated with hepatic lipidosis, or secondary to a variety of other diseases/conditions (see Risk Factors above).

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- On the basis of histopathologic findings, three distinct entities exist within the CCHC, as defined by the World Small Animal Veterinary Association Liver Diseases and Pathology Standardization Research Group:
    - Acute neutrophilic (suppurative)
    - Chronic (lymphoplasmacytic or mixed)
    - Lymphocytic (nonsuppurative)
- The forms can be quite different clinically (history, initial presentation, chief complaint, etiology, progression, and outcome).
- Chronic lymphocytic cholangitis is a form seen predominantly in Europe and is progressive.
    - Some pathologists classify this as low-grade (well-differentiated) lymphoma.
- Lymphocytic portal hepatitis is a separate entity confined to portal triads and is often an incidental finding in older cats.

HISTORY, CHIEF COMPLAINT

- Patients with the suppurative form of CCH usually present for an acute onset of illness: anorexia, fever, and vomiting in an icteric cat with abdominal discomfort.
- Patients with the nonsuppurative form of CCH usually present for a more chronic condition with subtle nonspecific signs, and less commonly present with acute signs.
- Patients with concurrent IBD and pancreatitis ("triaditis") may present with a wide variety of signs and varying degrees of severity, depending on the severity of inflammation in these other organs.
- Patients with either form are usually icteric, and a few may have ascites.
- Patients with the chronic condition may rarely be polyphagic, although usually they will be presented for lethargy, anorexia, vomiting, and weight loss.

PHYSICAL EXAM FINDINGS

- Suppurative CCH: The patient is usually febrile, dehydrated, and icteric and may have abdominal discomfort with palpation.
- Patients with the nonsuppurative form of CCH may have minimal physical exam abnormalities or may present icteric.
    - Hepatomegaly may be appreciated with abdominal palpation.

ETIOLOGY AND PATHOPHYSIOLOGY

- Bacterial infection *(Escherichia coli, Streptococcus, Clostridium, Salmonella [serovar typhimurium], Enterococcus faecium*, other enteric organisms, anaerobes); ascending infection of the biliary tract (acute suppurative/neutrophilic cholangitis)
- In association with other infectious agents (i.e., toxoplasmosis, FIP)
- Immune-mediated disorder (chronic nonsuppurative/lymphocytic cholangitis)
- Extrahepatic biliary obstruction
- Secondary or concurrent pancreatitis, especially with suppurative form; pancreatic and bile ducts enter duodenum through a common opening in the cat (see p. 135)
- IBD

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Lethargy and anorexia in a cat with elevated liver enzymes is consistent with CCH but also several other hepatobiliary disorders. The diagnosis is confirmed histologically from a liver biopsy.

DIFFERENTIAL DIAGNOSIS

- Hepatic lipidosis
- Hepatic neoplasia (especially lymphoma)
- Extrahepatic biliary duct obstruction
- Pancreatitis
- Inflammatory bowel disease
- FIP
- Sepsis

INITIAL DATABASE

- CBC:
    - Leukocytosis; neutrophilia with a left shift and/or toxic neutrophils
    - Lymphocytosis (nonsuppurative CCH)
    - Mild nonregenerative anemia with poikilocytes and/or Heinz bodies
- Serum biochemistry panel:
    - Elevated liver enzyme activities (alanine aminotransferase, ALP, aspartate aminotransferase, γ-glutamyltransferase)
    - Possibly elevated total bilirubin concentration
    - Increased bile acids concentration (fasting and postprandial)
    - Hyperglobulinemia (nonsuppurative CCH)
- Other:
    - High feline pancreatic lipase immunoreactivity (fPLI) possible with pancreatitis
    - Low serum cobalamin concentration with severe IBD
    - Possible clotting time abnormalities (prothrombin time, activated partial thromboplastin time, activated clotting time [ACT], proteins induced by vitamin K absence [PIVKA]), or portal vein thrombus (PVT).

- Hepatomegaly (radiographs or laparoscopy)

ADVANCED OR CONFIRMATORY TESTING

- Abdominal ultrasound:
  - Hepatic parenchyma: mixed echogenicity, multifocal hyperechogenicity, diffuse hypoechogenicity, or a coarse or nodular appearance (nonspecific)
  - Prominent portal vasculature
  - Gallbladder distension, cholelithiasis, biliary sludge, thickened gallbladder wall
  - Abdominal lymphadenopathy
  - Evidence of pancreatic or intestinal inflammation
  - Ascites (nonsuppurative CCH; high protein, low cellularity)
- Fine-needle aspiration (FNA) of the liver:
  - Hepatocellular vacuolation (concurrent lipidosis is possible).
  - Cellular infiltration: neutrophils, lymphocytes, or mixed, +/− intraluminal biliary inflammation
  - Bacterial culture and sensitivity.
  - In general, FNAs result in a greater number of false-negative and false-positive diagnoses compared to core or wedge biopsies.
- Percutaneous ultrasound-guided cholecystocentesis
  - Minimally invasive; identification, culture and sensitivity for bacterial isolates
- Liver biopsy (wedge [laparotomy, laparoscopy] or ultrasound-guided core):as above for FNA, plus:
  - Periportal hepatocellular necrosis, bile duct dilation and proliferation (suppurative)
  - Periductal fibrosis, diminished bile duct number, and sclerosing cholangitis (nonsuppurative)
- Laparoscopy:
  - Abdominal lymphadenopathy
  - Ability to obtain wedge biopsy sample
- Laparotomy, as above for laparoscopy:
  - Assess biliary system for extrahepatic biliary obstruction.
  - Feeding tube placement possible

TREATMENT

TREATMENT OVERVIEW

In addition to supportive care and specific treatment, the treatment plan must address concurrent conditions (frequent) for optimal patient outcomes.

ACUTE GENERAL TREATMENT

- Treatment should be tailored to the individual patient.
- Fluids (Normosol, lactated Ringer's solution) with potassium supplementation
- Antibiotics (based on culture and sensitivity when possible):
  - Amoxicillin-clavulanate, 62.5-125 mg/cat PO q 12 h, 1-2 weeks beyond normalizing liver enzymes, *or*
  - Amoxicillin, 10-20 mg/kg PO q 12 h, *or*
  - Cephalexin or cefadroxil, 22 mg/kg PO q 8 h, *or*
  - Enrofloxacin, 5 mg/kg PO q 24 h, combined with metronidazole, 7.5 mg/kg PO q 12 h
  - Vancomycin has been reported for one case of multidrug-resistant *Enterococcus faecium*
- Ursodeoxycholic acid (10-15 mg/kg PO q 24 h) for choleresis, unless physical obstruction to gallbladder outflow exists
- Vitamin K1 (5 mg/cat PO q 24 h) in cases of coagulation abnormalities
- Cannulation for removal of inspissated bile, surgery for extrahepatic biliary obstruction, and necessary treatments for associated conditions (especially pancreatitis, IBD, hepatic lipidosis).

CHRONIC TREATMENT

- Long-term management is highly dependent on an accurate diagnosis and requires histopathologic analysis of a liver biopsy.
- Continued antibiotics and ursodeoxycholic acid (see Acute General Treatment above) 3-6 months if suppurative CCH
- Prednisolone (for chronic or nonsuppurative CCH; 4 mg/kg/d initially, gradual taper over 2-4 months) combined with metronidazole (see Acute General Treatment above)
- Refractory cases of nonsuppurative CCH may require chemotherapeutics (e.g., methotrexate [0.13 mg PO q 8 h for 3 doses at 7-day intervals, if tolerated], cyclosporine [3-5 mg/kg PO q 12 h], or chlorambucil [4 mg/m^2 PO q 48 h]). Given the potential for severely detrimental side effects with these drugs and the need for close monitoring, their use is recommended only in consultation with an internist.

- Vitamin E (a-tocopherol acetate, 10-30 IU/kg) for all forms of CCHS
- *S* -adenosylmethionine (20 mg/kg PO q 24 h [enteric-coated tablet]) for all forms of CCHS
- Ursodeoxycholic acid, carnitine (see Acute General Treatment above)
- Continued treatment of concurrent conditions such as pancreatitis and/or IBD
- Treatment for ascites if present (furosemide [1-3 mg/kg PO q 12 h, ACE inhibitors [enalapril, 0.5 mg/kg PO q 12-24 h], salt restriction)
- For biliary cirrhosis (sclerosing CCHC), consider the addition of pulsatile therapy with methotrexate (0.13 mg PO q 8 h for 3 doses at 7-day intervals if tolerated), being cognizant of potentially adverse side-effects (GI, hepatic toxicity, renal toxicity, bone marrow suppression).

NUTRITION/DIET

- Route determined by clinical condition
- Protein restriction in cats is problematic because they are strict carnivores; protein restriction should be avoided unless there is clear evidence of hepatic encephalopathy (rare).
- Consider supplementation with L-carnitine (250 mg/cat PO q 24 h), taurine(250-500 mg/cat PO q 24 h), thiamine(B1) 50-100 mg PO q 24 h for 3 days, and vitamin B12 (1 mg SQ repeated weekly).

POSSIBLE COMPLICATIONS

- Hepatic lipidosis with prolonged anorexia or inadequate nutritional support
- Diabetes mellitus with corticosteroid treatment of nonsuppurative disease or IBD
- Hepatic sclerosis
- Progression of acute to chronic disease
- Necrotizing cholecystitis, choleliths
- Portal vein thrombosis

RECOMMENDED MONITORING

- Hepatic enzyme activity and total bilirubin concentration (at 2-week intervals until stable, then monthly)
- PIVKA and/or clotting times if abnormalities are present or to monitor vitamin K1 therapy
- Consider repeat bile acids measurement to monitor liver function.

PROGNOSIS AND OUTCOME

- Acute suppurative cholangiohepatitis may be a single curable event, or it may recur (especially if antibiotic therapy is curtailed prematurely), but the prognosis is generally good with timely diagnosis and appropriate treatment.
- Nonsuppurative cholangiohepatitis is a chronic condition but carries a fair to good prognosis with lifelong therapy.
- Concurrent pancreatitis and/or IBD may also affect the prognosis negatively.

PEARLS & CONSIDERATIONS

COMMENTS

- The cholangitis/cholangiohepatitis complex of cats is a complex or constellation of distinct clinical signs, biochemical abnormalities, and structural derangements. The underlying etiology may be distinct as well, and determining whether an infectious process is a contributing factor has a critical bearing on treatment decisions. Following the appropriate and sufficient diagnostic steps in the workup of a cat with inflammatory liver disease is critical for therapeutic success.
- Acute (suppurative) CCH is often infectious in nature (and therefore treated initially with antibiotics), whereas chronic (nonsuppurative) CCH may have an immune-mediated basis (and is therefore treated with immunosuppressive drugs).

PREVENTION

Avoid and/or treat contributing or concurrent conditions such as chronic pancreatitis or IBD.

CLIENT EDUCATION

- Vigilant monitoring is important for early detection of anorexia, lethargy, vomiting, or abdominal discomfort, because suppurative cholangiohepatitis may recur.
- Compliance with medication administration may be a lifelong commitment.

- Proper nutritional support (optimal high-protein diet) is important.

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Chocolate Toxicosis

BASIC INFORMATION

DEFINITION

Clinical signs caused by ingestion of chocolate products and byproducts

SYNONYM

Methylxanthine toxicosis

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs are most commonly affected; all breeds, ages, both sexes susceptible.

RISK FACTORS

Animals with cardiac or seizure disorders may be at increased risk for signs.

GEOGRAPHY AND SEASONALITY

Toxicosis can occur year-round; most prevalent (greater opportunity for exposure) during holiday seasons such as Easter, Christmas, and Valentine's Day.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Severity and onset of signs depend on amount and type of chocolate ingested.
- Chocolate and its by products contain methylxanthines—theobromine (primary) and caffeine (secondary)—plus sugars and fat.
- See table for methylxanthine content of products.
- Variable individual sensitivity to methylxanthines
- Methylxanthine dosages:
    - 20-40 mg/kg: mild to moderate clinical signs
    - 40-50 mg/kg: cardiac arrhythmias; potentially life-threatening
    - >60 mg/kg: seizures

HISTORY, CHIEF COMPLAINT

- Known ingestion of chocolate most common
- Onset of signs up to 6-12 hours post ingestion possible
- Initially: polydipsia, bloating, vomiting, diarrhea; restlessness
- Can progress to polyuria, agitation, tremors, rigidity, ataxia, seizures, collapse, coma

PHYSICAL EXAM FINDINGS

- Agitation, nervousness
- Tachycardia
- Tachypnea
- Hypertension
- Hyperthermia
- Cardiac arrhythmias (premature ventricular contractions, sinus tachycardia, sinus bradycardia, others)
- Ataxia, tremors, seizures

ETIOLOGY AND PATHOPHYSIOLOGY

- Behavior changes, central nervous system stimulation, and cardiovascular abnormalities: competitive inhibition of cellular adenosine receptors
- Enhanced cardiac and skeletal muscle contractility: increase in free intracellular calcium concentrations from inhibition of sarcoplasmic calcium reuptake and increased calcium entry into cells
- Death likely due to cardiac arrhythmias, respiratory failure, or hyperthermia-induced disseminated intravascular coagulation (DIC)
- High sugar and fat contents in chocolate: gastrointestinal signs, possibly pancreatitis

*Exact methylxanthine content varies with growing conditions for cocoa beans as well as individual commercial formulations of products. Approximate methylxanthine dose ingested (in mg/kg) is: 1. Add product's theobromine concentration, in mg/oz (above) + product's caffeine concentration, in mg/oz (above). 2. Multiply this number by number of ounces of chocolate product ingested. 3. Divide by dog's body weight in kg. Metric conversion 1 oz = 28.5 g.

Approximate Methylxanthine Content of Various Products*

Product	Theobromine	Caffeine
Cocoa powder	737 mg/oz	42 mg/oz
Baker's chocolate	393 mg/oz	118 mg/oz
Semisweet chocolate	138 mg/oz	22 mg/oz
Instant cocoa mix powder	136 mg/oz	15 mg/oz
Milk chocolate	56 mg/oz	6 mg/oz
White chocolate	0.25 mg/oz	0.85 mg/oz
Unprocessed cocoa bean shell mulch	285-1140 mg/oz (54-849 mg/oz in processed mulch)	20-103 mg/oz

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis based on any combination of history, presence of chocolate in the vomitus, and clinical signs consistent with chocolate toxicosis

DIFFERENTIAL DIAGNOSIS

- Other toxicoses that can cause central nervous system (CNS) excitation: amphetamines, pseudoephedrine, phenylpropanolamine, metaldehyde, cocaine, antidepressants, antihistamines
- Causes of cardiac arrhythmias (see p. 1165 , p. 1027, and p. 1025)
- Causes of dyspnea/tachypnea (see p. 327)
- Causes of hyperthermia (see p. 480)
- Causes of systemic hypertension (see p. 1068)

INITIAL DATABASE

- ECG (see p. 1253)
- Blood pressure (see p. 1209)
- Serum biochemistry panel:
  - Renal values in animals with severe clinical signs
  - Serum electrolyte levels in animals with overt clinical signs
- Evaluation of pancreas (serum assays, ultrasound) in animals with severe or persistent gastrointestinal clinical signs

TREATMENT

TREATMENT OVERVIEW

Intensity of treatment is guided by dose of intoxication (type and amount of chocolate ingested), time since ingestion (expected efficacy of emesis induction and charcoal administration; onset of clinical signs), and presence or absence of preexisting cardiac or renal disorders. Mild intoxications may be treated as benign gastroenteritis cases (after patient decontamination).

ACUTE GENERAL TREATMENT

- Manage clinical signs:
  - CNS signs/neuromuscular
    - Diazepam (0.5-2 mg/kg IV) for seizures
    - Barbiturates, gas anesthetics if diazepam ineffective
    - Methocarbamol (50-200 mg/kg slow IV; do not exceed 330 mg/kg/24 h) for tremors, rigidity
- Cardiac arrhythmias:
  - Beta-blockers for severe, sustained supraventricular tachyarrhythmias, especially if preexisting heart disease
    - Propranolol (0.04-0.06 mg/kg slow IV over 2-3 minutes; max 0.2 mg/kg), *or*
    - Esmolol (0.2-0.5 mg/kg IV or 25-200 mcg/kg/min IV CRI), *or*
    - Metoprolol (0.2-0.4 mg/kg PO q 8 h)
  - Lidocaine for rapid sustained ventricular arrhythmias
    - Dogs: 1-4 mg/kg IV, then 30 to 50 mcg/kg/min if necessary (if beta-blockers ineffective). Cats (use with caution): 0.5-2 mg/kg IV.
  - Atropine (0.01-0.02 mg/kg IV) for bradyarrhythmias
- Control hyperthermia:
  - Fluids, fans (see p. 480)
  - Control vomiting (if needed)
    - Maropitant 1 mg/kg SQ q 24 h or 2 mg/kg PO q 24 h up to 5 days; *or*
    - Metoclopramide 0.2-0.5 mg/kg PO or SQ q 6-12 h
- Decontaminate patient after life-threatening issues addressed:
  - Subclinical (or stabilized clinical) patient only
    - Emesis: effective up to 8-12 h post ingestion (see p. 1364)
- Gastric intubation, gavage, lavage (see p. 1281)
  - Consider when emesis is contraindicated (comatose, anesthetized)
- Activated charcoal:
  - 1-4 g/kg (or labeled dosage) after emesis/lavage; repeat q 8 h during clinical signs of toxicosis
- Animals without clinical signs/pre-clinical cases: monitor 8-12 hours for development of signs:
  - Maintain urine output (IV fluid diuresis) potassium supplementation
- Urinary catheter placement:
  - Caffeine is reabsorbed from the urine; urinary catheter helps increase caffeine excretion.

NUTRITION/DIET

Bland diet may be indicated for 3-5 days for diarrhea.

DRUG INTERACTIONS

Erythromycin, cimetidine, corticosteroids may delay methylxanthine clearance and should be avoided.

POSSIBLE COMPLICATIONS

- DIC from hyperthermia
- Myoglobinuria from seizure-induced rhabdomyolysis; renal failure
- Pancreatitis

RECOMMENDED MONITORING

- ECG, blood pressure, body temperature
- Serum electrolytes
- Fluid ins/outs
- Urinalysis
- Pancreatic ultrasound enzymes

PROGNOSIS AND OUTCOME

- Prognosis is generally good with prompt and thorough care.
- If severe clinical signs are not controlled, prognosis is guarded to poor.
- Signs generally resolve in 12-72 hours, depending on methylxanthine dose, severity of signs, and aggressiveness of treatment.

PEARLS & CONSIDERATIONS

COMMENTS

- The darker the chocolate, the more dangerous it is.
- To estimate amount of methylxanthine ingested, add amount of caffeine and theobromine together (see table), multiply by number of ounces ingested, and divide by body weight in kilograms.
- Half-life in dogs: theobromine = 17.5 hours; caffeine = 4.5 hours
- Chocolate may form a clump in the stomach, delaying absorption and onset of clinical signs for up to 12 hours.

PREVENTION

- Keep chocolate-containing products away from pets.
- Avoid leaving chocolate-containing gifts unsupervised (e.g., under the Christmas tree).

TECHNICIAN TIPS

Induction of emesis even several hours after exposure can prevent signs or substantially reduce the severity of signs.

CLIENT EDUCATION

Pets fed small amounts of chocolate may develop a taste for it and actively seek out chocolate, leading to intoxication.

SUGGESTED READING

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Chlamydiosis, Cat

BASIC INFORMATION

DEFINITION

A bacterial infection associated mainly with acute and chronic conjunctivitis in cats

SYNONYMS

- *Chlamydia psittaci* infection (outdated; current name is *Chlamydophila felis)*
- *Chlamydophila felis* infection
- Feline pneumonitis (outdated term; the organism is primarily a conjunctival pathogen)

EPIDEMIOLOGY

SPECIES, AGE, SEX

The prevalence of *C. felis* in cats with upper respiratory tract disease has ranged from 10%-31%. Cats < 5 years old, and especially < 1 year old, are predisposed. There is no strong sex predilection.

RISK FACTORS

Young age is the most significant risk factor.

CONTAGION & ZOONOSIS

Highly contagious between cats (aerosol, direct contact, fomites). *C. felis*-associated conjunctivitis has been described in a single immunocompromised human. Other reports associating *C felis* infection with keratoconjunctivitis in people did not provide definitive evidence of infection. The DNA of *C. felis* has also been detected uncommonly in respiratory samples from humans. Maintenance of hygienic conditions and prompt treatment of cats should help prevent human disease.

GEOGRAPHY AND SEASONALITY

Worldwide distribution; may be more common in summer.

ASSOCIATED CONDITIONS & DISORDERS

May be associated with concurrent feline respiratory viral infections such as feline herpesvirus 1 or feline calicivirus infection.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Ocular discharge and redness
- Occasionally decreased appetite
- Nasal discharge
- Sneezing

PHYSICAL EXAM FINDINGS

- Ocular signs: blepharospasm, chemo-sis, conjunctivitis, serous to mucopurulent ocular discharge
- Serous to mucopurulent nasal discharge (always accompanied by conjunctivitis)
- Possible fever
- Possible vaginal discharge

ETIOLOGY AND PATHOPHYSIOLOGY

- *C. felis* is an obligately intracellular bacterium related to gram-negative bacteria.
- The life cycle alternates between an extracellular, infectious elementary body, and an intracellular reticulate body.
- Reticulate bodies divide within a cytoplasmic vacuole called an *inclusion*, and are released from the host cell as elementary bodies.
- Natural transmission probably occurs by close contact with other cats and their aerosols, and via fomites.
- The incubation period is 3-5 days, and infection may persist for months.
- Feline chlamydiosis is a systemic disease, and organisms are shed from the conjunctiva, vagina, and rectum.
- Recently, another chlamydial species has been identified in cats, *Neochlamydia hartmannellae;* the clinical significance of this organism is yet to be determined.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis may be suspected based on clinical signs (i.e., marked persistent conjunctivitis) and response to appropriate antimicrobials.

DIFFERENTIAL DIAGNOSIS

- Infectious causes:
  - Feline herpesvirus 1
  - Feline calicivirus
  - *Bordetella bronchiseptica*
  - *Mycoplasma* spp.
  - *Cryptococcus neoformans*
  - *Aspergillus* spp.
- Noninfectious causes:
  - Eyelid and nasal neoplasia (including nasopharyngeal polyps)
  - Dental disease
  - Congenital eyelid malformations
  - Palate defects
  - Chemical irritants
  - Foreign bodies
  - Trauma
  - Immune-mediated/inflammatory (e.g., eosinophilic keratoconjunctivitis)

INITIAL DATABASE

Conjunctival scrapings: may reveal inclusion bodies within epithelial cells when stained with Giemsa. Low sensitivity and specificity.

ADVANCED OR CONFIRMATORY TESTING

- Human ELISA antigen kits for *Chlamydia trachomatis:* performed on conjunctival swabs, variable sensitivity and specificity
- Cell culture: available in specialized laboratories, requires special transport media, and sensitivity varies depending on equipment and technical expertise
- PCR: performed on conjunctival swabs; sensitivity and specificity varies with the laboratory; quality control may be problematic in some laboratories; ensure positive and negative extraction controls are included with each run
- Positive serologic titers: correlate well with infection in unvaccinated cats, but reliable assays not yet readily available

TREATMENT

TREATMENT OVERVIEW

The cornerstone of treatment is antibiotics (doxycycline), with supportive care as needed.

ACUTE GENERAL TREATMENT

- Doxycycline, 10 mg/kg PO q 24 h for at least 4 weeks
- Treat all cats in the household simultaneously.
- Because infection is systemic, use of topical ocular treatment alone is not likely to be effective.

- Doxycycline is superior to azithromycin.
- A 4-week course of amoxicillin-clavulanic acid (2.5 mg/kg PO q 12 h) may also eliminate *C. felis*.

POSSIBLE COMPLICATIONS

- Risk of teeth discoloration in kittens if tetracyclines are used in the last 2-3 weeks of pregnancy or for kittens in the first few months of life.
    - Little evidence that this occurs with doxycycline; amoxicillin-clavulanic acid is an acceptable alternative in this situation.
- Administration of doxycycline liquid oral suspension minimizes the risk of doxycycline-induced esophagitis associated with tablets (or follow tablet administration with a water bolus by syringe).

RECOMMENDED MONITORING

Consider retesting with PCR or cell culture in problem cattery situations after treatment to ensure infection has been eliminated.

PROGNOSIS AND OUTCOME

- Excellent in households with low numbers of cats
- Fair in cattery situations; recurrent cases involve large numbers of cats and poor compliance. All cats in the household must be treated with the full course of antimicrobials and proper hygiene and quarantine maintained. Concurrent infections with feline calicivirus and feline herpesvirus 1 are a common problem.

PEARLS & CONSIDERATIONS

COMMENTS

- There is some evidence that *C. felis* may infect the reproductive tract and cause vaginal discharge. Abortion and infertility have been documented in some cats infected with *C. felis*, but in general it appears that *C. felis* does not cause feline reproductive disease.
- There is experimental evidence that *C. felis* may be associated with lameness in cats.

PREVENTION

- Maintenance of environmental hygiene in catteries and disinfection of fomites with a 1:32 solution of bleach in tap water, to which detergent may be added
- Modified live and inactivated cell culture vaccines are available, which do not prevent infection or clinical signs, although the latter are reduced in severity.
    - Associated with atypical reactions in a small percentage of cats, including fever, anorexia, and lameness 7-21 days after vaccination
    - May be useful as part of a control program in catteries with endemic chlamydiosis

SUGGESTED READING

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Cheyletiellosis

BASIC INFORMATION

DEFINITION

Cheyletiellosis is a highly contagious, zoonotic skin disease of dogs, cats, and rabbits caused by the surface-living mite, *Cheyletiella* spp.

SYNONYM

Walking dandruff

EPIDEMIOLOGY

SPECIES, AGE, SEX

Young animals are more frequently affected.

GENETICS & BREED PREDISPOSITION

Long-haired cats appear to be more commonly affected.

RISK FACTORS

More common in dogs and cats from shelter and breeding establishments or that have been in boarding and grooming facilities.

CONTAGION & ZOONOSIS

- *Cheyletiella* spp. mites are very contagious and not host specific; they may transfer readily between dogs, cats, and rabbits.
- Cheyletiellosis is a zoonotic disease; humans are at risk if exposed to an infested pet (whether or not overt clinical signs are present in the pet).

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

Reason for presentation can be any combination of scaling, pruritus, or zoonosis.

PHYSICAL EXAM FINDINGS

- Scaling (“dandruff”) noted primarily over the dorsum and neck *and/or*
- Mild to moderate pruritus or over-grooming in cats *and/or*
- Dorsal erythema, papules and crusting can be noted occasionally, particularly in cats (miliary dermatitis)
- Among the exfoliated epidermal cells, *Cheyletiella* mites can be seen moving. hence the name “walking dandruff.” The term should not be overinterpreted; the mites are much smaller than skin scales, and a pet has to be very still to enable the clinician to see the subtle movement of mites carrying scales and/or the mites themselves.
- Some pets not noted by the owner to have clinical signs are presented for evaluation because of suspected zoonotic lesions in a human in contact with the animal.

ETIOLOGY AND PATHOPHYSIOLOGY

- *Cheyletiella* is a relatively large mite (0.05 mm, barely visible to the naked eye) with prominent hooklike mouth parts; it lives on the skin surface and feeds on surface debris and exudates. These mites form pseudotunnels in the surface keratin.
- The mite eggs, smaller than lice eggs, are loosely attached to hair shafts.
- The entire life cycle is completed on the host within approximately 3 weeks.
- Although adult mites may survive in the environment for 10 days off the host, eggs are shed into the environment with the pet's hair and may be an important source of reinfestation beyond those 10 days.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected from the history and clinical signs, which include any combination of scaling, pruritus, and/or zoonosis (possibly in presence of an animal without cutaneous lesions).

DIFFERENTIAL DIAGNOSIS

In dogs, differential diagnosis depends on the clinical presentation.

- If only scaling is present, differential diagnoses include:
  - Ectoparasites (fleas, lice)
  - Ill thrift or nutritional imbalance (e.g., intestinal parasitism, poor nutrition)
  - Cornification disorders (ichthyosis, primary seborrhea)
- If pruritus is present, differentials include:
  - Ectoparasites (lice, sarcoptic mange)
  - Hypersensitivities (flea bites, atopic dermatitis, food)
  - Pyoderma
  - Fungal infections *(Malassezia*, dermatophytosis)

In cats, miliary dermatitis due to other causes such as hypersensitivity (flea bites, food, environmental) and dermatophytosis should be considered, as well as other causes of generalized scaling and pruritus.

In humans, the pruritic papular eruption (papular urticaria) induced by a hypersensitivity reaction to *Cheyletiella* mites is often undistinguishable from other zoonotic (fleas, *Sarcoptes* spp., *Dermanyssus* spp.) or nonzoonotic arthropod (harvest mites, straw itch mites, bedbugs) bite reactions.

INITIAL DATABASE

- Confirmation relies on the collection and identification of the mites.
- Mites and eggs can be harvested using adhesive acetate tape (transparent “Scotch tape”) preparations, superficial skin scrapings, flea combing, fecal flotation, or simply by collecting dislodged scales from the skin surface following rubbing/petting the animal's back.
- The epidermal debris is examined with a magnifying lens or put on a glass slide, mixed with mineral oil, covered with a cover slip and examined under microscope at low power.
- The mites and eggs can be found in fairly large numbers, but occasionally they may be difficult to recover, especially in adult cats, owing to their grooming habits.

ADVANCED OR CONFIRMATORY TESTING

- *Cheyletiella* eggs and mites can sometimes be identified in a fecal flotation.
- Therapeutic trials with reliable acaricides are essential to confirm or rule out cheyletiellosis in pruritic or scaling animals with negative samplings, as well as when a human in contact has a pruritic papular eruption evocative of skin lesions caused by zoonotic arthropod bite reactions.

TREATMENT

TREATMENT OVERVIEW

- The goal of treatment is to thoroughly eradicate the mites. All affected and in-contact animals should be treated with an appropriate acaricide regardless of presence or absence of clinical signs.
- All suspected cheyletiellosis cases should be treated even if the parasite has not been isolated.
- Environmental treatment may be required in severe cases.

ACUTE GENERAL TREATMENT

- Selamectin (Revolution/Stronghold [Pfizer]) and moxidectin/imidacloprid (Advantage Multi/Advocate [Bayer]) are not approved for the treatment of cheyletiellosis but appear effective when applied topically every 2-4 weeks for a treatment course of 2 months.

- Off-labeled ivermectin remains a popular treatment option in cats and can still be a therapeutic alternative in dogs but should never be used in collies or related breeds carrying the ABCB1 (MDR1) mutation (see p. 706). The injectable product (Ivomec 1% injection for cattle and swine [Merial]) is usually given at a dosage of 0.3 mg/kg q 7 days PO or q 14 days SQ for a 6- to 8-week course of treatment. The 0.5% alcohol based pour-on ivermectin formulation (Ivomec Pour-On for cattle [Merial]) is also effective and practical when applied to the interscapular skin q 14 days at 0.5 mg/kg for 3-4 treatments.
- Milbemycin oxime (Interceptor [Novartis]) was shown to be effective in dogs but may require up to 9 weekly oral doses (at 2 mg/kg) for eradication of the mites.

POSSIBLE COMPLICATIONS

In collies and other herding breeds, the MDR1 (ABCB1) mutation can cause intoxication with commonly recommended dosages of ivermectin or other off-label macrocyclic lactones (see pp. 625 and p. 706).

PROGNOSIS AND OUTCOME

- Prognosis is excellent.
- In humans, the zoonotic infestation is transient, with resolution of the pruritic papular eruption when the mites are eradicated from the dog.

PEARLS & CONSIDERATIONS

COMMENTS

- Infested animals may show no clinical signs.
- Cheyletiellosis is possible even if there is only one animal with clinical signs among a household full of dogs and cats without any clinical signs whatsoever.
- Due to cross sensitization, a positive intradermal skin test result for the house dust mite antigen is seen in 50% of dogs with cheyletiellosis. All clinical signs resolve and intradermal reaction to house dust mites are generally negative within a few months following acaricidal therapy. This illustrates the importance of ruling out cheyletiellosis prior to testing for atopic dermatitis.

CLIENT EDUCATION

- Humans transiently infected with *Cheyletiella* spp. mites may develop an uncomfortable, pruritic papular eruption, especially on the arms, trunk, and buttocks. This should spontaneously resolve within 3 weeks when the mites are eradicated from the animals and the environment. Symptoms should prompt the person to consult with a physician.

SUGGESTED READING

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AUTHOR EDITOR: MANON PARADIS

Chemotherapy: Adverse Reactions

BASIC INFORMATION

DEFINITION

Chemotherapy targets rapidly dividing cells. However, normal proliferating cells (gastrointestinal [GI] epithelial, bone marrow, others) may be affected, resulting in adverse reactions. In addition, some chemotherapy agents cause unique toxicities.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Drugs that should not be administered to cats:
  - Cisplatin: fatal pulmonary edema
  - 5-Fluorouracil: fatal neurologic signs
- Toxicities not generally observed clinically in cats:
  - Cyclophosphamide: hemorrhagic cystitis
  - Doxorubicin: despite documented histologic changes, cardiotoxicity not seen clinically

GENETICS & BREED PREDISPOSITION

Several herding breeds (collie, Australian shepherd, Shetland shepherd, German shepherd, border collie, Old English sheepdog, and others), sight hounds (longhaired whippet and silken wind-hound), and mixed breed dogs have been reported to have mutations in the ABCB1 gene, which may result in decreased expression of P-glycoprotein (P-gp) and increased risk of toxicity with drugs that are substrates for this protein (see p. 706).

RISK FACTORS

- ABCB1 mutation (see Genetics & Breed Predisposition above): increased toxicity with P-gp substrates including vincristine, vinblastine, doxorubicin, and others
- Significant infiltration of bone marrow by neoplastic cells: myelosuppression
- Neoplastic GI involvement: GI toxicity
- Clinically ill patients may be more likely to develop adverse effects and should receive concurrent supportive care.
- Preexisting cardiomyopathy: increased risk of doxorubicin cardiotoxicity
- Preexisting renal dysfunction: increased risk of toxicity with renally excreted drugs; increased risk of cisplatin nephrotoxicity
- Preexisting hepatic dysfunction: increased risk of toxicity with drugs eliminated by the liver and possible increased risk of hepatotoxicity

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

Administration of associated chemotherapeutic agent

PHYSICAL EXAM FINDINGS

- Adverse reactions occurring during administration:
  - Allergic reactions (L-asparaginase, doxorubicin, taxanes [rarely used])
    - Facial swelling, erythema, urticaria, panting, agitation, vomiting, diarrhea, dyspnea, tachypnea, collapse, hypotension
  - Extravasation injury (vincristine/vinblastine, doxorubicin, actinomycin D, dacarbazine, mechlorethamine, cisplatin)
    - No immediate signs
    - Erythema, inflammation, licking site 7-14 days post treatment
    - Can progress to slough of skin and subcutis
  - Acute vomiting—Common: cisplatin, dacarbazine, streptozotocin. Less common: doxorubicin, cyclophosphamide, mechlorethamine, procarbazine
    - Vomiting during/within 24 hours of chemotherapy
- Delayed adverse reactions:

    - GI toxicity—Common: doxorubicin, MOPP (mechlorethamine, vincristine, procarbazine, prednisone) protocol, cisplatin, dacarbazine. Less common: vincristine, vinblastine, cyclophosphamide, CCNU (lomustine, rare), mitoxantrone, carboplatin, actinomycin
        - Vomiting, diarrhea, lethargy, anorexia 2-5 days after chemotherapy
        - Vincristine: may cause paralytic ileus and associated GI signs
        - Doxorubicin: may cause life-threatening hemorrhagic colitis
    - Myelosuppression/sepsis—Most common: CCNU, carboplatin. Possible: doxorubicin, mitoxantrone, cyclophosphamide (especially when combined with vincristine).
        - Usually no overt manifestations
        - Possible: lethargy, loss of appetite, fever with febrile neutropenia/sepsis, generally 1 week post administration
        - Neutrophil count nadir (lowest) typically occurs 7 days after ad ministration.
        - Neutrophil nadir and onset of signs with cisplatin, carboplatin, and CCNU (in cats) is more variable; can occur 1, 2, or 3 weeks post chemotherapy (rarely later) and may be prolonged
- Unique adverse reactions:
    - Cardiac toxicity (doxorubicin)
        - Arrhythmias, exercise intolerance, weakness, collapse, tachypnea, tachycardia
    - Hemorrhagic cystitis (cyclophosphamide, ifosfamide)
        - Stranguria, pollakiuria, hematuria, incontinence, pain
    - Nephrotoxicity (cisplatin, streptozotocin; uncommon: doxorubicin [cats], CCNU; extremely rare: carboplatin)
        - Often no clinical signs
        - With progression, polyuria, polydipsia, lethargy, decreased appetite
    - Hepatotoxicity (CCNU, streptozotocin)
        - Often no clinical signs
        - If progresses, icterus, lethargy, loss of appetite, GI signs, and abdominal effusion

ETIOLOGY AND PATHOPHYSIOLOGY

- Allergic reactions—L-asparaginase: type I hypersensitivity reaction. Doxorubicin: directly stimulates mast cell degranulation.
- Extravasation injury: vesicant injury to local tissue; multiple mechanisms
- Acute vomiting: irritation of chemoreceptor trigger zone
- Gastrointestinal toxicity: injury to GI crypt epithelium
- Myelosuppression/sepsis: injury to proliferating bone marrow cells causes neutropenia and possibly thrombocytopenia. Severe neutropenia allows opportunistic infection, usually by GI bacteria (usually gram-negative, but gram-positive and anaerobic infections possible).
- Cardiac toxicity: doxorubicin induces acute arrhythmias by increasing circulating catecholamines. Free radical formation by doxorubicin causes cumulative injury to myocardium and fibrosis (doses = 180-240 mg/m^2) because of low levels of cardiac catalase and because doxorubicin decreases glutathione peroxidase activity. In addition, changes in transcriptional activity alter cardiac protein expression. Consequences include arrhythmias and decreased contractility, progressing to dilated cardiomyopathy weeks to months after treatment.
- Hemorrhagic cystitis: metabolite of cyclophosphamide (acrolein) directly toxic to the bladder urothelium
- Nephrotoxicity: cisplatin, streptozotocin: tubular injury and decreased glomerular filtration (cisplatin)
- Hepatotoxicity: CCNU causes hepatocellular and ductal epithelial injury with inflammation and cholestasis, eventually progressing to cirrhosis.

DIAGNOSIS

INITIAL DATABASE

- CBC, serum biochemistry profile, urinalysis:
    - Neutropenia, possibly thrombocytopenia (myelosuppression)
    - Azotemia, low urine specific gravity (nephrotoxicity)
    - Hematuria (hemorrhagic cystitis)
    - Elevated liver enzymes (hepatotoxicity)
- Additional tests (e.g., diagnostic imaging) as determined by history, exam, and lab test results

TREATMENT

TREATMENT OVERVIEW

Control of toxic effects and prevention of secondary complications are the therapeutic goals.

ACUTE GENERAL TREATMENT

- Adverse reactions occurring during administration:
  - Allergic reactions
    - Depends on severity.
    - Dexamethasone, SP 0.2-0.5 mg/kg IV
    - Diphenhydramine, 1-2 mg/kg IM
    - Intravenous fluids, 90 mL/kg/h (dog) or 50 mL/kg/h (cat)
    - Epinephrine if severe (Dilute 1 mL of 1:1000 solution in 9 mL of 0.9% NaCl. Give 0.1 mL/kg of 1:10,000 solution IV.)
  - Extravasation injury
    - Aspirate drug back before removing catheter.
    - Apply compresses (cold for doxorubicin; warm for vincristine/vinblastine) for 10 minutes q 6 h for 72 hours after extravasation.
    - Vincristine/vinblastine: infuse 1 mL 1% hyaluronidase for each mL extravasated.
    - Doxorubicin: administer dexrazoxane (anecdotal dose used by author: 400-600 mg/m^2 IV in a different vein within 3 hours of administration; repeat at 24 and 48 hours). Topical DMSO (dimethyl sulfoxide) gel q 8 h for 14 days (wear gloves when applying) may also be helpful.
    - Wound management: E collar, clip/clean, topical or systemic antibiotic, topical or systemic antiinflammatory
    - Surgical débridement/grafting if severe
  - Acute vomiting
    - Stop administration
    - Nothing by mouth
    - Antiemetic therapy (See section on delayed vomiting for drugs and dosages below.)
    - IV fluid support if indicated
- Delayed adverse reactions:
  - Gastrointestinal toxicity
    - Nothing by mouth
    - Patient acting normally, self-limiting vomiting: antiemetics (maropitant citrate [dogs] 2 mg/kg PO q 24 h for up to 5 days (in cats has been used at 1 mg/kg PO q 24 h); metoclopramide [dogs or cats] 0.2-0.5 mg/kg PO q 8 h); water trial then bland diet trial. Decreased appetite: tempting bland foods, appetite stimulant (mirtazapine [dogs] 0.6 mg/kg, not to exceed 30 mg/d, PO q 24 h, [cats] 3-4 mg/cat PO q 72 h; or cyproheptadine [cats]: 1-2 mg PO q 12-24 h).
    - Patient acting normally, diarrhea not bloody or watery: bland diet, consider metronidazole, 15 mg/kg PO q 12 h for colitis.
    - Patient lethargic, vomiting/diarrhea continuing, or watery or bloody diarrhea: admit to hospital for supportive care.
      - Intravenous fluids
      - Antiemetics
        - Maropitant citrate (dogs and cats): 1 mg/kg SQ q 24 h, up to 5 days, *or*
        - Metoclopramide (dogs/cats): 0.2-0.5 mg/kg SQ q 8 h or IV as a CRI at 1.1-2.2 mg/kg/d (if maropitant does not control nausea; also for vincristine-induced ileus).
        - If refractory:
          - Dolasetron: (dogs/cats) 0.6-1 mg/kg IV slowly q 12-24 h
          - Ondansetron: (dogs) 0.1-1 mg/kg IV slowly q 12-24 h; (cats) 0.1-0.15 mg/kg IV slowly q 6-12 h
      - H2 receptor antagonist
        - Famotidine, 0.5-1 mg/kg IV slowly q 12-24 h
      - Antibiotic therapy if bloody vomiting/diarrhea, neutropenic, or febrile
      - Parenteral feeding if prolonged vomiting, enteral feeding tube if prolonged anorexia (rare)
      - Usually resolves in 2-3 days
  - Myelosuppression/sepsis
    - Usually no treatment required. Counts generally normalize within 2-3 days (except carboplatin-prolonged nadirs and CCNU in cats).
    - If neutrophil count < 1000 cells/mcL, consider prophylactic antibiotics for dogs. A common choice is amoxicillin/clavulanic acid, 20 mg/kg PO q 12 h for 4-7 days. For breeds other than Doberman pinschers and if dogs have normal tear production, sulfadiazine-trimethoprim, 15 mg/kg PO q 12 h for 5-7 days is an option. Cats do not usually need prophylactic antibiotics.
    - If febrile or ill, admit to hospital for intravenous fluids and intravenous antibiotics:
      - Base on culture and sensitivity if available (urine, blood, infected site)
      - Empirical treatment option while culture results pending: ampicillin, 22 mg/kg IV q 8 h, with enrofloxacin, 5 mg/kg (cats) or 10 mg/kg (dogs); dilute and give slowly IV q 24 h.
- Unique adverse reactions:
  - Cardiac toxicity (doxorubicin)

        - No treatment beyond management of cardiac disease
        - Avoid additional doxorubicin.
    - Hemorrhagic cystitis (HC)
        - Treat bacterial cystitis if present.
        - Generally self-limiting, but may take weeks to months to resolve. Some dogs show lifelong signs of cystitis.
        - Antiinflammatory: nonsteroidal antiinflammatory drug or prednisone
        - Analgesic: tramadol, 2-4 mg/kg q 8 h PO or another opioid agent
        - Oxybutynin hydrochloride (0.2 mg/kg PO q 8-12 h) has been recommended for straining, pollakiuria
        - Instillation of diluted dimethyl sulfoxide into the bladder may be helpful if refractory. Consultation with an oncologist is recommended for refractory HC.
        - After HC, cyclophosphamide should not be administered again. Often chlorambucil is substituted.
    - Nephrotoxicity
        - Discontinue drug.
        - Treatment usually not necessary, but if clinical or acute renal failure, hospitalize for therapy.
    - Hepatotoxicity
        - Discontinue drug.
        - *S* -adenosyl-L-methionine (SAMe): anecdotally may be helpful; 18 mg/kg PO q 24 h or divided dose q 12 h. Administer on empty stomach.
        - Treat hepatic dysfunction if indicated.

CHRONIC TREATMENT

Cardiac toxicity, chronic bone marrow toxicity, nephrotoxicity, and hepatotoxicity may require ongoing therapy.

DRUG INTERACTIONS

Many possible interactions of chemotherapy agents with each other and other drugs. It is the responsibility of veterinarians treating patients with chemotherapy to review possible interactions associated with each agent before administration.

RECOMMENDED MONITORING

For all patients undergoing chemotherapy:

- CBC at the expected time of the neutrophil nadir the first time they receive each drug. CBC rechecked as indicated, especially before administration of potentially myelosuppressive chemotherapy.
- Serum chemistry profile should be performed every 2-3 months or more frequently if indicated (see p. 503 , p. 501).
- Urinalysis should be performed every 6 months or more often if indicated.

PROGNOSIS AND OUTCOME

With appropriate treatment and supportive care, most patients will recover from delayed adverse reactions and those that occur during administration. Cardiac toxicity, chronic bone marrow toxicity, nephrotoxicity, and hepatoxicity generally do not resolve but may improve or stabilize.

PEARLS & CONSIDERATIONS

COMMENTS

- Clinicians treating veterinary cancer patients must know the complications associated with chemotherapeutic agents and be able to take appropriate preventive measures and manage adverse effects.
- It is essential to understand the metabolism and excretion of chemotherapy agents when treating patients with organ dysfunction, because dose reductions or avoidance of certain drugs may be necessary.
- It is also essential to understand drug interactions that might exacerbate toxicity with chemotherapeutic agents.

TECHNICIAN TIPS

- Multiple toxicities are possible during chemotherapy administration. It is critical that technicians administering these drugs know these toxicities and how to prevent them, recognize them, and manage them.
- Signs of serious chemotherapy toxicity may be as subtle as lethargy and loss of appetite. It is important to educate clients to communicate with the veterinarian and veterinary technicians if their pet is not normal to them.
- The majority of adverse effects associated with chemotherapy occur on a predictable timetable. Veterinarians and technicians

treating patients with these drugs should know when relevant toxicities would be expected and be able to recognize signs of these toxicities.
- It is important to remember that veterinary cancer patients receiving chemotherapy can develop illnesses unrelated to their cancer or chemotherapy.

PREVENTION

- Double-check all dose calculations, route of administration, and patient's history, exam, and lab test results prior to administration. Consider testing breeds at risk for MDR-1 mutation.
- Allergic reactions
  - L-Asparaginase: premedicate (20 minutes pretreatment): diphenhydramine, 2 mg/kg IM, then monitor patient 30-60 minutes post treatment. If allergic reaction, patient should not receive this drug again.
  - Doxorubicin: administer slowly (1 mg/min, not faster than 10 minutes for doses <10 mg). If allergic reaction, premedicate with diphenhydramine (as above) dexamethasone SP, 0.5 mg/kg SQ, and administer more slowly.
- Extravasation injury
  - Administer chemotherapy through intravenous catheter placed perfectly on first attempt in vein not punctured within 24 hours.
  - Comfortably restrain patient; sedate if fractious.
  - Flush catheter with 3 to 5 mL of 0.9% NaCl before and after administration.
  - Monitor site during treatment.
- Acute vomiting
  - Administer chemotherapy slowly.
  - Pretreatment antiemetic agents are given prior to cisplatin, streptozotocin, or dacarbazine administration. Options include:
    - Maropitant citrate (dog and cat): 1 mg/kg SQ 1 hour prior to chemotherapy. Effective.
    - Butorphanol (dog): 0.2-0.4 mg/kg IM 20 minutes prior to chemotherapy. Not used as frequently now that maropitant is available.
    - Dolasetron: (dog/cat) 0.6-1 mg/kg slow IV immediately prior to chemotherapy
    - Ondansetron: (dog) 0.1-1 mg/kg PO or IV slowly 30 minutes prior and 90 minutes after starting cisplatin; (cat) 0.1-0.3 mg/kg IV slowly 15 minutes before and 12 hours after chemotherapy
  - For less emetogenic agents:
    - Maropitant citrate: (dog/cat) 1 mg/kg SQ or (dog) 2 mg/kg PO; (cat) 1 mg/kg PO 1 hour prior to chemotherapy
    - Metoclopramide: (dog/cat) 0.2-0.5 mg/kg PO or SQ q 8 h starting at least 30 minutes before treatment
- Gastrointestinal toxicity
  - Double-check chemotherapy doses.
  - If patient hospitalized with gastrointestinal toxicity, reduce subsequent doses of that drug by 20%.
  - Prophylactic antiemetic if history of gastrointestinal toxicity (maropitant citrate, [dog] 2 mg/kg PO, [cat] 1 mg/kg PO q 24 h up to 5 days; or metoclopramide, 0.2-0.5 mg/kg PO q 8 h)
- Myelosuppression/sepsis
  - CBC before myelosuppressive chemotherapy. Do not treat if <2500 neutrophils/L or <150,000 plate-lets/mcL. If suspect platelet count is below normal due to chronic bone marrow injury, recommend consultation with oncologist before further chemotherapy.
  - Due to the potential for cumulative thrombocytopenia, CCNU chemotherapy may need to be discontinued if a pretreatment CBC reveals a platelet count that has decreased below the reference range.
  - Double-check chemotherapy doses.
  - CBC at expected neutrophil nadir the first time patient receives each agent
  - If neutrophil count at nadir is <1000 cells/mcL, reduce subsequent doses of that drug by 20%.
  - If overdose, treat with recombinant human granulocyte colony stimulating factor (rhG-CSF) 5 mcg/kg q 24 h SQ for 3-5 days starting 24 hours after treatment.
- Cardiac toxicity
  - Do not treat dogs with cardiotoxic agents if they have myocardial dysfunction.
  - Cardiac evaluation for breeds at risk for dilated cardiomyopathy and dogs with cardiac abnormalities (heart murmur, arrhythmia, cardiomegaly) before doxorubicin
  - Limit total lifetime cumulative doxorubicin dose to <180-240 mg/m^2; substitute noncardiotoxic agents (mitoxantrone, actinomycin-D) after 150 mg/m^2.
  - Dexrazoxane: 10 mg for every 1 mg of doxorubicin given IV within 30 minutes of each dose. Not helpful once cardiac injury present. Not used routinely in veterinary oncology, owing to cost.
- Hemorrhagic cystitis
  - Administer in morning.
  - Give furosemide (2 mg/kg PO, IV, or SQ) with cyclophosphamide.
  - Ad lib access to water
  - Encourage frequent urination.
  - After HC, cyclophosphamide should not be administered again. Often chlorambucil is substituted.
- Nephrotoxicity

    - Urine specific gravity and serum creatinine before every dose of cisplatin, streptozotocin
    - Serum biochemistry profiles and urinalyses for all patients at least every 3 months, more frequently if indicated
    - Fluid diuresis protocol required with cisplatin, streptozotocin
- Hepatotoxicity
    - Check liver enzymes with every other dose of CCNU or streptozotocin or more frequently if indicated; discontinue drug if an increase in liver enzymes is noted.
    - It is unknown whether SAMe can help prevent this toxicity.

CLIENT EDUCATION

Provide information that allows clients to recognize adverse effects of chemotherapy and encourage them to seek veterinary care promptly.

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Chagas Disease

BASIC INFORMATION

DEFINITION

Chagas disease is a relatively rare, geographically specific condition caused by infection with the hemoflagellate protozoa, *Trypanosoma cruzi*. It results in chagasic myocarditis, which is characterized by brady- and/or tachyarrhythmias with or without a dilated cardiomyopathy clinical picture indistinguishable from idiopathic dilated cardiomyopathy.

SYNONYMS

American trypanosomiasis, chagasic myocarditis

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs:

- Young dogs (<1 year of age) develop a more severe form of the acute stage of the disease which is often rapidly progressive and fatal.
- Hunting dogs may be at increased risk because of increased exposure to the vector and reservoir hosts, but house dogs have been infected.

CONTAGION & ZOONOSIS

- Humans and dogs may be infected via common source (reduviid beetle) but not directly zoonotic or contagious. Exception: blood-blood contact (e.g., animal blood on open human wound).

GEOGRAPHY AND SEASONALITY

In the United States, most canine cases occur in Texas and elsewhere along the U.S.-Mexico border. *T. cruzi* infection is a major human health problem in South America, Mexico, and Central America.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

The disease occurs in three stages:

- Acute stage, 0-4 weeks post inoculation: severe ventricular tachyarrhythmias and often fatal (sudden death or severe heart failure) in puppies and dogs <1 year of age.
- An extended latent period lasting 1-60 months. No clinical signs, but chronic changes develop. Abnormalities are found as incidental findings (e.g., on echocardiography or electrocardiography [ECG]).
- Chronic stage: overt clinical signs due to congestive heart failure or cardiac arrhythmias occurring weeks to years postinfection.

HISTORY, CHIEF COMPLAINT

Most commonly related to heart failure with or without tachy- or bradyarrhythmias. History of travel to/residence in southernmost United States, Mexico, or Central or South America.

PHYSICAL EXAM FINDINGS

- Acute stage: normal if mature dog; as below for latent stage and chronic stage for young dogs and puppies; peripheral lymphadenopathy possible.
- Latent stage: normal or signs consistent with progressive cardiac remodeling, such as weak femoral arterial pulse, soft heart murmur, arrhythmia with or without pulse deficits

- Chronic stage: brady- or tachyarrhythmias with/without pulse deficits, weak pulse, soft heart murmur, crackles or wheezes or increased bronchovesicular sounds, absent lung sounds, signs of right-sided heart failure (abdominal distension from ascites/hepatomegaly, jugular distension, positive hepatojugular reflux test). Bradyarrhythmias (e.g., AV block) seem to be more common in the chronic stage of the disease.

ETIOLOGY AND PATHOPHYSIOLOGY

- Acute stage (0-4 weeks postinoculation)
- Trypomastigotes (flagellated form) enter the blood via infected reduviid bite (*Triatoma gerstaeckeri* vector in United States) or ingestion of infected reduviid bug or infected reservoir host (armadillo, opossum, raccoon, mouse, squirrel, rat, dog). Blood transfusion–mediated and transplacental and transmammary transmission also occur.
- Trypomastigotes are taken up by monocytes and macrophages in cardiac and skeletal tissue (possibly nervous tissue) and transform into amastigotes (nonflagellated form) then multiply rapidly, leading to cell rupture.
- The amastigotes transform back to trypomastigotes prior to cell rupture. Rising parasitemia occurs, peaking at 2-3 weeks post inoculation and decreasing by 4 weeks post inoculation.
- Latent stage (4 weeks to 5 years postinoculation)
- After 4 weeks, clinical signs diminish or disappear while chronic changes develop (via myocardial necrosis/fibrosis, local coronary spasm, and possible immune-mediated pro gression +/− low levels of persistent parasitism).
- Chronic stage (months-years post inoculation)
- Progressive myocardial changes lead to systolic dysfunction (dilated cardiomyopathy), pathologic bradycardias (advanced 2nd-degree or 3rd-degree AV block), and/or congestive heart failure; ventricular tachyarrhythmias are less common than in the acute stage.
- Protective immunity does not develop in infected dogs or people.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

In puppies/young dogs with signs of heart disease living in (or traveling to) endemic areas, every effort should be made to find the organism on a blood smear or buffy coat smear. In mature dogs, a Chagas titer should be performed.

DIFFERENTIAL DIAGNOSIS

- Dilated cardiomyopathy (idiopathic)
- Other causes of myocarditis (see p. 743)
- Other causes of right heart failure (see p. 468)
- Other causes of AV block (see p. 117)

INITIAL DATABASE

- Young dog or puppy (listed from most to least useful):
  - Blood smear or buffy coat (better) stained with Giemsa or Wright stain: definitive diagnosis if organism is seen (trypomastigotes; flagellate organisms, two to three times as long as the diameter of erythrocytes). Ascitic or pleural fluid can also be tested if available.
  - With respiratory signs: thoracic radiographs are indicated. Cardiomegaly, with or without evidence of congestive heart failure (e.g., pulmonary edema), can occur.
  - With weakness, collapse, or arrhythmia in the absence of respiratory distress: ECG is indicated before radiographs (expect ventricular premature complexes/ventricular tachycardia, or 2nd/3rd-degree AV block).
  - Echocardiography is indicated to identify chamber dilation and poor systolic function if present.
  - Serum biochemistry profile: liver enzymes may show mild to moderate elevation.
  - CBC: lymphocytosis is common.
  - Serum cardiac troponin I: elevated; not specific for chagasic myocarditis
- Mature dog (listed from most to least useful):
  - Chagas titer in dogs suspected of chagasic myocarditis. Titer is typically positive by 3 weeks postinfection.
  - If dog presents with respiratory signs, thoracic radiographs should be performed and may demonstrate cardiomegaly, with or without evidence of congestive heart failure (e.g., pulmonary edema)
  - If dog presents for weakness, collapse, or arrhythmia in the absence of respiratory distress, then ECG +/− Holter monitoring (24-hour ambulatory ECG) would be indicated before radiographs.
  - Echocardiogram is indicated to define cardiac lesion responsible for clinical presentation
  - Serum biochemistry profile: liver enzymes may be mild to moderately elevated. Blood smears and buffy coat smears typically will be negative.
  - Serum cardiac troponin I may or may not be elevated; elevations are nonspecific.

CONFIRMATORY TESTING

- Acute infection:
  - Cytologic identification of trypomastigotes in blood smear, buffy coat smear, abdominal effusion, lymph node aspirates
  - Histopathologic identification of amastigotes in myocardium
- Chronic infection:
  - Serologic testing: titer is typically positive by 3 weeks post infection.
    - Indirect fluorescent antibody (offered by Texas Veterinary Medical Lab [http://tvmdl.tamu.edu/] and Idexx [www.idexx.com])
    - ELISA
    - Radioimmunoprecipitation
- Flow cytometry
- Histopathologic evaluation of tissues, as above

TREATMENT

TREATMENT OVERVIEW

Supportive treatment for arrhythmias and congestive heart failure is recommended. There is no effective treatment to eliminate the organism. Therapeutic goals are:

- Control of the organism (elimination of infection is not considered possible)
- Palliation of clinical signs caused by congestive heart failure and/or arrhythmias
- Prevention of progressive ventricular systolic dysfunction (nonspecific cardioprotective therapies)

ACUTE AND CHRONIC TREATMENT

- See Heart Failure, Acute/Decompensated, p. 468
- See AV Block,
- See Ventricular Tachyarrhythmias,
- Nifurtimox and benznidazole may be useful in the acute stage but are not FDA approved for dogs, are difficult to obtain, and have clinically significant side effects.
- Glucocorticoids: antiinflammatory dose (prednisone 0.5-1 mg/kg PO q 12-24 h) may improve survival.
- Ketoconazole, gossypol, and allopurinol have been investigated, but proof of benefit is lacking.
- Albaconazole has been shown to re duce parasite proliferation without cure.
- Verapamil decreases mortality in acutely infected mice and reduces the severity of disease in chronically infected mice; no evidence of benefit in dogs.

POSSIBLE COMPLICATIONS

Refractory heart failure and/or cardiac arrhythmias. These complications may occur rapidly (weeks to months) in young dogs and puppies and typically occur between 8 and 36 months after the acute stage in mature dogs.

PROGNOSIS AND OUTCOME

- Overt clinical signs may occur rapidly (weeks to months) in young dogs and puppies, and typically occur between 8 and 36 months after the acute stage in mature dogs.
- Acute infection: dogs recognized with acute infections may live 0-60 months postdiagnosis or longer. Young dogs (<1 year of age), puppies, and dogs with overt signs of heart failure and/or severe ventricular arrhythmias typically have a more guarded prognosis.
- Chronic infection: dogs with systolic ventricular dysfunction or arrhythmias but no external manifestations of disease may live for years before developing clinical signs. Once clinical signs develop, appropriate palliative therapy may prolong life. Dogs with clinical signs of heart failure or severe arrhythmias have a guarded long-term prognosis, but appropriate palliative therapy can prolong their lives by months to years.

PEARLS & CONSIDERATIONS

TECHNICIAN TIP

Blood specimens in veterinary practice often are handled with less care than in human medical settings; in areas where Chagas disease is endemic, blood specimens and products from infected animals should be handled with caution by all staff (risk of blood-to-blood zoonosis).

PREVENTION

- Limitation of exposure to the vector (upgrading housing, using insecticides, limiting ingestion of raw reservoir hosts, and otherwise limiting contact between dogs and reservoir hosts). Blood donors should be screened, and breeding bitches in endemic/high-risk areas should also be screened to prevent transplacental and transmammary infection.
- Vector control and limiting canine contact with reservoir hosts is the primary form of prevention.
- Blood donors from endemic areas should be screened.

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Cervical Spondylomyelopathy

BASIC INFORMATION

DEFINITION

A combination of vertebral malformation and malarticulation that affects caudal cervical vertebrae and associated ligamentous structures

SYNONYMS

CSM, caudal cervical spondylomyelopathy (CCSM), cervical malformation/malarticulation syndrome, cervical vertebral instability, spondylolisthesis, “wobbler syndrome”

EPIDEMIOLOGY

SPECIES, AGE, SEX: Most commonly encountered in middle-aged to older large-breed dogs of either sex. Some reports describe a predilection in males (2 : 1 to 4 : 1) over females.

GENETICS & BREED PREDISPOSITION

Doberman pinschers appear to be most prone to developing CSM. Other commonly-affected breeds include rottweilers, German shepherds, and dalmatians.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Most cases have histories that include progressive gait abnormalities noted for months to years.
- Occasionally, CSM patients experience an acute-onset, rapid development of neurologic dysfunction.
- With CSM, abnormalities of thoracic limb gait are usually present but can be subtle and may be overlooked. When apparent, these abnormalities manifest as a stiff, stilted thoracic limb gait.
- Other less common historic/clinical complaints include nonambulatory tetraparesis or tetraplegia, neck pain, and thoracic limb lameness.

PHYSICAL EXAM FINDINGS

- Neurologic exam findings are consistent with a C6-T2 spinal cord lesion.
  - In ambulatory dogs, a characteristic “choppy,” short-strided forelimb gait with a wide-based, ataxic hind limb gait is common.
  - Chronicity may be suspected by soft-tissue lesions of the hind paws, including excessive wear of the nails and scuffing of the skin of the dorsum of the digits (common).
  - Patellar reflexes may be increased, and there may be delayed postural reactions in the pelvic limbs (including when the patient's weight is supported—delayed hopping response from proprioceptive deficits).
  - The remainder of the neurologic examination is unremarkable.
- Classic lower motor neuron signs to the thoracic limbs are not frequently encountered in ambulatory patients (more common in nonambulatory tetraparetic or tetraplegic dogs).
- Careful palpation of the ventral processes of the cervical vertebrae, as well as side-to-side movements of the head and neck, usually reveal some evidence of pain/cervical hyperesthesia.

ETIOLOGY AND PATHOPHYSIOLOGY

- Affected dogs are believed to have a malformation/malarticulation of caudal cervical vertebrae. The resultant instability of these abnormal vertebral segments leads to hypertrophy of supportive soft-tissue structures including the intervertebral disk. Such hypertrophy and movement lead to spinal cord impingement.
- Genetic (affected breeds), nutritional (overfeeding during growth), and conformational (long neck with large head) influences have been suggested as causative or contributory.
- Vertebral malalignment (“tipping”) as seen radiographically can be part of the malformation but is not necessarily indicative of a spinal cord lesion.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Cervical spondylomyelopathy is suspected when a large-breed, middle-aged to older dog has chronic progressive ataxia affecting the hind limbs more than the forelimbs. Being able to elicit pain during careful cervical manipulation on physical exam, and evidence of chronic soft-tissue trauma to the distal hind paws, further increases the likelihood of the diagnosis. Confirmation requires diagnostic imaging: MRI is ideal, but myelography is also effective.

DIFFERENTIAL DIAGNOSIS

- Type I disk extrusion
- Type II disk protrusion
- Neoplasia
- Spinal cord cyst

INITIAL DATABASE

- CBC, serum biochemistry profile, urinalysis: generally unremarkable
- Thoracic and cervical radiographs: if other diagnoses (e.g., vertebral neoplasia) are being considered
- Imaging of the cervical spine
    - Myelography or MRI are both acceptable.
    - MRI is preferable because it images within the spinal cord parenchyma, provides superior detail, and is better tolerated by the patient.
    - With either modality, static as well as dynamic views of the spine should be obtained.

TREATMENT

TREATMENT OVERVIEW

There are two goals of treatment for all cases: a return to normal or near-normal gait and elimination of cervical pain. These goals can be achieved through the use of medications in mild cases or cases where other factors (comorbidities, financial restrictions, etc.) limit treatment to medical intervention alone. Over time in many or most cases, lesions progress to such a degree that early surgical intervention is advantageous.

ACUTE GENERAL TREATMENT

- Exercise restriction
- Low-dose oral prednisone therapy (e.g., 0.5 mg/kg PO q 12 h)

CHRONIC TREATMENT

Most patients respond only transiently if at all to medical therapy. Surgical distraction/stabilization is recommended in most cases. Some cases may require dorsal decompression.

POSSIBLE COMPLICATIONS

- Tetraparesis/tetraplegia with lesion progression
- Severe chronic cervical pain
- Self-trauma to distal limbs; secondary infections

PROGNOSIS AND OUTCOME

The majority of dogs (>80%) respond favorably to surgical distraction/stabilization. Dogs that require dorsal decompression typically have a prolonged convalescent period (i.e., they may be nonambulatory for several months postoperatively).

PEARLS & CONSIDERATIONS

COMMENTS

- Poor responses to surgical correction tend to be dramatic and are usually due to either failure of surgical implants or spinal cord compression at a site cranial or caudal to the operative site.
- The radiographic appearance alone does not correlate to the clinical impact of the lesion; imaging and examination are complementary.

TECHNICIAN TIPS

- Affected patients are often large, heavy dogs that require assistance to rise and to walk. Self-protection to minimize the risk of back injuries is essential, and technicians caring for these dogs should be familiar with proper ergonomic methods for lifting and walking with such patients.
- Neck pain in these dogs may be significant, and the neck should be handled gently; use a harness if the patient is ambulatory.

CLIENT EDUCATION

- Avoid neck extension or side-to-side movement of the neck in these dogs.
- Purpose-made foot covers/booties made from dense, resistant fabric with rubberized soles for traction may be very helpful for reducing self-trauma to the hind paws.

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Cerebellar Abiotrophy

BASIC INFORMATION

DEFINITION

The spontaneous, premature, progressive degeneration of fully developed cerebellar tissue. Specifically, it involves the loss and degeneration of Purkinje cells (most commonly) within the cerebellar cortex. In contrast, cerebellar hypoplasia is the incomplete development of the cerebellum as a result of an in utero or perinatal insult or genetic abnormality.

SYNONYM

Cerebellar cortical degeneration

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs > cats
- The age of onset varies by breed and species:
  - Early (birth to 3-4 weeks of age): beagle, miniature poodle, rough-coated collie, Irish setter, Airedale terrier, coton de tulear, Finnish harrier, Jack Russell terrier, Rhodesian ridgeback, and Samoyed
  - Onset from 6 weeks to 6 months of age: Australian kelpie, Bernese mountain dog, border collie, bull mastiff, coton de tulear, Gordon setter, Kerry blue terrier, and Labrador retriever
  - Mixed-breed cats: between the ages of 6 and 16 weeks
  - Late-onset: English sheepdog, American Staffordshire terrier, Brittany spaniel, and the Siamese and domestic short-haired cat

GENETICS & BREED PREDISPOSITION

The genetic basis, where established, is an autosomal recessive pattern, affecting both sexes equally.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Animals are normal at birth and present for progressive cerebellar ataxia or other cerebellar clinical signs beginning at the age appropriate for the particular breed.
- There is no known trauma history or toxin exposure, and the animals are usually otherwise healthy.

PHYSICAL EXAM FINDINGS

- Clinical signs reflect cerebellar dysfunction and may include:
  - Cerebellar ataxia
  - Base wide stance
  - Truncal swaying
  - Intention tremors
  - Nystagmus
  - Poor menace response with normal vision
  - Hypermetric gait with preservation of strength
  - Opisthotonos
- Postural responses and spinal reflexes are within normal limits
  - When hopping these patients, the response may be spastic and hypermetric in character.

ETIOLOGY AND PATHOPHYSIOLOGY

The cause of cerebellar abiotrophy is unknown, but it is believed to be an intrinsic metabolic defect such as a defect in glutamate metabolism, causing excitotoxic injury to the cerebellar Purkinje cells.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Cerebellar abiotrophy is a clinical diagnosis of exclusion; a definitive diagnosis is reached only through histopathologic assessment of cerebellar tissue.

DIFFERENTIAL DIAGNOSIS

- Cerebellar abiotrophy should not be confused with cerebellar hypoplasia, because hypoplasia is a nonprogressive disorder, and clinical signs are present at the onset of ambulation.
- Differential diagnoses include in-herited lysosomal storage diseases (gangliosidosis, mannosidosis, hereditary neuroaxonal dystrophy, others), inflammatory causes such as granulomatous meningoencephalitis, and congenital causes such as quadrigeminal cisternal cysts and caudal occipital malformation syndrome. Less common differential diagnoses are encephalitides caused by *Cryptococcus neoformans*, canine distemper virus, feline infectious peritonitis, *Toxoplasma gondii*, and tickborne agents.

INITIAL DATABASE

- The diagnosis is based on signalment, history, and physical and neurologic clinical exams (see p. 1311).
- Typically, initial results of diagnostic tests are normal and not useful in the antemortem diagnosis of this disorder.

ADVANCED OR CONFIRMATORY TESTING

Definitive diagnosis of cerebellar abiotrophy is gained histologically at the time of necropsy. The only gross abnormality noted is a decreased cerebellar mass (<10% of the total brain weight). Unique to the Kerry blue terrier is a pallor, gelatinous change, and cavitation of the caudate nuclei. In advanced cases of cerebellar abiotrophy, a decrease in the size of the cerebellum is appreciated on MRI, though this does not differentiate this disorder from cerebellar hypoplasia.

TREATMENT

TREATMENT OVERVIEW

Because there are no effective treatments for this progressive disorder, treatment is palliative.

BEHAVIOR/EXERCISE

Patients with cerebellar disease are at risk for injuring themselves owing to a lack of balance and coordination. Therefore, keeping them safe, possibly confined, and away from stairs and furniture from which they can fall is advisable.

PROGNOSIS AND OUTCOME

Prognosis is grave because this disease is progressive (slowly in certain breeds and rapidly in others). Rarely, the clinical signs may stabilize, as seen in the rough-coated collie.

PEARLS & CONSIDERATIONS

COMMENTS

- Cerebellar abiotrophy must be differentiated from cerebellar hypoplasia, which is a nonprogressive disease that results from the abnormal development of the cerebellum, with some differentiation of tissue.
- Unlike abiotrophy, which involves an intrinsic metabolic defect, hypoplasia results from an extrinsic cause, most notably a parvovirus. For example, kittens infected with the feline panleukopenia virus either in utero or in the perinatal period may develop cerebellar dysfunction secondary to cerebellar hypoplasia. The virus causes inflammation and destruction of cells in the external germinal layer of the cerebellum, which results in failure to reach normal size.
- Another difference between hypoplasia and abiotrophy is that with hypoplasia, clinical signs are first noted at the onset of ambulation. Because of the disease's nonprogressive nature, most cats will compensate for the dysfunction, or the clinical

signs may lessen. Therefore, this disease carries a more favorable prognosis than cerebellar abiotrophy.

SUGGESTED READING

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Caudal Occipital Malformation Syndrome

BASIC INFORMATION

DEFINITION

A congenital malformation of the skull (caudal occipital bone region) that results in intracranial overcrowding and compression of the cervicomedullary junction at the level of the foramen magnum.

SYNONYMS

Chiari type I malformation, Chiari-like malformation, COMS, occipital bone hypoplasia

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Small-breed dogs predisposed; Cavalier King Charles spaniel (CKCS) overrepresented
- Variable age of onset of signs; mean age at diagnosis is 3-6 years. Age of onset/presentation appears to be decreasing, with more dogs being presented at younger than 1 yr of age.

GENETICS & BREED PREDISPOSITION

- Cavalier King Charles spaniel
  - Most common
  - Evidence of heritability, but mode of inheritance has not been determined
- Yorkshire terriers
- Miniature/toy poodles
- Maltese
- Brussels griffon

ASSOCIATED CONDITIONS & DISORDERS

- The vast majority of dogs with COMS also have syringomyelia, usually affecting the cervical spinal cord.
- Other malformations of the craniocervical junction have recently been identified in dogs, which may occur alone or in conjunction with abnormalities of the occipital region: hydrocephalus, intracranial intraarachnoid cysts (quadrigeminal cysts), and malformation of the C1 and/or C2 vertebrae (similar to basilar invagination in people).

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Dogs present for a wide variety of clinical manifestations, the most common of which are cerebellovestibular dysfunction and cervical myelopathy.
- A unique presentation of dogs with COMS that have concurrent cervical syringomyelia is incessant scratching at the shoulder region and head/neck region (suspected paresthesia). This appears to be most consistent in the CKCS breed.
- In a small percentage of COMS cases, seizure activity is the chief complaint.
- Clinical signs are often intermittent, often worsening in periods of stress or excitement.

PHYSICAL EXAM FINDINGS

- General examination is usually normal.
- Neurologic examination (see p. 1311) is usually indicative of cervical myelopathy (e.g., upper motor neuron signs to all four limbs), cerebellovestibular dysfunction (head tilt, resting nystagmus, circling, loss of balance, cerebellar ataxia, intention tremor, loss of menace response despite normal vision), or both.
- Neck and/or head pain is often detected on palpation.

ETIOLOGY AND PATHOPHYSIOLOGY

- The underlying problem is a malformed caudal occipital bone region, which is probably an inherited trait.
- The malformed occiput leads to cerebellar compression and constriction of the cervicomedullary junction at the level of the foramen magnum.
- Over time, the meninges at the constricted cervicomedullary junction become progressively hypertrophied.
- Pressure in intracranial and spinal compartments increases over time; CSF and/or extracellular fluid (more likely) is preferentially diverted into the spinal cord (with resultant syringo-hydromyelia).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is strongly suspected based on breed and presenting clinical signs, especially characteristic neurologic deficits. Exclusion of differential diagnoses is required, and confirmation of COMS is achieved with diagnostic imaging (MRI +/− CT) and cerebrospinal fluid (CSF) analysis.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis depends on the nature of the neurologic dysfunction in an individual patient:

- For example, in a dog with COMS that has multifocal central nervous system dysfunction, a likely differential diagnosis is granulomatous meningoencephalomyelitis.
- In a dog with COMS manifesting with neck pain alone, a likely differential diagnosis is intervertebral disk disease.

INITIAL DATABASE

- The diagnosis of COMS is dependent on MRI, especially the midsagittal T2-weighted view.
- In some cases, CT may also be necessary to completely assess bony abnormalities.
- CSF analysis is often performed to rule out concurrent inflammatory brain/spinal cord disease.

TREATMENT

TREATMENT OVERVIEW

The therapeutic goal is to halt disease progression and achieve either improvement or resolution of clinical signs of neurologic dysfunction; in most cases, this can be achieved most effectively with surgical correction.

ACUTE GENERAL TREATMENT

- Most dogs respond favorably to oral prednisone therapy (e.g., 0.5 mg/kg PO q 12 h, tapering if chronic use).
- Excessive scratching activity is usually ameliorated with oral gabapentin (10 mg/kg, PO, q 8 h).
- Pregabalin (2 mg/kg, PO, q 12 h initial dose) may also be effective for pain and scratching.
- Oral tramadol (2-4 mg/kg q 8-12 h) may also help relieve pain associated with this disorder.

CHRONIC TREATMENT

In most cases, surgical decompression of the foramen magnum (FMD) is indicated to achieve long-term therapeutic success.

POSSIBLE COMPLICATIONS

- Adverse effects of long-term corticosteroid administration
- Potential surgical complications include intraoperative/early postoperative death (rare), postoperative worsening of neurologic status (uncommon and usually temporary), and need for future reoperation (typically due to excessive scar formation at FMD site).

PROGNOSIS AND OUTCOME

- Most dogs respond favorably to medical therapy; however, the disease tends to progress over time. In one study, 5 of 10 dogs with COMS that were treated medically were euthanized within 2 years because of disease progression.
- Surgical therapy (FMD) is associated with an 81% success rate. A reoperative rate of 25%-47% has been reported. The

reoperative rate for FMD appears to be much lower when the decompression is combined with cranioplasty.

PEARLS & CONSIDERATIONS

COMMENTS

- Incessant scratching at the region of the shoulder (paresthesia) is a disproportionately common chief complaint with COMS and syringomyelia.
- Success of surgery appears to be inversely related to duration of clinical signs before surgical intervention.
- Anecdotally, the author and colleagues have seen substantially fewer postoperative recurrences (requiring reoperation) in cases that underwent cranioplasty in conjunction with FMD (<10%).

SUGGESTED READING

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Cataracts

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Any opacity, regardless of size, of the lens or its capsule is termed a *cataract*. A cataract results from a change in the lens protein composition or lens fiber arrangement and is one of the most common canine ocular abnormalities.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs and cats
- Variable age of onset depending on breed and cause
- Cataracts affect 16.8% of mixed-breed dogs ages 7-15+ years.

GENETICS & BREED PREDISPOSITION

- In dogs, most cataracts have an inherited component; most common mode of inheritance is autosomal recessive.
- Breeds of dogs with the highest prevalence of cataracts include: smooth fox terrier, Havanese, bichon frise, Boston terrier, poodles (toy, miniature, standard), silky terrier, American cocker spaniel, and miniature schnauzer. Cataracts have been reported in most purebred dog breeds.
- Canine cataracts can also occur secondary to diabetes mellitus, which has a genetic predisposition in some breeds (see p. 297)
- Presumed congenital feline cataracts reported in Persian, Birman, Himalayan, and domestic shorthair

RISK FACTORS

Diabetes mellitus, hypocalcemia, anterior uveitis, age, nutritional imbalance (milk replacement formulas), intoxication, retinal degeneration, retinal detachment, lens luxation, electric shock, radiation therapy/injury, when primary beam near or on globe

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Cataracts are classified by age at onset, location, and severity, in addition to etiology.

- Age at onset: congenital, present at birth; juvenile, few months to 6 years; senile, >6 years
- Location: capsule, anterior/posterior; cortex, anterior/posterior or equatorial; nucleus
    - Severity: incipient, <10% of retinal examination obstructed; immature (early, 10%-50% of retinal examination obstructed; late, 50%-99% of retinal examination obstructed); mature, 100% of retinal examination obstructed; hypermature, liquefaction/resorption with associated lens-induced uveitis (see p. 1151); morgagnian: nucleus falls ventrally in the capsule

HISTORY, CHIEF COMPLAINT

- Vision disturbance
- Cloudy white pupil
- The chief complaint may reflect a systemic cause of cataracts (e.g., polyuria/polydipsia, weight loss with diabetes mellitus)

PHYSICAL EXAM FINDINGS

- Opacity of the lens (unilateral or bilateral) with any or all of the following:
    - Anterior uveitis (see p. 1151)
    - Glaucoma (see p. 448)
    - Lens subluxation/luxation (see p. 644)
    - Retinal degeneration, retinal detachment (see and p. 985)
    - Systemic abnormalities may be present when cataracts are caused by a generalized disorder (e.g., weight loss with diabetes mellitus).

ETIOLOGY AND PATHOPHYSIOLOGY

- Regardless of etiology, all cataracts occur through a change in the lens protein composition or lens fiber arrangement:
  - Inherited: numerous breeds of dogs, some cats
  - Diabetes mellitus: increased blood glucose results in diffusion of increased glucose into the lens, overwhelming standard metabolism of the lens, causing excess glucose to be shunted to the sorbitol pathway, which forms polyols and subsequently osmotically draws water into the lens, causing opacification (dogs)
  - Secondary to intraocular disease: Uveitis, glaucoma, retinal degeneration/detachment, lens luxation
  - Trauma to lens: blunt or penetrating
  - Age-related
  - Nutritional: in puppies and kittens fed milk replacer. Proposed mechanism: amino acid deficiency, such as arginine, at crucial stage during lens development
  - Hypocalcemia (see p. 576)
  - Radiation therapy/injury (see p. 963) when primary beam near or on globe
  - Medications (e.g., long-term oral ketoconazole; mostly in young, large-breed dogs given higher doses [6-13.9 mg/kg/d])
  - Toxins (e.g., dinitrophenol; diazoxide)
  - Electric shock
- Not all cataracts are progressive.
- Cataracts can progress to become hypermature and result in lens-induced uveitis and increased risk of vitreal degeneration, retinal detachment, and secondary glaucoma

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis of cataract is suspected based on observation of a cloudy pupil in an animal that may be visually compromised. It is confirmed by the finding of a lens opacity following complete dilation of the pupil.

DIFFERENTIAL DIAGNOSIS

- Nuclear/lenticular sclerosis: normal aging change; usually seen in animals =7 years old; does not cause vision loss; center of lens becomes opalescent to hazy, but tapetal reflection in pupil (usually greenish) is still visible, versus cataracts, which obstruct this reflection
- Hyperlipidemia, which may result in lipid aqueous flare. This will obstruct the ability to see the iris and pupil. Most common in the miniature schnauzer.
- Diseases causing diffuse corneal edema (bluish-white opacity on *cornea*, not in pupil; may obstruct ability to see the pupil) including glaucoma, anterior uveitis, corneal endothelial degeneration or dystrophy
- Diseases causing secondary cataracts:
  - Retinal degeneration or detachment
  - Anterior uveitis (cataracts typically incomplete if due to inflammation; uveitis may also occur secondary to cataracts; if cataracts occupying large extent of lens in predisposed breed, assume lens-induced uveitis)
  - Lens luxation

INITIAL DATABASE

- Complete ophthalmic examination(see p. 1313) including:
  - Menace response
  - Evaluation of pupil size, symmetry, and pupillary light reflexes
  - Intraocular pressure (IOP): rule out glaucoma (>25-30 mm Hg)
  - After IOP assessment (assuming normal result), dilate pupil with 1% tropicamide
  - Penlight or transilluminator to characterize the cataract, evaluate for concurrent uveitis
  - Fundic (posterior segment) examination using indirect or direct ophthalmoscopy
- Blood and urine glucose determination (dogs primarily)

ADVANCED OR CONFIRMATORY TESTING

- CBC, serum biochemistry profile, and urinalysis to rule out systemic metabolic disease (e.g., diabetes mellitus, hypocalcemia) as cause of cataracts and/or to assess patient before considering referral for possible cataract surgery
- Ocular ultrasound if the cataract is immature or worse in severity and precludes accurate evaluation of the posterior segment of the eye
- Electroretinogram (ERG; see p. 1253) to assess retinal function (routinely conducted by veterinary ophthalmologists before

cataract surgery)

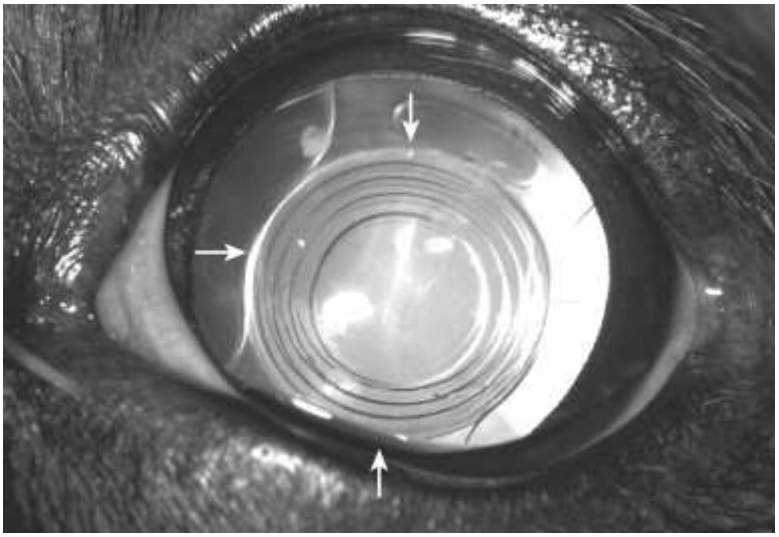
TREATMENT

TREATMENT OVERVIEW

- Incipient and nonprogressive early immature cataracts do not require treatment.
- Progressive immature, mature, and hypermature cataracts are treated to:
  - Restore vision (i.e., cataract surgery)
  - Prevent secondary sequelae of cataracts: uveitis, glaucoma, and retinal detachment
  - Referral to a veterinary ophthalmologist may help greatly in triage, diagnosis, and treatment of cataracts.

ACUTE GENERAL TREATMENT

- Treat associated uveitis with topical mydriatics and antiinflammatories (see p. 1151).
- Treat secondary glaucoma accordingly (see p. 448).
- Referral for cataract surgery if cataract is vision threatening and animal systemically stable (e.g., concurrent diabetes mellitus is controlled):
  - Cataract surgery requires preliminary ocular ultrasound and ERG that indicate the posterior segment of the eye is normal.
  - Phacoemulsification (ultrasonic lens fragmentation) to remove the cataract:
    - Followed by implantation of an artificial intraocular lens to restore emmetropia (normal vision, neither far- nor near-sighted)
    - Without an intraocular lens implant, animals are 14 diopters hyperopic (far-sighted) with little useful vision.



CATARACTS Canine eye 6 months after cataract surgery and foldable, acrylic intraocular lens implantation. The pupil has been dilated, and the intraocular lens implant is centered within the pupil.

CHRONIC TREATMENT

- After cataract surgery, treat as directed by the veterinary ophthalmologist:
  - Topical antibiotics and antiinflammatories
  - Exercise restriction/Elizabethan collar: 2 weeks
  - Antiinflammatory therapy may be continued in a decreasing fashion for months or, in some cases, indefinitely.
  - Frequent reevaluation of intraocular lens position, IOP, retinal examination, and inflammation control
- If cataract surgery is not an option:
  - Monitor cataracts for progression, and treat associated uveitis with topical antiinflammatories (see p. 1151) long term.
  - Use IOP-lowering drugs in combination with antiinflammatories if secondary glaucoma develops (see p. 448).
  - Enucleation or evisceration and intrascleral prosthesis of end-stage, blind, painful globes

DRUG INTERACTIONS

Corticosteroids (topical ophthalmic or oral) may interfere with management of diabetes mellitus.

POSSIBLE COMPLICATIONS

- Without cataract surgery, the following can occur: uveitis, glaucoma, lens luxation, retinal detachment, blindness.
- After cataract surgery, the following can occur: uveitis, glaucoma corneal ulceration, surgical wound/incisional dehiscence, intraocular infection (see p. 583), retinal detachment, intraocular lens displacement, lens capsule fibrosis (lessened through the use of new foldable, acrylic IOL implants), corneal endothelial degeneration and secondary corneal edema, keratoconjunctivitis sicca.

RECOMMENDED MONITORING

- Without cataract surgery, monitor for cataract progression and secondary complications (see Possible Complications above) q 2-4 mon, or more or less frequently, depending on the extent of cataract, rate of cataract development, and presence or absence of associated ocular complications.
- After cataract surgery, monitor according to veterinary ophthalmologist's recommendations; generally involves:
  - Reevaluations at postoperative weeks 2, 8, and 20
  - Long-term follow-up q 6-12 mon for life
  - In addition to routine ophthalmic examinations, Schirmer tear test, IOP, menace response, and pupillary light reflexes should be evaluated each time the animal is presented to the veterinarian.

PROGNOSIS AND OUTCOME 

- Rate of cataract progression variable depending on cause and location of the cataract and age of the animal
- Success of cataract surgery (i.e., phaco-emulsification), as determined by a positive visual outcome, is 90%-95%.
- Success is increased with early referral (i.e., before animal is blind) and surgery, and with diligent postoperative monitoring and treatment.

PEARLS & CONSIDERATIONS 

COMMENTS

- Early referral and prompt surgical intervention before the onset of hyper-maturity and lens-induced uveitis will result in a more successful outcome.
- Animals affected with cataracts, regardless of the severity, should not be used for breeding unless it is known specifically that the cataract is of nongenetic origin.

PREVENTION

- Ophthalmic screening of animals used for breeding by a board-certified veterinary ophthalmologist and registration through the Canine Eye Registration Foundation (http://www.vmdb.org/cerf.html) will help to remove affected animals from the breeding population.
- Prompt treatment of intraocular inflammation will decrease the likelihood of secondary cataracts.
- Early diagnosis and proper management of diabetes mellitus will help prevent cataract formation, but even the most well-managed diabetics may still develop cataracts. Once present, cataracts caused by diabetes mellitus are irreversible and will not resorb, even with good diabetic control.
- In the future, use of aldose reductase inhibitors and antioxidants may have a role in the delay and prevention of cataracts.

CLIENT EDUCATION

- It is essential that clients understand that not all cataracts are progressive.
- If a cataract is progressive, the client must make a decision with regard to surgery.
- Although surgery is associated with some risks, not opting for surgery is also associated with risks of lens-induced uveitis, secondary glaucoma, retinal detachment, and ocular pain.
- Animals undergoing cataract removal surgery that do not receive an intraocular lens implant have vision that, in human equivalence, is worse than 20/400 and corresponds to being “legally blind.”

SUGGESTED READING

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Castor Bean Toxicosis

BASIC INFORMATION

DEFINITION

Acute clinical signs, commonly including vomiting and diarrhea, initially and frequently progressing to coma and death. May occur in dogs or cats, as a result of eating castor beans.

SYNONYMS

African coffee tree, Mexico weed, mole bean, Palma Christi, wonder tree, *Ricinus communis*

EPIDEMIOLOGY

SPECIES, AGE, SEX

All breeds, ages, and both sexes susceptible; dogs involved more often than cats

RISK FACTORS

Presence of castor beans in pet's environment

GEOGRAPHY AND SEASONALITY

- Year round; more cases in October and November when castor beans mature and are released from their spiny pods
- Castor beans for jewelry and other ornamental purposes are available throughout the year.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- History of exposure to castor bean plant or ornamentals (e.g., jewelry)
- Lag period: 6-12 hours (up to 48 hours) before signs appear
- Vomiting and diarrhea (with or without blood), anorexia, lethargy

PHYSICAL EXAM FINDINGS

- No remarkable physical exam findings if recent exposure (<6 hours)
- Within 6-48 hours of exposure, anorexia, depression, lethargy, mild to severe vomiting, diarrhea, and abdominal tenderness may begin.
- In severe cases, dehydration, weakness, tremors, or seizures can ensue.
- Tachycardia, hypotension, and shock may be present (potentially fatal).
- Presence of castor beans or leaves in the vomitus

ETIOLOGY AND PATHOPHYSIOLOGY

- Castor bean is a large decorative, ornamental, Caribbean plant now present throughout the warmer parts of the United States. The beans are commercially grown for castor oil or may be used for ornamental purposes (e.g., jewelry). The plant produces spiny pods that burst open after drying, releasing seeds. The seeds have color markings resembling some ticks or beetles.
- All parts of the castor bean plant contain ricin and therefore are considered toxic if ingested; the highest concentration of ricin is in the bean. Ricin, a heterodimeric glycoprotein, is a cellular toxin (toxalbumin) that inhibits protein synthesis, causing cell death. Cell death results in vomiting, diarrhea, abdominal pain, and hemorrhages.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A working diagnosis made based on history/evidence of exposure (evidence of chewed up leaves/seeds in vomitus) and onset of vomiting, diarrhea, anorexia, or lethargy several hours after the ingestion.

DIFFERENTIAL DIAGNOSIS

- Dietary intolerance/garbage toxicosis
- Sago palm toxicosis
- Pancreatitis
- Viral and bacterial gastroenteritis
- GI tract obstruction

INITIAL DATABASE

- CBC: leukocytosis
- Serum biochemistry profile
  - Elevated alanine aminotransferase, aspartate aminotransferase, and lactate dehydrogenase, indicative of liver damage
  - Increased blood urea nitrogen and serum creatinine: may be renal or prerenal
  - Increased serum albumin and globulin possible, suggesting dehydration
- Changes may be seen 12-24 hours after ingestion.

ADVANCED OR CONFIRMATORY TESTING

Postmortem findings may include necrosis and hemorrhages in the heart, stomach, GI tract, lungs, liver, kidney, and pancreas.

TREATMENT 

TREATMENT OVERVIEW

- Risk of death means that treatment is implemented based on reasonable clinical suspicion alone (history of possible or proven exposure). If clinical signs are absent, treatment consists of patient decontamination and a period of monitoring. With overt clinical signs, intensive supportive care is indicated. Therapeutic goals are decontamination of patient, protecting GI mucosa, and supportive care.

ACUTE GENERAL TREATMENT

- Decontamination of patient:
  - Emesis: only animals not showing any clinical signs (see p. 1364). May be effective within several hours after exposure, especially if seeds have been ingested, since seeds are hard to digest
  - Gastric lavage (see p. 1281): only if a potentially lethal dose has been ingested (see Pearls & Considerations below) and emesis cannot be induced (comatose animal)
  - Activated charcoal 2-4 g/kg PO; may be effective even several hours after exposure if seeds have been ingested. Protect airway with cuffed endotracheal tube if patient is unconscious.
- Protect GI mucosa:
  - Administer GI protectants such as sucralfate (0.5-1 g/dog, or 125-250 mg/cat) PO q 8-12 h and H2 blockers (e.g., famotidine, 0.5 mg/kg PO, SQ, IM, or IV q 12-24 h
  - Control severe vomiting with metoclopramide (0.1-0.4 mg/kg PO, SQ or IM q 6 h) or maropitant (1 mg/kg, SQ, q 24 h for up to 5 doses), provided no evidence of GI obstruction is present.
- Supportive care:
  - IV fluids for 2-3 days or as long as needed, typically at 1.5 to 2 times maintenance rates
  - Diazepam for seizures (0.5-2 mg/kg IV PRN)
  - Lactulose (15-30 mL PO q 6-8 h in dogs; 0.25-1 mL PO q 8-12 h in cats) may reduce the risk of hepatic encephalopathy if acute hepatic injury (see p. 503) has occurred
  - SAMe (*S*-adenosylmethionine), 18 mg/kg PO in dogs and cats q 24-72 h for 1-3 months for hepatic injury
  - Dietary management: soft bland diet in small amounts for 1-5 days

CHRONIC TREATMENT

Management of chronic hepatopathy (see p. 212)

POSSIBLE COMPLICATIONS

Possible liver or renal compromise

RECOMMENDED MONITORING

- CBC
- Liver enzymes on presentation: q 24, 48 h, or until resolution of signs
- Kidney profile on presentation: q 24, 48 h, or until resolution of signs
- Serum electrolytes
- Blood pressure and heart rate

PROGNOSIS AND OUTCOME 

- Prognosis depends on the amount ingested and whether the beans were chewed or broken (prognosis worse) and if spontaneous vomiting occurred after the ingestion (prognosis better— self-decontamination).
- Most dogs respond well to supportive treatment.
- Poor prognosis if multiple organ damage, shock, or seizures occur.
- Mortality rate in dogs ingesting castor beans is approximately 9%.

PEARLS & CONSIDERATIONS 

COMMENTS

- Severity of signs increases if the seed is chewed open. Ricin is not likely to be released from the seed unless the coat is masticated, broken, or damaged.
- All known or potential ingestions should be considered serious and treated aggressively to avoid serious consequences.
- In humans, ingestion of 1-8 seeds can be lethal; the same may be true for dogs or cats.
- The toxalbumin is one of the most deadly substances known. Lethal dose in mice is 0.025 mg/kg IP and 1 mg/kg PO in humans.
- Latin name *(Ricinus)* means “insect,” since beans resemble some ticks or beetles.

PREVENTION

Keep castor beans out of reach of pets.

SUGGESTED READING

Albretsen JC, et al: Evaluation of castor bean toxicosis in dogs: 98 cases. J Am Anim Hosp Assoc 36:229–233, 2000.

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1ST EDITION AUTHOR: SAFDAR A. KHAN

Carpal Ligament Trauma/Breakdown

BASIC INFORMATION

DEFINITION

Carpal trauma includes ligamentous (sprain), fibrocartilaginous (hyperextension), fracture, or shearing injuries.

SYNONYMS

Palmar carpal breakdown, carpal laxity syndrome

EPIDEMIOLOGY

GENETICS & BREED PREDISPOSITION

Racing greyhounds: accessory carpal bone fractures. Carpal laxity syndrome: rapidly growing large/giant breed dogs.

RISK FACTORS

Racing or agility activities; distal forelimb trauma

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Sprains (hyperextension)
- Fractures
- Shearing/degloving wounds
- Coaptation-related injuries, including pressure sores from casts or splints; dermatitis from soiled bandages; and wound infection or dehiscence from old, dirty dressings

HISTORY, CHIEF COMPLAINT

- Forelimb trauma
- Lameness after competition; slowing or drifting wide on racetrack turns

PHYSICAL EXAM FINDINGS

- Lameness
- Carpal swelling
- Open wounds around the carpus
- Pain or crepitation during palpation of the carpus
- Gross instability characterized by plantigrade stance
- Gross instability characterized by “broken over” or flexed carpal stance

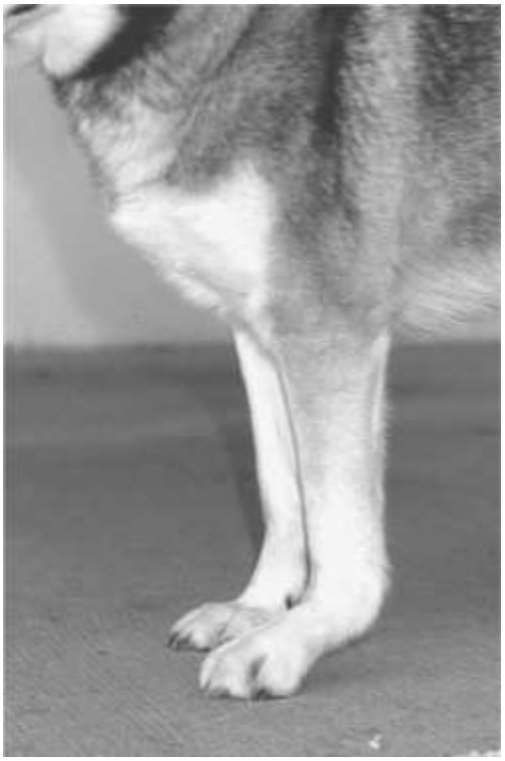
ETIOLOGY AND PATHOPHYSIOLOGY

- Track animals racing counterclockwise are predisposed to right-sided injuries (80%).
- In pets, carpal fractures (usually radial carpal bone) are less common than ligament injury.
- In racing animals, fractures usually involve the accessory carpal bone.
- Carpal laxity syndrome: potential ligamentous weakness

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis of carpal injury is based on physical and radiographic examinations.



CARPAL LIGAMENT TRAUMA/BREAKDOWN Lateral view of a mature malamute with a left forelimb lameness due to palmar carpal breakdown after a jump from a deck. Note hyperextension of the left carpus.

DIFFERENTIAL DIAGNOSIS

- Autoimmune polyarthropathy (systemic lupus erythematosus, rheumatoid arthritis)
- Infectious (Lyme borreliosis, rickettsial diseases)

INITIAL DATABASE

- Mediolateral and dorsopalmar radiographic projections of the distal limb (pes and carpus)
- CBC and chemistry panel based on American Society of Anesthesiologists (ASA) patient classification (see p. 1372)
- Electrocardiography and thoracic radiography (if part of massive trauma)

ADVANCED OR CONFIRMATORY TESTING

- Oblique radiographic views to outline nondisplaced fractures
- Stress radiography (mediolateral radiograph with carpus manually forced into hyperextension) for localizing joint instability

TREATMENT

TREATMENT OVERVIEW

The goal of therapy is to reestablish anatomic or functional joint and limb activities:

- Fractures: stabilization and anatomic reduction
- Ligamentous injuries: reestablishment of carpal support with ligament repair or arthrodesis
- Shearing injuries: wound management

ACUTE GENERAL TREATMENT

- Minimally displaced, nonarticular fractures, grade I, and most grade II ligament sprains are externally splinted for 6-8 weeks.
- Luxated joints, intraarticular fractures, and grade III sprains are initially supported in a modified Robert-Jones bandage until definitive surgery.

- Carpal laxity syndrome: soft exercise surfaces, with or without splintage
- Shearing injuries, after initial wound management protocols, are covered and supported until definitive treatment is performed.
    - Gentle lavage using warm saline, lactated Ringer's solution, dilute chlorhexidine solutions of open wounds to reduce gross contamination (patients are sedated and given analgesics).
    - Coverage of tissues with moistened (above solutions) gauze sponges useful in débridement (wet-to-dry-bandages), since they are changed daily.
    - Alternatively, direct application of sugar or honey has been used to reduce infection and promote healing in highly contaminated, traumatic open wounds, but the role of such treatment in the joint space is unclear.
    - Final surgical débridement and joint lavage can be performed during orthopedic stabilization surgery.
    - Wounds with healthy granulation tissue, reduced contamination, and early epithelialization can be closed with sutures or covered with a non-adherent dressing and allowed to heal via second intention.

CHRONIC TREATMENT

- Surgical repairs require 6-12 weeks of external coaptation (e.g., splint, cast, or external fixator) and exercise restriction.
- Radial carpal bone luxation is treated with open joint tissue repair.
- Large radial carpal and accessory carpal bone fractures are treated with lag-screw fixation.
- Small radial carpal and accessory carpal bone fractures are excised and have good outcomes.
- Avulsion fractures are treated with tension band techniques.
- Hyperextension injuries are managed with partial carpal arthrodesis (middle and distal carpal joints) or pancarpal arthrodesis (injuries involving the antebrachial carpal joint).
- Collateral ligament injuries are primarily repaired or replaced with synthetic suture.

POSSIBLE COMPLICATIONS

- Reduction/implant failure
- Delayed or failed arthrodesis
- Wound infection
- Coaptation-related morbidity
- Degenerative joint disease

RECOMMENDED MONITORING

- Lameness evaluation 1-3 months after injury and treatment
- Serial radiographic studies to evaluate fracture healing or progression of arthrodesis

PROGNOSIS AND OUTCOME 

- Good to excellent for noncompeting dogs
- Variable for athletic dogs needing to return to preinjury competition levels
- Severe shearing injuries with neurovascular compromise may necessitate limb amputation.

PEARLS & CONSIDERATIONS 

COMMENTS

- Complete palmar carpal breakdown (grade lll sprain) requires pancarpal arthrodesis.
- Intraarticular fractures, when treated conservatively, rarely heal with osseous bridging, thus leading to degenerative joint disease.
- Partial carpal arthrodesis can promote a return to most preinjury activities.
- In racing greyhounds, treatment of radial carpal or accessory carpal bone fractures with lag-screw fixation (preferred) or fragment excision provides a return to competitive performance.

SUGGESTED READING

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Carnitine Deficiency

BASIC INFORMATION

DEFINITION

Carnitine is an amino acid derivative. Carnitine deficiency is a relatively uncommon condition characterized by inadequate quantities of L-carnitine in blood, skeletal muscle, and cardiac muscle (systemic carnitine deficiency) or normal to elevated levels of carnitine in blood and low levels in cardiac muscle (myopathic form of carnitine deficiency).

SYNONYMS

Since L-carnitine is the biologically active isomer, the terms *carnitine* and *L-carnitine* are used interchangeably in the clinical setting.

EPIDEMIOLOGY

SPECIES, AGE, SEX

l-carnitine (β-hydroxy-γ-trimethylaminobutyric acid) appears to be a conditionally essential nutrient for dogs and cats. Although not essential under normal circumstances, deficiency can occur in certain cases secondary to decreased carnitine synthesis, decreased dietary intake, intestinal malabsorption, increased renal loss (such as with cystinuria), or membrane transport defects.

GENETICS & BREED PREDISPOSITION

- Cats: none reported
- Dogs: members of isolated families of various breeds, including American cocker spaniels and boxers, may develop carnitine deficiency. Breeds that develop cystinuria or urate urolithiasis may develop carnitine deficiency. Breeds predisposed to ceroid lipofuscinosis may also develop carnitine deficiency.

RISK FACTORS

- Cats: rapid weight loss in obese cats, idiopathic hepatic lipidosis
- Dogs: some dogs with cystinuria are also carnitinuric and develop carnitine deficiency due to excessive renal loss of carnitine. Dogs consuming vegetarian diets or protein-restricted diets that are not supplemented with carnitine may also develop carnitine deficiency.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Cats: idiopathic hepatic lipidosis. No cardiac effects of carnitine deficiency have been identified.
- Dogs: dilated cardiomyopathy (DCM), lipid-storage myopathy, juvenile-onset distal myopathy (rottweilers), ceroid lipofuscinosis (Tibetan terriers), and male infertility

HISTORY, CHIEF COMPLAINT

- Cats: compatible with idiopathic hepatic lipidosis (rapid weight loss in obese cats)
- Dogs: compatible with congestive heart failure (exercise intolerance and weight loss progressing to cough, respiratory distress, and eventually, ascites); compatible with myopathy; compatible with ceroid lipofuscinosis

PHYSICAL EXAM FINDINGS

- Cats: obesity; signs of idiopathic hepatic lipidosis (icterus, hepatomegaly, dehydration)
- Dogs: DCM; variable combinations of tachypnea, dyspnea, tachycardia, and lethargy
- Lipid-storage myopathy; stilted gait and muscle weakness
- Ceroid lipofuscinosis; progressive visual deterioration, behavioral changes, seizures, ataxia, and various degrees of motor and sensory dysfunction

ETIOLOGY AND PATHOPHYSIOLOGY

- Sources of carnitine include endogenous synthesis in the liver from lysine and methionine or dietary intake. Beef and lamb are the best dietary sources of carnitine; plant proteins generally are poor dietary sources of carnitine.
- In the body, 95%-98% of carnitine is stored in skeletal and cardiac muscle. Carnitine is necessary for transport of fatty acids into the mitochondria, the site of ATP generation for cardiac function. The heart obtains 60% of its total energy production from oxidation of long-chain fatty acids; therefore carnitine deficiency can result in cardiac dysfunction.
- Another important function of carnitine is its buffering capacity; prevents buildup of acyl-CoA derivatives in the mitochondria that inhibit oxidative metabolism.
- Dogs: myopathic form of carnitine deficiency occurs in some dogs with DCM and is thought to result from a membrane transport defect. Systemic form of carnitine deficiency can also result in DCM and may result from increased renal loss (such as with cystinuria) or inadequate dietary intake of carnitine or its precursor amino acids (such as with vegetarian or protein-restricted diets). Carnitine deficiency associated with ceroid lipofuscinosis is thought to involve a defect in the carnitine biosynthetic pathway involving e-*N*-trimethyllysine, a precursor for carnitine biosynthesis.
- Cats: association between L-carnitine and idiopathic hepatic lipidosis is less clear but may be related to inadequate synthesis or tissue availability.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis of carnitine deficiency in dogs is predicated on low plasma L-carnitine concentration; however, normal plasma carnitine levels do not rule out the myopathic form of carnitine deficiency where plasma carnitine levels are normal or elevated, but cardiac muscle levels are low.

DIFFERENTIAL DIAGNOSIS

- Cats: other hepatopathies, other influences on hepatic lipidosis
- Dogs: idiopathic DCM and other causes of myocardial failure; lipid storage myopathy and other causes of myopathies

INITIAL DATABASE

Samples for plasma carnitine levels are collected in heparinized (green-top) tubes or a syringe coated with heparin. Immediately place the sample on wet ice and centrifuge within 30 minutes of obtaining the sample; separate plasma from cells and freeze the plasma until it is analyzed. Be careful to avoid contaminating the plasma with cells from the buffy coat, and avoid using a sample that is hemolyzed. Ship sample on dry ice to lab for analysis.

ADVANCED OR CONFIRMATORY TESTING

- Dogs: myopathic carnitine deficiency is estimated to occur in 17%-60% of dogs with DCM. Evaluating carnitine levels in cardiac tissue requires fluoroscopic-guided endomyocardial biopsy, which is currently unavailable to most practices.
- Percutaneous skeletal muscle biopsies can be obtained in patients suspected of having a myopathy.
- Reported reference ranges for carnitine levels in various tissues (see tables).

TREATMENT

TREATMENT OVERVIEW

The therapeutic goal is to restore carnitine homeostasis:

- Cats: improve liver function
- Dogs: improve cardiac or skeletal muscle function

ACUTE GENERAL TREATMENT

- Cats: supportive care for idiopathic hepatic lipidosis
- Dogs: supportive care for congestive heart failure

CHRONIC TREATMENT

- Cats: L-carnitine, 200-500 mg PO per day during enteral nutritional support for idiopathic hepatic lipidosis has been recommended.

- Dogs: L-carnitine, 100-200 mg/kg PO q 8 h has been suggested. Use higher end of dosage range for myopathic carnitine deficiency. Approximately one third of dogs will develop diarrhea while receiving the high-end dose. If this occurs, reduce the dose of carnitine to the highest level the dog will tolerate without developing diarrhea.
- Even if plasma and tissue carnitine levels are unavailable in a patient, it is still strongly recommended to consider carnitine supplementation (plus taurine) in American cocker spaniels, boxers, and dogs with cystine or urate urolithiasis that develop DCM.
- Carnitine is a very safe substance. Most common side effect at high doses is diarrhea.
- It takes 3-4 months before any objective echocardiographic changes may occur, so don't stop prematurely.
- If purchasing carnitine through a health food store, only use products that contain the USP (produced under good manufacturing practices) seal. It can be very expensive to purchase carnitine through health food stores.
- Alternatively, buy carnitine in bulk (1 tsp = 2 grams of carnitine) from Lonza (http://www.carnitine.com/carnitine/en.html). Use the human-grade carnitine.

Feline Values

Feline Values	Plasma Free Carnitine	Plasma Ester Carnitine	Plasma Total Carnitine
Males (n = 9)	3.9-18.3 µmol/L	0-5.8 µmol/L	5.0-22.2 µmol/L
Females (n = 4)	5.0-33.8 µmol/L	0-11.6 µmol/L	5.2-44.4 µmol/L

NCP, Noncollaginous protein.*Reference range from 18 healthy adult beagle dogs.

Canine Values

Canine Values	Free Carnitine	Ester Carnitine	Short-Chain Acylcarnitine	Long-Chain Acylcarnitine	Total Carnitine
Plasma (µmol/L)	9-36	N/A	<7	N/A	12-40
Cardiac muscle (nmol/mg NCP)	3.5-11.5 or 0.94-9.8*	<5.0	0.05-2.7*	0-0.66	4.5-14.0 or 1.78-12.4*
Skeletal muscle (nmol/mg NCP)	2.2-15.4*	N/A	0.1-4.1*	0.05-0.81*	4.3-18.3*

RECOMMENDED MONITORING

- Cats: clinical condition, return to food intake
- Dogs: clinical condition, thoracic radiography, echocardiography

PROGNOSIS AND OUTCOME

- Cats: poor to good (± L-carnitine supplementation) depending on severity of idiopathic hepatic lipidosis and rapidity with which adequate nutritional support occurs
- Dogs: guarded to poor; few dogs with DCM respond to L-carnitine, but those that do have a much better prognosis than those not treated with carnitine. It is especially important to consider carnitine supplementation in American cocker spaniels, boxers, and dogs with cystine or urate urolithiasis that develop DCM. DCM has reversed in a few dogs supplemented with carnitine.
- Prognosis for other conditions associated with carnitine deficiency in dogs (e.g., ceroid lipofuscinosis, lipid storage myopathies) is not known.

PEARLS & CONSIDERATIONS

COMMENTS

In cats, recovery of appetite occurs within days to weeks of provision of L-carnitine and appropriate nutritional management.

CLIENT EDUCATION

Explain the importance of feeding a properly formulated diet.

SUGGESTED READING

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Sanderson SL: Carnitine. In Vaden SL, Knoll JS, Smith FWK, Tilley LP, editors: Blackwell's five-minute veterinary consult: laboratory tests and diagnostic procedures. Canine & feline, Ames, IA, 2009, Wiley-Blackwell, pp 160– 163.

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Cardiotoxic Plants

BASIC INFORMATION

DEFINITION

Toxicosis occurring as a result of ingestion of plants that produce substances harmful to the heart: cardiac glycosides or grayanotoxins.

EPIDEMIOLOGY

SPECIES, AGE, SEX

All ages and breeds are susceptible; dogs are more likely to be involved.

RISK FACTORS

Plants or flower bouquets present in pet's environment. Preexisting cardiac disease may increase risk.

GEOGRAPHY AND SEASONALITY

Toxicosis occurs throughout the year but more likely to occur in spring and summer months (outdoor exposures).

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- History or evidence of exposure (witnessed ingestion, chewed plant, or plant material present in the vomitus)
- Cardiac glycosides: onset of clinical signs within 2-8 hours of ingestion: salivation, vomiting, lethargy, depression, and ataxia. With severe intoxications, convulsions and death are possible.
- Grayanotoxins: signs occur within 6hours of ingestion: lethargy, salivation, vomiting, signs of abdominal pain, ataxia, lateral recumbency, and seizures are possible.

PHYSICAL EXAM FINDINGS

- Cardiac-glycoside–containing plants: pale mucous membranes, weak pulses, tachypnea, bradycardia, or paroxysmal tachycardias
- Grayanotoxin-containing plants: tachycardia, tachypnea, hyperthermia, vomiting, lethargy, hypotension, and bradycardia; diarrhea is uncommon.

ETIOLOGY AND PATHOPHYSIOLOGY

Source:

- Present in nature, landscaping, house plants, and floral arrangements
- Common cardiac-glycoside–containing plants: *Asclepias* spp. (some): milkweed; *Convallaria majalis*: lily of the valley; *Digitalis purpurea*: foxglove; *Hellebore* spp.; *Kalanchoe* spp.; *Nerium oleander*: oleander; *Thevitia nerifolia*: yellow oleander; *Thevetia peruviana*: yellow oleander
- Common grayanotoxin-containing plants: *Rhododendron* spp.: rhododendron, azalea, rosebay; *Kalmia* spp.: laurels; *Pieris* spp.: Japanese pieris, Mountain pieris; *Leucothoe* spp.: black laurel

Mechanism of Toxicosis:

- Cardiac glycosides:
  - Inhibition of Na^+/K^+-ATPase pump in the myocardial cell
  - Result: decreased intracellular potassium, increased intracellular sodium. Intracellular sodium is exchanged for calcium, raising intracellular calcium levels. In addition, excessive extracellular potassium may depress cardiac contractility.

- Effects noted include: AV block due to progressive interference with cardiac electrical conduction and increased vagal tone. Decrease in normal resting membrane potential. Decreased myocardial cell pacemaker activity, leading (in severe toxicoses) to malignant cardiac arrhythmias (ventricular) or asystole.

- Grayanotoxins: structurally distinct from cardiac glycosides but with a similar mechanism of action. Like cardiac glycosides, they bind to sodium channels, slowing their opening and closing and decreasing their ion selectivity, and therefore produce similar clinical signs. Many cells are affected, especially excitable cells (neurologic, cardiac, muscle cells).

CARDIOTOXIC PLANTS Foxglove plant *(Digitalis purpurea)* is a source of cardiac glycosides such as digitalis.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is made based on history of exposure and the presence of gastrointestinal and cardiac signs. Plant material present in pet's environment, vomitus, or lavage fluid may also be helpful in arriving at a diagnosis. Serum digoxin levels are confirmatory (cross-reactivity with cardiac glycosides); turnaround time limits utility in critical cases, but in cases that are less severe, the test is helpful for identifying whether preventive measures need to be taken to avoid reexposure in the future.

DIFFERENTIAL DIAGNOSIS

Toxicologic:

- Bufo toad ingestion
- Digoxin overdose (see online chapter: Digoxin Toxicosis)
- Antiarrhythmic medication ingestion

Spontaneous, nontoxicologic:

- Primary cardiac disease
- Systemic illness causing ventricular arrhythmias
- Gastroenteritis

INITIAL DATABASE

- CBC (no significant changes expected)
- Serum chemistry panel: hyperkalemia possible; *hypo*kalemia markedly worsens the toxic effects (including making the heart refractory to antiarrhythmics such as lidocaine and procainamide) and needs to be treated (see p. 577).
- Electrocardiogram (ECG) to assess cardiovascular status
  - A combination of first- or second-degree AV block together with possibility of exposure to incriminating plant and compatible clinical signs is highly suggestive of the clinical diagnosis of glycoside plant cardiotoxicity.
  - Ventricular or atrial arrhythmias of virtually any type are possible.
  - The most common electrocardiogram (ECG) changes include first-, second-, or even third-degree atrioventricular (AV)

block, ventricular arrhythmias, and ST segment changes.
- Blood pressure (may see hypotension)

ADVANCED OR CONFIRMATORY TESTING

- Serum digoxin levels (cardiac-glyco-side–containing plants). Any detectable amount in a patient not receiving digoxin pharmaceutically confirms the diagnosis. Test can be performed at a local human hospital.
- Presence of oleandrin in gastrointestinal (GI) contents and body fluids can confirm exposure (available in some veterinary diagnostic laboratories).

TREATMENT 

TREATMENT OVERVIEW

Treatment is aimed at management of severe cardiac arrhythmias and systemic disturbances (e.g., dehydration), and early decontamination of the patient (emesis induction and administration of activated charcoal). An intravenous antidote (Digibind) exists for cardiac glycosides but is often cost-prohibitive (see online chapter: Digoxin Toxicosis).

ACUTE GENERAL TREATMENT

- Decontamination of patient:
  - Emesis: see p. 1364
  - Activated charcoal; after emesis or if a few hours have elapsed after exposure; (1-4 g/kg) with a cathartic such as 70% sorbitol (3 mL/kg) PO
- Treat cardiac arrhythmias:
  - Bradyarrhythmias in a normotensive patient: atropine, 0.02-0.04 mg/kg IV, repeat as needed
  - Ventricular arrhythmias (see p. 1165).
  - Digoxin immune Fab (Digibind) may be used for treating refractory cardiac arrhythmias or hyperkalemia in cardiac glycoside toxicosis.
- Supportive care:
  - IV fluids as needed; avoid calcium-containing fluids (e.g., LRS) unless hypocalcemia
  - Correct acid-base status and electrolytes as needed.
  - Control central nervous system signs with benzodiazepine if needed (e.g., diazepam, 0.5-1 mg/kg IV).
  - Control severe vomiting with metoclopramide (0.1-0.4 mg/kg PO, SQ, or IM q 6 h) or maropitant, 1 mg/kg SQ q 24 h or 2 mg/kg PO q 24 h, provided GI obstruction is ruled out.

POSSIBLE COMPLICATIONS

Permanent cardiac damage

RECOMMENDED MONITORING

- ECG, electrolytes, blood pressure, heart rate, and pulse

PROGNOSIS AND OUTCOME 

- Cardiac glycosides: Animals with moderate to severe cardiovascular signs have a guarded prognosis; even with intensive supportive care, serious intoxications may require several days of in-hospital treatment.
- Animals with only GI signs but no subsequent cardiovascular signs have a good prognosis.
- Grayanotoxins: prognosis is generally good with grayanotoxin-containing plants.

PEARLS & CONSIDERATIONS 

COMMENTS

- Domesticated grayanotoxin plants, such as those sold in nurseries, are generally less toxic than their wild counterparts and mainly cause gastrointestinal signs.
- Cardiac glycosides are bitter tasting; however, when leaves dry, sugar is released and the leaves may be more attractive for ingestion.

- Cardiotoxicity of these plants is exclusively arrhythmogenic; structural heart disease (e.g., valve disease) is not caused by these plants.

CLIENT EDUCATION

Client should be made aware of toxic plants in their pet's environment.

SUGGESTED READING

Atkinson KJ, et al: Suspected lily-of-the-valley *(Covallaria majalis)* toxicosis in a dog. J Vet Emerg Crit Care 18(4):399–403, 2008.

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Cardiomegaly (Radiographic)

BASIC INFORMATION

DEFINITION

Enlargement of the cardiac silhouette relative to the thorax. This is a relatively common radiographic finding and may be due to underlying acquired or congenital cardiac disease.

- Radiographic assessment:
  - Subjective
    - Empirical: based on clinical experience
    - Compare to previous radiographs of same patient or other patient of same breed/conformation
  - Objective
    - Vertebral heart score: sum of long and short axes of cardiac silhouette on lateral view compared to length of thoracic vertebrae, beginning at T4 and continuing caudally
      - Canine normal = 9.7 ± 0.5
      - Feline normal = 7.5 ± 0.3
      - Has not proven to be more accurate than subjective assessment

EPIDEMIOLOGY

GENETICS & BREED PREDISPOSITION

Dog Breeds Predisposed to Heart Disease

Disease	Some Commonly Affected Breeds
Congenital	
Patent ductus arteriosus	Maltese, poodle, keeshond, bichon frise, Pomeranian
Subaortic stenosis (must be severe to cause cardiomegaly)	Newfoundland, bloodhound, boxer, golden retriever, rottweiler
Tricuspid dysplasia	Labrador retriever
Pulmonic stenosis	English bulldog, Scottish terrier, wirehaired fox terrier
Ventricular septal defect	Lakeland terrier, West Highland white terrier
Acquired	
Valvular endocardiosis	Cavalier King Charles spaniel, small breeds
Dilated cardiomyopathy	Doberman pinscher, Irish wolfhound, Great Dane, boxer, Saint Bernard, Afghan hound, Newfoundland, Old English sheepdog
Pericardial effusion	Retrievers, German shepherds, other large breeds (hemangiosarcoma, idiopathic sterile pericarditis); brachycephalic dogs (chemodectomas)

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Dyspnea, tachypnea, cough, exercise intolerance, syncope
- May be incidental finding

PHYSICAL EXAM FINDINGS

Cardiac murmur, arrhythmia, tachycardia, muffled heart sounds, and in more advanced cases, increased lung sounds, pulse

alterations, ascites, jugular venous distension

ETIOLOGY AND PATHOPHYSIOLOGY

- Pressure overload: outflow obstruction, hypertension
- Volume overload: valvular insufficiency, cardiomyopathy, shunt
- Pericardial effusion: neoplasia, inflammation, hemorrhage; rarely, infection

Enlarged Chamber	Appearance on Lateral View	Appearance on VD/DV View
Left atrium	Dorsal deviation of left mainstem bronchus	Increase in soft-tissue opacity, causing splaying of the mainstem bronchi
Left ventricle	Dorsal deviation of trachea	Enlargement of apex at 3 to 5 o'clock
Right atrium	Bulge at cranial aspect of cardiac silhouette	Bulge at 9:30 to 11:30 o'clock
Right ventricle	Widening of the cardiac silhouette, increased cardiosternal contact	Rounding and ventricle enlargement at 5 to 8 o'clock "Reverse D" appearance

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Differential diagnosis of cardiomegaly is based on specific cardiac chamber enlargement and the appearance and size of the great vessels and pulmonary vasculature.

- Left-sided cardiomegaly:
  - Valvular disease: mitral insufficiency
  - Cardiomyopathy
    - Dilated (dilated cardiomyopathy, DCM): canine
    - Hypertrophic (hypertrophic cardiomyopathy [HCM]), restrictive: feline
  - Congenital
    - Left-to-right shunts: pulmonary overcirculation
      - Patent ductus arteriosus: ± main pulmonary artery, descending aorta, left auricular bulge
      - Ventricular or atrial septal defect
    - Subaortic stenosis: aortic arch dilation
    - Mitral dysplasia
- Left-sided congestive heart failure:
  - Enlarged left atrium
  - Interstitial to alveolar pulmonary infiltrates; perihilar, caudal distribution
  - In dogs with DCM and in cats, cardiogenic edema may have patchy, diffuse distribution.
  - ± Enlarged pulmonary veins
- Right-sided cardiomegaly:
  - Valvular disease: tricuspid insufficiency
  - Congenital
    - Pulmonic stenosis: main pulmonary artery dilation
    - Tetralogy of Fallot: no main pulmonary artery enlargement, ± pulmonary underperfusion
    - Tricuspid dysplasia: can resemble generalized cardiomegaly, pericardial effusion on radiographs
    - Right-to-left patent ductus arteriosus or ventricular septal defect: heart may be of normal size, ± pulmonary underperfusion, main pulmonary artery, and lobar artery dilation
  - Cor pulmonale
    - Secondary to pulmonary hypertension: main pulmonary artery and lobar artery dilation
    - Example: heartworm disease, pulmonary thromboembolism, chronic pulmonary disease
- Right-sided congestive heart failure:
  - Pleural effusion
  - Enlarged caudal vena cava
  - Hepatomegaly
- Generalized cardiomegaly:
  - Pericardial effusion: globoid appearance; loss of normal heart shape. No enlarged left atrium.
    - Idiopathic

        - Heart base, right atrial/auricular mass
        - Mesothelioma
        - Congestive heart failure
        - Left atrial rupture
        - Peritoneal-pericardial diaphragmatic hernia
    - Dilated cardiomyopathy
    - Mitral and tricuspid insufficiency
        - Individual chamber enlargement, including left atrial enlargement
- Great vessels:
    - Pulmonary trunk dilation: 1 to 2 o'clock on ventrodorsal/dorsoventral (VD/DV) view
        - Pulmonic stenosis, pulmonary hypertension
    - Aortic arch dilation: 11 to 1 o'clock on VD/DV view
        - Aortic stenosis, patent ductus arteriosus. May be normal in geriatric cats.
    - Caudal vena cava enlargement
        - Right-sided congestive heart failure, cardiac tamponade, right atrial obstruction
- Pulmonary vasculature: corresponding pulmonary arteries and veins should be of equal size:
    - Large pulmonary arteries
        - Pulmonary hypertension: heartworm disease, pulmonary thromboembolism, chronic pulmonary disease
    - Large pulmonary veins
        - Venous congestion associated with left atrial enlargement
    - Large pulmonary arteries and veins
        - Left-to-right shunts
    - Small pulmonary arteries and veins
        - Right-to-left shunts, low cardiac output

INITIAL DATABASE

- Right or left lateral and VD or DV thoracic radiographs made during full inspiration
- Electrocardiogram, blood pressure, serum biochemistry profile

ADVANCED TESTING

- Echocardiography
- Nonselective or selective angiography

TREATMENT

TREATMENT OVERVIEW

Treatment is specific to underlying cause. The general goal is to optimize preload and afterload, as well as improve diastolic and systolic cardiac function if abnormal.

ACUTE AND CHRONIC TREATMENT

As required based on underlying cause

PROGNOSIS AND OUTCOME

Variable depending on underlying disease

PEARLS & CONSIDERATIONS

COMMENTS

- Things that mimic cardiomegaly:
    - Chondrodystrophic, shallow-chested patient (especially lateral view)
    - Films made during expiration
    - Excess pericardial fat
    - Patient obliquity

- Things that mimic pulmonary disease:
  - Films made during expiration
  - Underexposure
  - Excess intrathoracic and/or extrathoracic fat
- Positional differences:
  - Cardiac apex is normally rounded and dorsally displaced on left lateral view.
  - Cardiac silhouette is normally more elongated on VD view and more oval in shape on DV view.
  - With pleural effusion, cardiac silhouette is better outlined on VD view.
- Breed/conformation differences:
  - Deep-chested patients: cardiac silhouette more narrow and vertically oriented on lateral projection compared to patients with other chest conformations.
  - Chondrodystrophic, shallow-chested patients: cardiac silhouette appears large relative to thorax. Trachea deviated dorsally on lateral projection (normal).
- Normal geriatric felines:
  - Horizontal orientation of heart
  - Tortuous, prominent aorta
- Cardiomegaly is present in 80% of dogs with hemodynamically significant pericardial effusion (cardiac tamponade); for the remaining 20%, diagnosis depends on physical exam (tachycardia + weak pulse + muffled heart sounds) and echocardiography.

SUGGESTED READING

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Campylobacter Enteritis

BASIC INFORMATION

DEFINITION

Well-recognized diarrheal disease resulting from invasive and toxigenic effects of *Campylobacter* spp. infection

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Most commonly occurs in young animals <6 months old
- Pathogen of dogs, cats, humans, and various wild and domestic animals

RISK FACTORS

- Young age
- Crowded conditions such as kennels, catteries, or animal shelters
- Conditions with poor hygiene and sanitation
- Immunocompetence/immunodeficiency of individual patient
- Concomitant gastrointestinal infections
- History of antibiotic therapy

CONTAGION & ZOONOSIS

- Contagious between humans and numerous animal species
- Commonly spread between animals by fecal-oral route through contaminated food and water sources.
- Humans appear to be more susceptible than dogs or cats to clinical disease.
    - Dogs and cats are a major source of *C. jejuni* infection in people, especially puppies or kittens recently acquired from pet stores or kennels.
    - Other sources of infection to humans include eating raw or undercooked meat, especially poultry.
    - Owners of pets should be warned of the risks and practice good hygiene to minimize risk of zoonosis.

GEOGRAPHY AND SEASONALITY

Appears to be more common in the summer and fall months. In the United States, young cats in the upper Midwest commonly carry *C. upsaliensis*.

ASSOCIATED CONDITIONS & DISORDERS

May be associated with other gastrointestinal infections or parasites:

- Parvovirus
- Coronavirus
- Giardiasis
- Salmonellosis

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Most carriers of *Campylobacter* show no clinical signs.
- Clinical disease usually occurs in young dogs and cats.

HISTORY, CHIEF COMPLAINT

- Acute diarrhea ranging from mild to severe, with watery to mucoid diarrhea with or without blood.
- Animals may have tenesmus, possibly vomiting, or inappetence.

- Chronic diarrhea that may be intermittent
- Cholecystitis has been reported in two dogs associated with *C. jejuni*.
- May cause abortion and fetal resorption in the bitch

PHYSICAL EXAM FINDINGS

Acute cases may have fever and/or signs of dehydration.

ETIOLOGY AND PATHOPHYSIOLOGY

- Gram-negative, curved, motile, microaerophilic bacterial rods
- Component of the normal intestinal flora
- Clinical disease depends on number of organisms ingested as well as degree of development of protective antibody
- Disease localizes in jejunum, ileum, cecum, and colon
- Virulence factors, including cytotoxin production, allow organism to invade epithelium.
- Enterotoxin results in secretory diarrhea.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis should be suspected in a young animal with diarrhea and fecal cytologic findings that identify slender, curved rods and leukocytes. Confirmation, which is often undertaken given the risk of contagion and/or zoonosis, requires culture identification or positive PCR.

DIFFERENTIAL DIAGNOSIS

- Viral diarrhea: parvovirus, coronavirus, rotavirus
- Bacterial diarrhea: *Salmonella*, *Clostridium*
- Parasites
- Dietary indiscretion

INITIAL DATABASE

CBC, serum chemistry profile, and urinalysis results usually normal or nonspecific

- Mild hemoconcentration may be seen with dehydration
- Leukocytosis may be seen with invasion of mucosa
- Serum chemistry profile may show elevated total proteins and prerenal azotemia with dehydration

ADVANCED OR CONFIRMATORY TESTING

- Microscopic examination of feces:
  - Evaluation of stained smears of fresh feces for presence of characteristic organisms.
  - Increased numbers of fecal white blood cells should be observed if intestinal inflammation is present.
  - *Campylobacter* may be difficult to distinguish from other similar species, including *Helicobacter*, on cytologic evaluation alone.
  - *Campylobacter* enteritis is difficult to diagnose cytologically, because many dogs have this organism as part of normal flora.
  - Darkfield or phase contrast microscopy if available
- Fecal culture:
  - Requires special *Campylobacter* plates and microaerophilic conditions
  - Samples of fresh feces or rectal swabs can be submitted.
  - Organisms remain viable for 3 days at room temperature and 1 week if refrigerated, but viability is improved with shorter delays.
- Polymerase chain reaction:
  - The most reliable method of definitive identification of *Campylobacter* species
  - Fecal samples should be placed in isopropyl alcohol and are stable for 72 hours.

TREATMENT

TREATMENT OVERVIEW

Treatment for latent carriers should only be performed if an immunocompromised person or animal is in the home and at risk or showing signs of infection. Otherwise, the treatment goal is confined to elimination of clinical signs in animals showing them.

ACUTE GENERAL TREATMENT

- Efficacy of antibiotic therapy in altering course of disease is unknown.
- Erythromycin, 10 to 20 mg/kg PO q 8 h, is the treatment of choice.
- Tetracyclines also have activity against *Campylobacter* (doxycycline, 5 mg/kg PO q 12-24 h).
- Quinolones (e.g., enrofloxacin, 5-10 mg/kg PO q 24 h) thought to be effective, but a high rate of drug resistance may develop.
    - Deleterious effects on joint cartilage are a concern, because many patients are young, growing animals.
    - Marbofloxacin should be considered as an alternative in cats, owing to ocular toxicity of enrofloxacin.
- Chloramphenicol has mixed results.
- Duration of treatment with any of these antibiotics is typically 2-3 weeks.

CHRONIC TREATMENT

May be indicated in carrier animals (treatment for 4-6 months has been reportedly necessary to completely clear the organism).

POSSIBLE COMPLICATIONS

Erythromycin commonly causes vomiting in dogs and cats.

RECOMMENDED MONITORING

- Monitor clinical signs.
- Recheck fecal culture to assess fecal shedding and potential exposure to humans.

PROGNOSIS AND OUTCOME

- Prognosis for recovery is good in the absence of other serious concomitant disease.
- Worse prognosis if underlying immunodeficiency or complicating disease

PEARLS & CONSIDERATIONS

COMMENTS

- May be difficult to attribute *Campylobacter* as cause of diarrhea in dogs and cats, since also part of normal flora
- Latent carriers may need to be treated if potential exposure and transmission to humans is a concern (e.g., immunocompromised persons).
- Lack of response to therapy should prompt investigation into other concurrent intestinal disease or possible antibiotic resistance.

PREVENTION

- Good sanitation and avoidance of overcrowding
- Avoid undercooked meats

TECHNICIAN TIPS

- Care should be taken to avoid any risk of fecal contamination to other hospital patients or staff.

CLIENT EDUCATION

- Owners should be informed that this is a zoonotic disease and humans are very susceptible.
- Good hygiene is essential, especially with a puppy or kitten with diarrhea.

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Callus/Pressure Sore

BASIC INFORMATION

DEFINITION

- Callus: a thickened, hyperkeratotic, alopecic area of skin over a pressure point
- Pressure sore (decubital ulcer): an area of tissue damage or necrosis concentrated over a bony prominence, resulting from prolonged application of pressure

SYNONYM

Decubital ulcer (pressure sore)

EPIDEMIOLOGY

SPECIES, AGE, SEX

Any patient can develop a callus or pressure sores.

GENETICS & BREED PREDISPOSITION

Large- or giant-breed dogs, because of their size and weight, are disproportionately more commonly affected.

RISK FACTORS

- Animals that are weak or emaciated, as well as those that are recumbent for long periods on hard surfaces, are at a high risk for developing pressure sores.
- Immunosuppressed individuals may be more prone to secondary infections of pressure point lesions.
- Hypothyroid dogs may develop unusually severe calluses or calluses in unusual areas.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Often have a history of prolonged recumbency or sleeping on hard surfaces such as wood, cement, or brick
- Owner may notice progressive lesions over bony prominences. Some owners may not notice sores until they break open, or see the patient further aggravating the lesions by licking them.

PHYSICAL EXAM FINDINGS

- A callus initially appears as a thickened, hyperkeratotic, lichenified, and alopecic area of skin over a bony prominence, commonly affecting the elbows, hocks, and sternum.
- The severity of pressure sores is variable:
    - They can be erythematous to purple in color, with a serous, sanguineous, or purulent discharge. Ulcers with undermined edges are common sequelae.
- Either of these lesions may develop secondary infections with abscessation and draining tracts.

ETIOLOGY AND PATHOPHYSIOLOGY

- A callus is caused by pressure-induced ischemia and inflammation.
- Prolonged pressure compresses capillary circulation, causing tissue damage or necrosis, producing a pressure sore:
    - Grade I lesions affect the epidermis and superficial dermis.
    - Grade II lesions extend to the subcutis. Within 24-48 hours, the ulcer edges become undermined.
    - Grade III lesions extend to the deep fascia.
    - Grade IV lesions involve the underlying bone.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Ulcerated neoplasm
- Infected/necrotic wound as a result of trauma
- Calcinosis circumscripta

INITIAL DATABASE

- A thorough history and physical exam are most important.
  - Diagnosis is generally based on physical location of the lesion(s) over pressure points, typical appearance (see above), and owner's description of the environment and surfaces on which the animal lies.
- Radiographs of the affected area may help to ascertain bony involvement (uncommon).

ADVANCED OR CONFIRMATORY TESTING

- Cytologic examination and culture and susceptibility testing may be indicated for the management of secondary infections.
- Histopathologic evaluation of biopsies can be used for distinguishing infected/necrotic callosities and pressure sores from neoplasms and calcinosis circumscripta.

TREATMENT

TREATMENT OVERVIEW

- Recognition and elimination of the cause(s) is paramount.
- Providing a soft, padded environment may be all that is required to decrease the size of callus lesions and prevent progression.
- Resolving pressure sores and preventing new lesions depend on providing an optimum environment for healing by treating infection and encouraging blood supply to the area.

GENERAL TREATMENT

- Pressure sores should be cleaned daily with an antiseptic solution such as chlorhexidine diluted to 0.05%.
  - With standard 4% chlorhexidine solution, dilute 1 part chlorhexidine to 80 parts water (or 12 mL in 1 L of water) to obtain a 0.05% concentration.
- Various treatments have been suggested to accelerate healing of pressure sores, including wound-healing creams, raw honey, or a topical antibiotic, mupirocin.
- Although systemic antibiotics do not penetrate well, owing to the area of capillary and venous congestion at the base and tissue margins of a pressure sore, coverage is prudent.
  - Cephalexin, 30 mg/kg PO q 12 h for 30 days may be beneficial.
- Grade II-IV pressure sores often require surgical débridement and closure, but not until the patient is ambulatory. Otherwise, the wound may dehisce.
- Physical barriers such as Elizabethan collars may help deter self-trauma to pressure point lesions.

POSSIBLE COMPLICATIONS

- Wound dehiscence after surgery
- Slow healing

PROGNOSIS AND OUTCOME

- Callus lesions can be controlled by attention to home environment and bedding.
- Since the severity of pressure sores varies, severe lesions are accordingly more difficult to manage.
- If the patient recovers from the underlying disease/reason for recumbency quickly, the pressure sore should heal spontaneously, but often slowly.

PEARLS & CONSIDERATIONS

COMMENTS

Prevention of pressure sores is of utmost importance because they can be difficult to manage, prone to infection, and slow to heal.

PREVENTION

- Prevention is vastly superior to any kind of treatment.
- All recumbent patients should be turned frequently and given massage, physiotherapy, and/or hydrotherapy to stimulate blood flow.
- Recumbent animals should be kept on a well-padded surface such as a waterbed, soft egg crate, foam rubber pad, or airbed.

TECHNICIAN TIP

The keys for preventing pressure sores in recumbent patients are “dry and clean, soft, and shift”: bedding should be changed when damp or soiled; well-padded; and the patient's recumbency should be altered periodically (e.g., every 4-6 hours) to avoid extended time spent on the same pressure points.

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Calicivirus, Cat

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Common viral disease in domestic and some exotic cats, characterized by upper respiratory signs, oral ulceration, and less commonly arthritis

SYNONYMS

Upper respiratory infection (calicivirus is one possible etiology); limping kitten syndrome; older literature: classification as picornavirus. Virulent systemic feline calicivirus (VS-FCV) is also known as *hemorrhagic fever–like FCV*

EPIDEMIOLOGY

SPECIES, AGE, SEX

- All domestic cats and some exotic feline species are susceptible.
- All ages affected, but susceptibility for typical upper respiratory infection is highest in kittens.
- Adults are more likely to experience the virulent systemic form of infection.
- No gender predilection

RISK FACTORS

- Multiple-cat environments
- Crowding
- Stress
- Poor husbandry
- Coinfection with other respiratory pathogens worsens disease

CONTAGION & ZOONOSIS

FCV is a highly contagious disease of cats. No zoonotic implications are known.

GEOGRAPHY AND SEASONALITY

Worldwide with no seasonality

ASSOCIATED CONDITIONS & DISORDERS

- Lymphocytic-plasmacytic stomatitis and gingivitis linked to chronic carriers
- Frequent coinfection with other upper respiratory pathogens

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Pneumotropic isolates affect primarily the upper, and uncommonly the lower, respiratory tract.
- Rheumatic isolates cause joint pain and lameness in naturally infected kittens.
    - Joint disease also reported after administration of modified-live calicivirus vaccine
- Virulent systemic form may cause more severe clinical signs in adults.
    - Vaccinated cats can be affected.

HISTORY, CHIEF COMPLAINT

- Malaise: lethargy, listlessness
- Inappetence/anorexia
- Ocular signs (see Physical Exam Findings below)

- Sneezing
- Nasal discharge (serous or purulent)
- Drooling
- Reluctance to walk, lameness

PHYSICAL EXAM FINDINGS

Pneumotropic form:

- Conjunctivitis: diffuse, bilateral
- Epiphora
- Blepharospasm
- Chemosis: may be dramatic; entire globe may become hidden behind swollen conjunctiva
- Oculonasal discharge (serous or purulent)
- Fever
- Vesicles or erosions on tongue, palate, nasal planum:
  - Visible during routine examination of mouth
  - Characteristic of calicivirus, but also occurs less commonly from herpesvirus infection and exposure to topical irritants, especially hospital and surgical disinfectants
  - May cause drooling
- Dehydration
- Cough is uncommon

Rheumatic form:

- Fever; temperature often >104°F (>40°C)
- Joint swelling
- Pain
- Myalgia
- Oral ulcers possible
- Kitten/cat may eat well but be reluctant to walk

Virulent systemic form:

- Fever
- Facial and limb edema that may progress to necrosis
- Upper respiratory signs
- Icterus with pancreatitis
- Dyspnea
- Epistaxis and/or hematochezia
- Ulcerations in mouth, face, muzzle, pinna, and extremities
- Pneumonia
- Pericarditis
- Death

ETIOLOGY AND PATHOPHYSIOLOGY

- Infection with FCV, an RNA virus with multiple subtypes of varying degrees of virulence and cross-reactivity, is acquired predominantly via ingestion.
  - Spread by aerosol route less likely
- Replication occurs in oropharyngeal tissues, with spread primarily to epithelium of conjunctiva, nose, and oral cavity, including the tongue and palate.
  - Rapid cytolysis of infected cells ensues.
  - In the virulent systemic form, signs result from vasculitis and development of disseminated intravascular coagulation/systemic inflammatory response syndrome.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

- Presumptive diagnosis is primarily based on history, physical examination, and clinical signs. Virus identification must be interpreted carefully; it rarely affects treatment and is mainly of academic interest.

DIFFERENTIAL DIAGNOSIS

- Feline herpesvirus 1:
  - Cough and keratitis more likely with feline herpesvirus infection
  - Oral ulceration less likely with feline herpesvirus infection
- Chlamydiosis
- Mycoplasmosis
- Bordetellosis
- Corneal injury/trauma
- Oral/lingual ulceration accompanied by fever may be caused by licking of surgical and/or hospital disinfectants from feet or fur.

INITIAL DATABASE

- Fluorescein staining of corneas to rule out corneal ulcers/injury
- Feline leukemia/feline immunodeficiency virus tests to rule out underlying immune compromise
- No characteristic findings on CBC, biochemical profile, or urinalysis

ADVANCED OR CONFIRMATORY TESTING

- Viral culture
- Viral identification usually not warranted except in cases of virulent systemic calicivirus infection

TREATMENT

TREATMENT OVERVIEW

Treatment is aimed at controlling pain, maintaining supportive care, treating secondary bacterial infection, and preventing spread to unaffected cats. Therapeutic goals are to maintain hydration and nutrition; provide pain relief for ulcers, joint/muscle pain; and control secondary bacterial infection.

ACUTE GENERAL TREATMENT

- Fluids to maintain hydration
- Syringe feeding if anorexic
- Erythromycin ophthalmic ointment to combat potential secondary *Chlamydia* or *Mycoplasma* infections
- Buprenorphine (0.01-0.03 mg/kg q 8-12 h IM, IV, PO) may be considered for analgesia.
- Sucralfate slurry dribbled on lingual ulcers may be beneficial.
- α-Interferon may inhibit viral replication.

CHRONIC TREATMENT

- Recrudescence of clinical disease is uncommon.
- Cats may be susceptible to infection with new subtypes.

NUTRITION/DIET

Feeding tubes may be required for nutritional support in cases with severe or protracted oral ulceration (see p. 1270).

DRUG INTERACTIONS

Nonsteroidal antiinflammatory drugs and steroids are discouraged, owing to risks and interference with therapeutic benefits of fever and cytokine release.

POSSIBLE COMPLICATIONS

- Interstitial viral pneumonia and/or secondary bacterial pneumonia can be life-threatening complications.
- Oral ulcers and arthritis usually resolve without complication.
- Sudden dyspnea may occur if pneumonia develops.

RECOMMENDED MONITORING

Clinical signs

PROGNOSIS AND OUTCOME

- Prognosis is good for recovery from typical calicivirus infection with supportive care.
- By contrast, a mortality rate of 40% is reported for the virulent systemic form.

PEARLS & CONSIDERATIONS

COMMENTS

- Constant viral mutation within individuals and endemically infected populations may account for extreme variation in virulence between subtypes.
- Recovered cats remain lifelong carriers. Virus is shed continuously from oral cavity, regardless of health status or stress.
- Properly vaccinated cats may become infected with different subtypes.

PREVENTION

- Proper husbandry to prevent cat-to-cat contact and cross-contamination during cleaning and feeding procedures.
- FCV is stable and resistant to many disinfectants, except bleach (sodium hypochlorite) diluted 1 part bleach to 32 parts tap water.
- Proper vaccination at 8-10 weeks, after 12 weeks of age, 1 year later, and every 3 years afterward.

TECHNICIAN TIPS

All cats, especially kittens, seen with signs of upper respiratory tract infection should be considered FCV-infected so that appropriate precautions can be taken to limit spread within the hospital.

CLIENT EDUCATION

- Emphasize proper vaccination
- In catteries, consider immunizing kittens from carrier queen as early as 6 weeks of age.

SUGGESTED READING

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Calcium Channel Blocker Drug Toxicosis

BASIC INFORMATION

DEFINITION

Calcium channel blocker (CCB) drugs are commonly used for the treatment of hypertension and tachyarrhythmias in human and veterinary medicine. Adverse effects at therapeutic dose or with overdose result in hypotension and bradycardia or tachycardia, causing weakness, ataxia, and inappetence within 30 minutes to 12 hours after ingestion.

EPIDEMIOLOGY

SPECIES, AGE, SEX

Animals of all breeds, ages, and both sexes are susceptible. Exposure is more common in dogs.

RISK FACTORS

- Preexisting renal or cardiovascular disease may predispose to signs.
- Hepatic disease may reduce metabolism and elimination of CCBs.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Sustained/controlled/extended/delayed-release preparations may delay onset of signs (6-12 hours), whereas immediate-release preparations can cause signs within 30 minutes.

HISTORY, CHIEF COMPLAINT

- History of suspected or observed exposure
- Weakness, depression, ataxia, vomiting possible

PHYSICAL EXAM FINDINGS

- Hypotension and bradycardia are common; reflex tachycardia is possible if hypotension predominates (dihydropyridine CCBs).
- Pale mucous membranes
- Hypothermia possible (due to hypotension)
- Depression, ataxia, seizures, or coma possible
- Dyspnea possible (pulmonary edema)

ETIOLOGY AND PATHOPHYSIOLOGY

Source:

- Prescription medication (human or veterinary)
- Dihydropyridine-type CCBs (e.g., amlodipine [Norvasc]) have effects that are confined to vascular smooth muscle. Thus they are used for treating hypertension.
- Nondihydropyridine-type CCBs (benzothiazepines such as diltiazem [Dilacor, Cardizem] or phenylalkylamines such as verapamil [Isoptin, Calan]) have greater potency in cardiac muscle and cardiac nodal tissues than in the vasculature. Thus they are used for treating arrhythmias and cardiomyopathy.

Mechanism of Toxicosis:

- CCBs close L-type calcium channels by binding to their α-subunit. Decreased calcium influx results in vasodilation (dihydropyridine-type) or a decrease in cardiac contractility and electrical impulse conduction at the SA and AV nodes (nondihydropyridine-type).
- CCBs decrease pancreatic insulin secretion, resulting in hyperglycemia.

- CCBs may cause noncardiogenic pulmonary edema (mechanism unknown)

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on observation or evidence of ingestion (chewed container) along with physical exam findings of hypotension and/or bradycardia. Confirmation with plasma drug levels is uncommonly performed, and treatment generally should be initiated without such results.

DIFFERENTIAL DIAGNOSIS

- Toxicologic:
  - β-Adrenergic receptor antagonists overdose (propranolol, metoprolol), α2-adrenergic receptor agonists (imidazoline-type decongestants), cardiac glycosides (example: digoxin, some cardiac glycoside containing plants; bufo toad toxicosis), antidepressant toxicosis, organophosphate and carbamate insecticides
- Spontaneous, nontoxicologic:
  - Primary cardiac disease, systemic illness causing hypotension

INITIAL DATABASE

- Blood pressure (see): hypotension
- Electrocardiogram (ECG; see):
  - Sinus bradycardia, AV block with verapamil or diltiazem
  - Sinus tachycardia with dihydropyridines
- Serum chemistry profile: hyperglycemia, hypokalemia, hypophosphatemia, hypomagnesemia possible
- Acid-base status: lactic acidosis possible

ADVANCED OR CONFIRMATORY TESTING

Plasma CCB levels may be measured at a human hospital for confirmation. Therapeutic monitoring to assess response to treatment is not useful, as reference ranges have not been established for animal.

TREATMENT

TREATMENT OVERVIEW

Treatment consists of decontamination (emesis and charcoal administration), stabilizing the cardiovascular system, and maintaining tissue perfusion by maintaining adequate blood pressure during the course of toxicosis. If no clinical signs are present, continuous monitoring in a veterinary facility for 12-24 hours or longer following ingestion is recommended; signs can be delayed, especially with extended release formulations.

ACUTE GENERAL TREATMENT

- Decontamination
  - Emesis with a recent ingestion or in an animal showing no overt signs of toxicosis (see)
  - Activated charcoal: 1-2 g/kg (or labeled dosage) with a cathartic PO following emesis (if performed); repeat half the original dose q 6 h for large ingestions or extended-release preparations.
  - Gastric lavage: if large number of tablets, which can form concretions
  - Enema (see p. 1258): consider if the medication is an extended-release preparation, as significant absorption can occur in colon; 2.5-5 mL/kg of warm tap water or isotonic saline
- Fluid therapy
  - Fluid rate should be guided by blood pressure monitoring; avoid volume overload (iatrogenic pulmonary edema).
- Treatment of hypotension
  - IV crystalloid fluids
  - Hetastarch for persistent hypotension
    - Dogs: 20 mL/kg/d IV; initial 5 mL/kg bolus over 15-30 minutes, followed by CRI of 15 mL/kg/day
    - Cats: 10 mL/kg/d IV
  - Calcium chloride or calcium gluconate for refractory hypotension; monitor continuous ECG, and discontinue if bradycardia worsens.
    - Calcium chloride provides 3 times more calcium per mL than calcium gluconate.

        - Calcium chloride and calcium gluconate are very irritating and can cause tissue necrosis if extravascular; use indwelling catheter.
        - Calcium chloride (10% solution; 27.2 mg Ca/mL): 0.1-0.5 mL/kg slow IV bolus or CRI of 0.01 mL/kg/h (5 mg/kg/h), *or*
        - Calcium gluconate (10% solution; 9.3 mg Ca/mL): 50-150 mg/kg (0.5-1.5 mL/kg) slow IV over 5 minutes to effect or CRI of 5 mg/kg/h (0.05 mL/kg/h).
    - If hypotension persists after crystalloids, hetastarch, and calcium supplementation, dopamine (1-20 mcg/kg/min IV CRI) may be used, provided the patient is volume-expanded/well hydrated.
- Severe bradycardia/AV block:
    - Atropine: 0.02-0.04 mg/kg IV, SQ, or IM; repeat as needed; *or*
    - Isoproterenol: 0.4 mg in 250 mL of D5W, drip slowly IV to effect; *or*
    - Temporary cardiac pacing (see)
- Control seizures (see p. 1009) with diazepam (0.5-1 mg/kg IV) or pentobarbital (3-15 mg/kg IV slowly to effect).
- Supplement potassium in hypokalemic patients when the potassium is below 2.5 mEq/L.
- Oxygen therapy if pulmonary edema occurs

CHRONIC TREATMENT

Some animals may need continued treatment for renal insufficiency.

DRUG INTERACTIONS

- CCBs will increase blood levels of propranolol and digoxin.
- Propranolol, ketoconazole, and itraconazole increase CCB levels by reducing clearance of CCBs.
- Cimetidine will increase bioavailability of CCBs.
- Phenobarbital will increase clearance of CCBs.

POSSIBLE COMPLICATIONS

- Pulmonary edema
- Renal insufficiency due to decreased renal perfusion

RECOMMENDED MONITORING

- Blood pressure
- ECG
- Electrolytes
- Serum chemistry panel, especially renal parameters
- Respiration (rate, lung sounds, pulse oximetry)
- CNS signs

PROGNOSIS AND OUTCOME

- Prognosis is generally good with prompt treatment. Refractory hypotension, severe hyperglycemia, and pulmonary edema may convey a guarded prognosis.
- After recovery, long-term effects are uncommon. Organ dysfunction secondary to sustained hypotension is possible, such as myocardial ischemia or renal failure.

PEARLS & CONSIDERATIONS

COMMENTS

- Many preparations of CCBs are sustained-, controlled-, extended-, or delayed-release medications, which may substantially lengthen the onset and duration of signs.
- Bezoar formation is possible with ingestion of large quantities of sustained/controlled/extended/delayed-release preparations, especially nifedipine.
- Signs of toxicosis can occur at veterinary therapeutic doses of CCBs. These medications have a narrow margin of safety.
- Noncardiogenic pulmonary edema is possible as a toxic effect; fluid overload should be avoided.

PREVENTION

Owners should keep all medications out of reach of pets.

TECHNICIAN TIPS

It is important to know whether CCB involved in the intoxication is regular or extended-release medication.

CLIENT EDUCATION

Owners should be made aware of possible adverse effects when veterinary patients are prescribed CCBs.

SUGGESTED READING

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AUTHOR: CRISTINE HAYES

EDITOR: SAFDAR KHAN

Calcipotriene/Vitamin D3 Analog Toxicosis

BASIC INFORMATION

DEFINITION

Synthetic vitamin D3 analogs are used topically for treating psoriasis in human and occasionally for treating some skin conditions in dogs and cats. Toxicosis manifests acutely with nonspecific signs of illness and within days may cause kidney disease/renal failure.

SYNONYMS

Calcipotriene, calcipotriol = 1,25 dihydrocholecalciferol (= calcitriol) analog; Tacalcitol = 1,24 dihydrocholecalciferol analog; vitamin D2 = ergocalciferol; vitamin D3 = cholecalciferol. Popular brands (calcipotriene): Dovonex; Taclonex, Dovobet (calcipotriene 0.005% or 50 mcg/g)

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs appear to be very sensitive to toxicosis

RISK FACTORS

- Dogs, especially young dogs, with indiscriminate eating habits
- Patients with chronic kidney disease may be at higher risk for adverse renal effects
- Presence of vitamin D3 analog in pet's environment

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- History of ingestion of vitamin D3 analog (chewed up tube/capsules) possible
- Anorexia, vomiting, lethargy, diarrhea within 12-24 hours of ingestion
- PU/PD (due to renal failure) within24-72 hours

PHYSICAL EXAM FINDINGS

- Depression, lethargy, and weakness
- Vomiting (hematemesis), diarrhea (melena)
- Signs of dehydration
- Cardiac arrhythmias
- Seizures (usually seen within 1-3 days of ingestion, if at all)

ETIOLOGY AND PATHOPHYSIOLOGY

Source:

- Vitamin D3 analogs are available by prescription as creams, lotions, ointment, and capsules. Toxicosis occurs secondary to acute accidental ingestions by the patient.

Mechanism of Toxicosis:

- Through calcium-binding proteins, vitamin D3 analogs increase the amount of calcium absorbed from the intestines, as well as increasing bone resorption of calcium and renal tubular resorption of calcium.
- The result is hypercalcemia and hyperphosphatemia.
- Unregulated increases in calcium and phosphorus result in soft-tissue mineralization, especially kidneys, myocardium, large blood vessels, and GI tract.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is based on suspected or confirmed history of exposure to calcipotriene or other vitamin D3 analogs and development of clinical signs including vomiting, anorexia, weakness, and lethargy initially; polydipsia, polyuria, and renal failure >24-72 hours after exposure. Hypercalcemia and hyperphosphatemia are noted in virtually all clinically important cases at first and may normalize while renal values rise (renal damage is due to precipitation of calcium in kidneys, and in certain cases, serum calcium and phosphorus levels may have normalized while azotemia persists), indicating renal failure. A patient with normal serum Ca, P, and renal values 3 or more days after exposure either was not exposed or received a minor exposure.

DIFFERENTIAL DIAGNOSIS

- Rodenticide cholecalciferol ingestion
- Other causes for hypercalcemia (see pp. 553 and 1397) plus hyperphosphatemia include chronic kidney disease, hypoadrenocorticism, lymphoma, perianal adenocarcinoma, multiple myeloma, osteolytic tumors.

INITIAL DATABASE

- CBC and serum biochemical profile (hyperphosphatemia and/or hypercalcemia usually in 12 hours; increased BUN, creatinine within 1-3 days if at all; monitor at least every 24 hours for 3-4 days or longer if abnormalities noted.
- Calcium (mg/dL) phosphorus (mg/dL) product (historically, >70 has suggested greater risk for dystrophic mineralization)
- Urinalysis including specific gravity
- Abdominal and thoracic radiographs +/− ultrasound (dystrophic mineralization)

ADVANCED OR CONFIRMATORY TESTING

Rarely practical during active management of toxicosis

- Increased serum 25-hydroxycholecal-ciferol; no assays available to detect calcipotriene in clinical cases
- Total wet weight calcium may be elevated in kidneys.
- Histopathologic evidence of tissue mineralization (kidneys, aorta, GI mucosa, lungs, heart)

TREATMENT

TREATMENT OVERVIEW

- Immediate treatment of renal failure, cardiac arrhythmias, and seizures as needed
- Prevention of absorption by inducing emesis and administering activated charcoal in promptly presented patient (no clinical signs)
- Promote calciuresis and limit calcium and phosphorus absorption from intestine.
- Inhibit release of calcium and phosphorus from bone.
- Judicious supportive care, notably with intravenous fluids

ACUTE GENERAL TREATMENT

- Prevent absorption: emesis if <4 hours (hydrogen peroxide 3%, 0.25-0.5 mL/kg PO once [dogs] or xylazine hydrochloride, 0.44 mg/kg IM [cats] followed by activated charcoal, 2 g/kg suspended in 10 mL tap water PO; follow label directions for brands) and a cathartic, given q 8 h 24 hours
- Promote calciuresis: saline diuresis using isotonic crystalloids (e.g., 0.9% saline) at 130 mL/kg/d barring cardiovascular contraindications; furosemide, 2.5-4.5 mg/kg PO, IM, or IV q 6-8 h; prednisolone, 1-3 mg/kg PO q 8-12 h
- Inhibit release of calcium and phosphorus from bone (specific antagonist): pamidronate, 1.3-2 mg/kg IV infusion over 2 hours. Repeat in 3-7 days if needed based on persistent hypercalcemia.
- Phosphate binders (e.g., aluminum hydroxide, 10-30 mg/kg PO q 8 h)

CHRONIC TREATMENT

Several days or even weeks of ongoing treatment (including hospitalization) may be needed for treating hypercalcemia, hyperphosphatemia, and renal failure in some cases.

NUTRITION/DIET

Kidney disease dietary therapy (optimized protein, low calcium diet)

POSSIBLE COMPLICATIONS

Calcification of soft tissues—especially in kidneys, lungs, walls of great vessels

RECOMMENDED MONITORING

Follow serum renal, calcium, phosphorus values—initially daily, then weekly until they remain normal without medical support.

PROGNOSIS AND OUTCOME

- Good if treatment is initiated before persistent hypercalcemia, azotemia, and soft-tissue calcification
- Guarded for several months after a patient recovers from hypercalcemia and hyperphosphatemia of several months' duration; calcified plaques in walls of great vessels are intrinsically weaker, can rupture

PEARLS & CONSIDERATIONS

COMMENTS

- Ingestion of 40-60 mcg/kg of calcipotriene or more in dogs can lead to marked hypercalcemia, hyperphosphatemia, renal failure and death.
- Several human supplements contain large amounts of vitamin D, up to 5000 IU (= 0.125 mg).
- 40 IU of vitamin D = 1 mcg or 1 IU of vitamin D3 = 0.025 mcg of cholecalciferol
- The recommended dose of calcitriol for treatment of renal secondary hyperparathyroidism in dogs is 1.65-3.63 ng/kg *(please note it is nanogram not microgram)* PO q 24 h. This corresponds to 0.00165-0.00363 micrograms per kilogram.

PREVENTION

- Prevent pet access to vitamin D3-containing products.
- Store medications in pet-proof cabinets.

TECHNICIAN TIPS

Keep in mind that topical creams/ointments may be potent (contain vitamin D analogs) and can cause life-threatening intoxications. If an owner is using a human skin cream on a pet's skin abrasion, be sure the cream does not contain calcipotriene or other similar compound.

CLIENT EDUCATION

- Maintain information on types of topical medications used in the home.
- Keep a list of all medications in the home, separate from the medications themselves.

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Calcinosis Cutis and Calcinosis Circumscripta

BASIC INFORMATION

DEFINITION

- Calcinosis cutis is uncommon and characterized by inappropriate deposition of calcium within the skin. Calcinosis cutis typically denotes a specific form of dystrophic calcification associated with spontaneous or iatrogenic hyperadrenocorticism.
- Calcinosis circumscripta is a localized nodular deposition of calcium in subcutaneous tissue or in other areas such as the tongue, tendons, and ligaments.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Calcinosis cutis develops as a result of another underlying disorder in dogs, most commonly spontaneous or iatrogenic hyperadrenocorticism. It has been reported in three dogs being treated for blastomycosis with amphotericin B, one dog with atypical fungal infection, and another dog with suspected leptospirosis.
- Calcinosis circumscripta is an uncommon disorder found in dogs younger than age 2 years. It is rare in cats.

GENETICS & BREED PREDISPOSITION

Calcinosis circumscripta is typically found in large-breed dogs, with German shepherds being predisposed.

RISK FACTORS

- Increased risk of calcinosis cutis with chronic administration of exogenous corticosteroids
- Calcinosis circumscripta lesions develop at sites of repetitive trauma.

ASSOCIATED CONDITIONS & DISORDERS

- Calcinosis cutis: hypertrophic osteodystrophy and idiopathic polyarthritis

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Calcinosis cutis is classified as dystrophic, metastatic, idiopathic or iatrogenic.

- *Dystrophic calcification* is either localized or generalized. Localized dystrophic calcification occurs as a result of tissue abnormalities or injury. Generalized dystrophic calcification most commonly occurs in dogs with spontaneous or iatrogenic hyperadrenocorticism.
- *Metastatic calcification* is the calcification of normal skin secondary to an underlying abnormality in calcium or phosphorus metabolism. Although rare, canine and feline metastatic calcification has been reported with chronic renal failure and is restricted to the footpads.
- *Idiopathic calcification* occurs in localized (calcinosis circumscripta) or generalized forms. The underlying cause is unknown.
- *Iatrogenic calcinosis cutis* occurs secondary to percutaneous absorption or penetration of calcium-containing products (e.g., calcium chloride). It has been reported in both dogs and cats as a consequence of subcutaneous injections of calcium-containing solution.

HISTORY, CHIEF COMPLAINT

- Dogs affected with calcinosis cutis may present for evaluation of erythematous papules or plaques with gritty surfaces, with or without concurrent pruritus.
- In calcinosis circumscripta, dogs present with a solitary mass over bony prominences or in the oral cavity, particularly the tongue.

PHYSICAL EXAM FINDINGS

- Calcinosis cutis lesions may be found anywhere on the body but typically develop along the dorsum of the trunk, inguinal region, and axillae. Early lesions are erythematous papules that coalesce to form firm, gritty plaques. A chalky white to pink material can be seen through intact epidermis of early nonulcerated lesions. Ulceration and crusting occur during transepidermal elimination of mineralized debris. Lesions can be quite pruritic, leading to extreme self-trauma.
- Calcinosis circumscripta is usually a solitary lesion, but multiple masses are possible. The lesion is a firm, haired to alopecic, well-circumscribed, subcutaneous or deep dermal mass that may ulcerate and discharge a chalky or gritty substance.

ETIOLOGY AND PATHOPHYSIOLOGY

- The pathogenesis of calcinosis cutis and calcinosis circumscripta probably involves abnormally high mitochondrial calcium phosphate levels, resulting in crystal formation and cell death. Calcium salts are deposited along collagen and elastin fibers.

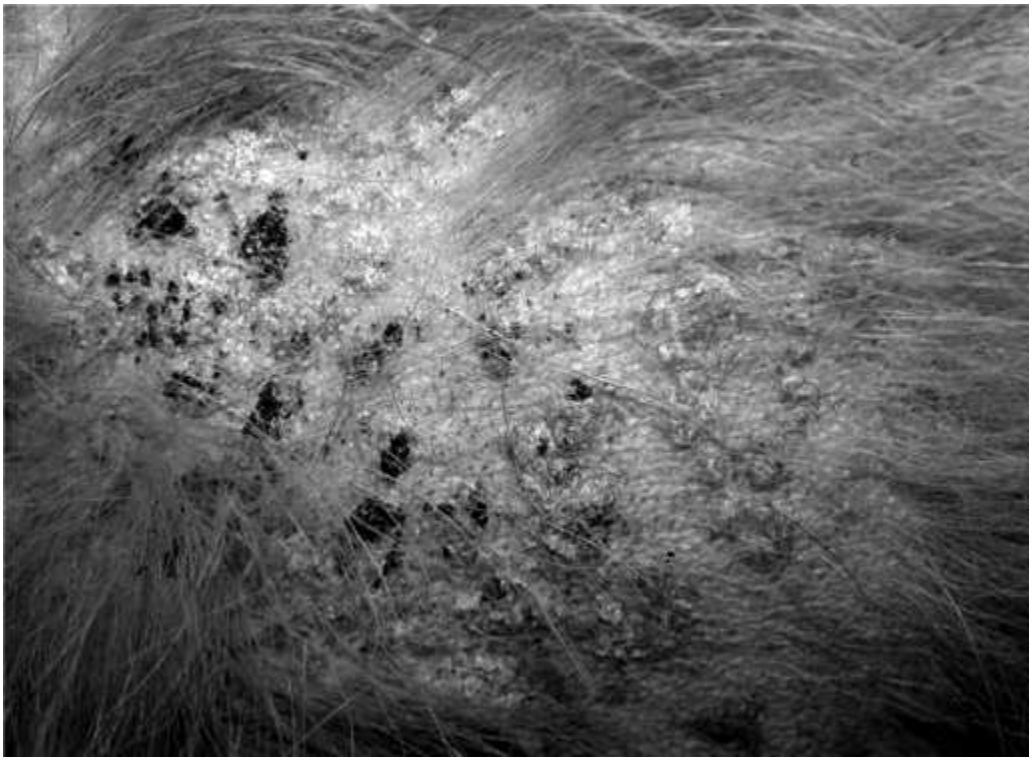
DIAGNOSIS

DIAGNOSTIC OVERVIEW

Physical examination is the cornerstone of diagnosis: calcinosis cutis is suspected when erythematous papules or plaques that may exude a gritty white substance develop in dogs with iatrogenic or spontaneous hyperadrenocorticism. Biopsies are usually performed for confirmation.

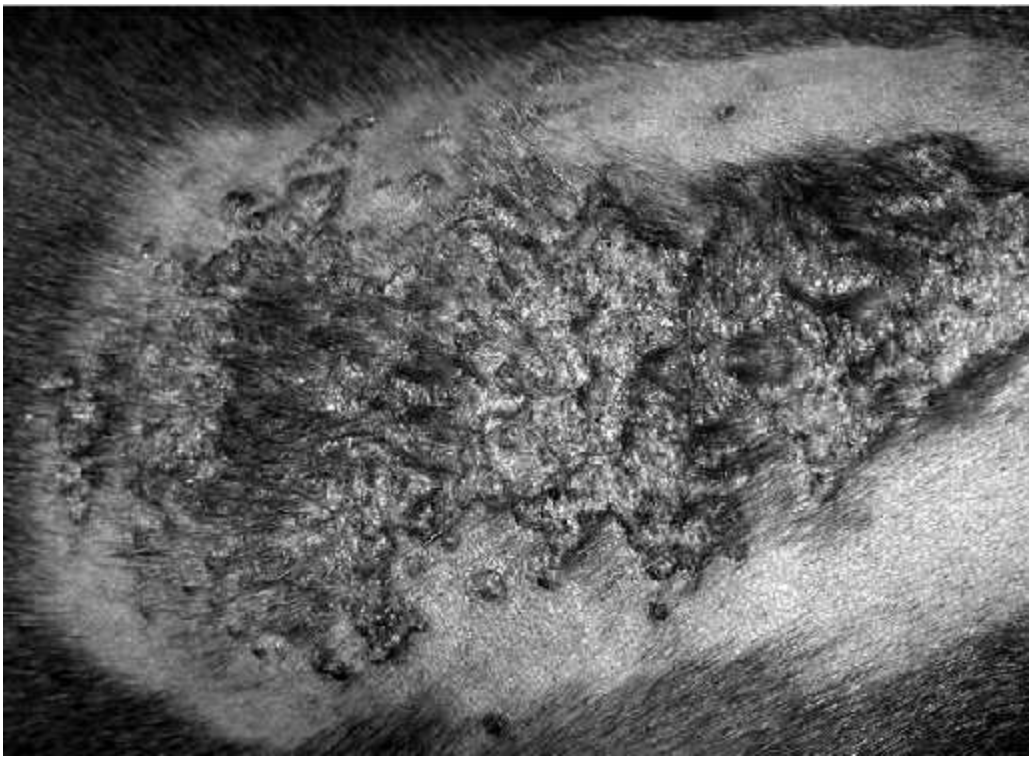
DIFFERENTIAL DIAGNOSIS

- Calcinosis cutis: bacterial pyoderma, deep fungal infection, demodicosis, neoplasia
- Calcinosis circumscripta: neoplasia, foreign body



EARLY LESIONS OF CALCINOSIS CUTIS. Note the crusted, erythematous papules.

(Courtesy Dr. J. Wellington.)



CALCINOSIS CUTIS Calcinosis cutis on dorsal cervical region of a boxer with spontaneous hyperadrenocorticism.

(Courtesy Dr. J. Wellington.)

INITIAL DATABASE

- Cytologic evaluation of exudates: amorphous gritty material
- Skin scrapings: sample has gritty consistency when smeared onto microscope slide
- Routine hematologic and biochemical profile: changes associated with hypercortisolism are usually noted in spontaneous and iatrogenic hyperadrenocorticism cases
- Normal calcium and phosphorus levels are typically found, except in patients with metastatic calcification.

ADVANCED OR CONFIRMATORY TESTING

- Skin punch biopsies and histopathologic analysis: multifocal accumulations of finely or coarsely granular amorphous basophilic debris in deep dermal or subcutaneous tissue encompassed by granulomatous inflammation
- Radiographs: conglomerated calcified mass in skin or subcutis with calcinosis circumscripta

TREATMENT

TREATMENT OVERVIEW

In most patients with calcinosis cutis, lesions slowly resolve spontaneously once the underlying disease is controlled or resolved. Surgical excision is curative for solitary lesions of calcinosis circumscripta.

ACUTE GENERAL TREATMENT

- Discontinue or reduce dosage of systemic corticosteroids.
- Oral antihistamines and bathing with oatmeal-based shampoo may be effective in controlling pruritus associated with calcinosis cutis.

CHRONIC TREATMENT

- Topical dimethyl sulfoxide applied to up to one-third of body each treatment may dissolve the calcium. If lesions are extensive, serum calcium levels should be monitored for hypercalcemia with this therapy.
- Hydrotherapy and frequent bathing with antibacterial shampoo will reduce pruritus and potential for secondary bacterial

infection.

PROGNOSIS AND OUTCOME

- Calcinosis cutis may regress spontaneously without treatment over weeks to months, with resolution or control of the underlying disease.
- Recurrence of calcinosis circumscripta lesions post surgical excision does not occur.

PEARLS & CONSIDERATIONS

COMMENTS

In patients with calcinosis cutis associated with excessive glucocorticoids, lesions increase in size, or new lesions may appear for up to 3 months after discontinuing the steroid or treatment of spontaneous hyperadrenocorticism.

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Cachexia, Cardiac

BASIC INFORMATION

DEFINITION

Weight and lean tissue loss commonly associated with congestive heart failure (CHF)

EPIDEMIOLOGY

SPECIES, AGE, SEX

More common in dogs than in cats

RISK FACTORS

More common in right-sided or biventricular than in isolated left-sided CHF but can occur regardless of underlying cause

ASSOCIATED CONDITIONS & DISORDERS

Occurs secondary to CHF

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Cachexia ranges in severity from subtle muscle loss to severe, end-stage muscle wasting.

HISTORY, CHIEF COMPLAINT

Heart failure (see p. 470)

PHYSICAL EXAM FINDINGS

- Loss of lean body mass first noted in epaxial, gluteal, scapular, or temporal muscles; may be subtle initially
- Carefully palpate obese animals and animals with ascites or subcutaneous edema to determine whether muscle loss is present.

ETIOLOGY AND PATHOPHYSIOLOGY

- Cardiac cachexia reduces strength, immune function, and survival.
- Decreased food intake, increased energy requirements, and production of the inflammatory cytokines, tumor necrosis factor (TNF) and interleukin 1 (IL-1)
    - TNF and IL-1 cause anorexia, increased energy requirements, catabolism of lean body mass, myocardial fibrosis, and decreased cardiac contractility (negative inotropy).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

All animals with CHF should be assessed carefully for early signs of muscle loss so that cachexia can be detected at its early stages when intervention is more likely to be successful.

DIFFERENTIAL DIAGNOSIS

Cachexia from other diseases (e.g., cancer, renal failure)

INITIAL DATABASE

- Diet history, including specific types and amounts of food eaten, dietary supplements, treats, and foods used for administering medications
- Evaluation for potential causes of anorexia (e.g., worsening CHF; medication side effects such as azotemia, hyperkalemia, or hypotension; unpalatable diet)

TREATMENT

TREATMENT OVERVIEW

The goals of treating cardiac cachexia are to (1) optimally manage CHF, (2) minimize anorexia, (3) reduce energy requirements, (4) ensure adequate protein intake, and (5) modulate cytokine production.

ACUTE GENERAL TREATMENT

- In acute CHF episodes, avoid diet changes until the patient is home and stabilized on medications.
- To avoid food aversions, introduce new diet gradually when patient is stabilized.

CHRONIC TREATMENT

- Ensure optimal medical therapy for CHF (see p.470).
- Nutritional management is key to the effective chronic treatment of cardiac cachexia (see below).

NUTRITION/DIET

- Tips to minimize anorexia (see p.1377):
  - Reduced sodium diet palatable to individual patient may require diet changes (e.g., dry to canned, or different brand or flavor).
  - Balanced homemade diet formulated by veterinary nutritionist
  - Smaller, more frequent meals
  - Palatability enhancers (cooked meat or low-sodium broth)
  - Fish oil supplementation (see “Modulate cytokine production” below)
- Reduce energy requirements:
  - Optimal management of CHF
  - Exercise restriction
- Ensure adequate protein intake:
  - Avoid protein-restricted diets (e.g., “renal” diets or cardiac diets with <5.1 g/100 kcal protein)
- Modulate cytokine production:
  - Administer one 1-gram fish oil capsule (containing 180 mg eicosapentaenoic acid and 120 mg docosahexaenoic acid) per 5 kg body weight q 24 h.
  - Fish oil should contain vitamin E as an antioxidant, but no other nutrients.
  - Cod liver oil and flaxseed oil should not be used (ineffective).

DRUG INTERACTIONS

Medication side effects can contribute to cachexia by causing anorexia (e.g., digoxin toxicity, azotemia secondary to angiotensin-converting enzyme inhibitor or overzealous diuretic use).

RECOMMENDED MONITORING

- Body weight (be sure to adjust for ascites) and assessment of muscle loss
- Appetite and food intake

PROGNOSIS AND OUTCOME

Prognosis depends on the underlying cardiac disease. However, anorexia is a common contributing factor to an owner's decision for euthanasia.

PEARLS & CONSIDERATIONS

COMMENTS

- Animals with CHF often have variable and cyclical appetites. Reassure owners that this is common, and that they can offer favorite (low-sodium) foods when this occurs. However, anorexia longer than 24-48 hours should trigger reevaluation of CHF and medications.
- Centesis should be performed on anorectic animals with a significant ascites or pleural effusion to reduce fluid accumulation (for comfort).
- Animals with CHF may prefer foods at a particular temperature (e.g., room temperature, warmed, refrigerated, or even frozen).
- Dogs with CHF often prefer sweet tastes, particularly as the disease progresses. Adding items such as maple syrup, fruit-flavored yogurt, or applesauce to the dog's food may improve food intake.

PREVENTION

- None known
- Early detection in more subtle stages
- Minimize by ensuring adequate food intake and optimal therapy for CHF

CLIENT EDUCATION

- Sodium intake:
  - Provide owner-specific instructions regarding foods high in sodium (to be avoided), appropriate dog foods, acceptable low-salt treats, and methods for administering medications.
- Appetite:
  - Provide the owner with suggestions for improving the animal's appetite (see Nutrition/Diet above and).

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EDITOR: KATHRYN E. MICHEL

Cachexia, Cancer-Associated

BASIC INFORMATION

DEFINITION

The term *cancer cachexia* refers to weight loss in an animal or person with underlying neoplastic disease. Classic defining clinical features of the syndrome include severe involuntary weight loss, fatigue, anemia, and progressive depletion of both lean body mass and adipose stores.

SYNONYM

Cancer-associated weight loss

EPIDEMIOLOGY

SPECIES, AGE, SEX

Cancer cachexia has been reported in association with neoplastic disease in many species, including people, cats, and dogs with naturally occurring malignancies, as well as laboratory rodents bearing implanted tumors. Animals of any age and either sex may be affected.

RISK FACTORS

- Advanced clinical stage of neoplastic disease
- Tumors of the upper gastrointestinal tract (esophagus, stomach, and pancreas) in humans
- Lower risk in people with treatment-responsive lymphomas, soft-tissue sarcomas, and breast cancer
- Cancer cachexia is less common in dogs than in people.
- Cats appear to be at greater risk for cancer cachexia than dogs: up to 90% of cats with neoplastic disease experience clinically apparent loss of lean body mass.

ASSOCIATED CONDITIONS & DISORDERS

Cancer cachexia is a form of protein-energy malnutrition, the most common form of malnutrition found in critically ill animals and people. It occurs when protein and energy intake is insufficient to meet requirements. Protein-energy malnutrition is associated with hypoproteinemia, delayed wound healing, immunosuppression, and compromised gastrointestinal, pulmonary, and cardiovascular function. Multiorgan failure and death will be the eventual outcome unless nutritional support is provided and the primary underlying disease process is resolved.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

Although weight loss is the primary abnormality in all cats and dogs with cancer cachexia, specific historical findings differ substantially from animal to animal. Weight loss may be mild to profound in severity, ranging from acute to chronic in duration. Weight loss is also superimposed on any clinical signs associated with the underlying neoplastic disease, which vary with the specific diagnosis.

PHYSICAL EXAM FINDINGS

Physical exam findings in animals with cancer cachexia can be divided into two groups: abnormalities related to cancer cachexia, and abnormalities caused by the animal's underlying cancer. The clinical signs associated with cancer cachexia are nonspecific, initially may be subtle, and can easily be overlooked. Findings may include muscle wasting, pallor, weakness, poor haircoat, hepatomegaly, splenomegaly, evidence of chronic infections, and lymphadenopathy. Peripheral edema could be present in severe cases. Physical exam findings related to the underlying malignancy are highly variable and depend on the animal's specific histopathologic diagnosis and stage of disease. No two animals with cancer cachexia have exactly the same presentation.

ETIOLOGY AND PATHOPHYSIOLOGY

- The etiology of cancer cachexia is highly variable and multifactorial.
- There are two major categories of cancer cachexia: primary and secondary.
- Primary cancer cachexia is an incompletely understood paraneoplastic syndrome in which tumor-related changes in host metabolism lead to inefficient use of consumed calories, in turn leading to gradual depletion of lean body mass and adipose stores. No matter how many calories are fed or by what route, host requirements cannot be met.
- Recent studies suggest that primary cancer cachexia may be an inflammatory disorder caused by alterations in proinflammatory mediators such as interleukin (IL)-1 alpha, IL-1 beta, IL-6, tumor necrosis factor alpha (TNF-α), and various eicosanoids.
- Secondary cancer cachexia is caused by one or more of a variety of functional abnormalities that decrease nutrient intake, digestion, or absorption. Examples include the physical presence of tumor within the digestive tract, causing gastrointestinal dysfunction, or side effects of radiotherapy or chemotherapy such as stomatitis, vomiting, and gastroenteritis.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Dogs and cats with cancer-associated cachexia have objective evidence of loss of lean body mass and adipose stores as demonstrated by weight loss and a decline in body condition score.

DIFFERENTIAL DIAGNOSIS

Differential diagnoses for weight loss in a cat or dog with cancer:

- Primary cancer cachexia (paraneoplastic abnormalities in energy metabolism)
- Secondary cancer cachexia:
    - Tumor involving the intestinal tract
    - Paraneoplastic syndromes other than cancer cachexia:
        - Hypercalcemia
        - Fever
    - Treatment-related toxicity:
        - Altered taste and smell perception
        - Learned food aversions
        - Stomatitis/mucositis
        - Gastroenteritis
        - Centrally mediated nausea and vomiting
- Concurrent disease:
    - Infection:
        - Bacterial, viral, fungal, oomycotic, or rickettsial
    - Organ dysfunction/failure (i.e., liver, kidney, lung)
    - Diabetes mellitus
    - Hyperthyroidism (cats)
- Inappropriate nutritional management (unsuitable diet, inadequate caloric intake)

INITIAL DATABASE

- Diet history (specific ration fed and quantity consumed, plus all treats, supplements, and medications)
- Body weight and body condition score
- CBC
- Serum biochemistry profile
- Urinalysis
- Chest and abdominal radiographs
- Retroviral screening (cats)
- Serum thyroxine concentration (cats)

ADVANCED OR CONFIRMATORY TESTING

- Thoracic and abdominal ultrasonography
- Cross-sectional imaging (CT, MRI)
- Endoscopy
- Urine culture and sensitivity
- Fine-needle aspiration cytology, impression smears, or tissue biopsy to confirm the presence or absence of neoplastic cells, organisms, or other abnormalities in suspected lesions

TREATMENT

TREATMENT OVERVIEW

The basic goals of therapy in the cat or dog suffering from cancer cachexia are twofold:

- Return the animal to ideal body condition.
- Maintain the animal in ideal body condition long term.

These goals are accomplished by diagnosing and treating the underlying malignancy and providing appropriate nutritional support.

ACUTE GENERAL TREATMENT

- Cancer cachexia is a paraneoplastic syndrome, so eradication of the underlying neoplastic disease is the best treatment. This goal can be met by:
    - Obtaining a rapid and accurate definitive diagnosis of neoplasia, including neoplasm type and clinical stage
    - Initiating timely and effective antineoplastic therapy
- An individualized feeding protocol is instituted concurrently and is based on the animal's nutritional assessment as defined by the minimum database outlined previously.

CHRONIC TREATMENT

Nutritional recommendations are adjusted as necessary based on repeat nutritional assessment, with the goal of maintaining ideal body condition:

- Food intake is increased or decreased as needed in response to changes in body weight and condition.
- Assisted feeding can be used intermittently to maintain nutrient intake.
- The specific ration recommended for an individual animal may change depending on the progression of the underlying neoplastic disease and concurrent conditions.

NUTRITION/DIET

- Components of the feeding protocol for an animal with cancer-associated cachexia must include:
    - Fluid requirement in milliliters per day

    - Energy requirement in kilocalories per day
    - A choice of commercial ration that meets the animal's needs:
        - Calories appropriately distributed among protein, fat, and carbohydrate
        - All necessary nutrients (i.e., vitamins and minerals) present in correct quantities and ratios
    - A method of feeding that will be tolerated by the animal
- No single diet is appropriate for every animal with cancer cachexia, because underlying disease, nutritional status, and nutrient requirements are highly variable from case to case.
    - Rations with ample protein and fat are often recommended for weight-losing cats and dogs with cancer.
    - Individual restriction of protein, fat, or carbohydrate intake may be indicated, depending on preexisting or concurrent conditions such as renal or hepatic insufficiency, pancreatitis, or diabetes mellitus.
- Voluntary intake is the most practical feeding technique, but quantities of food and water consumed must be measured to ensure that requirements are actually met.
- Assisted feeding should be instituted without delay in animals unable to meet their own nutrient requirements.
- Assisted enteral feeding using some type of feeding tube is usually preferred, because it allows nutrients to be metabolized through normal pathways and is more effective in maintaining gut health.
- Fluid deficits and electrolyte or acid-base imbalances should be corrected before any type of assisted feeding is attempted.

POSSIBLE COMPLICATIONS

- Gastrointestinal intolerance
- See online chapter: Refeeding Syndrome

RECOMMENDED MONITORING

- Nutritional assessment, including diet history, body weight, and body condition score, should be repeated at regular intervals.
- Diagnostics are repeated as indicated based on underlying neoplastic disease and nutritional status; this commonly includes CBC, serum biochemistry profile, urinalysis, and imaging studies.

PROGNOSIS AND OUTCOME

- Cancer cachexia has a well-documented negative effect on quality of life and prognosis in people, and its impact is highly likely to be the same in cats and dogs.
- Increased incidence and severity of treatment-related toxicities, lower treatment response rates, shorter remission durations, and shorter survival times should be expected in weight-losing animals when compared to weight-stable animals with the same tumor.

PEARLS & CONSIDERATIONS

COMMENTS

- Several studies now show that many dogs with cancer are actually obese. Indiscriminate use of high-fat diets in these animals will simply promote additional weight gain and its associated health problems. The primary goal of nutritional therapy in any cat or dog with cancer is always to maintain ideal body weight and condition.
- Recent work suggests that cats with cancer are more likely to have weight loss than dogs. However, it is not yet clear if this weight loss is specifically related to the presence of underlying neoplastic disease, or if it is a generic response to critical illness in the cat.

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Dystocia

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Difficulty in the normal vaginal delivery of a neonate from the uterus

SYNONYM

Ineffective labor

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs > cats, older > younger

GENETICS & BREED PREDISPOSITION

- Brachycephalic breeds have a higher incidence due to fetal head/birth canal size mismatch and a steep angle of the entrance of the maternal pelvic canal from the abdomen.
- Some purebred colonies (assistance-dog colonies) have a higher-than-breed-average incidence of dystocia, suggesting heritability.
- Breed, parity (number of previous litters), and litter size can influence gestational length (determined to be 65 +/− 1 day from the LH surge or the initial rise in progesterone between 1.5-3 ng/mL) by 1-2 days.

RISK FACTORS

- Large litters
- Poor prepartum condition of the dam
- Small litters with oversized fetuses or prolonged gestation
- Breed conformation, obesity, preeclampsia, malnutrition, vaginal canal abnormalities (strictures, vaginal hyperplasia), pelvic abnormalities (healed fractures with reduction in pelvic canal), and abdominal wall defects (hernias) can predispose a dam to dystocia.
- A previous normal caesarean section does not predispose a bitch to dystocia.

ASSOCIATED CONDITIONS & DISORDERS

Hypocalcemia, hypoglycemia, hypovolemia

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Dystocia can be categorized as resulting from maternal causes, fetal causes, or most commonly a combination of maternal and fetal causes.

HISTORY, CHIEF COMPLAINT

- A client's perception that labor is not initiated or progressing as expected, most commonly due to:
  - Time between stages of labor. Stage I labor typically lasts no more than 12-24 hours.
  - Time between sequential deliveries of neonates. Typically, sequential deliveries should be within 1 hour.
- Alternatively, the presence of stillbirths can prompt presentation for dystocia.
- The clinician must quickly obtain a careful reproductive history detailing: ○ Breeding dates
  - Onset of diestrous behavior
  - Any ovulation timing performed
  - Previous dystocia
  - General medical history

PHYSICAL EXAM FINDINGS

- Physical examination may be unremarkable; normal physical exam findings do not rule out dystocia.
- Typically, dams in stage I labor (uterine contractions) or stage II labor (uterine and abdominal contractions) are euthermic, mildly agitated, trembling, mildly hyperpneic, and nesting.
- Variable abnormal physical findings include atypical vulvar discharge (green, malodorous, frankly hemorrhagic), a fetus or fetal membranes in the birth canal (i.e., presence of a fetus caudal to the cervix, which may be palpable over the brim of the pelvis or may be partially protruding out of the vulva), muscle tremors, fatigue, persistent vomiting, and protracted tenesmus (abdominal efforts).
    - Uteroverdin (green vaginal discharge) indicates placental separation and indicates the need for veterinary medical or surgical intervention if fetal delivery is not prompt.
    - Malodorous discharge suggests fetal death and necrosis or metritis.
    - Inappropriately voluminous hemorrhage should prompt evaluation for uterine trauma (surgical exploration) or abnormal placental site coagulation (medical ± surgical evaluation) or a coagulopathy.
- Protracted muscle tremors, vomiting, or marked fatigue suggest metabolic abnormalities (hypoglycemia, hypocalcemia, ketosis) or exhaustion.
- Protracted tenesmus suggests obstruction or uterine inertia.

ETIOLOGY AND PATHOPHYSIOLOGY

- Normal labor proceeds through three stages:
    - Stage I labor: onset and increase in the frequency and strength of uterine contractions. The dam may be restless or agitated. No external contractions are visible.
    - Stage II labor begins when abdominal efforts (tenesmus) coincide with uterine contractions, resulting in the delivery of a neonate through the birth canal.
    - Stage III labor consists of the delivery of the placenta.
    - Dams typically progress through stage I labor in 12-24 hours and alternate between stages II and III until all neonates and placentae are delivered. Placentae normally may be delivered with the neonate or separately.
- Etiology of dystocia: maternal/fetal causes
    - Maternal dystocia: primary or secondary uterine inertia, birth canal or abdominal wall defects (strictures, hernias), severe perivulvar edema, lack of lubrication in the birth canal, uterine torsion or tear, metabolic derangements
    - Fetal dystocia: oversized, malformed (anasarca), malpositioned, malpostured fetus
    - Combined maternal/fetal dystocia: mismatch of birth canal size versus fetal size
    - Caudal presentations in dogs and cats are normal.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A correct diagnosis of dystocia is dependent on taking an accurate history and performing a thorough physical examination in a timely manner.

DIFFERENTIAL DIAGNOSIS

- Normal labor
- Misinformation about gestational length (see p. 909), in which case lack of labor is then normal
    - In the bitch, gestation is normally terminated 64-66 days from the initial rise in progesterone corresponding to the LH surge, or 56-58 days from the first day of diestrus (the first day vaginal cytology is <50% superficial cells). If no ovulation timing was performed, establishing the first day of behavioral diestrus (refusing the male) can provide guidance.
    - Gestational length from the first breeding date can vary from 58-72 days; this makes determination of due dates from breeding dates risky.
    - In the queen, the mean gestation is 65-66 days from breeding.
    - Ultrasound measurements of gestational sac diameter, crown-rump length, body diameter and/or head diameter can be helpful in determining gestational age when ovulation timing data is not available:
- Completion of labor, misinformation about litter size

Formulas to Predict Gestational Age and Days Before Parturition in the Dog and Cat

GESTATIONAL AGE IN THE DOG (+/− 3 DAYS)

Less than 40 days

Gestational age = (6 × Gestational sac diameter) + 20

Gestational age = (3 × Crown-rump length) + 27

Greater than 40 days

Gestational age = (15 × Head diameter) + 20

Gestational age = (7 × Body diameter) + 29

Gestational age = (6 × Head diameter) + (3 × Body diameter) + 30

DAYS BEFORE PARTURITION IN THE DOG

Days before parturition = 65 - Gestational age

GESTATIONAL AGE IN THE CAT (+/− 2 DAYS)

Greater than 40 days

Gestational age = 25 × Head diameter + 3

Gestational age = 11 × Body diameter + 21

DAYS BEFORE PARTURITION IN THE CAT

Days before parturition = 61 - Gestational age

Gestational age (GA) is based on days post luteinizing hormone (LH) surge in the dog and days post breeding in the cat. Gestational sac diameter (GSD), crown-rump length (CRL), head diameter (HD), and body diameter (BD) measurements are in centimeters. Days before parturition (DBP) is based on 65 +/− 1 days post LH surge in the dog and 61 days post breeding in the cat. Data modified from Nyland et al.

INITIAL DATABASE

- Minimally, hematocrit and total protein (mild decreases expected due to dilution), blood glucose (decreased with prolonged labor), serum electrolytes, and ionized calcium (hypocalcemia possible with prolonged labor) should be evaluated. Urine can be checked for ketones (indicating prenatal mal-nourishment).
- Vaginal digital and/or vaginoscopic examination to determine if a vaginal obstruction exists. In the dog, the cervix (assessing for dilation) and cranial vagina (assessing for obstruction) are beyond the reach of the human finger. Abdominal ultrasound or fetal Doppler evaluation to assess fetal viability.
- Abdominal radiograph to evaluate litter size, relative fetal size and position

ADVANCED OR CONFIRMATORY TESTING

Uterine monitoring (tocodynamometry) to assess strength and frequency of contractions.

- Currently, canine and feline uterine monitors are available for short- or long-term lease through Veterinary Perinatal Services Inc. (www.whelpwise.com).
- Tocodynamometry is the only method of confirming uterine inertia.

TREATMENT

TREATMENT OVERVIEW

Therapeutic goals are to:

- Facilitate delivery of viable neonates, with minimal morbidity to the dam.
- Avoid unnecessary surgical intervention via timely diagnosis and medical intervention.
- Differentiate cases requiring surgical versus medical intervention: surgery is warranted if:

- Refractory (unresponsive) uterine inertia
- Fetal distress and suboptimal response to medical management
- Intractable pain in bitch or queen
- Obvious mismatch of fetal-maternal birth canal size
- Birth canal abnormalities such as strictures or pelvic stenosis that cannot be remedied
    - Minimize fetal stress; neonatal death during the first week of life is related to stress during labor and the immediate postpartum period.
    - Avoid fetal or maternal mortality.
    - Preserve the reproductive capacity of a valuable dam.

ACUTE GENERAL TREATMENT

- Supportive: intravenous balanced electrolyte solution with 5% dextrose if appropriate (dam is hypovolemic, dehydrated, or hypoglycemic)
- Calcium: calcium gluconate 10% solution (= 10 g/100 mL solution, or 0.465 mEq Ca^{++}/mL) (Fujisawa Inc., USA).
    - Given SQ at 1 mL/4.5 kg (10 lb) body weight as indicated by the strength of uterine contractions—generally no more frequently than every 4-6 hours during the second stage of labor.
    - Large volumes of calcium gluconate given subcutaneously may cause local irritation; doses >6 mL should be divided.
    - Intravenous use: generally unnecessary unless systemic signs of severe hypocalcemia are present (see p. 576 for signs and intravenous doses).
    - While most dams are eucalcemic, the benefit of calcium administration is still seen, suggesting a cellular or subcellular effect.
- Oxytocin:
    - The administration of oxytocin increases the frequency of uterine contractions, whereas the administration of calcium increases their strength.
    - Oxytocin, 10 USP units/mL (American Pharmaceutical Partners Inc., Los Angeles) is most effective at mini doses, starting with 0.25 units SQ or IM to a maximum dose of 4 units per bitch or queen.
    - The frequency of oxytocin administration is dictated by the labor pattern, and it is generally not given more frequently than every 30-60 minutes.
    - Uterine contractions compromise placental blood flow and cause fetal hypoxia. Excessive contractions (due to uterine hypertonicity, over-dosage of oxytocin, obstruction) can compromise fetal survival. Uterine relaxation between contractions allows normal placental blood flow to resume.
    - Absolute contraindications to oxytocin therapy: fetal obstruction in any part of the uterus or birth canal, uterine torsion, uterine laceration or rupture.
- Persistence of a fetus in the birth canal beyond 5-10 minutes warrants assisted delivery.
    - Placental separation and the potential for fetal hypoxemia are likely.
    - Caution: traction applied to a fetus retained in the birth canal must be very gentle to avoid trauma to the fetus.
    - Traction is only advised if the veterinarian can position his/her fingers around the fetus's shoulders or hips for gentle traction.
    - Lubrication delivered via a red rubber catheter and water-soluble lubricant jelly can be helpful.
    - Elevation of the bitch's forequarters can assist in manipulation of the fetus in the birth canal.

CHRONIC TREATMENT

Medical therapy for dystocia, based on the administration of calcium gluconate and oxytocin, can be directed and tailored based on the results of tocodynamometry.

DRUG INTERACTIONS

Calcium is given before oxytocin in most cases, improving contractile strength before increasing frequency of contractions. The action of oxytocin is improved when given 15 minutes subsequent to calcium.

POSSIBLE COMPLICATIONS

- Hypercalcemia-induced arrhythmias if calcium solution is given intravenously at too rapid a rate.
- Fetal hypoxia secondary to placental compression during uterine contractions induced by parenteral oxytocin administration, particularly if given inappropriately (too early in labor, when fetal obstruction is present, if uterine torsion is present, too frequently, too rapidly) or at excessive doses.
- Uterine rupture, with fetal and maternal morbidity and mortality if ecbolic agents (oxytocin) are given excessively, inappropriately (too early in labor, when fetal obstruction is present, if uterine torsion is present, too frequently, too rapidly) or when the uterine wall is compromised or torn.

RECOMMENDED MONITORING

- Progression of labor with viable neonates delivered
- Using real-time transabdominal ultrasonography, fetal heart rates should be >180 bpm.
- Sustained fetal heart rates <180 bpm are associated with fetal distress.
- Continued uterine monitoring using tocodynamometry, showing continuation and progression of appropriate contractile strength and frequency

PROGNOSIS AND OUTCOME

Fair to good with timely intervention and appropriate monitoring

PEARLS & CONSIDERATIONS

COMMENTS

Obstruction of the birth canal, regardless of cause (fetal malposition, fetal-dam size mismatch, or anatomic defects of dam), must be ruled out by vaginal palpation. It is an indication for caesarean section and an absolute contraindication for treatment with oxytocin.

PREVENTION

- Complete prebreeding evaluation of the bitch, including a vaginal examination
- Prepartum abdominal radiography to estimate fetal number and relative size in comparison to the dam

CLIENT EDUCATION

Client education about proper prenatal husbandry, accurate gestational length interpretation based on ovulation timing, client recognition of dystocia

SUGGESTED READING

Davidson AP: Dystocia management. In Bonagura JD, editor: Kirk's veterinary therapy XIV. St Louis, 2009, Elsevier Saunders, pp 992–998.

Nyland TG, Mattoon JS: Small animal diagnostic ultrasound. St Louis, 2002, WB Saunders.

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Dyspnea

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Abnormal breathing. In clinical practice, *dyspnea* specifically refers to difficulty breathing.

SYNONYM(S)

Labored breathing, respiratory difficulty, shortness of breath. Severe dyspnea: respiratory distress.

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs and cats of any breed and either sex.

CONTAGION & ZOONOSIS

- Animal-to-animal contagion with certain infectious etiologies
- Public health concern: severely dyspneic dog or cat may bite if distressed/disoriented.

GEOGRAPHY AND SEASONALITY

Dependent on etiology

ASSOCIATED CONDITIONS & DISORDERS

Respiratory stridor, hypoxemia, syncope

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Inspiratory dyspnea: generally caused by upper-airway obstruction
- Inspiratory-expiratory dyspnea, or expiratory dyspnea: generally caused by lower-airway, pulmonary circulatory, pleural, mediastinal, or metabolic problems

HISTORY, CHIEF COMPLAINT

- Dyspnea may be the presenting complaint if severe and/or the owner is observant.
- Nonspecific systemic complaints (anorexia, lethargy; hiding [cats]) may be reported in pets that are more mildly dyspneic or with owners who are less observant.
- Owners may describe excessive abdominal wall excursions (“belly breathing”) as the first manifestation of dyspnea, especially in cats.
- Concurrent complaints, including exercise intolerance, lethargy, and inappetence are common but nonspecific.
- Medical history may be very informative (previous respiratory or systemic problems, current medications, etc.).
- Inciting cause (observed foreign-body inhalation, anticoagulant ingestion few days earlier, etc.) occasionally is reported by the owner.

PHYSICAL EXAM FINDINGS

- Respiratory effort: should be assessed immediately at the beginning of the consultation (e.g., exam room) before the hands-on physical examination increases the respiratory rate in nervous patients.
- Animals with moderate or severe dyspnea often manifest an anxious facial expression, reluctance to lie down, and other signs of discomfort.
- Inspiratory dyspnea
    - Severity varies from mild inspiratory wheeze to extreme gasping actions.

    - The sound of turbulent air at the level of the obstruction may suggest the site of obstruction (e.g., nasal versus tracheal).
    - If nasal obstruction, dyspnea disappears when the animal breathes with the mouth open.
    - Other than potentially severe respiratory distress, animals with upper-airway dyspnea are otherwise generally well: no weight loss, no other physical abnormalities.
- Expiratory or expiratory-inspiratory dyspnea.
    - With lower-airway disease, dyspnea is often accompanied by cough, with or without other general systemic signs (lethargy, anorexia, etc.) or signs more closely related to respiratory disease (e.g., cyanosis).
    - If lower-airway dyspnea is severe, the animal's posture can include abducted elbows, an extended neck, and the canthi of the lips drawn caudally.
    - Cough inducible with tracheal pressure does not indicate whether the problem originates from the upper or lower airway.
- Auscultation
    - Decreased intensity or absence of lung sounds suggests pneumothorax, pleural effusion, intrathoracic mass, or diaphragmatic hernia.
    - Presence of crackles and wheezes is nonspecific.

ETIOLOGY AND PATHOPHYSIOLOGY

- Respiratory center in medulla oblongata and pons is stimulated by ↑CO2, ↑H^+, but not ↓O2.
- Chemoreceptors (carotid bodies, aortic bodies) are stimulated by ↑CO2, ↑H^+, and ↑O2, feeding back to the respiratory center.
- Impulses from the respiratory center activate the intercostal muscles (intercostal nerves, which are branches of thoracic spinal nerves) and diaphragm (phrenic nerves).
- Disturbances in this process can occur at many levels, causing dyspnea.
    - Hypercapnia
    - Acidosis
    - Hypoxemia
    - Physical reduction of lung volume (obesity, diaphragmatic hernia, severe ascites)
    - Respiratory paralysis
    - Airway obstruction
- Causes of dyspnea: pulmonary edema, pleural effusion, upper-airway obstruction (laryngeal paralysis, foreign body, brachycephalic syndrome), pneumonia, chronic sterile bronchitis, pulmonary hypertension, pulmonary thromboembolism, pulmonary hemorrhage, marked ascites, hyperthermia, neuromuscular weakness/paralysis, compensation for metabolic acidosis, anxiety.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The location of an anatomic lesion causing dyspnea may be surmised from the sound of breathing: upper-airway obstructions produce audible turbulence of air on inspiration, and the associated raspy or loud whistling noise is heard to occur close to the mouth (nasal, tracheal, pharyngeal, laryngeal disorders) or in the nasal passages on inspiration. Conversely, lower-airway disorders and metabolic causes for dyspnea typically cause a mixed inspiratory-expiratory dyspnea and no such noise. Thoracic radiographs are the initial diagnostic test of choice.

DIFFERENTIAL DIAGNOSIS

- Panting. Unlike dogs that are panting, dogs with dyspnea are likely to show wide chest excursions, an anxious facial expression, and unwillingness to lie down or rest.
- Reverse sneezing. Loud, inspiratory noises that are sudden in onset and in termination can be abolished by opening the animal's mouth.

INITIAL DATABASE

- Thoracic radiographs: diagnostic test of choice for expiratory or expiratory-inspiratory dyspnea
- Oral/pharyngeal exam (may require sedation) and lateral cervical radiograph if upper-airway dyspnea is suspected
- CBC/serum biochemistry profile/urinalysis: no specific changes; results depend on etiology.
- Serum levels of a cardiac myocyte protein, N-terminal proBNP, are significantly elevated when dogs have dyspnea of cardiac origin (congestive heart failure; median = 24.6 pg/mL) versus of noncardiac origin (median = 2.6 pg/mL) ($P < 0.0001$). This excellent differentiating test is limited by central laboratory availability (not in-house/snap).

ADVANCED OR CONFIRMATORY TESTING

- Arterial blood gas: degree of hypoxemia helps determine intensity of acute treatment.
- Pulse oximetry: results may fluctuate; less invasive than arterial blood sampling.
- Coagulation profile: if rodenticide/pulmonary hemorrhage is suspected.
- Transtracheal wash: for evaluation of mild dyspnea associated with chronic cough.
- Bronchoscopy: for tracheal and bronchial visualization, and retrieval of secretions, tissue samples, foreign bodies.
- Rhinoscopy: if nasal obstruction, discharge, or other physical nasal signs are present.
- Echocardiography: if a cardiac cause is suspected (e.g., cardiomegaly; heart murmur).
- Computed tomography (thorax, nose): especially to identify/characterize mass lesions.

TREATMENT

TREATMENT OVERVIEW

- Control dyspnea immediately if life threatening.
- Address/eliminate underlying cause.

ACUTE GENERAL TREATMENT

- Oxygen supplementation (see p. 1318)
- Specific treatment is highly dependent on underlying cause and is initially based on history, physical findings, and thoracic radiographs. Acute general treatment may include removal of upper-airway foreign body; thoracocentesis; diuretic; tracheostomy; or many others, depending on etiology.

CHRONIC TREATMENT

Depends on underlying cause

POSSIBLE COMPLICATIONS

Uncontrolled dyspnea, producing hypoxemia, cyanosis

RECOMMENDED MONITORING

- Respiratory effort
- Thoracic radiographs
- Arterial blood gases

PROGNOSIS AND OUTCOME

Highly variable, based mainly on severity of dyspnea at presentation and ability to control underlying cause

PEARLS & CONSIDERATIONS

COMMENTS

- Dyspneic patients may be fragile. Simple procedures such as thoracic radiography or thoracocentesis need to be accomplished with the lowest effective degree of restraint in severely dyspneic patients, or else postponed.
- A simple way of establishing whether nasal obstruction is present and if so, which side(s) is/are affected involves simply occluding the nostrils, one at a time, and watching to see if airflow flutters a tuft of a few hairs plucked from the patient's coat and held in front of the nonoccluded nostril.

CLIENT EDUCATION

- At the time of diagnosis, patients are usually in serious or critical condition even if they do not appear to have been very ill.
- The long-term outlook depends on the cause of the labored breathing, and tests are necessary to find what the most likely cause is.

SUGGESTED READING

DeFrancesco TC, Rush JE, Rozanski EA, et al: Prospective clinical evaluation of an ELISA B-type natriuretic peptide assay in the diagnosis of congestive heart failure in dogs presenting with cough or dyspnea. J Vet Intern Med 21(2):243–250, 2007.

Forney S: Dyspnea and tachypnea. In Ettinger SJ, Feldman EC, editors: Textbook of veterinary internal medicine, ed 7, St Louis, 2010, Elsevier Saunders, pp 253–256.

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Dysphagia

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Difficulty in swallowing resulting from the inability to prehend, form, and/or move a bolus of food from the mouth into the esophagus

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dependent on underlying cause:

- Young dogs: congenital, foreign objects, facial trauma
- Young cats: congenital, inflammatory polyps
- Older animals: neoplasia

GENETICS & BREED PREDISPOSITIONS

Cricopharyngeal achalasia (toy breeds), myasthenia gravis (Jack Russell and fox terriers, English spaniel, Samoyed, Siamese)

RISK FACTORS

Neuromuscular conditions may have breed predispositions.

CONTAGION & ZOONOSIS

Rabies, especially if the animal's rabies vaccination status is unknown or if has been exposed to a potentially rabid animal

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Oral dysphagia:
  - Modified eating behavior (eating with head tilted to one side and throwing head back while eating) common
  - Mandibular/tongue paralysis, dental disease, masticatory muscle swelling or atrophy, inability to open the mouth, and food packed in the buccal folds without retention of saliva
- Pharyngeal dysphagia:
  - Normal prehension
  - Repeated attempts at swallowing while repeatedly flexing and extending the head and neck, excessive chewing, and gagging
  - Saliva-coated food retained in the buccal folds, diminished gag reflex, and nasal discharge from nasopharyngeal aspiration may exist.
- Cricopharyngeal dysphagia:
  - Repeated, nonproductive efforts to swallow and gag associated with regurgitation immediately after swallowing
  - Normal gag reflex and prehension

HISTORY, CHIEF COMPLAINT

Some or all may be present:

- Ptyalism/hypersalivation, gagging, weight loss, ravenous appetite, repeated attempts at swallowing, swallowing with the head in an abnormal position, coughing, regurgitation, painful swallowing, and occasionally anorexia
- Foreign bodies cause acute-onset dysphagia.
- Pharyngeal dysphagia may be chronic and intermittent.

ETIOLOGY AND PATHOPHYSIOLOGY

- Anatomic or mechanical lesions:
  - Pharyngeal inflammation (trauma, abscess, eosinophilic granuloma)
  - Retropharyngeal lymphadenopathy/neoplasia
  - Pharyngeal/retropharyngeal foreign body
  - Salivary mucocele
  - Temporomandibular joint disorders (luxation, fracture, craniomandibular osteopathy)
  - Mandibular fracture
  - Cleft palate
- Pain due to dental disease, trauma, stomatitis, glossitis, and pharyngeal inflammation
- Neuromuscular disorders (trigeminal neuropathy, lingual paralysis)
- Masticatory myositis
- Pharyngeal weakness/paresis/paralysis:
  - Infectious polymyositis (toxoplasmosis, neosporosis)
  - Immune-mediated polymyositis
  - Muscular dystrophy
  - Polyneuropathies
  - Myoneural junction disorders (myasthenia gravis, tick paralysis, botulism)
- Rabies can cause dysphagia by affecting both the brainstem and peripheral nerves.
- Other brainstem disorders

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Dysphagia is a nonspecific chief complaint; thorough oral exam and observation of the patient's attempts to eat food are indicated to determine whether the problem is one of oral, pharyngeal, or cricopharyngeal dysphagia. Further tests are then selected accordingly.

DIFFERENTIAL DIAGNOSIS

- Vomiting
- Regurgitation

INITIAL DATABASE

- CBC: inflammatory conditions can cause leukocytosis, sometimes with a left shift.
- Urinalysis:
  - Usually normal
  - Isosthenuria can be associated with kidney disease.
- Biochemistry: elevated serum creatine phosphokinase activity with muscular disorders

ADVANCED OR CONFIRMATORY TESTING

- Other laboratory tests:
  - Type 2M-muscle antibody serology for masticatory myositis
  - Acetylcholinesterase receptor antibody test for acquired myasthenia gravis
  - Antinuclear antibody test for immune-mediated diseases
- Imaging:
  - Survey radiographs of the skull and neck, with attention to the mandibles, temporomandibular joint, teeth, pharyngeal and retropharyngeal area, and position of the hyoid apparatus
  - Ultrasonography of the pharynx may be useful with mass lesions and for obtaining ultrasound-guided biopsy specimens.
  - Fluoroscopy to evaluate pharyngeal movement in patients with suspected pharyngeal or cricopharyngeal dysphagia (see p. 1205)
  - CT or MRI for suspected intracranial mass
- Other diagnostic procedures:
  - Biopsy of a mass lesion
  - Pharyngoscopy
  - Electromyography of the pharyngeal musculature to confirm the presence of a neuromuscular disorder
  - Repetitive nerve stimulation and edrophonium chloride test for suspected myasthenia gravis (suboptimal)
  - Cerebrospinal fluid analysis

TREATMENT

THERAPEUTIC OVERVIEW

- Determine underlying cause.
- Direct primary treatment at the underlying cause.
- Nutritional balance to maintain optimal body condition

NUTRITION/DIET

- Nutritional support:
  - Care taken to avoid aspiration when feeding orally
  - Animals with oral dysphagia may be able to swallow if a bolus of food is placed in the caudal pharynx; other animals may find a gruel that can be lapped easier to swallow.
  - Elevating the head and neck may make swallowing easier for animals with pharyngeal or cricopharyngeal dysphagia and help prevent aspiration of food.
- If nutritional requirements cannot be met by oral feeding, an esophagostomy or gastrostomy tube may be necessary (see p. 1267,p. 1270).
- Surgical excision of a mass lesion
- Foreign-body removal
- Cricopharyngeal myotomy may benefit patients with cricopharyngeal dysphagia, but a correct diagnosis is essential; cricopharyngeal myotomy will exacerbate dysphagia with oropharyngeal dysphagia.

POSSIBLE COMPLICATIONS

Aspiration pneumonia is a common complication.

RECOMMENDED MONITORING

- Daily for signs of aspiration pneumonia
- Body condition and hydration status daily
- If oral nutrition does not meet requirements, use esophagostomy/gastrostomy tube feeding.

PROGNOSIS AND OUTCOME

Dependent on the cause and the associated complication of aspiration pneumonia

PEARLS & CONSIDERATIONS

COMMENTS

- Uncommon problem
- Dysphagia is not a diagnosis but a clinical sign

CLIENT EDUCATION

Monitor for aspiration pneumonia

SUGGESTED READING

Hitt ME: Pharyngeal and swallowing disorders. In Morgan RV, Bright RN, Swartout MS, editors: Handbook of small animal practice, ed 4, Philadelphia, 2003, WB Saunders, pp 305–306.

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Dysautonomia

BASIC INFORMATION

DEFINITION

Dysautonomia is characterized by a degeneration of the autonomic ganglia, with failure of parasympathetic and sympathetic function in multiple organs.

SYNONYMS

Key-Gaskell syndrome, pure autonomic failure, pandysautonomia, autonomic neuropathy

EPIDEMIOLOGY

SPECIES, AGE, SEX

- In the United States, dogs are most commonly affected; occasional feline cases. In the United Kingdom, horses are most commonly affected.
- Any age animal may be affected, but dysautonomia most commonly affects young adult dogs (median age 18 months).

RISK FACTORS

Free-roaming, rural dogs are at higher risk.

CONTAGION & ZOONOSIS

- Except for rare reports of multiple dogs in a household affected, no evidence of contagion
- No evidence of zoonosis

GEOGRAPHY AND SEASONALITY

- In the United States, the greatest concentration of dysautonomia centers around the borders between Missouri, Kansas, and Oklahoma. Cases are also seen in the northern Colorado and southern Wyoming front range, with occasional cases elsewhere in the country.
- The disease is most common in the late winter/early spring, with the incidence dropping off during the summer months.

ASSOCIATED CONDITIONS & DISORDERS

Autonomic failure can be a part of a more diffuse peripheral neuropathy or neuromuscular junction disorder.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Different combinations of organ failure may be seen.
- Dogs will sometimes present in the early stage of disease with only one obvious sign (e.g. dilated pupils or gastrointestinal [GI] atony). Other signs rapidly develop, allowing a diagnosis of dysautonomia.

HISTORY, CHIEF COMPLAINT

Acute disease: most cases <5-14 days duration

- Most common complaint is GI disturbance: vomiting/regurgitation and diarrhea; some animals instead are constipated.
- Dysuria
- Photophobia, dilated pupils, or third eyelid elevation
- Coughing
- Nasal discharge
- Weight loss

PHYSICAL EXAM FINDINGS

- Diminished anal sphincter tone
- Dry eyes and mucous membranes, with normal hydration; crusty nose
- Midrange or dilated pupils with no pupillary light reflex but normal vision
- Elevated third eyelid, enophthalmos, and ptosis
- Distended, easily expressed bladder
- Abdominal discomfort
- Heart rate and blood pressure are usually at the low end of normal range.
- Nasal discharge or crackles on lung auscultation if secondary rhinitis or aspiration pneumonia
- Cachexia can be dramatic even in relatively short-duration disease.

ETIOLOGY AND PATHOPHYSIOLOGY

- Histologically there is loss of neurons in the autonomic ganglia, with little inflammation.
- Cause is unknown, but toxic and immune-mediated hypotheses are being investigated.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

- To establish the diagnosis, it is necessary to document autonomic failure in multiple organs, without significant deficits in sensory or motor function. Not all patients show all clinical signs.
- Dysautonomia can mimic other diseases in the early stages when only one or two functions are affected.

DIFFERENTIAL DIAGNOSIS

- The most dramatic signs reflect parasympathetic loss, so anticholinergic toxicosis needs to be ruled out.
- Other differentials would be determined by the specific organ most prominently affected.
    - GI: gastroenteritis, GI foreign body, metabolic causes, idiopathic mega-esophagus, focal myasthenia gravis
    - Dry eyes and mucous membranes: dehydration, keratoconjunctivitis sicca (eyes only)
    - Dilated pupils: intraocular or retro-bulbar disease
    - Photophobia: corneal ulcer or anterior uveitis
    - Elevated third eyelid, enophthalmos and ptosis: any cause of Horner's syndrome, especially retrobulbar, mediastinal, or middle ear disease
    - Dysuria: urinary tract infection, disease affecting sacral spinal cord, cauda equina, or pelvic nerves
    - Loss of anal sphincter tone: disease affecting sacral spinal cord, cauda equina, or pudendal nerves
    - Respiratory: any cause of pneumonia or rhinitis

INITIAL DATABASE

- CBC, serum biochemistry panel, urinalysis: unremarkable
- Radiographs may reveal evidence of ileus, distended bladder, megaesophagus, and/or aspiration pneumonia.
- Abdominal ultrasound or barium series may show lack of intestinal motility.
- Ocular pilocarpine test will rule out anticholinergic toxicity in animals with dilated pupils:
    - Place 2-3 drops of 0.05% pilocarpine (1% diluted 1:20 with saline or eye flush) in one eye.
    - Compare pupil size every 15 minutes for up to one hour.
    - Pupil should constrict in dysautonomia; anticholinergic toxicity or normal pupil would not respond.
- Atropine test: does not rule out anticholinergic toxicity but documents cardiac involvement.
    - Measure heart rate before and after IV atropine.
    - Rate should increase in normal animal; may not change in dysautonomia.

ADVANCED OR CONFIRMATORY TESTING

Diagnosis can be confirmed histopathologically by cell loss and gliosis in autonomic ganglia. The celiacomesenteric ganglia can be found surrounding the origin of the cranial mesenteric artery from the aorta, and there are usually autonomic ganglia in the periadrenal tissues.

TREATMENT

TREATMENT OVERVIEW

Since the cause is unknown, treatment is supportive and thus dictated by the signs shown.

ACUTE AND CHRONIC TREATMENT

- Prokinetic drugs (metoclopramide or cisapride)
- Eye lubrication
- Humidification of air
- Manually express the bladder. Low-dose bethanechol may help bladder contraction but may cause increased vomiting.
- Antibiotics for secondary infections

NUTRITION/DIET

- Support nutrition and hydration
  - IV fluids
  - PEG tube may be of value, but if complete GI atony TPN may be necessary (see p. 1270 and p. 1322).

DRUG INTERACTIONS

Animals with dysautonomia develop supersensitivity to direct-acting cholinergic or adrenergic drugs, as evidenced by the ocular pilocarpine test. Therefore any of these drugs should be used cautiously beginning at about 10% of the normally used dose and escalating the dose as needed.

POSSIBLE COMPLICATIONS

Aspiration pneumonia can occur at any time in animals that are vomiting or regurgitating.

PROGNOSIS AND OUTCOME

- Prognosis is grave, with 70%-90% fatality
- Animals either die of aspiration pneumonia or are euthanized because of poor quality of life.
- Occasionally an animal will recover but may have permanent dysfunction of one or more organs.

PEARLS & CONSIDERATIONS

TECHNICIAN TIPS

Supportive care is the cornerstone of these patients' treatment, particularly when the disease is advanced. Technicians involved in their care should be proficient in ophthalmic treatments, elevated feedings for megaesophagus, and management of urinary retention, among other skills.

CLIENT EDUCATION

Because the cause is unknown, it is difficult to provide clients with firm recommendations for preventing future occurrences. Dogs in the same household do not appear to be at greater risk.

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EDITOR: CURTIS DEWEY

Drug Eruption

BASIC INFORMATION

DEFINITION

Development of cutaneous or mucocutaneous lesions following drug administration (topical, oral, or injectable). The lesions may be limited to the cutaneous/mucocutaneous areas or may be part of a systemic reaction. These uncommon reactions can be either predictable (pharmacologic) or unpredictable (idiosyncratic).

SYNONYM

Cutaneous adverse drug reaction (CADR)

EPIDEMIOLOGY

SPECIES, AGE, SEX

The incidence of drug eruptions in dogs and cats has been reported as 2% and 1.6%, respectively. It is likely that many cases of drug reaction, by their subtlety, go unreported.

GENETICS AND BREED PREDISPOSITION

No clear breed predisposition

RISK FACTORS

The number of drugs administered, a concomitant infection suppressing the immune system, or other immunosuppressive state might increase the risk of developing a CADR.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- History of drug administration
- The chief complaint may be variable because of the wide spectrum of clinical signs.
- Depending whether the reaction is predictable or not, it can occur following the first treatment or as the result of several days to years of drug administration (see below).

PHYSICAL EXAM FINDINGS

Several clinical presentations have been described:

- Erythroderma/exfoliative dermatitis: localized or diffuse erythema that can lead to scales, crusts, and alopecia
- Urticaria/angioedema: edematous papules and wheals; variable erythema and pruritus
- Autoimmune diseases (pemphigus, bullous pemphigoid, systemic lupus erythematosus): clinical presentation varies from pustules and crusts to vesicles, bullae, and ulcers depending on the autoimmune dermatosis mimicked.
- Erythema multiforme (EM)/toxic epidermal necrolysis (TEN): group of diseases manifested by an acute reaction pattern of skin and mucous membranes; EM characterized by erythematous maculopapules and flat or raised annular or polycyclic lesions, with minimal epidermal detachment; TEN involves widespread erythema, blistering, and severe epidermal detachment (see online chapter: Erythema Multiforme and Toxic Epidermal Necrolysis).
- Fixed reactions: well-demarcated erythematous lesions sometimes associated with blistering and necrosis
- Macules and papules: usually erythematous; pruritic or not
- Pruritus: localized or widespread, can lead to self-induced lesions
- Injection-site reactions: local reaction characterized by alopecia, inflammation, necrosis, or ulceration
- Vasculitis: purpura, necrosis, and punctate ulcers, especially localized over extremities, pressure points, and oral mucosa

ETIOLOGY AND PATHOPHYSIOLOGY

- Although some drugs are more frequently associated with drug reactions, all kinds of drugs are at risk to cause a CADR.
- CADR may be immediate after first administration or after weeks to months of administration without prior apparent reaction.
- The predictable (pharmacologic) reactions are related to the pharmacologic actions of the drugs and thus more common. They are associated to the dose, the pharmacologic side effects/toxicity or drug interactions, and reversed when the drugs are discontinued.
- The unpredictable (idiosyncratic) reactions are usually considered immunologically mediated. They can also be associated with individual genetic differences in the metabolism of drugs, leading to inappropriate generation or accumulation of toxic metabolites (e.g., MDR1 gene mutation in collie and other herding breeds; see p. 706). These reactions (cutaneous and/or systemic) are often serious and potentially fatal.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The key elements necessary for identifying a CADR are a thorough history, including drug administration and appropriate timing for the development of skin eruptions, a lack of alternative explanations for the lesions, and dechallenge, with resolution of skin lesions within 1-2 weeks. Rechallenging with the suspected drug confirms the diagnosis but is generally not recommended.

DIFFERENTIAL DIAGNOSIS

- Erythroderma/exfoliative dermatitis: epitheliotropic lymphoma
- Urticaria/angioedema; macules/papules; pruritus: hypersensitivity disorders, ectoparasitosis, superficial bacterial or fungal infection, and mast cell tumor
- Autoimmune skin diseases: spontaneous autoimmune disease not related to drugs, which is more common
- EM/TEN: superficial and deep infection (bacterial and fungal), urticaria, autoimmune skin diseases, burns, ulcerative stomatitis, and epitheliotropic lymphoma
- Fixed reactions: contact dermatitis, hypersensitivity disorders, pyoderma, and fungal infection
- Injection-site reactions: traction alopecia, hypersensitivity disorders, pyoderma, dermatophytosis, alopecia areata, and neoplasia
- Vasculitis: urticaria, autoimmune skin diseases, EM/TEN, disseminated intravascular coagulation, coagulopathy, frostbite, and neoplasia

INITIAL DATABASE

- History of drug administration before onset of skin lesions
- Routine dermatologic diagnostics should be performed as appropriate (skin scrapings, skin cytology, skin biopsy, fungal culture) based on differential diagnosis.
- Although a wide range of dermatohistopathologic patterns exists in CADR, it is recommended to perform skin biopsies in order to confirm the diagnosis or eliminate differential diagnoses.

ADVANCED OR CONFIRMATORY TESTING

- Suspected vasculitis: rickettsial titers, if other clinical signs suggestive of rickettsial diseases are present
- Suspected systemic lupus erythematosus: antinuclear antibody test
- Cats: feline immunodeficiency virus (FIV)/feline leukemia virus (FeLV) serology, if considered appropriate based on clinical signs

TREATMENT

TREATMENT OVERVIEW

- Stop the pharmacologic or immunologic reactions causing the drug eruption.
- Prevent secondary skin infection if the cutaneous barrier is ruptured.
- Supportive care is important when the animal is debilitated.

GENERAL TREATMENT

- Discontinue use of the offending medication.
- Supportive care as needed, including fluid therapy, nutritional support, analgesics, antipruritic therapy, or wound care. Depending on the clinical presentation, corticosteroids may be used (controversial).

PROGNOSIS AND OUTCOME

Good, except if internal organs are affected or if there is extensive epidermal necrosis

PEARLS & CONSIDERATIONS

COMMENTS

- Lesions can persist for days to weeks after discontinuing the medication.
- Hospitalization may be indicated.
- Consider short-term glucocorticoid or immunosuppressive therapy if severe pruritus or immune-mediated dermatosis exists and concurrent infection is absent.
- Immunomodulatory therapy can be beneficial in EM/TEN, injection-site reactions, or vasculitis.
- Avoid future use of the offending medication or chemically related drugs.

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AUTHOR: FRÉDÉRIC SAUVÉ

EDITOR: MANON PARADIS

Drowning

BASIC INFORMATION

DEFINITION

Potentially fatal disorder characterized by asphyxia and possibly dysfunction of multiple organ systems due to submersion in a liquid medium (typically water)

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs and cats of either sex and any age

RISK FACTORS

Preexisting disorders (orthopedic injury, neurologic dysfunction, visual deficits, respiratory abnormality) can predispose an incapacitated patient to fall into water or become submerged during aquatic activity.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Fresh water versus salt water aspiration

HISTORY, CHIEF COMPLAINT

There is almost always a known submersion incident. If possible, it is helpful to obtain information regarding factors that have been reported to influence prognosis in human medicine.

- Circumstances surrounding submersion (severe internal injuries worsen prognosis)
- Duration of submersion (prognosis worsens with increased time)
- Tonicity and temperature of the water (prognosis better with fresh/ice water)
- Apnea after rescue (spontaneous breathing improves prognosis)
- Immediate neurologic condition after rescue (poor condition may worsen prognosis)

PHYSICAL EXAM FINDINGS

Variable depending on severity. May include wet fur, collapse, dyspnea, tachypnea, tachycardia, bradycardia, cyanosis, hypoperfusion, hypothermia, increased bronchovesicular breath sounds, or cardiac or respiratory arrest.

ETIOLOGY AND PATHOPHYSIOLOGY

- Pulmonary, fresh water: affects the surface-tension properties of pulmonary surfactant (surfactant washout), leading to alveolar instability, the possibility of noncardiogenic pulmonary edema, and altered ventilation/perfusion ratio. Because of the relative hypotonicity of fresh water, aspirated fluid is generally quickly absorbed into the circulation. If enough fluid is absorbed, hyponatremia causes hemolysis.
- Pulmonary, sea water: elicits fluid influx into the pulmonary parenchyma (osmotic gradient) and alveolar flooding; volume may be so great as to cause hypovolemia.
- Hepatocellular: hepatic ischemia as a result of hypoxia and compromised cardiovascular function causes direct hepatic injury and lobar necrosis.
- Hematologic dysfunction: hypoxemia, vascular stasis, and acid-base disturbances predispose animals to development of disseminated intravascular coagulation.
- Acute kidney injury: renal hypoxia contributes to tubular cell death.
- Cardiovascular effects: elevated systemic and pulmonary vascular resistance, cardiac arrhythmias, and cardiac arrest are primarily due to hypoxemia. They are positively related to the length of anoxic insult and negatively related to the effects of hypothermia and effectiveness of resuscitation in humans.
- Neurologic effects: ischemia leads to an elevation in extracellular central nervous system tissue glutamate concentration,

which is thought to be directly related to neuronal damage. Both cerebral ischemia and hypoxia can lead to irreversible neurologic dysfunction.
- In all, 90% of drowning victims aspirate fluid into the lungs; in 10%, drowning is associated with laryngospasm and inhalation against a closed glottis, causing noncardiogenic pulmonary edema without aspiration of water.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Known history of recent submersion is generally sufficient to make the diagnosis. Involvement of other organ systems such as hepatocellular, hematologic, cardiovascular, renal, and neurologic systems can be common.

INITIAL DATABASE

- Arterial blood gas analysis (hypoxemia variable with degree of aspiration/noncardiogenic pulmonary edema; metabolic acidosis possible and appears detrimental to prognosis)
- Pulse oximetry: low Spo2
- Electrocardiogram: ventricular arrhythmias
- CBC (usually unremarkable)
- Serum chemistry (increased liver enzymes, possibly hypoproteinemia or azotemia)
- Urinalysis (usually unremarkable)
- Thoracic radiographs (pulmonary infiltrates of varying location and type)
- Blood pressure (monitor for hypotension)

ADVANCED OR CONFIRMATORY TESTING

Bronchoalveolar lavage or transtracheal wash is indicated if warranted by clinical suspicion of pulmonary infection; not required for diagnosis of drowning.

TREATMENT

TREATMENT OVERVIEW

- Improve ventilation (goal: PaCO2 = 30-40 mm Hg or less)
- Maintain appropriate intravascular volume and tissue perfusion (*mean* arterial blood pressure >60-80 mm Hg, central venous pressure = 2-5 cm H2O, urine production >1-2 mL/kg/h)
- Ensure adequate blood oxygen saturation (Spo2 > 92%, Pao2 > 80 mm Hg [room air])
- Correct electrolyte imbalances or severe acidosis (e.g., if pH < 7.1)
- Referral for therapeutic ventilation may be warranted early in the course of disease and should be considered in those animals with severe respiratory distress (SpO2 < 92%, Pao2 < 80 mm Hg) despite oxygen supplementation.

ACUTE GENERAL TREATMENT

- Regain spontaneous ventilation and circulation (see p. 1223).
- Oxygen supplementation (see p. 1318).
- IV fluid administration as indicated.
- Mechanical ventilation with positive end expiratory pressure where indicated (see p. 1362).
- Abdominal thrust or gravitational drainage offers *no* advantage and may increase complications such as regurgitation and aspiration and delaying adequate treatment.
- Antibiotic therapy is not indicated unless clinical and radiographic evidence of pulmonary infection. Ongoing antibiotic use should be based on culture and sensitivity results.
- Corticosteroid therapy was once suggested but has failed to demonstrate any therapeutic advantage in large studies and may predispose patients to infection.

POSSIBLE COMPLICATIONS

- In addition to being risk factors that led to the incident, preexisting problems such as respiratory disease, heart disease, or seizure disorders should be identified; they may complicate resuscitation.
- Infrequently, grossly contaminated water can cause lower-airway obstruction (particulate matter) or pulmonary infection.
- Uncommonly, renal function can become compromised due to decreased renal perfusion, hypoxemia, or severe

hemoglobinuria.
- Cerebral hypoxia, cerebral hypoperfusion, or carbon dioxide narcosis can cause varying degrees of neurologic impairment but are rarely permanent.

RECOMMENDED MONITORING

- Thoracic auscultation
- Respiratory rate and effort
- Arterial blood gas analysis
- Urine output
- Serial neurologic evaluation and modified Glasgow Coma Score designation (see p. 235)
- Hematocrit, electrolyte and pH imbalances
- Electrocardiogram

PROGNOSIS AND OUTCOME

- Most near-drowning animals are markedly improved within 24 hours. Failure to rapidly improve is associated with a grave prognosis, as is persistent hypoxemia.
- By extrapolation from human medicine, the need for CPR on presentation, blood pH < 7.0, and apnea or coma are poor prognostic indicators.
- Similar to human beings, submersion for >25 minutes, resuscitation for >25 minutes, cardiac arrest at time of presentation, and lack of return of purposeful movements within 24 hours of the incident are associated with severe neurologic deficits or death.

PEARLS & CONSIDERATIONS

COMMENTS

Abdominal thrust and gravitational pull (suspended upside down) offer no benefits and may increase complications such as regurgitation, aspiration, and delayed resuscitation.

PREVENTION

- Outdoor supervision
- Avoidance of swimming by dogs with disorders causing episodic lack of control (seizures, syncope)
- Precautionary poolside safety measures such as pool covers and gated pool areas
- Boating safety measures: flotation devices; keeping animals in boat cabin, on boat floor, or away from railings
- Avoid semifrozen lakes, ponds, or rivers

TECHNICIAN TIPS

- Early placement of an arterial catheter may allow for rapid, accurate interpretation of pulmonary gas exchange, since intermittent SpO2 can require the oxygen cage to be open for longer periods of time, can be difficult to interpret in a panting animal, and does not give information pertaining to changes in acid-base status or PaCO2.
- A urinary catheter and closed collection set allows for frequent, accurate calculation of urine output and may aide in nursing care.
- Many dogs presented on emergency for near-drowning have visual, neurologic, musculoskeletal, or other deficits that existed previously and predisposed them to the incident. It is useful and important to be aware of these preexisting deficits when monitoring recovery so as to avoid misinterpreting the long-standing condition as a complication of near-drowning.

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EDITOR: ELIZABETH ROZANSKI

Draining Tracts, Cutaneous

BASIC INFORMATION

DEFINITION

A tract that connects an area of subcutaneous or deeper soft-tissue inflammation to the skin surface

SYNONYMS

Fistulous tract, sinus tract

EPIDEMIOLOGY

SPECIES, AGE, SEX

Variable depending on etiology

RISK FACTORS

- Penetrating injuries, chronic exposure of the skin to trauma or moisture, wound contamination, contact with infected individuals, immunodeficiency syndromes

CONTAGION & ZOONOSIS

Pathogens with zoonotic potential include: *Nocardia*, *Blastomyces*, *Sporothrix*, and *Leishmania* among others.

GEOGRAPHY AND SEASONALITY

In warm, dry climates: grass awns as penetrating foreign bodies

ASSOCIATED CONDITIONS & DISORDERS

- Frequently associated with cutaneous nodular disease
- May be associated with additional systemic signs depending upon the etiology

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

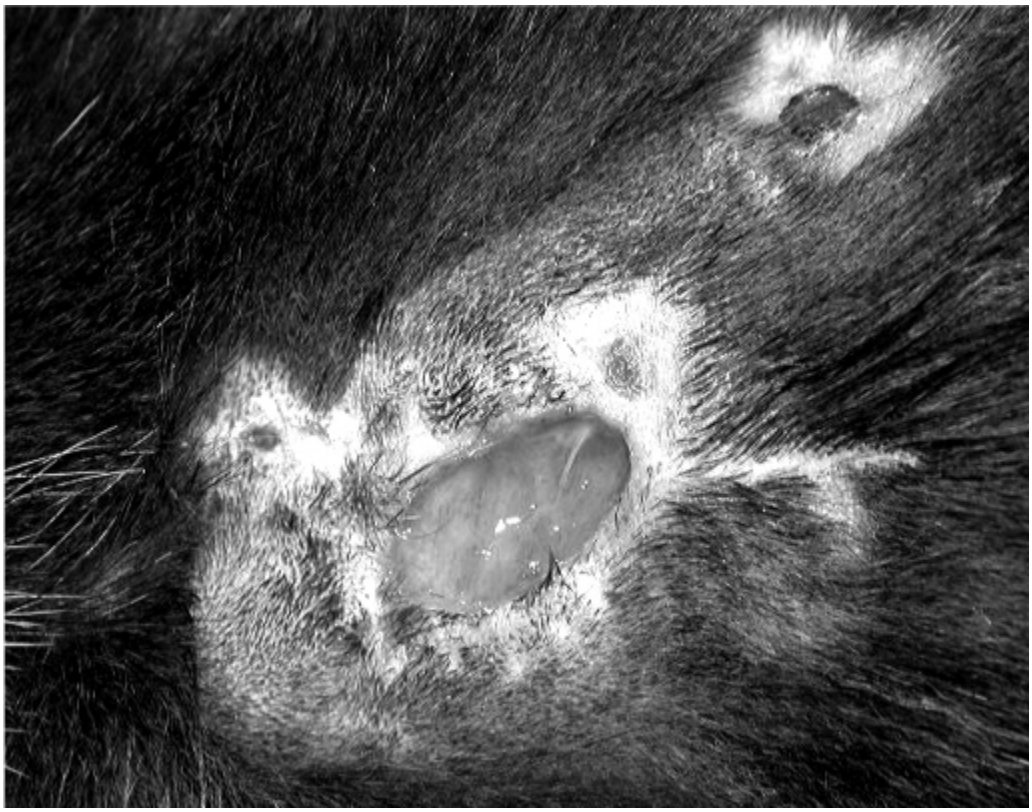
- Infectious
- Noninfectious
- Neoplastic

HISTORY, CHIEF COMPLAINT

There may be a history of a previous penetrating injury, typically associated with infectious causes. For all three forms/subtypes, a common complaint is of a nonhealing cutaneous wound that may fail to respond to antimicrobial therapy.

PHYSICAL EXAM FINDINGS

- Lesions may be solitary or multiple.
- Draining tracts are often associated with cutaneous nodules (fungal or bacterial granuloma, idiopathic sterile pyogranuloma/granuloma, sterile nodular panniculitis)
- Lesions may or may not be painful.
- Exudate from the tracts may be serous, serosanguineous, or purulent. Tissue granules may be found within the exudate (e.g., actinomycosis, actinobacillosis, nocardiosis, and bacterial pseudomycetoma).



DRAINING TRACTS, CUTANEOUS Draining tract in a cat with panniculitis due to nocardiosis.

(Courtesy Dr. Andrew Lowe.)

ETIOLOGY AND PATHOPHYSIOLOGY

- Infectious causes are often the result of direct inoculation of the organism into the subcutaneous tissue via penetrating injury. A major exception is the systemic mycoses (histoplasmosis, blastomycosis, coccidioidomycosis, cryptococcosis), which are acquired mainly through inhalation and only very rarely through direct inoculation. Immunosuppressive diseases may increase the risk of infection or colonization with opportunistic pathogens.
    - Bacterial (including feline subcutaneous abscesses, actinomycotic infections *[Actinomyces, Nocardia], Streptomyces griseus*, *Dermatophilus congolensis*, actinobacillosis, mycobacteria, deep bacterial infections and bacterial pseudomycetoma)
    - Fungal (as above, plus zygomycosis, pythiosis, sporotrichosis, and dermatophytic pseudomycetoma)
    - Parasitic (including leishmaniasis, neosporosis, *Cuterebra*, dracunculiasis, and cutaneous dirofilariasis)
- Noninfectious:
    - Foreign bodies (although secondary bacterial infection is virtually inevitable)
    - Immune-mediated (sterile nodular panniculitis, systemic lupus erythematosus, perianal furunculosis, drug eruption)
    - Xanthomatosis
    - Neoplasia

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A draining cutaneous tract is a readily visible but nonspecific clinical sign for which the underlying cause must be determined. Additional testing, usually beginning with cytologic evaluation of exudate, is almost always necessary. Further tests are then indicated based upon the cytologic results.

DIFFERENTIAL DIAGNOSIS

Persistent exudation of fluid from subcutaneous or deeper tissues through an opening in the skin is characteristic of a draining tract. Few differential diagnoses exist; hemorrhage and serum exudation from a superficial wound should be easily differentiated by nature of fluid and depth of wound.

INITIAL DATABASE

A thorough diagnostic approach is indicated with draining tracts: all of the following diagnostic tests are indicated for a complete evaluation.

- Cytologic evaluation: as well as the exudate, any tissue granules present should be crushed between two slides and examined. Fine-needle aspirates of nodules or impression smears of biopsy samples may also prove useful (Diff-Quik followed by acid-fast and periodic acid–Schiff staining). If samples are submitted to an outside laboratory, be sure to send unstained slides, and advise the lab of differential diagnoses being considered.
- Diagnostic imaging/radiographs: may help identify foreign bodies or diseases with systemic manifestations, such as pulmonary involvement with blastomycosis, or underlying bony lesions (e.g., osteomyelitis, neoplasia)
- Culture and sensitivity: bacterial (aerobic and anaerobic), fungal, and mycobacterial cultures should be considered in cases of persistent draining tracts. Culture of the superficial exudate will likely not reflect the true, deeper disease process. Samples of deep tissue should be obtained by biopsy for culture. Many of the potential pathogens are difficult to successfully culture (false-negative results). Notify the lab as to which differentials are being considered so appropriate sampling, transport, and culture procedures are performed (many organisms are highly infectious to humans under laboratory conditions).
- Histopathologic evaluation: obtain multiple specimens from both open and closed lesions. Wedge or elliptical biopsies provide a better yield for deep subcutaneous lesions than punch biopsies. Special stains may be required for positive identification (notify pathologist of differential diagnoses).
- A lack of organisms on cytologic and histopathologic evaluation and culture, if performed correctly, may indicate a noninfectious etiology.
- Routine CBC, serum biochemistry profile, urinalysis: nonspecific

ADVANCED OR CONFIRMATORY TESTING

- Serologic testing: a fourfold rise in antibody titer from samples taken 3 weeks apart may help confirm some mycoses (e.g., cryptococcosis, blastomycosis, *Pythium*).
- Urine *Blastomyces* antigen test: blastomycosis (see 138)
- Fundic examination
- Antinuclear antibody (see p. 1070)

TREATMENT

TREATMENT OVERVIEW

Treatment varies widely, depending on the etiology; more specific treatment information may be sought once this is determined.

ACUTE GENERAL TREATMENT

- In general, an inciting cause (e.g., foreign body, neoplasm) should always be identified and, if present, should be removed for an optimal outcome/potential for cure.
- Lavage and débridement of the lesions in combination with appropriate antimicrobial therapy based on culture and sensitivity are indicated for infectious etiologies.
- Noninfectious etiologies (e.g., sterile nodular panniculitis, perianal fistulae) may respond to immunosuppressive doses of glucocorticoids and other immunosuppressive therapies (e.g., cyclosporine).

PROGNOSIS AND OUTCOME

Variable depending on etiology

PEARLS & CONSIDERATIONS

COMMENTS

- Patients with chronic or recurrent infectious draining tracts should be evaluated for underlying immunosuppressive diseases or persistent local/focal abnormalities (foreign body, neoplasm, etc.).
- Only after infectious agents have been completely ruled out and a definitive diagnosis has been reached should treatment be considered for noninfectious diseases that respond to glucocorticoid therapy.

TECHNICIAN TIPS

- Patients with draining tracts should be handled with gloves, and contact with exudates should be minimized until a definitive etiology is determined (zoonosis risk).

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AUTHOR: ANDREW LOWE

EDITOR: MANON PARADIS

Dracunculus insignis Infection

BASIC INFORMATION

DEFINITION

Rare parasitic infection of dogs

SYNONYMS

Canine guinea-worm, canine dracunculiasis

EPIDEMIOLOGY

SPECIES, AGE, SEX

Infects dogs (any wild carnivore and member of the Canidae family). Also recovered from raccoons and mink (reservoir hosts).

GENETICS & BREED PREDISPOSITION

Sporting breeds of dogs are predisposed.

RISK FACTORS

Hunting/foraging and drinking water from freshwater environments (inhabited by aquatic crustaceans ["water fleas"], intermediate hosts belonging to genus *Cyclops*).

CONTAGION & ZOONOSIS

Although they have their own species of this parasite *(Dracunculus medinensis),* humans are not susceptible to infection with this canine parasite.

GEOGRAPHY AND SEASONALITY

Found in definitive hosts throughout North America. No seasonality.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- One or more blisterlike cutaneous swellings/nonhealing ulcers. Often on the extremities or ventral abdomen.
- Some owners may notice the characteristic protruding end of the female worm in the lesion.

PHYSICAL EXAM FINDINGS

- Ulcerative nodules or abscesses can be found on the skin of the limbs, head, and abdomen.
- The worm typically protrudes from the ulcerated lesion, making it easily visible to the owner and/or veterinarian.
- Lesions may be painful or pruritic.
- The dog may or may not be febrile.
- The veterinarian should exercise caution and not pull or attempt to manually extract the worm. The female worm's body is extremely fragile and subject to breakage.

ETIOLOGY AND PATHOPHYSIOLOGY

- The adult worm may be up to 100 cm (3 feet) in length.
- This is an unusual parasite in that the female possesses no vulva to allow exit of her offspring.
- The female worm lives in the subcutaneous connective tissues of the dog's extremities, producing a large cutaneous swelling that eventually develops into a nonhealing ulcer. From this ulcer, the female worm extrudes her anterior end.
- Whenever the female worm makes contact with water, her uterus will prolapse through her anterior, releasing a mass of

first-stage larvae into the water. These larvae are 500-750 mm in length with unique, characteristic long tails. The larvae are ingested by the intermediate host, a copepod aquatic crustacean (water flea) usually belonging to the genus *Cyclops;* eventually, larvae develop into infective third-stage larvae.
- Dogs become infected by drinking the water containing the *Cyclops* harboring the infective larvae.
- In approximately 1 year, the ingested larvae mature to adult parasites. Male and female worms copulate. The female eventually migrates to the extremities, where she produces the nodule which eventually will develop into a cutaneous ulcer in the dog.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Suspicion of dracunculiasis is first raised with the appearance of a cutaneous ulcer and is greatly heightened if a fine, threadlike structure is seen protruding from the lesion. Confirmation is simple, using a test tube full of cold water, a centrifuge, and a microscope.

DIFFERENTIAL DIAGNOSIS

- In heartworm-endemic areas (or with appropriate travel history), this nematode may be confused with a single aberrant (erratic) adult *Dirofilaria immitis*, which can be found in a variety of ectopic sites throughout a dog's body. These “lost” adult heartworms may produce subcutaneous nodules or abscesses, but adult heartworms usually do not protrude from the lesion.
- Foreign bodies within the skin which may produce nonhealing ulcerous lesions; however, these lesions usually do not resemble a protruding female worm.

INITIAL DATABASE

- CBC and serum chemistry profile: unremarkable
- Impression smears of the lesion may reveal inflammatory cells and first-stage larvae.

ADVANCED OR CONFIRMATORY TESTING

With the worm still embedded in tissues and protruding from the nonhealing ulcer, the protruding (anterior) end of the worm should be dipped into a test tube containing cool water to elicit release of a mass of first-stage larvae into the water; a cloudy discharge (containing microscopic larvae) may be observed. The test tube should be centrifuged and the water supernatant collected off. The larvae may be found in the sediment at the bottom of the test tube. Microscopic examination of the sediment will reveal the first-stage larvae (500-750 mm in length) with their characteristic long tails.

TREATMENT

TREATMENT OVERVIEW

- Manually extract the adult female parasite from the ulcerous lesion.
- Careful surgical intervention with blunt dissection is recommended.

ACUTE GENERAL TREATMENT

- Do not attempt to pull on the worm; it is entwined within the subcutis and prone to breaking. Surgical extraction using blunt dissection is recommended. Some antiinflammatory drugs may ease removal.
- There is no effective medical treatment; surgical extraction is recommended. Possible experimental treatments include:
  - Niridazole, 12.5 mg/kg PO q 12 h for 10 days, *or*
  - Thiabendazole, 50 mg/kg PO q 24 h for 2 to 3 days
- Multiple infections in a single ulcerative lesion do not occur. Once the sole female is removed, healing should take place quickly.

CHRONIC TREATMENT

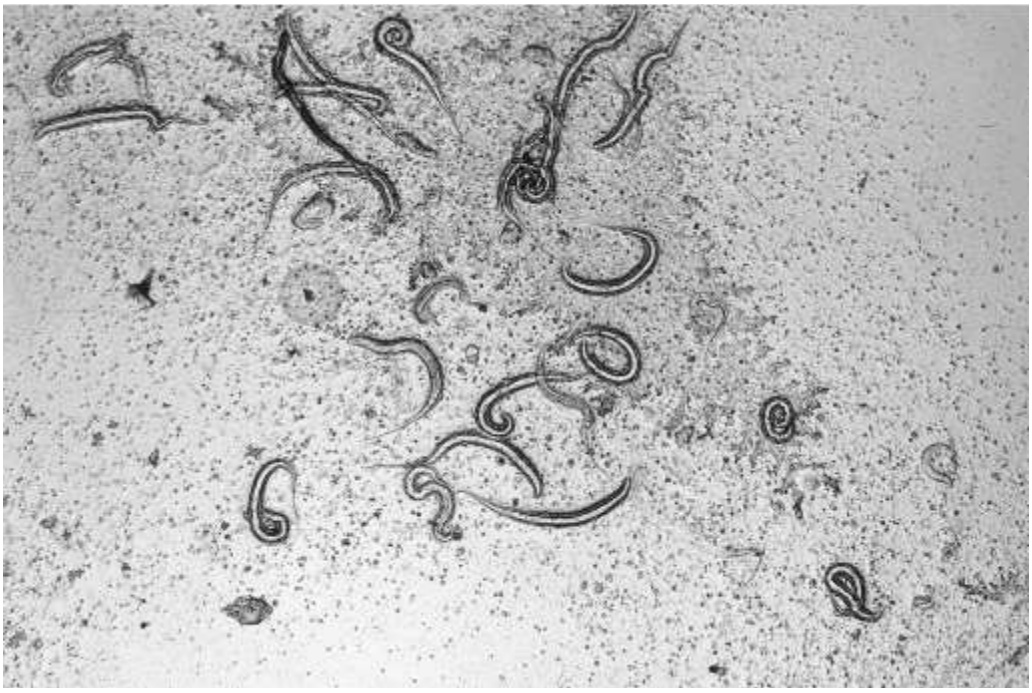
As needed for dermatologic complications:

- Secondary bacterial infection
- Cellulitis

- Culture and sensitivity of skin lesion with appropriate antimicrobial therapy

BEHAVIOR/EXERCISE

- The "old school"/Old World therapy of removing *D. medinensis* in humans is to tie the worm to a small stick and gradually roll the worm up over the course of a few days or weeks. Dogs are not likely to tolerate this therapy.
- Depending on the location of the lesion, an Elizabethan collar may be indicated.



***DRACUNCULUS INSIGNIS* INFECTION** Third stage larvae of *Dracunculus insignis* (500-750 mcm in length). Note the characteristic long tail of each larva.

POSSIBLE COMPLICATIONS

Breaking the friable body of the female worm in situ and not being able to recover the remnants of the parasite

RECOMMENDED MONITORING

Visual assessment of the healing process of the lesion

PROGNOSIS AND OUTCOME

Excellent prognosis if the parasite is surgically extracted and no portions remain in situ.

PEARLS & CONSIDERATIONS

COMMENTS

- These worms are singular in their appearance in ulcerated skin lesions.
- Although this nematode is extremely rare, it is easy to diagnose. Blunt dissection of tissues and manual extraction of the worm without breakage are paramount.
- *D. insignis* is closely related to the human scourge, *D. medinensis*, the human guinea-worm, the "serpent on the stick," or the serpent of the Staff of Aesculapius, the symbol of the medical profession.

PREVENTION

Prevent dogs from roaming and coming into contact with freshwater aquatic environments containing *Cyclops* species harboring

infective larvae of *D. insignis.*

TECHNICIAN TIPS

The use of a compound microscope to detect the presence of the unique first-stage larvae with their characteristic long tails is the key to diagnosis.

CLIENT EDUCATION

Dogs should never be allowed to roam freely, thus avoiding contact with infested water.

SUGGESTED READING

Beyer TA, Pinckney RD, Cooley AJ: Massive *Dracunculus insignis* infection in a dog. J Am Vet Med Assoc 214:351, 366–368, 1999.

Johnson GC: *Dracunculus insignis* in a dog. J Am Vet Med Assoc 165:533, 1974.

Panciera DL, Stockham SL: *Dracunculus insig-nis* infection in a dog. J Am Vet Med Assoc 192:76–78, 1988.

AUTHOR: CHARLES HENDRIX

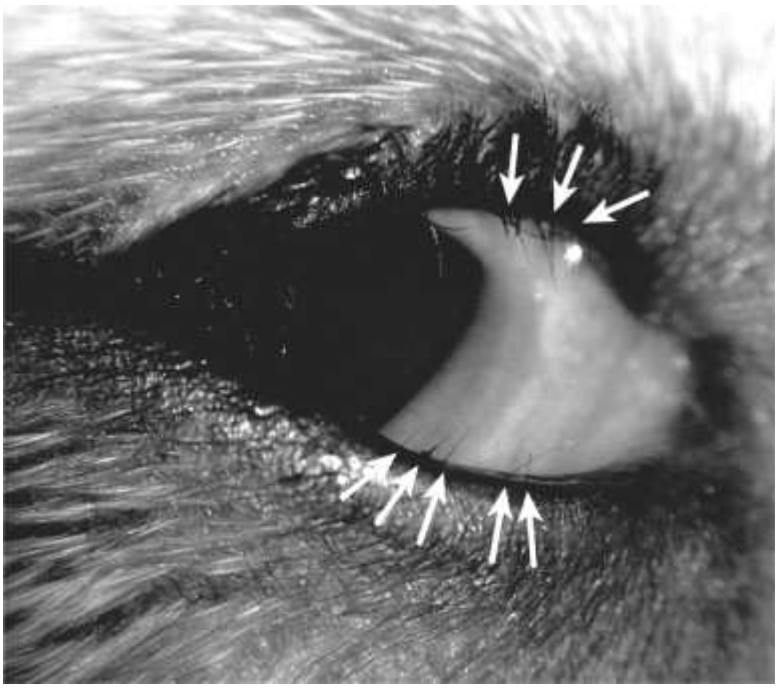
EDITOR: DOUGLASS MACINTIRE

Distichiasis/Ectopic Cilia/Trichiasis

BASIC INFORMATION

DEFINITION

- Distichiasis: common condition represented by the presence of an additional row of adventitious lashes on the eyelid margin arising from the meibomian glands, in addition to the normal eyelashes emerging from the usual peripheral eyelid margin
- Ectopic cilia: well-recognized condition consisting of aberrant individual eyelashes that arise from the meibomian glands and grow through the palpebral conjunctiva toward the globe
- Trichiasis: common condition associated with normal eyelid/facial hair that is directed toward and contacts the conjunctiva or cornea



DISTICHIASIS/ECTOPIC CILIA/TRICHIASIS Distichiasis in a dog. Note the numerous long, aberrant hairs along the upper and lower eyelid margins and arising from the meibomian gland ducts *(arrows).* These hairs were an incidental finding and caused no clinical signs, so no treatment was warranted.

SYNONYMS

Aberrant cilia, “abnormal eyelashes,” distichia

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Common in dogs, rare in cats
- Most often in young dogs, but can occur at any age

GENETICS & BREED PREDISPOSITION

- *Distichiasis:* any breed, but common in American and English cocker spaniels, miniature long-haired dachshund, English bulldog, golden retriever, Cavalier King Charles spaniel, Pekingese, toy and miniature poodles, Yorkshire terrier, and Shetland sheepdog
- *Ectopic cilia:* any breed, but common in boxers
- *Trichiasis:*
    - Congenital trichiasis: English cocker spaniel and small breed dogs such as brachycephalic breeds with prominent

facial folds (e.g., Pekingese, pug)
- Acquired trichiasis: breeds with redundant dorsal skin folds (English bulldog, shar-pei, chow chow, bloodhound, Saint Bernard)

ASSOCIATED CONDITIONS & DISORDERS

- Conjunctivitis (see p. 239)
- Ulcerative keratitis (see Corneal Ulceration, p. 250)
- Nonulcerative keratitis (see Corneal Pigmentation, p. 246; Corneal Vascularization, p. 254)

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- *Distichiasis:*
  - Generally does not produce clinical signs; most cases are clinically silent.
  - Epiphora and blepharospasm may be seen if ocular irritation is present.
- *Ectopic cilia:*
  - Acute onset of signs of ocular pain, such as severe blepharospasm and epiphora
- *Trichiasis:*
  - Signs of ocular irritation, such as blepharospasm and epiphora

PHYSICAL EXAM FINDINGS

- *Distichiasis:*
  - Single to multiple cilia along eyelid margin (incidental finding [see figure])
  - Epiphora, mild conjunctivitis, and nonulcerative keratitis are seen if cilia are causing ocular irritation; blepharospasm, ulcerative keratitis, +/− entropion (secondary/spastic) in severe cases.
- *Ectopic cilia:*
  - Most common at the 12 o'clock position (center of upper eyelid)
  - Emerge through the palpebral conjunctiva 4-6 mm posterior (caudal) to the eyelid margin
  - Magnification is needed to identify the cilia.
  - Acute blepharospasm and epiphora are typical; focal signs of nonulcerative and ulcerative keratitis often present (in a vertical pattern that follows the path of eyelid movement).
- *Trichiasis:*
  - Congenital trichiasis: The cilia or hair that contact the cornea occur on the lateral two-thirds of the upper eyelid.
  - Medial canthal trichiasis: The hairs that contact the cornea arise along the medial eyelid margin and in the area of the caruncle (aberrant dermis at the medial canthus and present on the conjunctiva).
  - Trichiasis is a common consequence of agenesis of the lateral two-thirds of the upper eyelid in cats.
  - Signs of ocular irritation, such as epiphora, if mild
  - Keratitis (ulcerative and nonulcerative) if severe

ETIOLOGY AND PATHOPHYSIOLOGY

- Meibomian glands without cilia may spontaneously develop distichiasis or ectopic cilia if the glands become metaplastic.
- *Distichiasis:*
  - Cilia originate from the meibomian glands, develop from metaplastic meibomian glands, and arise secondary to chronic inflammation (meibomitis); acquired condition.
  - May or may not contact cornea
- *Ectopic cilia:*
  - Cilia originate from the meibomian glands and emerge through the palpebral conjunctiva.
  - Always contact cornea
  - Can occur at any time in the animal's life
- *Trichiasis:*
  - Normal hairs that are abnormally directed toward the eye
  - Congenital trichiasis of the upper eyelid can be bilateral or unilateral.
  - Acquired trichiasis develops secondary to ptosis associated with redundant skin folds (see Genetics & Breed Predisposition).
  - Acquired trichiasis develops secondary to loss of muscle tone in older dogs.
  - Associated with entropion, prominent nasal folds, and medial canthal hairs (eyelids and caruncle)

DIAGNOSIS

OVERVIEW STATEMENT

Ocular disease associated with distichiasis is suspected based on the presence of conjunctivitis or ulcerative and/or nonulcerative keratitis. It is confirmed when adventitious lashes are seen to originate from the meibomian glands (no magnification necessary for most clinicians).

Ocular irritation related to ectopic cilia is suspected based on acute blepharospasm and epiphora with signs of focal ulcerative and/or nonulcerative keratitis; confirmation requires magnification to identify cilia emerging from the palpebral conjunctiva.

Ocular disease associated with trichiasis is suspected when conjunctivitis or ulcerative and/or nonulcerative keratitis is present and when normal eyelid/facial hair is directed toward and contacts the conjunctiva or cornea.

DIFFERENTIAL DIAGNOSIS

- Trichomegaly (excessively long eyelashes)
- Other causes of blepharospasm, including corneal ulceration, conjunctivitis, uveitis, epiphora
- Entropion

INITIAL DATABASE

Complete ophthalmic examination (see p. 1313) including:

- Schirmer tear test (normal >15 mm after 1 minute in dogs, variable in cats)
- Fluorescein dye application
- Intraocular pressure (normal: 10-25 mm Hg)
- Examination of the eyelid margin and palpebral conjunctiva with magnification and a good light source
- Examination of the cornea

ADVANCED OR CONFIRMATORY TESTING

Magnification 5 to 10× is often needed to visualize ectopic cilia.

TREATMENT

TREATMENT OVERVIEW

Treatment goals are to eliminate ocular irritation; to determine if distichiasis, trichiasis, or ectopic cilia are responsible for clinical signs of ocular disease; and to remove the offending cilia or direct the cilia away from the globe. The presence of distichiasis and/or trichiasis without signs of ocular irritation does not require treatment.

ACUTE GENERAL TREATMENT

- *Distichiasis:*
  - Usually does not produce clinical signs; no treatment required
  - Hairs regrow within 4-5 weeks with mechanical epilation/plucking.
  - If clinical signs are present, consider surgical treatment:
    - Before removal, expression of the meibomian glands pushes hidden hairs from the glands.
    - Cryotherapy along the palpebral surface of the meibomian glands using a double freeze/thaw cycle is effective treatment for a large number of distichia in a patient.
    - Electrolysis is useful for single or a low number of cilia; procedure is tedious, and excessive current may cause tissue damage.
    - Carbon dioxide laser removal is tedious and can predispose to excessive tissue damage.
    - Resection from the conjunctival surface effective for single or multiple cilia
    - Eyelid-splitting techniques are not recommended because of the potential for postoperative eyelid deformities and regrowth of hairs.
- *Ectopic cilia:*
  - Typically produce clinical signs; therefore treated surgically
  - En-bloc resection of aberrant cilia, including associated conjunctiva and underlying meibomian gland
  - Surgical removal usually successful, but regrowth can occur.
- *Trichiasis:*
  - If minor ocular irritation, conservative management may be effective:
    - Clipping hairs short to prevent ocular contact
  - Variable surgical therapies depending on location of trichiasis:

- Many procedures complex; consider referral to veterinary ophthalmologist.
- Medial canthal trichiasis may be corrected by permanent medial canthoplasty (pocket technique or Wyman technique) or cryotherapy.
- Nasal fold trichiasis may require resection of prominent nasal skin folds.
- Trichiasis associated with ptosis (drooping of the upper eyelid) may be corrected by a Stades procedure.
- Trichiasis associated with redundant dorsal skin folds may be corrected by extensive removal of tissue or by the use of anchoring sutures to the periosteum.
- Trichiasis associated with eyelid agenesis in cats may be corrected by cryotherapy until kitten is old enough for permanent surgery (e.g., rotational flap).

CHRONIC TREATMENT

If recurrence, repeat treatment may be required

POSSIBLE COMPLICATIONS

- The most common complication to correction of distichiasis, ectopic cilia, and trichiasis is recurrence.
- Postoperative eyelid scarring ± entropion

RECOMMENDED MONITORING

Have owner monitor animal for signs of recurrent ocular irritation postoperatively; may indicate regrowth of offending hair(s).

PROGNOSIS AND OUTCOME

Generally good prognosis, but recurrence is possible regardless of treatment.

PEARLS & CONSIDERATIONS

COMMENTS

- Distichiasis and trichiasis are among the most common eyelid abnormalities.
- Goal is not simply to diagnose distichiasis or trichiasis, but to determine if the abnormal hair(s) is/are causing ocular irritation, as this determination will help decide whether treatment is necessary.
- Keratitis that presents in a vertical pattern that follows the path of eyelid movement should raise the suspicion of an ectopic cilium in the upper eyelid.
- Magnification commonly is needed to identify ectopic cilia, and without a magnifying glass or loupe, the diagnosis should not be ruled out based on absence of visualization.
- Ectopic cilia and hairs causing distichiasis will regrow within 4-5 weeks with mechanical epilation/plucking.
- No single treatment guarantees permanent resolution of distichia, ectopic cilia, or trichiasis.

PREVENTION

Avoid breeding affected or closely related dogs.

CLIENT EDUCATION

- Presence of distichiasis or trichiasis does not indicate disease.
- Animals with distichiasis, ectopic cilia, or trichiasis are monitored for signs of ocular irritation.
- Recurrence is possible regardless of treatment.

SUGGESTED READING

Stades FC, Gelatt KN: Diseases and surgery of the canine eyelid. In Gelatt KN, editor: Veterinary ophthalmology, ed 4, Ames, 2007, Blackwell Publishing, p 563.

AUTHOR: PHILLIP A. MOORE

EDITOR: CHERYL L. CULLEN

Distemper, Canine

BASIC INFORMATION

DEFINITION

Viral disease principally of young dogs and caused by a morbillivirus of the family Paramyxoviridae. Clinical disease includes mild to severe systemic illness with high morbidity and variable mortality (mortality often related to central nervous system [CNS] infection).

SYNONYMS

Distemper, hardpad disease

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs, especially urban or suburban dogs between 3 and 6 months of age
- Other susceptible species include additional members of the order Canidae (coyote, dingo, wolf, fox), ferrets, mink, skunk, raccoon, panda, and select members of the order Felidae (lion, cheetah, jaguar, margay, ocelot).

GENETICS & BREED PREDISPOSITION

More common, with higher mortality rates, in dolichocephalic breeds versus brachycephalic breeds

RISK FACTORS

Inadequate vaccination, exposure to animals with clinical or subclinical disease, transplacental transmission, and exposure of vaccinated but immunocompromised animals to an infected animal

CONTAGION & ZOONOSIS

Highly contagious (aerosol route most common) between infected, shedding individuals and susceptible individuals. Not considered zoonotic.

ASSOCIATED CONDITIONS & DISORDERS

- Hyperkeratosis of the footpads (hardpad disease)
- Ocular signs (anterior uveitis, optic neuritis, retinal degeneration, keratoconjunctivitis) can develop with systemic disease or as a sequela.
- Postencephalitic epilepsy
- Myoclonus
- Persistent anosmia (loss of sense of smell) possible in recovered patients

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Subclinical to mild disease is probably most common, but systemic/generalized form is the most recognized.
- Generalized distemper: manifests initially as a respiratory infection followed by gastrointestinal (GI) signs and often CNS signs; CNS signs may manifest concomitant with or after resolution of respiratory and GI signs.
- Old-dog encephalitis (ODE) likely results from an inflammatory reaction associated with persistent canine distemper virus infection of the CNS gray matter. Clinical signs can include ataxia, compulsive movements such as head pressing or continual pacing, and uncoordinated hypermetric gait. Systemic signs are not associated with this form.
- Inclusion-body polioencephalitis is a variant of the disease, can occur after vaccination, and only manifests as a CNS disease. The pathogenesis is similar to ODE.

HISTORY, CHIEF COMPLAINT

With the generalized form of the disease, initial presentation typically includes one or more of the following: lethargy, ocular and nasal discharge (serous or mucopurulent), cough, inappetence, vomiting, diarrhea. A patient with a more advanced form of the disease often has a history of neurologic signs (seizures, ataxia, etc.).

PHYSICAL EXAM FINDINGS

- Systemic disease: as above; fever, ocular signs (keratitis, conjunctivitis, uveitis), loud breath sounds on auscultation, dehydration, cachexia, poor haircoat. Dental abnormalities in dogs that survive neonatal infections (dental enamel hypoplasia, tooth impaction, oligodontia).
- Neurologic disease: signs indicative of encephalitis or encephalomyelitis (seizures, vestibular signs, cerebellar signs/hypermetria, paresis). Seizures are commonly manifested as “chewing-gum” seizures (vigorous repetitive opening and closing of the mouth) but can also be generalized. Hyperesthesia attributable to viral meningitis is uncommon. Myoclonus (rhythmic twitching of the head, neck, or one or more limbs) occurs as the disease progresses and is very suggestive of canine distemper. Optic neuritis and chorioretinitis can be observed.
- Systemic and neurologic signs are not always present at the same time. More often, neurologic disease occurs 1-3 weeks after recovery from systemic signs, but the two forms can coincide. Rarely, the neurologic signs will occur weeks to months later.

ETIOLOGY AND PATHOPHYSIOLOGY

- Certain strains of canine distemper virus (CDV) are more virulent and neurotropic; Snyder Hill strain is associated with polioencephalomyelitis; A75/17 and R252 strains are associated with CNS demyelination.
- Shedding of the virus begins by the seventh day after infection and may continue for up to 90 days.
- Shedding is primarily aerosol, but virus can also be recovered from urine, feces, nasal and ocular secretions, and skin.
- After initial exposure, CDV replicates in the upper-respiratory epithelium tissue macrophages. These cells are carried by the local lymphatics to the tonsils and retropharyngeal and bronchial lymph nodes. Here, the virus multiplies and disseminates systemically in mononuclear cells, creating an initial fever and leukopenia 3-6 days after exposure. Lymphopenia is associated with viral damage to both T and B lymphocytes.
- Viremia occurs by the ninth day post infection as the virus spreads hema-togenously to epithelial tissues and the CNS. Occurrence of viremia depends on host humoral and cell-mediated immunity. Infection of epithelial tissue correlates with shedding of the virus and occurs through all epithelial secretions, even in animals with subclinical infections.
    - Dogs with adequate humoral and cell-mediated immunity clear the virus by day 14.
    - Dogs with an intermediate level of immunity have infection of the epithelial tissues by day 14. Clinical signs that develop eventually resolve if the antibody titer increases and the virus is cleared from most tissues. Some virus may persist in footpads and CNS.
    - In dogs with poor immunity, virus spreads to many tissues by day 14, including skin, endocrine glands, exocrine glands, and epithelial cells of the intestinal tract, the respiratory system, and the genitourinary tract.
- Clinical signs are usually severe; secondary bacterial infections are common (although this advances morbidity, studies indicate it does not increase mortality).
- CNS infection occurs hematogenously. CDV enters the CNS through meningeal perivascular spaces, the choroid plexus, and the ventricular ependymal cells. Acute CDV encephalomyelitis occurs early in the course of the disease of young and immune-deficient dogs, causing a polioencephalomyelitis.
- Full recovery from CDV infection in young animals is uncommon, but likely produces lifelong immunity.
- Transplacental infections can result in abortions or stillbirths. Puppies that survive transplacental infections can develop neurologic signs by 6 weeks of age and often have lifelong immunodeficiency.
- Some dogs will continue to shed the virus for up to 2 months after infection.

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

A presumptive diagnosis in a young, unvaccinated dog is made based on presentation of clinical signs that include oculonasal discharge, vomiting, and/or diarrhea with or without a recent onset of neurologic signs. Older dogs can initially present with signs consistent with infectious tracheobronchitis. Clinical confirmation typically comes from a blood sample submitted for immunofluorescent antibody testing of white blood cells, or anti-CDV antibody titers in cerebrospinal fluid (CSF).

DIFFERENTIAL DIAGNOSIS

- Canine infectious tracheobronchitis
- Canine parvoviral enteritis
- Other CNS diseases of young dogs

INITIAL DATABASE

- CBC can reveal an absolute lymphopenia; rarely, CDV inclusions are identified in lymphocytes, monocytes, neutrophils, or erythrocytes.
- Serum biochemistry profile and urinalysis are variable and not definitive for CDV.
- Thoracic radiographs: interstitial pattern in early phases; evidence of bronchopneumonia in later stages with secondary bacterial infection

ADVANCED OR CONFIRMATORY TESTING

- Serum antibody testing: elevated serum IgM titers in unvaccinated dogs confirm recent exposure or current infection.
- CSF
  - Elevated CSF protein and lymphocytic pleocytosis are typical.
  - Presence of CSF antibody titers to CDV are confirmatory when there is no blood contamination of the sample.
  - With potential blood contamination of the CSF sample, paired samples of CSF and serum are tested for CDV and canine parvovirus (CPV) antibody titers; since CPV does not cross the blood-brain barrier, a CDV/CPV ratio that is higher in CSF than in blood suggests CDV infection.
  - Severely immunosuppressed patients or those with the noninflammatory demyelinating form of CDV may have normal CSF, often with low CSF protein (<5 mg/dL).
- Fluorescent antibody testing
  - Cytologic smears from buffy coat, tonsillar or conjunctival epithelial scrapings, CSF, bone marrow, urine sediment
  - More rewarding on conjunctival scrapings early in course of the disease
- PCR test for CDV: whole blood, serum, CSF
- Postmortem testing: immunofluorescent techniques for frozen samples of tonsils, lymph nodes, GI epithelium, spleen, urinary bladder, brain

TREATMENT

TREATMENT OVERVIEW

Affected animals are treated with supportive care, antibiotics to control secondary bacterial infection, and anticonvulsants to control seizures. No medication is known to eradicate the virus.

ACUTE GENERAL TREATMENT

- Broad-spectrum antibiotics (parentally initially) such as ampicillin, 22 mg/kg IV q 8 h, and enrofloxacin (not in growing puppies), 5 mg/kg diluted 1:1 in saline and given slowly IV q 12 h for secondary bacterial infections
- Nebulization and coupage if pneumonia apparent radiographically
- Antidiarrheals (e.g., loperamide, 0.1-0.2 mg/kg PO up to q 8 h), antiemetics (e.g., dolasetron, 0.3-0.6 mg/kg IV or SQ q 12-24 h; or metoclopramide, 0.2-0.4 mg/kg SQ q 8 h), and GI protectants (e.g., omeprazole, 0.7 mg/kg PO q 24 h) as needed for GI signs
- IV fluid resuscitation to correct dehydration and electrolyte disturbances
- Diazepam or midazolam if acute seizure control is needed (0.5 mg/kg IV or 1 mg/kg per rectum PRN up to 4 times in 2 hours)
- Isolation: patients are in an infectious phase of the disease and contagious.

CHRONIC TREATMENT

- Anticonvulsant therapy (phenobarbital, 2-4 mg/kg PO q 12 h; or leve-tiracetam, 20 mg/kg PO q 8 h) for seizure control. Sodium valproate (60-100 mg/kg PO q 8 h) can be considered in early stages of myoclonus but is ineffective in later stages.
- The use of corticosteroids is controversial. Antiinflammatory doses are considered useful to combat optic neuritis. Immune-suppressive doses are sometimes advocated for acute inflammatory CDV encephalitis in older dogs without systemic disease. Corticosteroids are advocated in the treatment of ODE and vaccine-induced CDV. Corticosteroid doses should be tapered to the lowest effective dose and are *contraindicated* in the presence of systemic disease with mucosal (respiratory, ocular, GI) signs and any evidence of secondary bacterial infections.

POSSIBLE COMPLICATIONS

- Recovery from systemic signs of the disease may precede development of neurologic signs weeks to months later.
- A possible link has been noted between rheumatoid arthritis and CDV.

PROGNOSIS AND OUTCOME

- Development of CNS signs is the most important negative prognostic factor.
- Dogs with adequate immunity do not develop clinical signs, and they clear the virus within 14 days post infection. The incidence of late-onset CNS signs in these dogs is low.
- Dogs with inadequate immunity develop mild to severe systemic signs and frequently develop CNS signs.

PEARLS & CONSIDERATIONS

COMMENTS

- CDV has a worldwide distribution and most commonly affects puppies and young, unvaccinated adults. Unvaccinated puppies exposed to an infected dog in the waiting room of a veterinary hospital should be vaccinated at that time and usually develop sufficient immunity before the virulent virus produces systemic signs.
- Weimaraners may have an unusual susceptibility to vaccination (see below).

PREVENTION

- Routine vaccination with a modified live canine distemper (ML-CDV) vaccine is indicated in puppies (every 3-4 weeks beginning at 6 weeks and ending at 16 weeks). A booster vaccine is given 1 year later and then periodically (every 3 years).
- Vaccination usually confers adequate immunity. Immunocompromised dogs or dogs exposed to a large amount of highly virulent CDV strain can still develop disease.
- Vaccine-induced infections are very rare and only produce CNS signs.
- Complications from the vaccine can occur but are also rare. Complications can include hypertrophic osteodystrophy (HOD) and juvenile cellulitis. Clinical signs usually develop within 10 days of vaccination (range 4-21 days) and have been associated with all ML-CDV vaccine strains. Weimaraners are the most frequently affected breed, and some evidence suggests there are familial tendencies. A corticosteroid-responsive neutrophilic meningitis/arteritis has also been described in this breed in association with ML-CDV vaccination. The use of a recombinant CDV vaccine in young Weimaraners instead of ML-CDV is suggested to reduce the risk of such complications. Additional vaccinations in Weimaraners after 1 year of age have not shown the same problems.
- Recombinant CDV vaccines are currently available and showed comparable efficacy to ML-CDV vaccines in initial studies.

TECHNICIAN TIPS

- Affected dogs should be isolated from other hospitalized patients, and gowns and gloves should be worn by personnel when handling these patients to prevent transmission of disease to other dogs.
- Transmission via fomites can be devastating; be sure that nebulization equipment and other objects are thoroughly disinfected before and after each use.

CLIENT EDUCATION

- Vaccination of young dogs is essential.
- Dogs with CDV infections should be isolated from healthy dogs for at least 2 weeks after cessation of signs in survivors. Some dogs will continue to shed the virus for up to 2 months after infection.
- In the environment, CDV is very sensitive to UV light, heat, and drying.

SUGGESTED READING

Greene CE, Appel MJ: Canine distemper. In Greene CE, editor: Infectious diseases of the dog and cat, ed 3, Philadelphia, 2006, WB Saunders, pp 25–41.

AUTHOR: ANDY SHORES

EDITOR: DOUGLASS K. MACINTIRE

1ST EDITION AUTHOR: JODI D. SMITH

Disseminated Intravascular Coagulation

BASIC INFORMATION

DEFINITION

An acquired syndrome of coagulation system dysregulation in which coagulation is abnormally and inappropriately activated, resulting in widespread deposition of fibrin in the microvasculature. Depletion of platelets and coagulation factors then causes bleeding in a subset of patients with disseminated intravascular coagulation (DIC).

SYNONYM

Dysfibrinogen syndrome

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs of any age and either sex; rarely identified in cats

RISK FACTORS

Primary disorders that initiate DIC: neoplasia, sepsis, polytrauma, shock, multiple organ dysfunction syndrome, gastric dilation-volvulus, severe inflammatory and immune reactions (pancreatitis, immune hemolysis, envenomation), liver failure

ASSOCIATED CONDITIONS & DISORDERS

DIC always develops secondary to an underlying or primary disease process (see Risk Factors above).

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Acute DIC: associated with fulminant diseases (e.g., sepsis, anaphylaxis, heatstroke, pancreatitis, envenomation)
- Chronic DIC: develops secondary to solid tumors and hematopoietic neoplasia; common in dogs with hemangiosarcoma

HISTORY, CHIEF COMPLAINT

Typically reflects the primary disease (see above); signs of DIC are nonspecific and to most owners, indistinguishable from signs of the underlying disorder.

PHYSICAL EXAM FINDINGS

Variable, depending on primary disease and extent of thrombosis/factor depletion. None, one, or several of the following may be apparent:

- Collapse, pale mucous membranes, tachycardia, tachypnea, diffuse bruising (ecchymoses), melena, icterus

ETIOLOGY AND PATHOPHYSIOLOGY

- Two major pathways initiate DIC:
  - Systemic inflammatory response accompanied by cytokine activation and coagulation cascade activation (e.g., sepsis, polytrauma)
  - Release or exposure of procoagulant stimuli into the vascular space initiates widespread activation of coagulation (e.g., hemangiosarcoma, mammary carcinoma).
- Systemic fibrin deposition is insufficiently balanced by opposing anticoagulant mechanisms.
  - Antithrombin depletion from consumption, degradation, and suppressed synthesis
  - Protein C system: downregulated by proinflammatory cytokines
- Fibrinolysis is concomitantly suppressed.

- High plasminogen activator inhibitor levels impair fibrinolysis.
- Subsequent depletion of coagulation factors, including consumption of platelets, develops in some patients.
- Local thrombosis contributes to acidosis, ischemia, and tissue necrosis, which can perpetuate the syndrome.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

No single laboratory test is diagnostic for DIC. Early diagnosis of the thrombotic phase of DIC is especially challenging and requires an elevated index of clinical suspicion. The presence of nonspecific physical exam abnormalities (see above), especially together with a documented recent (hours/days) decrease in platelet count and/or altered coagulation parameters in a patient with a recognized risk factor, should alert the clinician to the possibility of DIC. The suspicion is further increased if signs of hemorrhage are present, but at the hemorrhagic stage, DIC is more likely advanced and more difficult to treat effectively.

DIFFERENTIAL DIAGNOSIS

- Hemorrhagic DIC:
  - Anticoagulant rodenticide exposure
  - Severe thrombocytopenia
  - Inherited or acquired platelet dysfunction
  - Dextran or hetastarch administration (prolonged clotting times)
  - Liver failure
- Thrombotic DIC: organ failure or pulmonary thromboembolism (PTE) due to cardiac disease, heartworm disease, tumor emboli, or “hypercoagulability” associated with antithrombin loss

INITIAL DATABASE

- CBC, platelet count, blood smear evaluation
  - Thrombocytopenia
  - Schistocytosis (fragmented red blood cells) from shredding effect of intravascular fibrin strands
- Serum biochemistry profile, urinalysis: evidence of underlying disease; effects of thromboembolism (e.g., renal, hepatic)
- Chest and abdominal radiographs: evidence of underlying disease and/or thromboembolism, hemorrhage
- Coagulation testing (prothrombin time [PT], activated partial thromboplastin times [APTT], fibrinogen [hypofibrinogenemia])
- D-dimer or fibrin/fibrinogen degradation product (FDP) concentration: typically increased in DIC
- Antithrombin III activity: typically decreased in DIC

TREATMENT

TREATMENT OVERVIEW

DIC can be thought of as a secondary complicating factor of other serious disorders. Therefore treatment involves two parallel approaches: control of hemo-static abnormalities (thromboembolism or hemorrhage, whichever is predominant) and control or reversal of the underlying disorder.

ACUTE GENERAL TREATMENT

- Always treat the primary condition.
- Support adequate perfusion with intravenous fluids as needed.
- Supplemental oxygen therapy if indicated (e.g., pulmonary disease including PTE)
- Red blood cell transfusion or polymerized hemoglobin solution: considered in anemia cases (see p. 1347).
- Fresh-frozen plasma (FFP) transfusion if fibrinogen and clotting factor depletion cause overt signs of hemorrhage, or if fibrinogen-deficient patients require surgery (see p. 1347). High volume and repeated doses of FFP may be needed (10-15 mL/kg IV q 8-12 h).
- Heparin (either unfractionated or low-molecular-weight heparin) should be considered in cases with signs of dyspnea due to PTE or organ failure due to thrombosis.
  - “Regular” unfractionated heparin (UFH): 100-200 U/kg SQ q 8 h, or 15-25 U/kg/h IV continuous rate infusion
  - Low-molecular-weight heparin: dalteparin (Fragmin), 100 IU/kg SQ q 12 h; or enoxaparin (Lovenox), 1-1.5 mg/kg SQ q 12 h.

CHRONIC TREATMENT

DIC is always a sequela, and chronic treatment should be directed toward the primary condition.

DRUG INTERACTIONS

Avoid heparin, hetastarch, and dextrans when prolonged clotting times due to severe factor and fibrinogen depletion or severe thrombocytopenia are present.

POSSIBLE COMPLICATIONS

- PTE
- Thromboembolism to other organs (e.g., renal, brain, hindlimb, hepatoportal)
- Hemorrhage into other organs, leading to organ dysfunction

RECOMMENDED MONITORING

- Serial platelet counts and coagulation times
- Monitor organ function and tissue oxygenation.
- If heparin treatment: closely monitor to detect signs of hemorrhage, falling platelet count, or excessive prolongation of in vitro clotting time (UFH therapy).
- A target prolongation of APTT to 1.5 to 2 times patient baseline is considered evidence of UFH high-dose anticoagulant effect.
- UFH and low-molecular-weight heparins can be monitored based on their inhibition of Factor Xa. In human studies, the target range of anti-Xa activity for UFH = 0.3-0.7 U/mL (UFH) and for low-molecular-weight heparin = 0.5-1 U/mL.

PROGNOSIS AND OUTCOME

- Guarded because diagnosis is often reached late (inadequate suspicion), syndrome is challenging to treat (both thromboembolic and hemorrhagic phases exist), and a primary disorder is concurrent. Prognosis depends primarily on the underlying condition and the extent of thromboembolic/hemorrhagic sequelae if any.

PEARLS & CONSIDERATIONS

COMMENTS

- The development of DIC contributes to the morbidity and mortality of the primary disease.
- Treating DIC becomes less rewarding late in the disease process.
- Having an early suspicion that DIC may develop is important for selecting appropriate tests to document and monitor the syndrome.

PREVENTION

The critical factors in preventing or ameliorating DIC are specific and aggressive correction of the primary disease process.

CLIENT EDUCATION

Development of DIC represents a severe complication of many different systemic diseases.

SUGGESTED READING

Feldman B, Kirby R, Caldin M: Recognition and treatment of disseminated intravascular coagulation. In Bonagura JD, editor: Current veterinary therapy XIII. Philadelphia, 2000, WB Saunders, pp 190–194.

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Disorientation/Confusion

BASIC INFORMATION

DEFINITION

An inappropriate state of confusion with respect to time and/or place and/or identity

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs and cats, any age or gender

GENETICS AND BREED PREDISPOSITION

- Cats and dogs that are predisposed (brachycephalic and dome-headed breeds) to congenital hydrocephalus may be disoriented and confused.
- Inherited inborn errors of metabolism (e.g., various lysosomal storage diseases)
- Breeds predisposed to various diseases resulting in metabolic derangements (e.g., portosystemic shunts resulting in hepatic encephalopathy)
- Breeds of animals predisposed to epilepsy (i.e., disorientation/confusion during the postictal period)

RISK FACTORS

- Old age: canine and feline cognitive dysfunction syndrome (see p. 225)
- Access to psychoactive drugs or potentially neurotoxic substances
- Preexisting liver or kidney disease, diabetes mellitus, hypothyroidism, or other diseases causing osmotic, electrolyte, and/or acid-base disturbances

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- External trauma
- Ingestion of toxic substance with central nervous system effects
- Barring history or suggestion of observed trauma or intoxication, owners may describe any combination of the following signs:
  - Not responding to being called by name
  - Wandering aimlessly
  - Behaving unaware or “forgetful” of surroundings or of owner/family members
  - Urinating or defecating in inappropriate places
  - Not behaving in anticipatory manner with regard to daily routines (e.g., not being excited to being fed at usual time)
- Clear, concise description of primarycomplaint and ask questions pertaining to:
  - Vision or hearing changes
  - Potential access to toxins or psycho-tropic drugs
  - Signs associated with metabolic disturbances (e.g., alterations in thirst, appetite, gastrointestinal/urologic behaviors)
  - History of recent trauma
  - History of seizures (animals can be disoriented during the postictal period).

PHYSICAL EXAM FINDINGS

- Physical examination findings depend on the etiology (see specific diseases).
- For accurate treatment and prognosis, it is important to identify whether the cause of the disorientation is of:
  - Primary brain origin (e.g., canine or feline cognitive dysfunction syndrome, congenital hydrocephalus, brain neoplasia)
  - Secondary to some other cause (e.g., trauma, various metabolic encephalopathies, various toxicities)
  - Resulting from visual impairment: may note mydriasis in normal ambient lighting (see p. 141)
  - Resulting from hearing impairment
  - Benign behavioral origin

ETIOLOGY AND PATHOPHYSIOLOGY

- Disorientation can result when a disease affects the cerebrum.
- Exact pathophysiologic explanation of altered frontal and temporal lobe function varies with each disease but may include:
  - Alterations in neuronal metabolism (e.g., hypoglycemia, hypothyroidism, hypocalcemia)
  - Accumulation of neurotoxic substances (e.g., hepatic encephalopathy)
  - Chronic oxidative stress in the brain, leading to neurodegeneration (e.g., canine and feline cognitive dysfunction syndrome)
  - Alterations in brain neurotransmitters (e.g., hepatic encephalopathy, epilepsy)
  - Alterations in neuronal excitability (e.g., electrolyte disturbances)
  - Direct mechanical damage (head trauma)
- Animals can become disoriented despite normal cerebral function when they are blind and/or deaf (see pp.141 and 280).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The history and physical exam provide essential clues to investigate this nonspecific chief complaint. A neurologic examination is indicated in all cases, as are routine laboratory tests to investigate metabolic causes.

DIFFERENTIAL DIAGNOSIS

- See Etiology and Pathophysiology above for differentiation of specific inciting causes.
- Differential diagnosis for disorientation:
  - Stereotypic behavior
  - Complex partial seizure
  - Absence seizure

INITIAL DATABASE

- Age of onset
- Complete neurologic examination (see p. 1311)
- Complete ophthalmic examination (see p. 1313)
- CBC, serum biochemistry, urinalysis (1) to determine any underlying systemic condition and (2) as preanesthetic workup (if needed).
- NOTE: Diagnosis of age-related cognitive dysfunction is a diagnosis of exclusion in elderly patients; therefore, one should first consider other diseases resulting in disorientation.

ADVANCED OR CONFIRMATORY TESTING

- Brainstem auditory evoked response testing; rule out deafness.
- Scotopic and photopic maze testing/obstacle course: vision
- Electroretinogram: retinal function
- CT or MRI of brain
- Cerebrospinal fluid cytologic with biochemical ± serologic assessment
- Clinical laboratory diagnostic tests for various endocrinopathies, for liver function, toxicology screen, etc.

TREATMENT

TREATMENT OVERVIEW

Treat the underlying cause of disorientation when possible.

ACUTE GENERAL TREATMENT

Acute treatment varies according to the etiology (see specific etiology).

CHRONIC TREATMENT

Animals with incurable disorientation (e.g., age-related cognitive dysfunction) may need special care including:

- Being confined within a yard or home (e.g., to prevent wandering away and getting lost)
- Taking animal outside to urinate/defecate more frequently (dogs, if dog is inappropriately urinating/defecating in the house)

PROGNOSIS AND OUTCOME

Prognosis depends on the etiology.

PEARLS & CONSIDERATIONS

COMMENTS

- Up to 75% of dogs 7 years or older will demonstrate at least one clinical sign consistent with canine cognitive dysfunction syndrome.
- Animals with clinical signs of disorientation related to vision or hearing loss will commonly adapt to their surroundings and have a good quality of life, provided they are not used for tasks requiring these senses and if their home environment does not change drastically (e.g., moving furniture in new places frequently).

SUGGESTED READING

ASPCA Poison Control Center: http://www.aspca.org/site/PageServer?pagename–apcc (useful for information and links pertaining to toxicologic information on various plants and drugs).

Gunn-Moore DA, Moffat K, Christie LA, Head E: Cognitive dysfunction and the neurobiol-ogy of ageing in cats. J Small Anim Pract 48:546–553, 2007.

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Diskospondylitis

BASIC INFORMATION

DEFINITION

An inflammation/infection of the intervertebral disk and the adjacent end plates and vertebral bodies. Bacterial cause (usually *Staphylococcus*) is most common; occasionally, it is due to the fungal organism *Aspergillus*.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Most commonly seen in medium- to giant-breed male dogs (males outnumber females 2:1).
- Any age dog can be affected, but one large retrospective study found that older dogs were overrepresented, with the highest risk for dogs >10 years of age.
- Purebred dogs may be predisposed, especially Great Danes.
- Has also been seen in small-breed dogs as well as in cats.

GENETICS & BREED PREDISPOSITION

German shepherds are overrepresented for fungal diskospondylitis.

CONTAGION & ZOONOSIS

Diskospondylitis caused by *Brucella canis* carries the possibility of zoonosis.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Variable clinical presentation
- Most dogs show progressive clinical signs over several weeks, but some dogs develop clinical signs acutely.
- Clinical signs are often nonspecific (fever, anorexia, weight loss, lethargy, depression) but usually include spinal hyperpathia.

PHYSICAL EXAM FINDINGS

- General physical and neurologic examination findings (see p. 1311) vary depending on the location, severity, and secondary effects of the infection.
- Patients examined early in the course of the disease often show only signs of spinal hyperpathia without paraparesis.
- Later, patients may have more severe spinal hyperpathia with varying degrees of paraparesis.
- Occasionally, patients present with an acute onset of back pain with associated ambulatory or nonambulatory paraparesis/paraplegia.

ETIOLOGY AND PATHOPHYSIOLOGY

- Some dogs that develop diskospondylitis may have underlying immune compromise.
- Infectious organisms may gain access to the disk space and vertebrae via several mechanisms.
    - Hematogenous spread of bacteria or fungi: the most common mechanism, although the primary source of infection is not always found.
        - The urinary tract is the most likely source of infection.
        - Other sources, although rare, are bacterial endocarditis and dental disease.
    - Foreign-body migration: most commonly a grass awn. Plant materials have barbed ends that allow them to migrate through tissues (via inhalation and migration through the lungs or diaphragm, ingestion and subsequent penetration through the bowel wall, or transcutaneous penetration), carrying bacteria to the disk space.
    - Iatrogenic: infection may develop after spinal surgery or paravertebral injection.
    - Bacterial organisms that are involved are usually coagulase-positive *Staphylococcus* organisms *(S. pseud-intermedius*, *S. aureus.)* Other bacterial pathogens include *Streptococcus* species, *Brucella canis*, and *Escherichia coli*. Less frequently isolated bacteria are *Pasteurella*, *Proteus*, *Corynebacterium*, *Actinomyces*, *Nocardia*,

Bacteroides, and *Mycobacterium* species.
- Fungal organisms include *Aspergillus* and *Paecilomyces* species.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Radiographs are the most useful diagnostic tool. Changes first appear 2-4 weeks after the onset of clinical signs.

DIFFERENTIAL DIAGNOSIS

Radiographically, diskospondylitis must be distinguished from spondylosis deformans and spinal neoplasia:

- Spondylosis and sclerosis are common both in spondylosis deformans and diskospondylitis, but vertebral endplate lysis is seen only in diskospondylitis.
- Typically, in spinal neoplasia the lytic lesion is confined to a single vertebra, whereas in diskospondylitis, the lysis is associated with adjacent vertebrae.

INITIAL DATABASE

- CBC, serum biochemistry panel: typically unremarkable
  - Leukocytosis may be seen if there are concurrent systemic abnormalities (e.g., pyometra, prostatic abscess, endocarditis).
- Urinalysis reveals bacterial cystitis in up to 40% of cases.
  - The same organism is occasionally identified in both urine and blood cultures.
- Blood cultures should be obtained whenever possible.
- Cerebrospinal fluid is typically normal.
- *Brucella* titers may be positive. Because of the zoonotic potential, this titer should be performed in all sexually intact patients suspected of having diskospondylitis.
- Radiographs are the most useful diagnostic tool. Changes first appear 2-4 weeks after the onset of clinical signs.
  - Collapse of the disk space
  - Proliferative bony changes adjacent to the intervertebral disk space
  - Sclerosis at the bony margins
  - The first radiographic signs are usually a collapsed intervertebral disk space, with or without subtle vertebral endplate erosion.
  - With more chronic infections, the bone becomes more sclerotic, and ventral spur formation occurs. This is often accompanied by marked osteolysis and inflammatory new bone formation.
  - Multiple sites of involvement are found in approximately 40% of cases.
  - The most common site for diskospondylitis is L7/S1.

ADVANCED OR CONFIRMATORY TESTING

- The most sensitive procedure for identifying infectious organisms associated with diskospondylitis is culture of surgically obtained tissue. Samples can be taken at the time of surgery (if indicated for decompression), but otherwise it is an invasive diagnostic tool.
- Fluoroscopically guided percutaneous disk aspiration has been shown to be useful in obtaining a positive culture in approximately 75% of cases.
- Myelography and MRI are useful tools to identify spinal cord compression. The vertebral endplates often demonstrate strong contrast enhancement with MRI.

TREATMENT

TREATMENT OVERVIEW

Successful treatment of diskospondylitis depends on long-term antibiotic therapy.

ACUTE AND CHRONIC TREATMENT

- When a specific causative agent is not identified, empirical treatment with antibiotics is warranted. The most common causative bacteria are coagulase-positive *Staphylococcus* spp., which are generally sensitive to first-generation

cephalosporins or β-lactamase-resistant penicillins.

- Antibiotic treatment usually results in improvement of spinal hyperesthesia within 4-5 days. If there is no improvement within 7-10 days of starting antibiotics, the case should be reevaluated (if not already done, consider blood or urine culture, fungal titers, aspiration of the lesion, etc.).
- Antibiotic therapy should be continued for at least 6 weeks after clinical and radiographic improvement is seen. Specifically, antibiotic therapy should be continued until there is no additional or persistent bony lysis, which is considered a radiographic sign of progression of the disease. In most cases, antibiotic therapy is prolonged and may easily be required for a year from onset of therapy.
- With positive *Brucella* test results, options include antibiotic treatment, with strict control of exposure to other dogs, or euthanasia (see Brucellosis, Dog, p. 162).
- Limited success is seen using itraconazole in fungal diskospondylitis.
- Surgical treatment: based on imaging studies and clinical signs (e.g., vertebral instability or spinal cord compression associated with neurologic deficits); spinal cord decompression via a dorsal or hemilaminectomy may be indicated.

Organisms That Cause Diskospondylitis and Recommended Antibiotics (Pending Culture and Sensitivity)

Organism	Antibiotic	Dosage
Staphylococcus species	Cephalexin	22 mg/kg PO q 8 h
	Amoxicillin-clavulanate	13.75 mg/kg PO q 12 h
Streptococcus species	Amoxicillin	22 mg/kg PO q 12 h
Brucella canis	Enrofloxacin	5 mg/kg PO q 12 h
	Doxycycline	25 mg/kg PO q 12 h
Escherichia coli	Enrofloxacin	5 mg/kg PO q 12 h (dog)
	Cephalexin	22 mg/kg PO q 12 h
	Amoxicillin-clavulanate	13.75 mg/kg PO q 12 h
Actinomyces species	Penicillin G	100,000 U/kg IM, SC q 6 h
Aspergillus species	Itraconazole	5 mg/kg PO q 12 h

BEHAVIOR/EXERCISE

Exercise restriction is recommended for these patients to keep them comfortable and lessen the risk of trauma to the spine.

RECOMMENDED MONITORING

- In addition to clinical signs, radiographs should be monitored during the healing phase.
  - The radiographic signs of healing diskospondylitis lesions are disappearance of the lytic focus and its replacement by bridging or fusion of involved vertebrae.
- In young dogs (<1 year), radiographic improvement parallels clinical improvement and includes minimal additional bony lysis along with increased sclerosis and bridging.
- In older dogs, there is a lag of 3-9 weeks between the time of clinical improvement and the appearance of radiographic characteristics of recovery.
  - During the lag period, radiographic findings are consistent with progression of disease, showing increased bony lysis without additional sclerosis or bridging. The bony lysis is likely secondary to bone being resorbed at the site of the lesion before new bone formation can occur.

PROGNOSIS AND OUTCOME

- The prognosis is variable and depends mainly on the severity of neurologic deficits and the causative agent.
  - Patients with only spinal hyperpathia and no neurologic deficits have an excellent prognosis.
  - As the severity of the neurologic signs worsens, so does the prognosis.
- Prognosis is also based on response to treatment and is less favorable when the animal does not respond to medical management. In such cases, a different antibiotic may be considered or a disk/bone culture can be performed to rule out fungal disease and identify an organism.
- Fungal diskospondylitis carries a grave prognosis.

- Patients who require surgery carry a guarded prognosis that worsens with the degree of spinal instability.

PEARLS & CONSIDERATIONS

COMMENTS

Approximately 56% of dogs with diskospondylitis have associated spinal cord compression. In the majority of these dogs (76%), the compression is caused by soft tissue (i.e., proliferation of the annulus secondary to instability, steatitis) rather than subluxation (20%).

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Discolored Urine

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Urine that is any other color besides yellow or amber; most often caused by the presence of blood, hemoglobin, myoglobin, or bilirubin

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dependent on underlying cause

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Owner may note discolored urine with no other clinical signs.
- Signs may relate to primary cause. For example:
  - Pollakiuria, dysuria, stranguria associated with lower urinary tract disease
  - Weakness, collapse, pallor associated with severe hemolysis
  - Weakness or pain associated with severe muscle damage

PHYSICAL EXAM FINDINGS

- Lower urinary tract disease:
  - Vaginal disease (infection, inflammation, mass)
    - Vaginal discharge
    - Vaginal mass
    - Vulvar abnormalities
  - Prostatomegaly
  - Thickened, abnormal urethra
  - Distended bladder
- Hemolysis:
  - Pallor
  - Tachycardia
  - Weakness, collapse
  - Splenomegaly
- Muscle damage:
  - Weakness
  - Signs of pain
  - Signs of blunt trauma or prolonged recumbency
- Icterus:
  - Yellow mucous membranes, sclera, skin

ETIOLOGY AND PATHOPHYSIOLOGY

- Yellow, dark yellow
  - Normal
- Red, pink, red/brown, orange
  - Hematuria
  - Hemoglobinuria
  - Myoglobinuria
- Orange/yellow
  - Very concentrated normal urine
  - Excess urobilin
  - Bilirubin

- Yellow/brown, green/brown
  - Bile pigments
- Brown to black
  - Methemoglobin
  - Myoglobin
  - Bile pigments
- Colorless
  - Very dilute urine

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A comprehensive urinalysis is the most important step to help determine the source of discolored urine. Evaluation of urine color as compared to serum color also helps narrow the differential diagnosis list.

DIFFERENTIAL DIAGNOSIS

- Dark yellow/orange
  - Normal
  - Prehepatic icterus (extravascular hemolytic anemia)
  - Hepatic icterus:
    - Dogs/cats: hepatic neoplasia, toxin-induced hepatopathy
    - Dogs: idiopathic or breed-associated hepatitis
    - Cats: hepatic lipidosis, cholangitis/cholangiohepatitis
  - Posthepatic icterus (biliary disease, pancreatic disease, duodenal disease)
- Red, pink, red/brown, orange
  - Urinary tract infection
  - Idiopathic cystitis/feline lower urinary tract signs (FLUTS [cats])
  - Urolithiasis
  - Urethritis
  - Prostatitis, prostatic neoplasia
  - Vaginitis
  - Intravascular hemolytic anemia
  - Hemoglobin transfusion
  - Neoplasia (e.g., transitional cell carcinoma, renal carcinoma, others)
  - Coagulopathy
  - Trauma
  - Estrus
- Brown to black
  - Trauma
  - Heinz body hemolysis-inducing toxins:
    - Zinc
    - Copper
    - Onions, garlic, broccoli
    - Drugs (acetaminophen, methylene blue)
- Colorless
  - Normal
  - Fluid therapy/overhydration
  - See Polyuria/Polydipsia, 902:
    - Diabetes mellitus
    - Diabetes insipidus
    - Diuretics
    - Hepatic diseases
    - Hyperthyroidism
    - Hypoadrenocorticism
    - Hypokalemia
    - Pyometra
    - Renal failure
    - Glucocorticoid excess (hyperadrenocorticism, iatrogenic)
    - Psychogenic polydipsia

INITIAL DATABASE

- CBC
  - Anemia
- Serum biochemistry profile
  - Metabolic diseases (see Polyuria/Polydipsia above)
  - Evaluate color of serum:
    - Clear: consider myoglobin.
    - Pink: hemolysis
    - Yellow: icterus
- Urinalysis
  - Comparing free-catch to cystocentesis sample often aids in localization:
    - Discoloration of urine in both samples suggests a systemic, renal, ureteral, or urinary bladder disorder.
    - Discoloration of free-catch urine but normal-color cystocentesis urine suggests a urethral, uterine, prostatic, testicular, preputial, vulvar, or vaginal problem.
    - Discoloration of cystocentesis urine with a normal-color free-catch sample suggests erroneous switching of the samples or other error.
  - Hematuria:
    - Cystitis
    - Urolithiasis
    - Urethritis
    - Neoplasia
    - Prostatitis/prostatic abscess
    - Prostatic neoplasia
    - Bladder neoplasia
    - Trauma
    - Estrus
    - Idiopathic renal hematuria
  - Pyuria:
    - Cystitis, pyelonephritis
    - Inflammation, sterile (idiopathic cystitis/FLUTS)
    - Neoplasia
  - Hemoglobinuria: hemolysis
  - Myoglobinuria: muscle damage
- Urine culture and sensitivity
- Abdominal radiographs
  - Calculi
  - Mass effect
  - Prostatomegaly
  - Metal in gastrointestinal tract (e.g., zinc)
  - Enlargement/mineralization of sublumbar lymph nodes, suggesting prostatic or urinary bladder neoplasia
- Abdominal ultrasound
  - Renal disease (pyelonephritis, mass, diffuse infiltration, other)
  - Bladder wall tumor (transitional cell carcinoma, other)
  - Prostatic disease
  - Urolithiasis
  - Sublumbar lymphadenopathy
  - Other neoplasia/abnormality contributing to hemolysis
- Sedated vaginal examination
  - Mass
  - Inflammation/infection
  - Conformational abnormality

ADVANCED OR CONFIRMATORY TESTING

As dictated by findings for the individual case:

- Laboratory testing
  - Vaginal smear
  - Urine protein/creatinine ratio
  - Ejaculate examination
  - Fine-needle aspirate
- Imaging
  - Excretory urogram
  - Double contrast cystogram
  - Contrast vaginogram
- Biopsy

- Cystoscopy
- Exploratory laparotomy (virtually always replaced by less invasive means unless laparotomy is also therapeutic [e.g., urolith removal])

TREATMENT

TREATMENT OVERVIEW

- Correct underlying cause based on accurate diagnosis.
- Most life-threatening situations evaluated/addressed first

PROGNOSIS AND OUTCOME

Varies based on underlying cause

PEARLS & CONSIDERATIONS

- Physical examination and minimum laboratory work (CBC, serum biochemistry profile, urinalysis) essential to help quickly narrow the differential list.
- Comparison of urine color to plasma color and free-catch versus cystocentesis urine samples are simple but vital steps for narrowing the differential diagnosis list.
- Basic imaging (abdominal radiographs and ultrasound) can rule in or rule out many common causes of discolored urine.
- Color is not an indication of urine concentration; urinalysis with specific gravity is indicated for differentiation from pathologic conditions.
- Bilirubin conjugation and excretion is normal in the dog but not the cat; therefore trace or mild bilirubinuria in dogs may be normal and is not necessarily indicative of hepatobiliary or hemolytic disease.

TECHNICIAN TIPS

- Note color of urine before and after centrifugation.
- If red urine clears after centrifugation, the problem is hematuria. Hemoglobin and myoglobin stay in suspension, so urine color will not change with centrifugation.

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Disaster Working Dog Management and Health

BASIC INFORMATION

DEFINITION

Working dogs are highly trained for a specific task or tasks by an individual or organization for the purpose of assistance in a disaster, emergency, or disaster prevention. The nature of their work exposes them to environmental and physical risks less commonly encountered by pet dogs.

SYNONYMS

Accelerant-detection dog, bomb sniffer, drug-detection dog, search and rescue dog (Urban Search and Rescue [USAR]), cadaver dog, dual-purpose dog (does patrol and some type of detection work), explosives-detection dog, military working dog (MWD), patrol dog, guard dog

EPIDEMIOLOGY

SPECIES, AGE, SEX

Primarily young adult male dogs (2-8 years old)

GENETICS & BREED PREDISPOSITION

German shepherd, Labrador retriever, Belgian malinois, other breeds or crossbreeds

RISK FACTORS

- Physical safety of working and training environment, risk of exposure, environmental conditions
- Specific risk factors include long hours; stressful environment; oral, dermal, and respiratory exposure to toxins; hazardous footing; work low to the ground and in inaccessible areas, risking exposure to pockets of toxins/gases not apparent to handlers.
- Weapons of mass destruction, chemicals (chemical agent or toxic industrial chemical), biologics, nuclear and radiologics, incendiaries and explosives

CONTAGION & ZOONOSIS

- Agents of bioterrorism, foreign animal diseases, biological weapons of mass destruction
- Infectious agents: *Leptospira,* rabies, other endemic infectious agents (tickborne, geologically specific agents, others), ectoparasites and endoparasites

GEOGRAPHY AND SEASONALITY

Consider effects of weather conditions, especially temperature extremes, on working dogs. Consider geographic location and local environmental conditions such as dust, mold, sand, floodwater, toxic plants, and the like as inhaled, ocular, dermal, or ingestion risks.

ASSOCIATED CONDITIONS & DISORDERS

Nutritional (dehydration, diet change, or anorexia when working), stress related (gastric dilatation/volvulus, anorexia/adipsia, “burnout”)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Environmental concerns, foot problems, trauma, explosives, toxins, lacrimators, pharmaceuticals and illicit drugs, weapons of mass destruction (biological, chemical, radiologic)

HISTORY, CHIEF COMPLAINT

- Known exposure
- Inability to work or perform task
- General signs of illness that may include vocalizing, hypersalivation, lameness, ocular signs, nasal discharge, sneezing, diarrhea, vomiting, poor or no appetite, manifestations of anaphylaxis, ataxia, depression, hyperactivity, cough, weakness, petechiae, hemorrhage, collapse, central nervous system depression, collapse, muscle tremors, polyuria/polydipsia, seizure, coma

PHYSICAL EXAM FINDINGS

- Variable, based on exact disorder
- Most commonly, abnormalities include dehydration, heat or cold stress, exhaustion, and foot disorders.
- Signs of toxin exposure may include coughing, choking or gasping for air; red eyes and gums, tearing, salivation; miotic or mydriatic pupils; nausea, ptyalism, emesis or diarrhea (+/- hemorrhagic), fatigue; disorientation, muscle twitching, seizures, paralysis, involuntary urination or defection.
- May be none initially (chronic, organ involvement, carcinogenic)

ETIOLOGY AND PATHOPHYSIOLOGY

- Environmental: dehydration, heat stroke, hypothermia, inadequate nutrition, inadequate conditioning, drowning, choking, plant toxins, moldy food (tremorgenic mycotoxins), zootoxins
- Foot problems: laceration, abrasion, torn nail(s), contact dermatitis
- Trauma: fracture, laceration, abrasion, projectiles, blunt trauma, crushing injury, sprain, strain
- Explosives: cyclonite (C-4); 2,4,6-trinitrotoluene (TNT); pentaerythritol tetranitrate, dynamite (nitroglycerin + stabilizing agent), nitrates, smokeless powders, chlorates, nitromethane, triacetone triperoxide
- Toxins: ethylene glycol; rodenticides; herbicides; insecticides; toxic agents released at disaster site (gas, smoke, particulates, liquids, solids) such as hydrocarbons, polychlorinated biphenyls, hazardous metals, asbestos, gases (hydrogen cyanide, hydrogen sulfide, Freon, halogenated gases, carbon monoxide), soaps/detergents/acids/alkalis, propylene glycol, phenol, alcohols
- Lacrimators: oleoresin capsicum (pepper spray), *o*-chlorobenzylidene malononitrile, 1-chloroacetophenone (mace), dibenzoxazepine
- Illicit/legal drugs/supplements: marijuana, cocaine, amphetamines, opiates, phencyclidine, prescription medications, over-the-counter medications; herbal preparations and supplements
- Routes of exposure: dermal, inhalation, ocular, or ingestion. Swallowing of inhaled large-particulate (2-5 mcg) material moved to the oropharynx by mucociliary apparatus.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis of disaster working dog health or management problems is based upon the handler's chief complaint, the signs exhibited by the dog, and the possible or known risk factors in the working environment.

DIFFERENTIAL DIAGNOSIS

Varies with presentation, history, and physical exam findings

INITIAL DATABASE

- CBC, serum biochemistry profile, urinalysis: common abnormalities include evidence of renal failure (azotemia + isosthenuria) from toxins, evidence of hepatopathy from trauma, thrombocytopenia and coagulopathy from heat stroke, calcium oxalate monohydrate crystalluria with ethylene glycol toxicosis, cylindruria (urinary casts) with renal trauma/toxin/heat stroke.
- Lactate level for dogs presenting in shock, acute abdomen, or circulatory compromise
- Arterial blood gas and/or pulse oximetry
    - Oxygen saturation (SpO_2) low with near-drowning, noncardiogenic pulmonary edema (shock, seizure, trauma)
    - Note for carbon monoxide poisoning (combustion of gasoline, fire/smoke): pulse oximetry cannot evaluate the true severity of hypoxemia because of its inability to differentiate between oxygenated hemoglobin and carboxyhemoglobin.
- Arterial blood pressure: for diagnosis and monitoring of hypotension in hypovolemic shock, or identification of hypertension with some intoxications
- Electrocardiogram: sinus tachycardia with some intoxications; ventricular arrhythmias with hypoxemia, myocarditis, ischemic events, heat stroke
- Radiographs as appropriate for trauma, respiratory signs, neurologic signs, gastrointestinal signs

- Ultrasound for suspected cardiac or pulmonary signs or gastrointestinal disorders

ADVANCED OR CONFIRMATORY TESTING

- Ethylene glycol test, coagulation profiles, infectious disease titers, cultures
- Specific diagnostic tests exist, but availability varies. Tests available include heavy metals, cholinesterase, polychlorinated biphenyl (PCBs), carboxyhemoglobin (CO poisoning), anticoagulants, pharmaceutical and illicit drugs, mycotoxins.
- Obtain and store preexposure blood.
- Necropsy for unexplained death, and consider for any working dog.

TREATMENT

TREATMENT OVERVIEW

- Treatment consists of appropriate therapy for the signs presented in the field and referral to veterinary hospital as appropriate and as available (on-site veterinary team, local practitioner or 24-hour emergency and/or specialty hospital). Therapeutic goals are to stabilize the patient, decontamination if necessary, decrease ongoing exposure and absorption, and the institution of appropriate supportive care.

ACUTE GENERAL TREATMENT

- Stabilize the patient:
  - General emergency medicine and stabilization of vital signs and specific derangements with appropriate cardiovascular and respiratory support
  - Control hemorrhage, shock.
  - Control dyspnea, oxygen therapy, move to fresh air.
  - Control seizures, tremors.
  - Control pain.
- Decrease ongoing exposure and absorption:
  - Induce vomiting, gastric lavage (exceptions include corrosive agents, hydrocarbons, PCBs, soaps and detergents [cationic agents], acids and alkalis, phenol).
  - Administer water or milk orally for dilution (useful for corrosive agents, soaps, detergents, acids and alkalis, explosives [C-4, nitrates, nitromethane]).
  - Activated charcoal ± saline cathartic or sorbitol for noncorrosive agents (minimally effective for some heavy metals or short-chain solvents, hydrocarbons, soaps and detergents, acids and alkalis, ethylene glycol)
  - Gastrointestinal protectants
  - Decontamination:
    - Using copious amounts of water and liquid dish detergent (rinse, wash, rinse—cycle 3 times); ocular and nasal flushing using water or saline (consider teaching working canine to sneeze when young); washing, brushing or clipping hair in feet if buildup of debris or concrete dust. Clip affected haired areas to facilitate removal. Body temperature of the patient must be monitored to avoid hypothermia.
    - Human Safety and Personal Protective Equipment (PPE): basic guidelines include gloves, protective eyewear and footwear, respiratory protection (i.e., N-96 particulate respirators), and durable clothing. Training ahead of time and continual monitoring and assessment of safety risks to modify the PPE as appropriate are paramount for human and canine safety.
    - Powders: use care brushing, as it may aerosolize; wipe only.
    - CAUTION: some hazardous materials become reactive when exposed to water. Alternate decontamination methods may include application of baking powder or flour then physical removal by wiping, brushing, or combing.
    - Caked on contamination: may need to try to scrape off or break down with mineral oil (for petroleum-based products) or mechanics' handwashing products.
    - Eye ointments: avoid, as they may absorb contaminant and worsen corneal damage.
    - Bleach: 0.5% hypochlorite rinse followed by routine soap-and-water decontamination protocol for blister agents (vesicants) or flood water exposure
    - Phenol exposure: (human PPE is a MUST). Use paper/disposable towels to blot fur and skin prior to washing.
    - Eye flush: 15 minutes required for exposure to blister agents, blood, or metabolic agents (0.9% saline or tepid clean water)
- Supportive care:
  - Fluid therapy: diuresis to help promote removal of agents that are primarily excreted renally and to address shock, dehydration, and metabolic derangements.
  - Treat dehydration, hypothermia/hyperthermia, stress colitis, hemorrhagic gastroenteritis, and hemorrhagic cystitis. Recognize metabolic differences between human and canine sensitivity to contaminants (can be more, the same, or

less). Sensitivity is also dependent upon such factors as health, conditioning, age, and concentration and length of exposure to contaminants. Treat appropriately based upon the patient's signs, test results, and response to treatment.

BEHAVIOR/EXERCISE

- Kenneling (housing, husbandry, and/or transportation) influences physical and psychological welfare. Long-term stress can result in poor training and working ability, behavioral and physiologic changes. Caretakers are advised to take positive steps to ensure the highest degree of welfare, with benefits from providing for all the animal needs; should include environmental enrichment (i.e., feeding devices).

CHRONIC TREATMENT

As indicated for specific case

DRUG INTERACTIONS AND CONTRAINDICATIONS

As indicated for individual treatments

POSSIBLE COMPLICATIONS

As indicated for individual case

RECOMMENDED MONITORING

- As indicated:
  - Monitoring may improve mentation and demeanor.
  - Temperature: during decontamination procedures and/or shock, to help prevent hypothermia
  - Hydration, electrolytes, hematocrit/total solids, blood glucose, blood urea nitrogen, urine production and serial urinalyses
  - Pain
- May be lifelong if injury or exposure leads to permanent lesions
- Baseline (yearly or biannually) blood work: CBC, serum biochemistry profile, heartworm antigen test, urinalysis, and thyroid profile. Consider infectious disease screening as appropriate for location: Lyme disease, ehrlichiosis, bartonellosis, leishmaniasis, foreign animal diseases, etc.
- Necropsy is advised for working animals to aid in monitoring and for future health and prevention strategies for other working dogs.

PROGNOSIS AND OUTCOME

Prognosis depends on source, speed of identification of inciting cause, and speed of appropriate decontamination, emergency, and supportive care. Prognosis improves with proper prevention, awareness, and monitoring work site for potential concerns.

PEARLS & CONSIDERATIONS

COMMENTS

- Important resources:
  - Center for Disease Control: www.cdc.gov
  - National Veterinary Response Teams (NVRT), part of the National Disaster Medical System (NDMS), Department of Health and Human Services: www.ndms.dhhs.gov/; www.hhs.gov/emergency/
  - American Veterinary Medical Association: www.avma.org
  - Veterinary Medical Assistance Team: www.VMAT.org
  - American Society for the Prevention of Cruelty to Animals, Animal Poison Control Center: www.ASPCA.org; 1-888-426-4435
  - Material Safety Data Sheet (MSDS)
  - Emergency Response Guidebook (U.S. Department of Transportation): www.labelmaster.com/ERG/
- Most common problems are conjunctival irritation, respiratory tract problems, decreased appetite, dehydration, exhaustion, cuts, and foot/pad disorders.
- Health problems should be treated with the highest standards of veterinary care. Chronic diseases (e.g., allergies, degenerative joint disease, epilepsy, cardiopulmonary disease, gastrointestinal diseases) may benefit from treatment by a specialist and/or by complementary therapies such as acupuncture, massage, physical rehabilitation, supplements, and

nutrition.
- Proper nutrition, housing, welfare, and adequate exercise/training are extremely important for working dogs and can affect behavior, willingness to work, scent-detecting ability, and ability to work long hours. Keep in mind safety of food and water sources.
- Handler physical and mental health must be appropriate to complement the teamwork needed.
- Handling and training should include obedience, crate training, restraint, and muzzling to aid in situations where working dog is injured, contaminated, or needs veterinary care. Also helpful are routine handling of the mouth, feet, brushing, bathing, clipping or shaving, rinsing of eyes, and teaching to sneeze. Positive reinforcement training in these areas could be lifesaving in an emergent situation, especially if the handler is unable to accompany the working dog.
- Person(s) providing treatment should utilize proper PPE, including gloves, eye protection, mask, apron, and so forth. Disasters with mass casualties may include human contamination as potential risk (human immunodeficiency virus, hepatitis, etc.). Dogs may carry infectious-disease agents, endo- or ectoparasites, zoonotic diseases, or topical chemicals.
- Knowledge of chronic medications' effects on work (i.e., prednisone may affect odor detection) and interactions with toxicants (i.e., hydrocarbons and certain medications) is important.

PREVENTION

- Heat Index guidelines are not established but should be considered. Rest and hydration at least every 30-60 minutes. (FEMA guidelines are equal rest time for every 20-45 minutes of work.) Cooling by convection and evaporation as means of heat dissipation (tepid water soak of body; not extremities, not ice [causes peripheral vasoconstriction], not alcohol). Fluids (subcutaneous by site veterinarian) before work in stressful environments are not likely to be beneficial.
- Working dogs should be in top health, conditioning, and have excellent nutrition to work at their best ability and without distraction.
- Ample time for play and rest and recovery from stressful work situations is essential.
- Routine veterinary preventive health care is paramount, with appropriate vaccinations for anticipated infectious diseases.
- Acclimation of dogs to personal protective devices such as goggles and foot protection before field work is important. Masks may not be appropriate, owing to panting and need for olfactory sense.
- Decontamination procedures including bathing and ocular and nasal flushing are particularly important in disaster situations. Dogs should be accustomed to bathing and trained for mass-decontamination procedures; may include muzzle (prevent drinking of decontamination effluent), crate or kennel for decontamination protocol, separation from handler, and handling by people in full PPE (such as level A or B suits).
- Regular cleaning during work of nose, muzzle, and body to prevent licking (including licking the nose, where material may collect on the nasal planum) and ingestion. Baby wipes could be used periodically, flush eyes regularly.
- Knowledge of the type of agent(s) at the scene, and regular reevaluation. Try to keep in well-ventilated area and upwind +/- upgrade area.
- Prevent drinking unknown sources by keeping well hydrated. Consider home water source or bottled water, electrolyte solutions, and/or flavoring of the water, which may encourage drinking.
- Prevent ingestion by using basket-type muzzle.
- Reflective safety vest
- Canine floatation device
- Appropriate holding/traveling area environment: fans/air conditioning or heat, water for cooling and bottled drinking water and/or electrolyte solution, crate, good footing/bedding while traveling or at staging area. Consider vehicle alarm for excessive vehicle temperatures.

TECHNICIAN TIPS

- Working dogs can be aggressive, fearful, or highly stressed! Communication with the handler is essential (if available), and many times their presence and restraint assistance is helpful, even if not routine handling protocol. Safety is critical—your own, the canine, and the safety of other people assisting.
- Working dogs are very often used to being muzzled, and the handlers do not associate this with a stigma as civilian owners may do. Use muzzles often for safety. Request chemical restraint as appropriate.
- PPE: always wear gloves and assume contamination or zoonotic threat (see Acute General Treatment above); decrease ongoing exposure and absorption; focus on decontamination, human safety, and personal protection.
- Training: work in hospital to set up disaster plan, train/volunteer with local and national groups for disaster veterinary medicine (see Client Education below).
- Save samples from working dogs in case needed for further diagnostics (blood, urine, fur, vomitus, feces, food/water, etc). If animal dies, save for necropsy.

CLIENT EDUCATION

- Search out veterinary and disaster assistance in advance: National Veterinary Response Teams (NVRT)—federal resource, Department of Health and Human Services, National Disaster Medical System [NDMS]); Veterinary Medical Assistance Teams (VMAT), part of American Veterinary Medical Association (AVMA); State and County Animal Response Teams; local Veterinary Medical Association and veterinary emergency hospital; Society for the Prevention of Cruelty to Animals (SPCA);

Office of Emergency Preparedness, State and County Emergency Management Resources.

- Employer should have access for handlers to ASPCA—Animal Poison Control Center (1-888-426-4435) with credit card on file or account established. Handlers should have phone number at all times.
- PPE for handler and dog. Keep extra supply of working-dog equipment; may be difficult to decontaminate and need to be discarded.
- Training in first aid procedures and kits: include bandaging and splint materials, sterile saline for flushing eyes and wounds, apomorphine and/or hydrogen peroxide for inducing vomiting, activated charcoal with a cathartic, resuscitator bag and mask (canine oxygen masks available such as for fire department use), stethoscope, thermometer, ophthalmic ointment, booties, moist toilettes, liquid dish soap for decontamination of skin and coat, towels for drying, water supply.
- Knowledge of normal vital signs and physical exam findings
- Canine field cardiopulmonary cerebral resuscitation
- Obtain or locate ample source of safe water for hydration and decontamination. Be sure food is stored safely, and avoid contamination.
- Knowledge of possible risks in animal's line of work: define ahead of time or search out site Safety Officer or official site disaster veterinarian.
- Save vomitus, urine, and/or feces if dog is not acting normally: may be diagnostic. Save sample of material or liquid the animal ingested or drank. (Keep sample bags or sterile plastic sample containers in vehicle or jump-pack.) Save water and food sample.
- Long-term health of disaster working dogs does not appear to be significantly compromised by their work (i.e., response to 9/11 terrorist attacks), although working dogs may have evidence of inhaled matter in pulmonary tissues (presence of anthracotic pigments or refractile particulate material).
- If working dog dies, save body in cool area for necropsy as soon as possible at a veterinary teaching hospital, military pathologist, or as available to the site. (Cooling could include refrigeration unit, ice bags, or wrapping in blankets to prevent deterioration of tissues for analysis.) Do not freeze.

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Dilated Cardiomyopathy

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

A primary myocardial disease characterized by impaired systolic function (pump failure) of one or both ventricles, leading to cardiac enlargement and potentially congestive heart failure, arrhythmias, or both. Diastolic dysfunction may also be observed.

SYNONYMS

Congestive/dilatative cardiomyopathy (obsolete), DCM

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs:
  - Adult-onset disease (4-10 years) except in Portuguese water dogs and toy Manchester terriers (juvenile; weeks/months of age)
  - Male > female
- Cats:
  - 2-20 years (mean, 9.8 ± 4.4 years)
  - Male > female

GENETICS & BREED PREDISPOSITION

- Dogs:
  - Large/giant-breed dogs overrepresented (Doberman pinscher, Irish wolfhound, Great Dane, Scottish deerhound, boxer, Afghan hound, Old English sheepdog, dalmatian).
  - Variety of spaniel breeds (English, American cocker spaniels; others)
  - Irish wolfhounds, Newfoundlands, Doberman pinschers, boxers: autosomal dominant trait. Portuguese water dogs: autosomal recessive trait (suspected).
- Cats: Abyssinian, Burmese, and Siamese overrepresented

RISK FACTORS

- Taurine deficiency in cats (common cause of DCM in cats, mainly before 1987)
- Dalmatians fed a low-protein diet
- Spaniel, retriever breeds: taurine deficiency

GEOGRAPHY AND SEASONALITY

Chagas' disease–associated DCM (southern United States): clinical presentation is indistinguishable from idiopathic dilated cardiomyopathy.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Occult DCM: earliest level. Overtly healthy dog with systolic dysfunction on echocardiography, ventricular arrhythmias, or both.
- Congestive heart failure (CHF)
- Cardiac arrhythmias: atrial fibrillation (especially giant breeds), ventricular arrhythmias (boxers, Doberman pinschers)
- Sudden cardiac death.

HISTORY, CHIEF COMPLAINT

- Occult DCM: by definition, without clinical signs (screening exam or incidental finding)

- CHF: any combination of tachypnea, coughing, restlessness, abdominal distension, lethargy, inappetence, respiratory distress
- Cardiac arrhythmias: syncope, collapse, lethargy, precipitation of CHF

PHYSICAL EXAM FINDINGS

- Some or all of the following are commonly observed: weakness, depression, tachypnea, respiratory distress, weight loss/advanced cachexia, cardiogenic shock due to decreased arterial blood pressure, soft grade 1-3/6 systolic left and/or right apical murmur, S3 or summation gallops, arrhythmia.
  - Right-sided CHF: jugular pulse/distension, muffled heart and ventral lung sounds with pleural effusion, hepatomegaly due to congestion (± ascites)
  - Left-sided CHF: pulmonary crackles/rales, muffled lung sounds with pleural effusion (cats)
- Hypokinetic femoral pulses; pulse deficits with premature beats or atrial fibrillation
- Subcutaneous pitting edema is rare; large/giant breeds almost exclusively.

ETIOLOGY AND PATHOPHYSIOLOGY

- Proposed etiologies for idiopathic DCM include viral infection, nutritional deficiency, immune-mediated, micro-vascular hyperreactivity, and a variety of genetic disorders.
- Deficiency in calstabin-2 implicates this cytoskeletal protein abnormality as a cause of DCM in Dobermans.
- Before clinical signs, onset of myocardial failure leads to reduced cardiac output followed by activation of various neurohormone and cytokine pathways to support blood pressure. This leads to short-term stability but long-term further myocardial damage.
- Very rare cases due to infection (parvoviral, protozoal) or toxicity (doxorubicin, radiation)

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is suspected—especially in predisposed breeds—if respiratory distress is noted with a gallop sound and/or systolic murmur over the mitral area and/or with arrhythmias (atrial fibrillation, premature ventricular complexes). Suspicion is heightened if radiographs suggest left atrial enlargement, pulmonary vein enlargement and/or pulmonary edema. The final diagnosis is reached with echocardiography. Diagnosis of occult (clinically inapparent) DCM requires echocardiography, 24-hour ECG recordings, or both. Blood-based markers of heart disease are currently in testing and might have a role in the future with diagnosis or prognosis of DCM.

DIFFERENTIAL DIAGNOSIS

- Clinical:
  - Primary respiratory disease, noncardiogenic pulmonary edema, pleural space disorders (pneumothorax, noncardiogenic effusions), heartworm disease, myxomatous valvular heart disease, infectious endocarditis or myocarditis, cardiac tumors and pericardial effusion, diaphragmatic hernia, pulmonary hemorrhage, airway obstruction (laryngeal paralysis, tumor, foreign body, collapsing trachea), congenital heart disease
- Radiographic:
  - Pericardial effusion, peritoneopericardial diaphragmatic hernia, myxomatous valvular heart disease and other causes of chronic cardiac volume overload (arteriovenous fistula: rare), congenital heart disease, other pleural effusions
- Echocardiographic:
  - Myocardial failure due to advanced or end-stage valvular disease (myxomatous valvular heart disease) or shunts (patent ductus arteriosus, fistulas, septal defects). Subnormal fractional shortening (FS)% may be normal in many healthy individuals; check left ventricle (LV) diameter, E-point to septal separation, or even premature ventricular complexes on ECG/Holter for support of DCM. Less common: myocarditis, ischemic cardiomyopathy, acute systemic hypertension.

INITIAL DATABASE

- Thoracic radiography: generalized cardiomegaly and signs of CHF (left-sided: interstitial or alveolar pulmonary edema [dogs, cats] and/or pleural effusion [cats]), (right-sided: pleural effusion, enlarged caudal vena cava, hepatomegaly, ascites [much more common in dogs]). Occult DCM: often unremarkable (poor screening tool), although left atrial and/or left ventricular enlargement may be noted.
- ECG: sinus tachycardia, possibly with atrial or ventricular premature complexes; atrial fibrillation; ventricular tachycardia, especially in boxers and Doberman pinschers; prolonged and/or increased voltage QRS complexes suggestive of LV enlargement; low-voltage QRS complexes with pleural or pericardial effusion.
- Routine hematologic tests and urinalysis: usually normal. Exceptions:

  - Severe DCM: prerenal azotemia, elevated alanine aminotransferase; hyponatremia and hypochloremia, if noted with CHF, confer a poorer prognosis because they indicate free water retention.
  - Concurrent disease
  - Result of therapy for heart failure (hypokalemia, metabolic alkalosis, prerenal azotemia)
- Effusion analysis: usually modified transudate (nucleated cell count< 2500/mcL, total protein < 4.0 g/dL); chylous effusion possible in cats

ADVANCED OR CONFIRMATORY TESTING

- Echocardiography: ventricular and atrial dilation, reduced myocardial systolic function (reduced left ventricular FS% and ejection fraction), increased E-point septal separation. Doppler studies often confirm mitral and tricuspid regurgitation, low-velocity transaortic flow, diastolic ventricular dysfunction, and possibly pulmonary hypertension (if severe left-sided heart failure).
- Taurine concentrations: deficiency if <40-50 nmol/mL (plasma) or <250 nmol/mL (whole blood). Taurine assays require special handling (green-top tube or myocardium only; frozen)
- Histopathologic study: lesions include absence of inflammation, myocyte loss, attenuated wavy fibers, and increased myocardial fibrosis.

TREATMENT

TREATMENT OVERVIEW

Treatment mainly consists of medications to relieve signs of congestive heart failure, and antiarrhythmics in cases with rapid atrial fibrillation or life-threatening ventricular arrhythmias. Other goals should focus on improved quality of life (e.g., appetite, exercise capacity). Treatment of “occult” (clinically inapparent) DCM remains controversial and may or may not help.

ACUTE GENERAL TREATMENT

In cases of severe cardiogenic pulmonary edema: see Heart Failure, Acute, p. 468 .

- Minimize stress (e.g., keep cats separated from canine patients).
- Oxygen supplementation
- Furosemide: Dogs—2-6 mg/kg IV or IM initial dose, then 1-2 mg/kg q 2-3 h as needed for resolution of pulmonary edema, then q 8-12 h for the first 3 days. Cats—1-4 mg/kg parenterally q 4-12 h as needed; duration of effect around 1-2 hours.
- Thoracocentesis if large-volume pleural effusion (therapeutic, diagnostic). Moderate to severe pleural effusion does not respond rapidly to diuretics, and in acute situations, it should be physically removed via centesis (see p. 1338)
- 2% nitroglycerin paste applied topically: 1” q 8 h (dog); 0.25” q 8 h (cat)
- Life-threatening arrhythmias (see pp. 1165 and)
- Sodium nitroprusside (dogs): effective for treating critical cardiogenic pulmonary edema but requires constant-rate infusion, protection from light, and careful monitoring. Start at 2 mcg/kg/min IV and titrate upward. Mean blood pressure must remain > 70 mm Hg. Maximum = 10 mcg/kg/min.
- Dobutamine (if severe heart failure or cardiogenic shock; ECG monitoring needed):
  - Dogs: start at 2.5-5 mcg/kg/min, titrate upwards q 30-60 min in 2.5 mcg/kg/min IV increments until heart rate increases by > 10% or PVCs develop/become more frequent. Maximum infusion rate 15 mg/kg/min IV.
  - Cats: >2.5 mcg/kg/min not recommended and should be used with extreme caution

CHRONIC TREATMENT

- Thoracocentesis and abdominocentesis as needed
- Diuretics (as needed to control edema):
  - Furosemide: Dogs—1-4 mg/kg PO q 8-24 h. Cats—1-2 mg/kg PO q 8-24 h.
  - For chronic treatment of CHF where fluid retention is refractory to furosemide alone, add:
    - Spironolactone (dogs, cats), 1-2 mg/kg q 12-24 h PO; *and/or*
    - Hydrochlorothiazide (dogs, cats), 2-4 mg/kg q 12 h PO (alternative use: BID q 48 h [q 12 h alternating one day on, one day off] to start, and monitor renal values more closely once adding this diuretic to furosemide)
- ACE inhibitors:
  - Enalapril: dogs, 0.5 mg/kg q 12-24 h PO; cats, 0.5 mg/kg q 24 h PO; *or*
  - Benazepril: dogs, 0.5 mg/kg q 12-24 h PO; cats, 0.25-0.5 mg/kg q 24 h PO; *or*
  - Lisinopril: dogs, 0.5 mg/kg q 24 h PO
- Digoxin: Dogs—0.003 mg/kg q 12 h PO (a dose preferred by author [other publications usually have a higher dose] that usually doesn't yield digoxin toxicosis and results in 70%-75% of dogs reaching therapeutic levels). Cats—0.01 mg/kg or ¼ of a 0.125 mg tablet PO q 48 h.

- Pimobendan: dogs, 0.2-0.3 mg/kg q 12 h PO for heart failure
  - Novel therapy (use after careful consideration of benefits and risks).
- Beta-blockers blunt cardiotoxic effects of sympathetic nervous system; however, heart failure must be well controlled first, and dose begun low and up-titrated slowly (days to weeks) with careful monitoring. Options include:
  - Carvedilol: dogs, up to 0.5 mg/kg q 12 h PO (start with ¼ dose initially)
  - Metoprolol: dogs and cats, up to 1 mg/kg q 8 h PO (start with ¼ dose initially)
  - Atenolol: dogs and cats, up to 1 mg/kg q 12 h PO (start with ¼ to ½ dose initially)
- Arrhythmias
  - In atrial fibrillation, slowing of ventricular response rate in DCM is achieved with digoxin and/or diltiazem (1-1.5 mg/kg PO q 8 h). If necessary, atenolol or carvedilol can be used instead of diltiazem. Use of atenolol or carvedilol in this situation should be done carefully, owing to their pronounced effect on contractility; consultation with a cardiologist might be warranted.
  - Serious ventricular arrhythmias are managed with identification and treatment of underlying causes (e.g., hypoxemia from pulmonary edema); if rapid or causing clinical signs, these must be controlled (see p. 1165).

NUTRITION/DIET

Diet: if CHF has occurred and is now controlled:

- Keep patient eating with adequate level of protein intake.
- Eliminate high-salt snacks.
- Sodium-restricted commercial diets such as Purina CV or Hills H/D (not at the expense of good appetite) or balanced home-cooked low-sodium diets
- Taurine: recommended in all cats (250 mg/cat PO q 12 h) with DCM until demonstrated that patient is unresponsive to taurine; dose in dogs is 500 mg/dog PO q 12 h.
- Omega-3 fatty acids may improve appetite and reduce cachexia (EPA, 30-40 mg/kg q 24 h; DHA, 20-25 mg/kg PO q 24 h).
- Consider L-carnitine (110 mg/kg PO q 12 h) in boxers and American cocker spaniels not responding to taurine.

BEHAVIOR/EXERCISE

- Absolute rest during treatment of CHF or life-threatening arrhythmias
- Once congestive heart failure is resolved, slowly increase activity back to normal; quality of life is important. Ask owner to use common sense (e.g., if patient is tired, take break from activity; if normally fetches the ball 100 times, consider 10 times now).

DRUG INTERACTIONS

- Quinidine, verapamil: will increase serum digoxin level (risk of toxicosis)
- Hypokalemia, hypercalcemia, renal dysfunction, and hypothyroidism predispose to digitalis intoxication (therefore, decrease dose of digoxin).

POSSIBLE COMPLICATIONS

- Sudden death due to arrhythmias (especially uncontrolled ventricular tachycardia)
- Renal insufficiency due to low cardiac output, medical treatment; however, mild to moderate azotemia (without associated clinical signs) is expected with diuretic treatment.
- Iatrogenic complications due to medical treatment (hypokalemia, azotemia, other electrolyte abnormalities)

RECOMMENDED MONITORING

- Monitor 7-10 days after discharge, then as needed (e.g., q 1-4 mon, barring decompensation): physical examination, thoracic radiographs, ECG, serum renal and electrolyte profile.
- Holter/event monitors, echocardiography, other: if significant or unexpected change in patient's condition
- Serum digoxin levels 1 week (dogs) or 2 weeks (cats) after start of therapy (therapeutic range = 0.8-1.8 ng/mL) taken 6-8 hours post pill.
- Renal/electrolyte panel 5-7 days after starting angiotensin-converting enzyme inhibitors
- Repeat echocardiogram in 3-6 months after initiating taurine supplementation to determine response to therapy.

PROGNOSIS AND OUTCOME

- Overall, death usually occurs 3-24 months after diagnosis.
- Paroxysmal ventricular tachycardia and atrial fibrillation are probable markers of shorter survival.
- Plasma cardiac Tn-I > 0.20 ng/mL is suggestive of shorter survival time.

- Prognosis is influenced by treatment, time of diagnosis, and client compliance.
- Prognosis generally worse in Portuguese water dogs and Doberman pinschers than in other breeds, but some Dobermans live months to years after diagnosis.
- Prognosis in Irish wolfhounds with DCM is fair; lifespan virtually unaffected.
- In cats with DCM not due to taurine deficiency, the prognosis is usually grave.

PEARLS & CONSIDERATIONS

COMMENTS

- Most dogs have left atrial enlargement, pulmonary venous enlargement, and perihilar/caudodorsal pulmonary edema if pulmonary infiltrates are cardiogenic, whereas cats usually have atrial enlargement with variable edema location and pulmonary vein enlargement.
- Low echocardiographic LV FS% is not pathognomonic for DCM; many normal hearts contract more in apical-to-basilar direction, and this motion is not accounted for by the FS%.
- Most small-breed dogs more likely to have chronic mitral valve endocardiosis > collapsing trachea > primary respiratory disease > DCM causing similar clinical presentation.
- DCM in cats is rare, hypertrophic cardiomyopathy is common; the opposite is true in dogs.

CLIENT EDUCATION

Monitor for signs associated with progression of disease (coughing [dogs], open-mouth breathing [cats], respiratory changes, lethargy, collapse) and adverse side effects of medications (vomiting, diarrhea, anorexia).

TECHNICIAN TIPS

- Unlike most hospitalized cases, heart failure patients do not need fluids because they are hypervolemic (“drowning in their own fluids”); an exception is low-dose fluids used for delivery of IV heart medications.
- Heart patients generally need to be stress free as possible (e.g., avoid cats mixing with dogs, avoid having inexperienced technician draw blood).
- One of the best and simplest ways to monitor the heart patient is to monitor respiratory rate per minute instead of physically handling these patients.

SUGGESTED READING

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Sisson DD, Thomas WP, Keene BW: Primary myocardial disease in the dog. In Ettinger SJ, Feldman EC, editors: Textbook of veterinary internal medicine, ed 5, Philadelphia, 2000, WB Saunders, pp 874–895.

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Digoxin Toxicosis

BASIC INFORMATION

DEFINITION

Clinical signs caused by excessive administration of, or individual intolerance to, normal doses of digoxin

SYNONYMS

Digitalis poisoning, digoxin intoxication. Digoxin and digitalis are used interchangeably; other digitalis derivatives, such as digitoxin, are no longer used clinically.

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs and cats of any age, either sex

GENETICS & BREED PREDISPOSITION

Doberman pinschers appear predisposed.

RISK FACTORS

- Renal failure
- Hypovolemia, dehydration
- Hypokalemia
- Concurrent administration of drugs that increase serum digoxin levels: diazepam, erythromycin, quinidine, tetracycline, verapamil
- Obesity (if digoxin is dosed on total body weight rather than lean body weight)
- Intravenous digoxin
- MDR-1 gene mutant

ASSOCIATED CONDITIONS & DISORDERS

Underlying heart disease prompting digoxin treatment

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Systemic signs
- Cardiac arrhythmias

HISTORY, CHIEF COMPLAINT

- Hallmarks of digoxin toxicosis: lethargy, anorexia, vomiting, and diarrhea, together or individually
- May be intermittent in mild cases
- Severe toxicosis: refractory vomiting, tenesmus, collapse, death
- Except for massive overdoses, digoxin treatment needs to have been underway for >24 hours (and usually weeks) to produce signs of toxicosis.
- Most commonly, patients are receiving digoxin as part of long-term cardiac treatment. Much less commonly, digoxin toxicosis occurs from a pet's consuming plants or human medication.

PHYSICAL EXAM FINDINGS

- Lethargy, dehydration
- Physical findings attributable to underlying heart disease

- Digoxin toxicosis can also produce virtually any cardiac arrhythmia.
  - Bradycardia or tachycardia on examination

ETIOLOGY AND PATHOPHYSIOLOGY

- Digoxin is a cardiac glycoside drug derived from the foxglove plant.
  - It is absorbed slowly (6-8 hours to peak serum concentration with oral tablets in dogs; faster with elixir) and is mainly excreted renally (>60%).
- The half-life is long: 14-56 hours (dogs), 30-173 hours (cats).
- Therefore, when intoxication occurs, it more often is a cumulative process (chronic treatment).
- Acute overdoses are amenable to activated charcoal administration for several hours after ingestion.
- All cardiac glycosides (therapeutic, e.g., digoxin, digitoxin [historic]; or botanical, e.g., foxglove, oleander) act on the sodium/potassium/adenosine triphosphate pump of mammalian cells to increase intracellular Na^{+} and Ca^{2+} concentrations.
- Cardiovascular, neurologic, and gastrointestinal effects are responsible for clinical signs.
- With digoxin toxicosis, systemic clinical signs precede or occur concurrently with cardiac arrhythmias.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is strongly suspected on the basis of medication history and clinical signs. Initial testing offers supportive evidence, but the diagnosis is often established based on resolution of clinical signs when the drug is stopped.

DIFFERENTIAL DIAGNOSIS

- Primary gastrointestinal disease
- Uremia/renal failure
- Cardiac arrhythmias of primary cardiac or systemic origin

INITIAL DATABASE

- Serum biochemistry profile, urinalysis:
  - Evidence of chronic kidney disease or hypokalemia increases likelihood of intoxication.
  - Concurrent treatment with diuretics may cause azotemia and isosthenuria.
  - Generally if azotemia is severe (blood urea nitrogen > 80 mg/dL and creatinine > 3 mg/dL), some degree of reduced renal function is expected, and digoxin elimination is likely reduced, predisposing to toxicosis.
- Electrocardiogram (ECG):
  - First-degree atrioventricular (AV) block (see p. 120): early ECG manifestation of digoxin toxicosis
  - Higher degrees of AV block, premature atrial or ventricular complexes common

ADVANCED OR CONFIRMATORY TESTING

- Serum digoxin concentration: confirmation (retrospective)
  - Therapeutic level: 0.8-2.0 ng/mL
  - >2-3 ng/mL with clinical signs: digoxin toxicosis
  - Turnaround time of test limits immediate usefulness, but some local human hospitals may provide stat service.
- Evaluations of renal/central nervous/gastrointestinal systems: as dictated by clinical signs

TREATMENT

TREATMENT OVERVIEW

- Acute overdoses: prevent digoxin assimilation.
- All cases: reduce serum digoxin concentration.

ACUTE GENERAL TREATMENT

- Acute overdoses (uncommon): activated charcoal and supportive care (see Etiology and Pathophysiology above)
- Toxicosis in dogs receiving normal digoxin doses chronically: the cornerstone of treatment is discontinuation of the drug.
  - Treatment may be restarted 48 hours later at half the dose after signs of toxicosis have resolved.

- Intravenous fluid therapy: judicious if patient has cardiac disease
- Potassium supplementation in hypokalemic patients: essential, since hypokalemia may potentiate arrhythmias
- Ventricular antiarrhythmics if rapid ventricular arrhythmias (see p. 1165)
- Treatment for supraventricular arrhythmias if very rapid (see p. 111).
- Soluble antidigoxin antibodies may be administered in severely ill patients.
    - Number of vials (38 mg each) given slowly IV = serum digoxin level [ng/mL] × body weight (kg)/100
    - For example, 2 vials slow IV, single dose for a 35-lb (16-kg) dog with serum digoxin level 12 ng/mL
    - Very costly ($500 per vial)

RECOMMENDED MONITORING

Monitoring serum concentrations is secondary to monitoring of clinical signs alone.

PROGNOSIS AND OUTCOME

- Dependent on dose, elimination (renal function, hydration), extent of signs, and response to treatment
- Severe digoxin intoxication can be fatal.

PEARLS & CONSIDERATIONS

COMMENTS

- Differentiation between digoxin toxicosis and an unrelated problem (e.g., primary GI disturbance, renal failure, other) may be challenging.
- It is virtually always preferable to assume that digoxin toxicosis exists and discontinue the drug and use other cardiac drugs (e.g., beta-blockers, inotropes) as replacements if necessary while evaluation of the other differential diagnoses takes place; response to discontinuation helps confirm toxicosis retrospectively.

PREVENTION

Early detection of clinical signs of toxicosis by owners, and if signs occur, discontinuation of the drug, monitoring, and supportive care

SUGGESTED READING

Knight DH: Efficacy of inotropic support of the failing heart. Vet Clin North Am 21:879-904, 1991.

Ward DM, Forrester SD, DeFrancesco TC, Troy GC: Treatment of severe chronic digoxin toxicosis in a dog with cardiac disease, using ovine digoxin-specific immuno-globulin G Fab fragments. J Am Vet Med Assoc 215:1808–1812, 1999.

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Dietary Intolerance

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Adverse reactions to an ingested food or food additive due to nonimmunologic mechanisms (common)

SYNONYMS

Adverse reaction to food, food intolerance, lactose intolerance

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs and cats: no age or gender predilection

RISK FACTORS

- Food contaminated with microorganisms or their toxic metabolites
- Specific foods (onions, chocolate)
- Toxic food preservatives (e.g., propylene glycol in cats)
- Preformed vasoactive amines (e.g., histamine) in food such as fish
- Dairy products
- Dietary indiscretion (gluttony, pica, ingestion of indigestible materials)

ASSOCIATED CONDITIONS & DISORDERS

- Dietary hypersensitivity
- Inflammatory bowel disease

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

Vomiting, diarrhea, intermittent abdominal pain, abdominal distension, soft feces, excessive flatulence, increased frequency of defecation

PHYSICAL EXAM FINDINGS

Diarrhea (small or large bowel), vomiting, abdominal distension, urticaria, angioedema

ETIOLOGY AND PATHOPHYSIOLOGY

- Food poisoning:
  - Eating foods (e.g., through scavenging, improperly cooked homemade foods, raw diets, contaminated moist or dry commercial foods [e.g., aflatoxin]) that are contaminated with bacteria, fungal toxins, or other toxins that cause an immediate gastrointestinal (GI) response (see p. 434)
- Idiosyncratic adverse reactions to food additives:
  - Examples include food colorings (azo or non-azo dyes), certain preservatives and emulsifying agents, thickeners or stabilizers (e.g., seaweed extracts, seed gums)
  - Occur infrequently and unpredictably in individuals, and are not apparently dose related
  - Histaminergic reactions mediated by type 1 (mast cell mediated) or 2 (receptors for gastric acid release in the stomach) histamine receptors
- Pharmacologic reactions to vasoactive amines (e.g., histamine) found in food
- Carbohydrate intolerance (lactase deficiency):
  - Mediated by lack of carbohydrate digestion (lactose intolerance) due to mucosal disease or lack of enzyme activity —either congenital or acquired

- A true allergic reaction to proteins in milk (e.g., bovine IgG) can mimic carbohydrate intolerance.
- Which of these types of reactions are causing the problem is rarely defined and not clinically relevant.

- Dietary indiscretion:
  - Typically defined as the consumption of unusual or spoiled foods (as can occur with scavenging or raiding the garbage can), the consumption of too much food (gluttony), or pica (eating nonfood substances such as hair, rocks, bones, etc.)
  - The insult occurring in the GI tract varies with the type of indiscretion observed, and thus no consistent clinical presentation is recognized.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Food intolerance is suspected on the basis of acute vomiting and/or diarrhea, often but not always occurring as a result of acute dietary alterations; confirmatory diagnosis is often retrospective, with resolution of clinical signs as a result of proper diet. In contrast to dietary hypersensitivity (food allergy), the response to the change in food is more rapid (few days to 2 weeks) with dietary intolerance. Therefore, if no response occurs during this time frame, the diagnosis of intolerance should be questioned.

DIFFERENTIAL DIAGNOSIS

- Any chronic disorder affecting the GI tract (e.g., hypoadrenocorticism, protein-losing enteropathy, infiltrative disease)
- Inflammatory bowel disease
- GI neoplasia
- Chronic parasitism
- Food hypersensitivity

INITIAL DATABASE

- CBC: nonspecific and usually normal
- Serum biochemistry profile: nonspecific and usually normal
- Urinalysis: nonspecific
- Fecal flotations to rule out parasitic causes of vomiting/diarrhea

ADVANCED OR CONFIRMATORY TESTING

- Proper nutrition/elimination food trial
- Further testing generally unnecessary for the primary diagnosis; used for identifying other disorders with similar signs or for identifying inciting causes (differential diagnosis)
- Abdominal radiography and ultrasonography: used for ruling out the other causes of vomiting and diarrhea for which imaging modalities are diagnostic (e.g., intestinal obstruction, intestinal mass)
- Endoscopy with biopsy and histopathologic evaluation of GI mucosa: mucosa may be normal or show increases in lamina propria lymphocytes or plasma cells, but inflammatory changes seen in dogs or cats with food intolerance are generally less profound than found in those with IBD or other diseases of the mucosa.

TREATMENT

TREATMENT OVERVIEW

Avoid exposure to food toxins, dairy products, certain carbohydrates, and dietary sources of vasoactive amines (e.g., certain types of fish). Control episodes of dietary indiscretion.

ACUTE GENERAL TREATMENT

- Nonspecific supportive care based on clinical signs (e.g., parenteral fluid administration for dehydration)
- Perform an elimination food trial (in general, a shorter trial of 7-10 days is all that is required to result in the resolution of the signs of dietary intolerance).
- Clinical signs of GI disease usually resolve within a few days on the new diet that does not contain the offending substance.

NUTRITION/DIET

- Maintain strict avoidance of offending foods or ingredients (e.g., dairy products).
- Find an acceptable commercial or homemade food for long-term maintenance.
- Control episodes of gluttony, pica, or ingestion of indigestible materials.

POSSIBLE COMPLICATIONS

Certain types of food poisoning can cause serious and life-threatening disease.

PROGNOSIS AND OUTCOME

Good prognosis if offending foods or ingredients are eliminated from the diet

PEARLS & CONSIDERATIONS

COMMENTS

In instances of recurrent food intolerance (versus one-time events), use of a food diary by the animal owner is important to monitor clinical response and compliance.

TECHNICIAN TIPS

Gradual transition to a new food is critical for a pet with health problems and may be the single most important thing you can do to help a pet accept a new food. Mix more of the new food with less of the old food over a period of at least 7 days. An alternative method for transitioning, especially for cats, is to offer the new food side by side with the old food in identical dishes, instead of mixing them both in the same dish.

CLIENT EDUCATION

Human food sources, snacks, treats, and food for other animals in the household (e.g., dog having access to cat food) can be a problem.

SUGGESTED READING

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Diarrhea, Chronic

BASIC INFORMATION

DEFINITION

An increase in frequency of defecation, stool fluidity, and/or fecal volume (increased water content or fecal solids) that is persistent (more than 2-3 weeks) or episodic.

EPIDEMIOLOGY

CONTAGION & ZOONOSIS

Potentially zoonotic organisms; see Diarrhea, Acute, p. 303.

GEOGRAPHY AND SEASONALITY

See Diarrhea, Acute, p. 303.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Small-intestinal (SI) diarrhea versus large-intestinal (LI) diarrhea or both

- Further segregated into diseases caused by maldigestion or malabsorption
- Malabsorption further segregated into nonprotein-losing versus protein-losing disease

Clinical Signs of Small-Intestinal Versus Large-Intestinal Diarrhea

Characteristic	Small Intestine	Large Intestine
Feces		
Mucus	Uncommon	Common
Hematochezia (fresh blood in/on feces)	Absent	Often present
Melena (digested blood in feces)	± Present	Absent
Volume	Often increased	Normal to decreased (due to increased frequency)
Quality	Nearly formed to watery (“cowpile”); ± undigested food/fat; possibly malodorous	Loose to semisolid
Shape	Variable (dependent upon amount of water present)	Normal or narrowed
Steatorrhea (undigested fat in feces)	Present with maldigestive or malabsorptive disorders	Absent
Defecation		
Frequency	Normal to mildly increased (2-4 times/d)	Greatly increased (4-10 times/d)
Dyschezia (inability to defecate without straining or signs of pain)	Absent	Dogs: frequent. Cats: less common.

Characteristic	Small Intestine	Large Intestine
Tenesmus (straining)	Absent	Dogs: common. Cats: less common; rule out stranguria.
Urgency	Less common, unless severe acute enteritis	Frequent
Associated Signs		
Weight loss	Common	Uncommon. Possible with severe chronic colitis, diffuse neoplasia, histoplasmosis, pythiosis.
Vomiting	Possible	May be seen, especially with acute colitis (30%). Possible before onset of abnormal stools.
Appetite	Usually normal; may be ↑ or ↓ in bowel infiltration/inflammation depending on severity of lesion	Normal to decreased if severe disease (neoplasia, histoplasmosis)
Halitosis	± Present (maldigestion/malabsorption)	Absent
Borborygmus	Possible	Absent
Flatulence	Possible	Common
Fecal incontinence	Rare	Possible
"Scooting" or chewing of perianal area	Absent	Possible with proctitis

HISTORY, CHIEF COMPLAINT

- Typical: persistent indoor fecal incontinence and/or loose stool
- Age, when/where the pet was acquired, vaccination and dietary history, environment, recent medications, and presence or absence of recent stressful episode (recent move, changes in family routine, etc.) help identify trigger factors.
- Differentiate SI diarrhea from LI (see table).

PHYSICAL EXAM FINDINGS

- Hydration status
- Depression/weakness/lethargy
- Emaciation: malnutrition, chronic malabsorption, protein-losing enteropathy
- Dull hair coat: malabsorption (fatty acids, protein, vitamins)
- Fever: inflammation, infection, neoplasia
- Edema, ascites, decreased lung/heart sounds (pleural effusion): protein-losing enteropathy
- Pale mucous membranes: chronic GI blood loss, anemia of chronic illness/inflammation
- Abdominal palpation may reveal a mass (foreign body, neoplasm, granuloma, abscess, mesenteric lymph-adenopathy), thickened bowel loops (inflammation, neoplastic infiltration), "aggregated" bowel loops (mass, peritoneal adhesions), "sausage-shaped" intestinal loop (chronic, intermittent intussusception), evidence of pain (inflammation, obstruction, ischemia, gas distension), gas/fluid distension (diarrhea, obstruction [mass], ileus)
- Rectal palpation (mandatory unless intractably painful): mass (polyp, neoplasm, granuloma), circumferential narrowing (stricture, spasm, neoplasm), irregular mucosal texture (colitis, neoplasm, perineal fistula)

ETIOLOGY AND PATHOPHYSIOLOGY

- Small intestine
  - Decreased fluid and electrolyte absorption
  - Incomplete nutrient absorption (fats, carbohydrates)
  - Increased fluid and electrolyte secretion
- Large intestine
  - Decreased fluid and electrolyte absorption
  - Secretion of fluid and electrolytes
  - Failure of reservoir function

CAUSES OF CHRONIC SMALL- AND LARGE-INTESTINAL DIARRHEA

- Parasites causing SI: *Isospora*, hookworms, roundworms
- Parasites causing LI: Whipworms *(Trichuris vulpis),* amoebiasis, *Balantidium coli*.
  - *Giardia* may be SI and/or LI.
- Dietary intolerance and dietary allergies may be SI and/or LI.
- Inflammatory bowel disease (IBD): lymphocytic-plasmacytic, eosinophilic, granulomatous enteritis may be SI and/or LI. Hypereosinophilic syndrome (cats primarily), neutrophilic (suppurative/purulent) enteritis and breed-specific (shar-pei, basenji, soft-coated Wheaten terrier) tend to cause SI. Chronic ulcerative colitis and histiocytic ulcerative colitis (primarily boxers) are most often LI.
- Neoplasia (lymphoma, adenocarcinoma, leiomyoma/leiomyosarcoma, mast cell tumour): SI and/or LI
- Infectious organisms causing:
  - SI signs: *Cryptosporidia parvum*
  - LI signs: salmonellosis, yersiniosis, *Bacillus piliformis*, pythiosis, protothecosis and *Tritrichomonas foetus* in cats
  - Both SI and LI: campylobacteriosis, *Clostridia* spp., histoplasmosis, feline leukemia virus (FeLV), feline immunodeficiency virus (FIV) and feline infectious peritonitis (FIP)
- Chronic small intestinal bacterial overgrowth (SIBO) in dogs may occur secondary to idiopathic antibiotic responsive enteritis or tylosin-responsive diarrhea. It may be idiopathic or occur secondary to diseases such as an immunoglobulin A deficiency, exocrine pancreatic insufficiency (EPI), a partial obstruction (chronic intussusception) or blind loops of bowel, or disease causing abnormal motility and thereby clearance of organisms, as well as a gastric acid deficiency.
- Villous atrophy (idiopathic, gastrinoma, gluten-sensitive enteropathy) causes SI diarrhea.
- Endocrine causes such as hyperthyroidism (cats) and hypoadrenocorticism may cause SI and/or LI diarrhea.
- Protein-losing enteropathy such as intestinal lymphangiectasia is primarily SI in nature.
- Any of the preceding disorders can cause protein-losing enteropathy, depending upon disease progression and severity.
- Maldigestive diseases (EPI, lactase deficiency [especially cats]) cause SI signs.
- Functional disorder (irritable bowel syndrome [IBS]) is a diagnosis by exclusion and causes LI diarrhea.
- Other: chronic active pancreatitis (cats and dogs) causes SI signs (lethargy, agitation/abdominal discomfort, vomiting, +/− diarrhea).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The list of causes of chronic diarrhea is exhaustive, hence the extreme importance of obtaining a thorough history from the client and considering the pet's environment prior to embarking on a battery of tests that may be unwarranted. Every animal with chronic large-bowel or mixed diarrhea should have a rectal exam and a direct smear performed. Fecal examinations should always be performed on *fresh* samples.

DIFFERENTIAL DIAGNOSIS

See Etiology and Pathophysiology above.

INITIAL DATABASE

- Fecal examinations
  - Cytology (fresh saline smears): ova, larvae, certain bacteria, protozoa *(Giardia, T. foetus, Entamoeba*, *Balantidium coli).*
  - *Campylobacter* fecal cytology alone not sufficient in making a diagnosis, as many are nonpathogenic.
  - Flotation
  - Gram stain
  - Zinc sulfate centrifugal flotation (*Giardia* cysts)
  - ELISA: *Giardia*-specific antigen
  - Iodine stain: enhances visualization of *Giardia* trophozoites, stops motion of organism and cysts (stain light brown).
- CBC: to assess hydration status (PCV/TS), presence of leukocytosis (inflammation, infection, stress), eosinophilia (eosinophilic IBD, endoparasitism), lymphopenia (lymphangiectasia), anemia (chronic GI blood loss, anemia of chronic illness/inflammation, nutrient malabsorption), thrombocytosis with microcytic, hypochromic anemia (iron deficiency)
  - Absence of a stress leukogram: hypoadrenocorticism
- Serum biochemical profile: hypoproteinemia (hypoalbuminemia, +/− hypoglobulinemia), elevated BUN (prerenal azotemia, GI bleeding, high-protein diet), elevated liver enzyme activities (primary hepatic disease, reactive hepatopathy, pancreatitis, or primary GI tract disease with portal bacterial translocation), hypocholesterolemia (lymphangiectasia, hepatopathy)
- Urinalysis to assess specific gravity (renal function [renal versus prerenal azotemia]), proteinuria
- Cats: serum thyroxine concentration (>6 years old), FeLV/FIV

ADVANCED OR CONFIRMATORY TESTING

- Abdominal radiographs: survey and/or contrast radiography
- Abdominal ultrasonography: mass lesion, thickened bowel loops, loss of detail of the layers of GI wall, evaluation of other abdominal organs
- Adrenocorticotropic hormone stimulation test (hypoadrenocorticism)
- Fecal cultures (*E. coli*, *Salmonella* spp., *C. jejuni*, *Clostridium* spp., *Y. enterocolitica*). Efficacy in determining true infection is controversial; many of these bacteria are commensal organisms, and their presence in feces does not necessarily correlate with disease.
- *T. foetus*: culture of feces using the InPouch TF (BioMed Diagnostics, White City, OR)—young cats from cattery or shelter
- *C. perfringens* fecal endospore enumeration (unreliable and not recommended)
- *C. perfringens* enterotoxin: caution, discordant results amongst detection methods
- Recommendations for *C. perfringens*: ELISA for enterotoxin combined with PCR for the enterotoxin gene
- *C. difficile:* test for the enzyme glutamate dehydrogenase (GDH; constitutively produced), available as a commercial kit. If positive on fecal culture or positive detection of GDH enzyme, further testing for enterotoxin A and B recommended. PCR of toxin genes should be interpreted with caution (no difference in toxigenic *C. difficile* shedding by diarrheic dogs versus nondiarrheic dogs).
- *Campylobacter:* PCR; positive PCR result requires further testing techniques such as sequencing of the 16S rDNA gene, etc.
- *Cryptosporidium:* fecal ELISA test
- *Salmonella:* positive PCR samples should be cultured followed by sero-typing of suspected colonies.
- Occult blood: chronic blood loss; meat-based diet may cause false positives with some kits.
- Trypsin-like immunoreactivity (TLI) test: EPI (species-specific test)
- Serum cobalamin (vitamin B12), folate
  - Folate: depends on jejunum's absorptive function (proximal SI)
  - Cobalamin: depends on pancreatic intrinsic factor secretion and absorption in ileum (distal SI)
  - ↓Folate and ↓cobalamin: diffuse malabsorptive disease
  - ↓Cobalamin, ↑folate: antibiotic-responsive enteritis/SIBO
  - TLI, cobalamin, and folate often run together.
- Species-specific pancreatic lipase immunoreactivity (PLI) test (spec CPL/cPLI, fPLI) for the diagnosis of chronic active pancreatitis
- If presence of hypoproteinemia and hypoalbuminemia, further diagnostics required to identify origin of loss; kidneys (urine protein/creatinine ratio if proteinuria noted on dipstick), liver (serum bile acids), or GI (fecal alpha-protease inhibitor)
- Serologic titers (histoplasmosis)
- Endoscopy: gastroduodenoscopy and colonoscopy indicated to determine extent of disease
- Exploratory laparotomy: full-thickness biopsies (biopsy even if no gross lesions)
- Molecular techniques (PCR, RT-PCR): increasing commercial availability (results highly dependent on laboratory's quality control)
- Empirical therapy may be elected because of client's financial constraints: probiotics, anthelmintics, antimicrobials (metronidazole, tylosin, enrofloxacin), dietary trials, antiinflammatories/immunomodulators.

TREATMENT

TREATMENT OVERVIEW

The goal of therapy is to treat the underlying cause of the diarrhea.

ACUTE GENERAL TREATMENT

- Low-fat, highly digestible low-fiber diets (low-fat cottage cheese, tofu, rice, potatoes)
- Small, frequent meals (3-6/d)
- High-fiber diets (colitis)
- Empirical treatment: anthelmintics (fenbendazole) or metronidazole, even with negative tests

CHRONIC TREATMENT

- Dependent on underlying cause; see specific disorders for details.
- Deworming medications
- Antimicrobials (see p. 303 and specific organism)
- Immunosuppressive agents such as prednisone/prednisolone/budesonide (use minimum effective dose), cyclosporine, azathioprine (not in cats), chlorambucil
  - Possible immunomodulating/antiinflammatory activities, such as metronidazole and tylosin
- Antiinflammatories (sulfasalazine/olsalazine/mesalamine)

- Adjunctive therapy: cobalamin supplementation and probiotics
- Antifungal agents (histoplasmosis)

NUTRITION/DIET

- Dietary modifications such as feeding a novel protein source or a hydrolyzed protein for a trial period (minimum 3 to 4 weeks). All other foods and antigen sources (treats, flavored medications) must be eliminated during this time.

POSSIBLE COMPLICATIONS

- Immunosuppressive therapy (azathioprine, chlorambucil): myelosuppression
- 5-aminosalicylates: keratoconjunctivitis sicca
- Iatrogenic hyperadrenocorticism with chronic glucocorticoid use, therefore use minimum effective dose
- Excessive protein loss: edema/cavity effusions
- Buccal mucosal irritation: pancreatic enzyme supplementation (EPI)

PROGNOSIS AND OUTCOME

- Dependent on underlying cause, response to treatment, owner compliance, and interindividual variation
- Guarded: histoplasmosis, protothecosis, pythiosis, yersiniosis, regional granulomatous enterocolitis, FIP
- Poor to guarded: basenji, shar-pei, soft-coated Wheaten terrier–associated IBD, villous atrophy (clinical signs often persist despite treatment), feline hypereosinophilic syndrome
- Fair: histiocytic ulcerative colitis (lifetime therapy needed, difficult to control)
- Fair to good: antibiotic-responsive enteritis/SIBO, depending on underlying cause. Some require frequent or continuous treatment; others have prolonged remission with one course of antibiotics. FeLV/FIV (when secondary infections controlled).
- Fair to excellent: IBD (realistic expectation: maintenance of remission/control of relapses, rather than cure)
- Good: dietary intolerance/food allergy, giardiasis, salmonellosis (although mortality rate can be high [hospitalized, young, immune-compromised]), campylobacteriosis, *Clostridium* spp. (although fatalities reported)
- Good to excellent: hyperthyroidism, EPI (continual treatment), hypoadrenocorticism (lifelong treatment), hook-worms/roundworms/whipworms
- Lymphangiectasia: unpredictable. Remission in some (months to years), cachexia, cavity effusions, intractable diarrhea in others with inability to control protein loss.
- Neoplasia: dependent on tumor type

RECOMMENDED MONITORING

- Body weight, serum protein and albumin concentrations, frequent CBCs if using immunosuppressive agents
- Schirmer tear test (sulfasalazine, TMS)

PEARLS & CONSIDERATIONS

COMMENTS

During diagnostic procedures (laparotomy, laparoscopy or endoscopy), it is vital to always obtain biopsies, even if tissues appear grossly normal.

TECHNICIAN TIPS

Proper hygiene is of paramount importance to avoid promoting contagion and to prevent zoonoses (handwashing between pets, gloves when cleaning a patient with diarrhea, never placing food in laboratory area where fecal analyses are performed).

CLIENT EDUCATION

Some of the preceding diseases can be frustrating to treat (waxing and waning nature). Inform owner at time of diagnosis: avoids unrealistic expectations/disappointment.

SUGGESTED READING

Hall, EJ, German, AJ: Diseases of the small intestine. In Ettinger SJ, Feldman EC, editors: Textbook of veterinary internal medicine vol. II, ed 6, Philadelphia, 2005, WB Saunders, pp 1332–1378.

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Diarrhea, Acute

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

- An increase in frequency of defecation, stool fluidity, and/or fecal volume (increased water content or fecal solids) that is sudden in onset and of short duration (<2 weeks).

EPIDEMIOLOGY

RISK FACTORS

- Environment: overcrowding, poor sanitation, immune compromise (infectious)
- Unsupervised activity (dietary indiscretion), stress (increased shedding of infectious organisms), close contact, animals from large geographic areas as associated with dog/cat shows (greater exposure to variety of pathogens)
- Raw diets: salmonellosis, *Escherichia coli* infection (young or immune-compromised patients)

CONTAGION & ZOONOSIS

- Potential zoonoses: *Ancylostoma caninum* (cutaneous larval migrans), *Balantidium coli, Campylobacter* spp., *Clostridium difficile, Cryptosporidium parvum, Echinococcus* spp., *Entamoeba histolytica, E. coli, Giardia lamblia, Pentatrichomonas hominis, Salmonella* spp., *Shigella* spp., *Toxocara* spp. (visceral and ocular larval migrans), *Toxoplasma gondii, Yersinia enterocolitica*
- Species-specific viral infections: feline leukemia virus (FeLV)/feline immunodeficiency virus (FIV)/feline infectious peritonitis (FIP)/feline panleukopenia (cat to cat); canine parvovirus (dog to dog)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Small or large intestine, or combination.

HISTORY, CHIEF COMPLAINT

- Typical reasons for presentation include owner observation of a new onset of indoor fecal incontinence and/or loose stool.
- Duration of clinical signs/course
- When/where the pet was acquired, vaccination history, dietary history, and environment, recent medications, and presence or absence of recent stressful episode (recent move, changes in family routine, etc.) help identify trigger factors. Differentiate small-intestinal diarrhea from large (see table in Diarrhea, Chronic, p. 305).

PHYSICAL EXAM FINDINGS

- Mentation: depression and dehydration make infections or intoxications more likely.
- Mucous membrane color
  - Brick red/injected: rule out sepsis, hemorrhagic gastroenteritis.
  - Pallor: hypoperfusion/shock/pain versus anemia due to gastrointestinal (GI) blood loss
- Hydration (caveat: nauseated animal may have slimy mucous membranes despite dehydration).
- Signs of shock, sepsis (fever/subnormal temperature, tachycardia [less consistent in cats], tachypnea, cool extremities [variable])
- Posture: possible “dog-praying” position/arched back (sign of abdominal pain).
- Abdominal palpation:
  - Lymphadenopathy (neoplasia, inflammation, infection)
  - Thickened bowel (inflammatory, neoplastic infiltration)
  - Fluid- or gas-filled bowel
  - Intussusception (sausage shape), especially in puppies with viral gastroenteritis or parasitism
  - Evidence of pain
  - Urinary bladder (urine production with respect to hydration status and renal function)
  - Abdominal mass (obstruction, foreign body)

- Perineum: perineal hernia and anal sac disorders may mimic signs of large-bowel disease.
- Rectal palpation; with large bowel diarrhea, the following signs are possible:
  - Pain/increased mucosal sensitivity
  - Palpable foreign material
  - Hematochezia
- Cats: palpate for thyroid nodule (hyperthyroidism).
- Observe animal defecating (tenesmus, signs of pain, character of feces)

ETIOLOGY AND PATHOPHYSIOLOGY

- Abnormality of transmucosal movement of water and solute:
  - Osmotic (decreased solute absorption)
  - Secretory (hypersecretion of ions)
  - Exudative (increased permeability)
  - Abnormal motility
- More than one mechanism possible, depending on underlying cause

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The list of causes of acute diarrhea is extensive, but it can be narrowed substantially based on a thorough history that includes information on the pet's environment and diet. Fecal examinations are indicated in all cases and should be performed on fresh samples. Further diagnostic testing is warranted in acute diarrhea cases if the patient shows signs of being systemically ill, if a zoonotic concern exists, if the history or physical exam reveals abnormalities that suggest a nontransient cause, or if follow-up reveals that a prolonged course is occurring (becomes chronic diarrhea rather than acute). Otherwise, a large proportion of acute diarrhea cases in dogs and cats is self-resolving and does not warrant testing beyond a fecal exam.

DIFFERENTIAL DIAGNOSIS

- Diet (food intolerance/allergy, poor-quality food, abrupt diet change, dietary indiscretion/toxin ingestion [mycotoxins, spoiled foods], overeating)
- Parasites (helminths [hookworms—*Ancylostoma/Uncinaria* spp.; whipworms—*Trichuris vulpis;* ascarids/roundworms —*Toxocara* spp., *Strongyloides* spp.], cestodes, trematodes, *Trichinella* spp., protozoa [*Isospora* spp.—coccidiosis; *Giardia* spp; *Cryptosporidium* spp.; *Pentatrichomonas/Tritrichomonas foetus; Balantidium coli; Entamoeba histolytica; Neorickettsia helminthoeca [salmon poisoning]*)
- Bacteria (*Campylobacter jejuni*, *Clostridium* spp. *[perfringens, difficile, upsaliensis], E. coli*, *Salmonella* spp., *Yersinia enterocolitica*, *Shigella* spp., *Bacillus piliformis*, antibiotic-responsive diarrhea/Enterobacteriaceae)
- Viral (astrovirus, coronaviruses, canine distemper virus, canine parvovirus, FeLV/FIV [secondary infections], feline parvovirus/panleukopenia, rotavirus)
- Other infectious (*Histoplasma capsulatum;* pythiosis/lagenidiosis; protothecosis)
- Heavy metals/organophosphates
- Drugs (several classes and types, notably: antibiotics, antineoplastics, anthelmintics, nonsteroidal antiinflammatory drugs, digoxin, lactulose)
- Hemorrhagic gastroenteritis (HGE)
- Intestinal foreign body
- Intussusception (especially puppies with viral gastroenteritis)
- Intestinal volvulus
- Irritable bowel syndrome
- Lymphangiectasia
- Neoplasia (lymphoma [most common], adenocarcinoma)
- Extraintestinal causes (acute pancreatitis, hypoadrenocorticism, hepatobiliary disease, renal disease, diabetes mellitus, exocrine pancreatic insufficiency, hyperthyroidism [cats])

INITIAL DATABASE

- Fecal examinations: basic
  - Cytology (fresh saline smears): ova, larvae, certain bacteria, protozoa (*Giardia, T. foetus, Entamoeba* spp., *Balantidium coli*)
  - Flotation
- CBC (if depressed, dehydrated, pyrexic):
  - Leukocytosis: rule out inflammatory, infection, stress.

  - Leukopenia (often seen with parvovirus, panleukopenia).
  - Elevated packed cell volume (PCV)/total solids (TS): rule out dehydration.
  - Elevated PCV without concomitant elevation in TS: rule out hemorrhagic gastroenteritis.
  - Absence of stress leukogram suggestive of hypoadrenocorticism
- Serum biochemical profile:
  - Decreased electrolytes: gastrointestinal (GI) tract loss
  - Hyperkalemia/hyponatremia: hypoadrenocorticism. Do not rule out hypoadrenocorticism based on normal serum electrolyte concentrations (atypical hypoadrenocorticism).
  - Hypoglycemia: sepsis (any age), anorexia, heavy parasitism (patients < 6 months old)
  - Elevated liver enzyme activities: rule out hepatic disease, pancreatitis, or primary GI tract disease with portal bacterial translocation.
- Urinalysis: specific gravity (renal versus prerenal azotemia), bilirubinuria in cats consistent with hepatic disease
- Serum thyroxine concentration (older cats—hyperthyroidism)
- Parvoviral fecal antigen test (ELISA)
- Abdominal radiographs, contrast radiography and/or ultrasonography, depending on history and physical exam (history of dietary indiscretion; mass, pain or “sausage-shaped” bowel loop on abdominal palpation)

ADVANCED OR CONFIRMATORY TESTING

As dictated by clinical suspicion based on history, exam, and initial diagnostic tests

TREATMENT

TREATMENT OVERVIEW

Many cases of acute diarrhea in otherwise normal dogs and cats are transient and self-resolving. If a diagnosis of benign acute diarrhea due to a spontaneous and temporary disorder such as dietary indiscretion has been established, then no treatment or simply palliative treatment for comfort (e.g., with antidiarrheal medications) are good options. However, in some individuals, acute diarrhea produces signs of volume depletion/dehydration, or is associated with disorders that are not likely to be self-resolving or may cause contagion or zoonosis. The goal of treatment in such cases is to correct any volume deficits with parenteral fluid therapy and eliminate the cause if one has been identified through diagnostic testing. Finally, to prevent infectious transmission to other patients or hospital personnel, it is important to have an established hospital protocol when dealing with such patients.

ACUTE GENERAL TREATMENT

See Colitis, Acute p. 227

DRUG INTERACTIONS AND CONTRAINDICATIONS

- Prochlorperazine and chlorpromazine may precipitate seizures in animals with a history of seizure activity.
- Metoclopramide and maropitant should not be used if an obstruction is suspected.
- Metronidazole: risk of neurotoxicity at higher dosages

POSSIBLE COMPLICATIONS

- Further/ongoing dehydration
- Severe mucosal damage: pyrexia, secondary sepsis/endotoxemia
- Development of intussusception/other intestinal accident

RECOMMENDED MONITORING

Adjusted based on physical examination

PROGNOSIS AND OUTCOME

- Dietary indiscretion: often benign and self-resolving
- Parasitic diseases generally good response to treatment, barring obstruction
- Infectious causes, intoxications, mechanical/functional obstruction, HGE, acute pancreatitis, hepatitis, renal disease, hypoadrenocorticism: potentially life-threatening

PEARLS & CONSIDERATIONS

COMMENTS

- Advanced diagnostic evaluation may not be necessary in a patient with first-time acute diarrhea when that patient is otherwise stable and well. However, if diarrhea fails to respond to treatment within 24-48 hours, or if deterioration occurs at any time, further diagnostic testing and treatment are warranted.
- Establish a hospital infectious protocol aimed at preventing contagion (quarantine as needed, parasite control, good sanitation habits, impervious flooring in kennels/dog runs).
- Routine deworming of bitches and puppies (every 2 weeks) decreases transmission.
- Routine antibiotic use in uncomplicated diarrhea is discouraged (alters GI flora, promotes antibiotic resistance).

TECHNICIAN TIPS

- Help establish a hospital infectious protocol and implement it upon admission of a patient with a suspicion of contagion.
- Proper hygiene is vital to avoid contagion and zoonoses (handwashing between patients, gloves when cleaning a patient with diarrhea, never placing human or animal food in laboratory area where fecal analyses are performed).

CLIENT EDUCATION

- Pets are occasionally reservoirs for human infection, so proper hygiene is essential: frequent handwashing, regular cleaning of pet's food bowls, bedding, and litterbox (cats).
- Feeding of raw diets is discouraged (risk of transmission of zoonotic pathogens (*E. coli.*, *Salmonella* spp.).

SUGGESTED READING

Willard M: Clinical manifestations of gastrointestinal disorders. In Nelson RW, Couto CG, editors: Small animal internal medicine, ed 4, St Louis, 2009, Mosby Elsevier, pp 346–369.

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EDITOR: ETIENNE CÔTÉ

Diaphragmatic Hernia

BASIC INFORMATION

DEFINITION

Disruption of the continuity of the diaphragm such that abdominal organs can shift into the thoracic cavity.

SYNONYM

Pleuroperitoneal hernia. (Note: peritoneopericardial diaphragmatic hernias are covered separately; see p. 864 .)

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Both dogs and cats
- Congenital pleuroperitoneal hernias are rarely reported, since many affected animals die soon after birth.
- Traumatic: commonly in male dogs 1-3 years old

RISK FACTORS

Trauma is the most common cause of diaphragmatic hernia.

ASSOCIATED CONDITIONS & DISORDERS

- Incarceration, obstruction, and strangulation of abdominal viscera
- Hepatic venous stasis, biliary tract obstruction, icterus, and ascites secondary to liver herniation
- Pleural effusion, hemothorax, chylothorax, bile pleuritis, and pneumothorax can complicate hernias.
- Musculoskeletal or neurologic abnormalities secondary to trauma

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Congenital pleuroperitoneal hernia
  - Animals are dead at birth or die soon after with severe respiratory deficiency.
- Traumatic diaphragmatic hernia
  - Clinical course can be acute or chronic.

HISTORY, CHIEF COMPLAINT

- Acute:
  - History of trauma
  - Shock
  - Respiratory distress
  - Pale or cyanotic mucous membranes
- Chronic:
  - Dyspnea or tachypnea
  - Exercise intolerance
  - Anorexia
  - Depression
  - Vomiting
  - Dysphagia
  - Diarrhea
  - Constipation
  - Weight loss
  - Difficulty in lying down
  - Abdominal distension

- Some animals can be clinically normal, and the hernia is an incidental (typically radiographic) finding.

PHYSICAL EXAM FINDINGS

- Signs of hypovolemic shock
- Dyspnea and/or tachypnea
- Pale or cyanotic mucous membranes
- Tachycardia
- Cardiac arrhythmias
- Muffled heart and lung sounds on thoracic auscultation
- Borborygmi on thoracic auscultation
- Hyporesonance on chest wall percussion (pleural effusion)
- Hyperresonance on chest wall percussion (gastric tympany)
- Tucked-up or empty appearance of the abdomen
- Abdominal distention with fluid wave if ascites

ETIOLOGY AND PATHOPHYSIOLOGY

- Congenital:
  - Defect in the dorsolateral part of the diaphragm
  - The intermediate part of the left lumbar muscle of the crus may be absent, or the defect may be more extensive with both crura and parts of the central tendon missing.
- Traumatic:
  - Direct:
    - Thoracoabdominal stab and gunshot wounds
    - Iatrogenic injury during thoracocentesis
  - Indirect:
    - Primarily motor vehicle accidents, but other blunt abdominal trauma can cause diaphragmatic hernia.
    - An abrupt increase in intraabdominal pressure with the glottis open results in a large pleuroperitoneal pressure gradient.
      - This pressure gradient causes the diaphragm to tear at its weakest points, which are usually the muscular portions.
      - The location and size of the tear are dependent on the position of the animal on impact and the location of the viscera.
      - Viscera malpositioned in the thoracic cavity can suffer ischemic injury from alterations in blood flow.
      - Venous congestion of entrapped liver lobes can lead to pleural or abdominal effusion.
    - Clinical signs reflect respiratory dysfunction secondary to loss of diaphragmatic integrity, pleural effusion, or displacement of pulmonary parenchyma.
    - Clinical signs may also reflect dysfunction of displaced abdominal viscera.

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

The diagnosis is usually established by demonstrating a loss of diaphragmatic integrity by thoracic or abdominal imaging (plain and contrast radiography, abdominal ultrasonography), particularly in patients with a history of pleural space disease following trauma.

DIFFERENTIAL DIAGNOSIS

- Peritoneopericardial diaphragmatic hernia (see p. 864)
- Other causes of pleural or peritoneal effusion
- Pneumothorax
- Pneumonia
- Other causes of abdominal distension or ascites

INITIAL DATABASE

- CBC, biochemistry panel, urinalysis: variable results depending on time of presentation, severity of clinical signs, and organs displaced into the thorax
- Thoracic radiographs may show:
  - Loss of the diaphragmatic line
  - Loss of cardiac silhouette

    - Dorsal displacement of lung fields
    - Pleural effusion
    - Presence of gas (stomach or intestines) in the thoracic cavity
- Thoracocentesis may be necessary for diagnostic thoracic radiographs (if large-volume pleural effusion).
- Abdominal radiographs may show absence or cranial displacement of normal abdominal viscera.

ADVANCED OR CONFIRMATORY TESTING

- Ultrasonography may demonstrate a rent in the diaphragm, the organs herniating through it, or viscera in abnormal positions.
- Positive contrast celiography may demonstrate contrast medium in the pleural cavity, absence of a normal liver lobe outline, and incomplete visualization of the abdominal surface of the diaphragm.
- Contrast radiography of the intestinal tract may show barium-filled stomach or intestine in the thoracic cavity.
- In some animals, the diagnosis is confirmed during exploratory surgery.

TREATMENT 

TREATMENT OVERVIEW

- Stabilize patient.
- Resolve respiratory distress.
- Return the abdominal organs to the abdominal cavity.
- Repair the diaphragmatic defect.

ACUTE GENERAL TREATMENT

- Oxygen administered via face mask, nasal cannula, or oxygen cage (see p. 1318)
- Fluid therapy as needed to stabilize cardiovascular status (particularly for acute trauma patients)
- Thoracocentesis if needed (see p. 1338)
- Position the patient in sternal recumbency with the head elevated above the rear limbs (forelimbs elevated) if tolerated.

CHRONIC TREATMENT

Surgical treatment:

- Diaphragmatic hernias are often repaired through a midline celiotomy. A median sternotomy may be required for additional exposure.
- Return the abdominal organs to the abdominal cavity.
    - The diaphragmatic defect can be enlarged if necessary to reposition organs that have become swollen/congested or that have developed adhesions.
- Close the diaphragmatic defect via standard herniorrhaphy, abdominal flaps, porcine small intestinal submucosal patches (Vet BioSIS), or synthetic material (Silastic sheeting).
- Remove air and fluid from the pleural cavity after closing the diaphragmatic defect.
- Explore the entire abdominal cavity for associated injuries if traumatic etiology.

POSSIBLE COMPLICATIONS

- Reexpansion pulmonary edema can follow rapid lung reexpansion.
- Hypoventilation or hypoxia due to pain, pneumothorax, hemothorax, or tight bandages

RECOMMENDED MONITORING

- Vital signs
- Respiratory patterns
- Pain

PROGNOSIS AND OUTCOME 

Prognosis is good if the animal survives the early postoperative period (12 to 24 hours).

PEARLS & CONSIDERATIONS

COMMENTS

- Findings on physical examination maybe normal in some animals.
  - Diaphragmatic hernias are occasionally discovered as incidental findings in patients evaluated for other reasons.
- The radiographic diagnosis of diaphragmatic hernia can be surprisingly difficult in some cases.
  - Ultrasonography may be more useful in making the diagnosis, especially if moderate to severe pleural effusion is present.
- Surgery should be delayed until the patient's condition has stabilized.
- Perform surgery as soon as possible if the stomach has herniated into the thoracic cavity.

PREVENTION

Routine use of leashes to avoid hit-by-car injuries

TECHNICIAN TIPS

Materials for thoracocentesis to evacuate pleural fluid just after anesthetic induction to better stabilize the patient while prepping for surgery include: 22-G over-the-needle catheter or butterfly needle, three-way stop cock, extension set, syringe, and collection bowl (see p. 1338). Extra towels or something to prop/elevate the cranial half of the body while prepping may help move abdominal contents out of the thoracic cavity and improve respiratory function.

CLIENT EDUCATION

Patients with diaphragmatic hernia usually have a history of trauma, but failure to perform radiographic examination of the thorax often results in delayed diagnosis.

SUGGESTED READING

Hyun C: Radiographic diagnosis of diaphragmatic hernia: review of 60 cases in dogs and cats. J Vet Sci 5:157, 2004.

Spattini G, et al: Use of ultrasound to diagnose diaphragmatic rupture in dogs and cats. Vet Radiol Ultrasound 44:226, 2003.

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Diabetic Ketoacidosis

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Diabetic ketoacidosis (DKA) is a lifethreatening metabolic disorder caused by insulin deficiency and/or insulin resistance that leads to excess hepatic production of ketoacids and progressively worsening metabolic acidosis, hyperosmolality, serum electrolyte derangements, and systemic signs of illness.

EPIDEMIOLOGY

See Diabetes Mellitus, p. (297)

CLINICAL PRESENTATION

HISTORY/CHIEF COMPLAINT

The history and physical examination findings are variable because of the progressive nature of DKA and the variable time between the onset of DKA and owner recognition of a problem. The classic clinical signs of diabetes (i.e., polyuria, polydipsia, polyphagia, weight loss) develop initially, followed by systemic signs of illness (lethargy, anorexia, vomiting) as ketonemia and metabolic acidosis develop and worsen. Underlying illness that precipitates DKA (e.g., pancreatitis, infection) also contributes to the clinical picture. The time interval from onset of diabetes to onset of DKA is unpredictable, but once ketoacidosis develops, severe illness usually becomes evident within days.

PHYSICAL EXAM FINDINGS

Findings are variable for reasons discussed above. Common physical exam findings in addition to those found in nonketotic diabetic dogs and cats (see p. ((() include dehydration, depression, weakness, tachypnea, and sometimes a strong odor of acetone on the breath. Slow, deep breathing (i.e., Kussmaul's respiration) may be observed in animals with severe metabolic acidosis. Such signs as vomiting and abdominal pain are common because of the common concurrent occurrence of pancreatitis.

ETIOLOGY AND PATHOPHYSIOLOGY

- Synthesis of ketone bodies (i.e., acetoacetic acid, β-hydroxybutyric acid, and acetone) requires mobilization of free fatty acids (FFAs) from triglycerides stored in adipose tissue and a shift in hepatic metabolism from fat synthesis to fat oxidation and ketogenesis.
- Accelerated production of ketones occurs as a result of insulin deficiency, insulin resistance, and increased production of diabetogenic hormones, most notably glucagon.
- Insulin deficiency “allows” lipolysis to increase, thus increasing the availability of FFAs to the liver and in turn promoting ketogenesis.
- Insulin deficiency may be absolute or relative; that is, DKA may develop in some diabetic dogs and cats despite daily injections of insulin.
- Increased concentrations of diabetogenic hormones (glucagon, epinephrine, cortisol, growth hormone) combined with concurrent illness and an altered metabolic milieu (e.g., increased concentrations of plasma FFAs and amino acids, metabolic acidosis) cause insulin resistance and stimulate lipolysis, ketogenesis, and gluconeogenesis, which worsen hyperglycemia and promote ketonemia.
- Progressive accumulation of ketones in the blood overwhelms the body's buffering system, causing metabolic acidosis, and surpasses the renal tubular threshold for complete resorption, causing ketonuria.
- Ketonuria contributes to the osmotic diuresis caused by glycosuria and enhances excretion of solutes (e.g., sodium, potassium, magnesium).
- Excessive renal loss of water and electrolytes combined with fluid loss secondary to vomiting leads to volume contraction, an underperfusion of tissues, and development of prerenal azotemia.
- Progressively worsening hyperglycemia combined with urinary losses of water leads to hyperosmolality, a shift of water out of cells, and marked cellular dehydration.
- The severe metabolic consequences of DKA, which include severe metabolic acidosis, hyperosmolality, obligatory osmotic diuresis, dehydration, and electrolyte derangements, quickly become life-threatening.
- Severe hyperglycemia with concurrent hyperosmolality and lack of ketonemia or ketonuria is characteristic of the hyperosmolar nonketotic diabetic syndrome. The pathogenesis of this disorder is similar to DKA; however, it is believed that insulin capacity in the body is sufficient to inhibit ketogenesis but not hyperglycemia.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

- The diagnosis of diabetes mellitus requires appropriate clinical signs and documentation of persistent fasting hyperglycemia and glycosuria. The concurrent documentation of ketonuria or ketonemia establishes the diagnosis of diabetic ketosis (DK), and documentation of metabolic acidosis establishes the diagnosis of DKA.
- Commonly used urine reagent strips do not detect β-hydroxybutyrate. If ketonuria is not noted but DKA is suspected, blood can be tested for acetoacetic acid and acetone using Acetest tablets (Ames Division, Miles Laboratories, Elkhart, Ind.) or for β-hydroxybutyrate using a benchtop or handheld chemistry analyzer.

INITIAL DATABASE

- The laboratory evaluation of a healthy dog or cat with ketosis is similar to the nonketotic diabetic.
- The laboratory evaluation of sick dogs and cats with DKA should include a CBC, serum biochemical profile, serum electrolytes, arterial acid-base evaluation, and urinalysis with bacterial culture and sensitivity.
- Additional data such as radiographs, abdominal ultrasound, or further clinical pathologic studies may be needed, depending on results of the history, physical examination, and nature of concurrent illnesses. Approximately 70% of dogs with DKA will have a concurrent illness.
- Typical findings in DKA include severe hyperglycemia, metabolic acidosis, hyperosmolality, hyponatremia, hypokalemia, hypochloremia, prerenal azotemia, increased liver enzyme activities, hypercholesterolemia, and urinary tract infection. Alterations associated with concurrent pancreatitis are also common.

TREATMENT

TREATMENT OVERVIEW

- Treatment of DKA requires intensive fluid therapy and insulin administration to correct existing metabolic misbalance and stop ketogenesis. Supportive care, close monitoring, and treatment of concurrent illness are required for successful treatment. Referral to a veterinary specialist should be considered for the treatment and management of severe cases or if 24-hour monitoring is unavailable.
- Provide adequate amounts of insulin to maintain the blood glucose concentration between 150 and 300 mg/dL (8.4-16.7 mmol/L).
- Restore water and electrolyte losses and maintain hydration and normal serum electrolyte concentrations.
- Correct metabolic acidosis.
- Identify and treat concurrent illness.
- Provide dextrose or food as needed to avoid hypoglycemia.
- Avoid overly aggressive therapy; slowly correct abnormalities over 24-48 hours.

TREATMENT

- For “healthy”-appearing dogs and cats with DK, short-acting regular insulin can be administered SQ q 8 h until ketonuria resolves. The patient should be fed a third of its daily caloric intake at the time of each insulin injection. The insulin dose should be adjusted based on blood glucose concentrations. Longer-acting insulin preparations can be administered once DK has resolved.
- Treatment for systemically ill dogs and cats with DKA includes intravenous fluids with appropriate supplements, regular (crystalline) insulin, bicarbonate, dextrose, and ancillary therapy, depending on concurrent illness.
    - Initial type of fluid depends on serum electrolyte concentrations. If not known, use 0.9% saline solution at a rate sufficient to correct dehydration over 12-24 hours; adjust based on hydration status, urine output, and persistence of fluid losses.
    - Potassium supplementation in fluids depends on serum potassium concentration; if unknown, initially add 40 mEq KCl to each liter of fluids.
    - Phosphate supplementation in fluids is indicated if serum phosphorus concentration <1.5 mg/dL (0.48 mmol/L) or hemolytic anemia develops; initial IV infusion rate is 0.01-0.03 mmol/kg/h in calciumfree fluids (e.g., 0.9% saline).
    - Dextrose supplementation in fluids is indicated when blood glucose approaches or falls below 250 mg/dL (13.9 mmol/L); initially add dextrose to make 5% solution. As insulin administration must be continued to resolve the ketosis, dextrose should be used to maintain the blood glucose concentration between 150-250 mg/dL (8.4-13.9 mmol/L).
    - Magnesium supplementation is not indicated unless persistent lethargy, anorexia, weakness, or refractory hypokalemia or hypocalcemia is encountered after 24-48 hours of fluid and insulin therapy, and hypomagnesemia is documented.
    - Bicarbonate supplementation is rarely indicated; adequate fluid therapy restores renal excretion of ketoacids, thus

lowering their concentration in blood. If serum bicarbonate is still <12 mEq/L (total venous CO2 <12 mmol/L) after several hours of fluid therapy, a onetime dose of bicarbonate can be given. The dose is based on the formula: mEq $HCO3^-$ = body weight (kg) × 0.4 × (12 - animal's serum [$HCO3^-$]) × 0.5; if animal's $HCO3^-$ or total co2 concentration is unknown, use 10 in place of (12 - animal's $HCO3^-$). Add to IV fluids and give over 6 hours; do not give as bolus infusion. Only re-treat if plasma bicarbonate concentration remains <12 mEq/L after 6 hours of $NaHCO3^-$ therapy.

- Begin insulin therapy 2-6 hours after initiating fluid therapy. If serum potassium level is normal, begin insulin treatment as described below. If hypokalemia is present, decrease insulin dose by 50% during the initial 2-3 hours, and provide adequate potassium supplementation.
  - Regular insulin is administered using one of two techniques:
    - For the intermittent IM technique, the initial insulin dosage is 0.2 U/kg IM, then 0.1 U/kg IM hourly; switch to regular insulin SQ every 6-8 hours once blood glucose approaches 250 mg/dL (13.9 mmol/L), and add dextrose to IV fluids as discussed above.
    - For the low-dose IV infusion technique, the initial insulin infusion rate is 0.05 U/kg/h (cat) or 0.1 U/kg/h (dog), diluted in 0.9% saline and administered via infusion or syringe pump as a continuousrate infusion (CRI) in a line separate from that used for fluid therapy. Adjust infusion rate based on hourly blood glucose measurements; as blood glucose level decreases and approaches 250 mg/dL (13.9 mmol/L), add dextrose to IV fluids as discussed above. The insulin administration rate may need to be adjusted when dextrose is added to the IV fluids.
  - The goal of insulin treatment is a gradual decline in blood glucose concentration, preferably 50-75 mg/dL/h (2.8-4.2 mmol/L/h).
  - Switch to longer-acting insulin preparations once the patient is nonketotic and eating (see p. 297).

POSSIBLE COMPLICATIONS

- Complications result from overzealous treatment, inadequate patient monitoring, inadequate fluid replacement, and failure to reevaluate biochemical parameters in a timely manner.
- Common complications include hypokalemia, hypoglycemia, hypernatremia, hemolytic anemia induced by hypophosphatemia, and neurologic signs secondary to cerebral edema.
- Slow correction of abnormalities over 24-48 hours will minimize complications.

RECOMMENDED MONITORING

- Blood glucose measurement every 1-2 hours initially; as blood glucose level decreases in response to treatment, adjust insulin therapy and begin dextrose infusion when approaches 250 mg/dL (13.9 mmol/L).
- Hydration status, respiration, pulse every 2-4 hours; adjust fluids accordingly.
- Serum electrolyte and total venous co2 concentrations every 6-12 hours; adjust fluid and bicarbonate therapy accordingly.
- Urine output, glycosuria, ketonuria every 2-4 hours; adjust fluid therapy accordingly.
- Daily body weight, packed cell volume, temperature, blood pressure
- Additional monitoring, depending on concurrent disease

PROGNOSIS AND OUTCOME

The prognosis for successful treatment of DKA is dependent in part on the severity of the metabolic derangements at the time DKA is diagnosed, underlying illnesses that precipitated DKA, and complications that develop during treatment. Close supervision and monitoring are imperative for a successful outcome. With optimal in-hospital treatment (intensive care), the rate of survival to discharge is approximately 70%.

PEARLS & CONSIDERATIONS

Anecdotally, addition of hydrogen peroxide to urine has been thought to convert β-hydroxybutyrate to acetoacetate, thus reacting with ketone reagent squares on urine dipsticks. However, the required concentration of β-hydroxybutyrate for this reaction to proceed is very high, and clinically such patients also have very high acetoacetate concentrations. Therefore the concept, while sound, is not clinically useful.

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Diabetes Mellitus

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Diabetes mellitus is a complex metabolic disorder caused by decreased production of insulin by the pancreatic β cells and/or decreased insulin utilization by peripheral tissues.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Diabetes mellitus typically occurs in older dogs and cats.
- Peak prevalence: dogs, 7-9 years, with 70% older than 7 years; cats, 9-11 years
- Juvenile-onset diabetes: dogs and cats <1 year of age; uncommon
- In dogs, females are affected twice as frequently as males. In cats, diabetes occurs predominately in neutered males.

GENETICS & BREED PREDISPOSITION

- The role of genetics remains to be determined. Genetic predispositions for diabetes have been suggested by familial associations in dogs and by pedigree analysis of keeshonden.
- Dog breeds at increased risk: Australian terrier, bichon frise, Cairn terrier, fox terrier, keeshond, miniature and standard poodle, Samoyed, miniature and standard schnauzer, spitz
- There is no clear-cut breed predisposition in cats, although Burmese cats are overrepresented in Australia.

RISK FACTORS

- Obesity
- Recurring pancreatitis
- Diestrus in the older intact female dog
- Diseases causing insulin resistance, most notably hyperadrenocorticism and acromegaly
- Insulin-antagonistic drugs, most notably glucocorticoids and progestagens

ASSOCIATED CONDITIONS & DISORDERS

- Renal insufficiency
- Hyperlipidemia
- Systemic hypertension
- Bacterial infections Cataracts and blindness (dogs)
- Peripheral neuropathy causing weakness and plantigrade stance (cats)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Insulin-dependent diabetes mellitus is present in 99% of dogs and 50%-70% of cats at the time diabetes is diagnosed. It is characterized by an absolute deficiency of insulin and mandatory need for insulin injections to control clinical signs of the disease. Historically, “type 1 diabetes.”
- Non–insulin-dependent diabetes mellitus is present in approximately 30% of cats at the time diabetes is diagnosed and it is characterized by a reduced population of pancreatic β cells and potential for clinical response to weight loss, diet, oral hypoglycemic drugs, and correction of concurrent insulin-antagonistic disease or drugs. Historically, “type 2 diabetes.”
- Transient or subclinical diabetes is present in approximately 20% of cats and is characterized by resolution of the clinical diabetic state weeks to months after initiating insulin treatment. Overt diabetes may or may not recur in the future.

HISTORY, CHIEF COMPLAINT

- Polydipsia, polyuria, polyphagia, and weight loss in virtually all diabetics
- Additional clinical signs can include:

- Lethargy
- Poor body condition
- Blindness from cataracts (dogs)
- Lack of grooming behavior, poor haircoat (cats)
- Decreased jumping ability, rear limb weakness, or development of a plantigrade posture (cats)

PHYSICAL EXAM FINDINGS

There are no specific physical exam findings. Body weight ranges from obese to thin. Lethargy is variable. A dry, lusterless haircoat and scales from hyperkeratosis; hepatomegaly from hepatic lipidosis; lenticular changes consistent with cataract formation (dogs); and impaired ability to jump, weakness in the rear limbs, ataxia, or a plantigrade posture from peripheral neuropathy (cats) may be identified.

ETIOLOGY AND PATHOPHYSIOLOGY

- The etiology of diabetes is multifactorial and involves a combination of genetic predisposition, environmental factors, insulin resistance, and decreased numbers of functioning β cells.
- Decreased numbers of β cells typically result from destruction secondary to vacuolar degeneration, islet amyloidosis (cats), immune destruction (dogs), hyperfunction-induced apoptosis (cats), pancreatitis, or congenital islet hypoplasia.
- Insulin deficiency causes decreased tissue utilization of glucose, amino acids, and fatty acids; accelerated hepatic glycogenolysis and gluconeogenesis; and accumulation of glucose in the circulation, causing hyperglycemia.
- Progressively worsening hyperglycemia leads to glycosuria, which creates an osmotic diuresis, causing polyuria. Compensatory polydipsia prevents dehydration as long as there is free access to water.
- The diminished peripheral tissue utilization of glucose and amino acids results in weight loss.
- Insulin deficiency results in failure of the satiety center to inhibit the feeding center in the hypothalamus, causing polyphagia.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is based on the presence of appropriate clinical signs (i.e., polyuria, polydipsia, polyphagia, weight loss), and documentation of persistent fasting hyperglycemia (blood glucose >200 mg/dL [11 mmol/L]) and persistent glycosuria.

INITIAL DATABASE

A thorough diagnostic evaluation is indicated to identify any disease that might be causing or contributing to the diabetic state, that may result from the diabetic state, or that may force modification of therapy.

- CBC: typically normal
- Common serum biochemical profile findings: hyperglycemia, hypercholesterolemia, and increased serum alanine aminotransferase and alkaline phosphatase activities.
- Common urinalysis findings: specific gravity >1.025, glycosuria, findings consistent with concurrent bacterial urinary tract infection (see p. 1596). Bacterial culture of urine is recommended in all diabetic patients irrespective of urinalysis results. Ketonuria establishes a diagnosis of diabetic ketosis or ketoacidosis.
- Findings on abdominal ultrasound may include hepatomegaly, changes suggesting pancreatitis, and bilateral adrenomegaly or an adrenal mass if concurrent hyperadrenocorticism is present.
- Additional diagnostic tests to consider include serum thyroxine concentration in an older diabetic cat, serum pancreatic lipase immunoreactivity for pancreatitis, serum progesterone concentration in an intact female diabetic dog.

DIFFERENTIAL DIAGNOSES

- Polyphagia (see pp. 899,)
- Polyuria/polydipsia (see pp. 902, p. 1419, p. 1420,p. 1585)
- Weight loss (see p. 1181 ,p. 1436)

TREATMENT

TREATMENT OVERVIEW

- The primary goal is elimination of owner-observed clinical signs and maintenance of a healthy, active pet while avoiding

clinical signs of hypoglycemia.
- Stable body weight once obesity is corrected
- Avoidance of chronic complications of diabetes mellitus, most notably recurring ketosis, clinical signs of poor control of glycemia (e.g., lethargy, weight loss, poor body condition), cataracts (dogs), and clinical signs of peripheral neuropathy (cats)

TREATMENT 

- For dogs, recombinant human or pork-source NPH or Lente insulin at an initial dosage of 0.25 U/kg SQ q 12 h
- For cats:
  - Glargine insulin at starting dose of no more than 3 U/cat SQ q12 h if blood glucose is >360 mg/dL (>20 mmol/L). Close monitoring of blood glucose is required; dose reduction is expected in the first 7 days. If close monitoring is not possible, it is safer to start with 1 U/cat SQ q12 h.
  - Alternatively, recombinant human or pork-source Lente or beef/porksource PZI insulin can be used at an initial dose of 1 unit per cat SQ q 12 h.
- Keep daily exercise fairly consistent for dogs.
- Identify and treat concurrent disorders that interfere with insulin effectiveness.
- Treatment with the oral sulfonylurea, glipizide, may be considered in diabetic cats when the owner refuses to administer insulin, if ketonuria and peripheral neuropathy are not identified, and if the cat is relatively healthy.
- Treatment of DKA: see p. 299

NUTRITION/DIET

- Adjust dietary caloric intake to correct or prevent obesity.
- Divide total daily caloric intake in half, and offer at the time of each insulin injection. Consumption may be immediate or intermittent throughout the 12-hour period, depending on eating habits of the dog or cat. Some cats may prefer to “graze” throughout the day.
- For maintenance in dogs, increase fiber content of the diet unless concurrent disease or adverse effects dictate otherwise. Amount of fiber depends on fiber type: insoluble fiber should be >10%, soluble fiber should be 4%-8%, and mixtures of soluble and insoluble fiber should be >8% of diet on dry-matter basis.
- In cats, restrict carbohydrate content of diet, ideally to 15% or less of metabolizable energy. Fiber content of the diet can also be increased as described for dogs.

POSSIBLE COMPLICATIONS

Insulin-induced hypoglycemia, diabetic ketoacidosis

RECOMMENDED MONITORING

- Initially, monitor clinical response and blood glucose concentrations weekly until diabetic control is attained, defined as resolution of clinical signs and blood glucose concentrations ranging between 100 and 300 mg/dL (5.5 and 16.7 mmol/L) during the 12 hours after insulin administration.
- With instruction, some clients may be able to obtain blood glucose curve results for their pet via home monitoring. However, any adjustments in insulin dose should only be done in consultation with the veterinarian.
- Monitor history, physical examination, body weight, and serum fructosamine concentration every 3-6 months once diabetes is controlled.
- Evaluate multiple blood glucose concentrations during the 12 hours after insulin administration if diabetic control is lost (i.e., return of clinical signs, abnormalities identified on physical examination, or progressive loss of body weight). Adjust insulin therapy accordingly.

TECHNICIAN TIPS

- Minimize stress to the patient.
- Perform blood sampling for glucose measurements in a quiet room, and have all equipment ready before taking the patient out of a cage for venipuncture.

PROGNOSIS AND OUTCOME 

- Prognosis depends on owner commitment to treating the disorder, ease of glycemic regulation, presence and reversibility of concurrent disorders, and avoidance of chronic complications associated with the diabetic state.
- Mean survival time for diabetic dogs and cats is approximately 3 years from time of diagnosis, although diabetic dogs and cats that survive the first 6 months can easily maintain a good quality of life for longer than 5 years with proper care.

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Diabetes Insipidus

BASIC INFORMATION

DEFINITION

Well-recognized disorder of insufficient antidiuretic hormone (ADH) secretion (central diabetes insipidus) or action (nephrogenic diabetes insipidus) resulting in inadequate urine-concentrating ability.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Affects both dogs and cats
- No breed, gender, or age predilection

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Central diabetes insipidus (CDI): hypothalamus/pituitary gland disorder
- Nephrogenic diabetes insipidus (NDI): renal disorder

HISTORY, CHIEF COMPLAINT

- Polyuria, polydipsia, loss of house training, perceived urinary incontinence
- Stupor, disorientation, ataxia, and seizures may be reported if an underlying neurologic disorder is present.

PHYSICAL EXAM FINDINGS

- Usually normal
- Dehydration may be noted if the animal has not had free access to water.
- Neurologic abnormalities (e.g., stupor, disorientation, ataxia) may be seen in CDI cases with underlying hypothalamic/pituitary lesions, or as a consequence of severe hypernatremia from hypertonic dehydration.

ETIOLOGY AND PATHOPHYSIOLOGY

- Normal daily water consumption: <70 mL/kg/d for dogs (higher in dogs <4 kg); <250 mL/d for the average-sized cat
- ADH is released by the neurohypophysis (segments of hypothalamus and posterior pituitary gland) in response to increased plasma osmolality, and to a lesser degree to reduced blood volume.
- ADH binds to receptors at the renal distal tubules and collecting ducts and allows water to be resorbed from the lumen of the duct into the renal interstitium, resulting in concentrated urine. Water resorption is also dependent on the osmotic gradient of the renal interstitium.
- CDI results from a lack of hypothalamic production of ADH secondary to cerebral trauma, cranial neoplasia (primary or metastatic), or hypothalamic/pituitary cysts. Those animals without a discernable underlying cause are classified as having idiopathic CDI.
- NDI results from a reduced capacity of ADH to bind to its renal receptors and exert its renal actions. Interference with the binding capacity of ADH can be secondary to *Escherichia coli* endotoxins (pyometra, pyelonephritis), hypercalcemia, hypokalemia, hyperaldosteronism, and hyperadrenocorticism.
- Congenital NDI and congenital CDI are very rare.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnostic approach to diabetes insipidus is directed at ruling out metabolic and other endocrine causes of polyuria/polydipsia, using a CBC, serum biochemistry profile, urinalysis, urine culture, and test(s) for adrenal gland disorders. Once other differentials are

excluded, differentiation of CDI from NDI or psychogenic polydipsia requires a modified water deprivation test or trial therapy with exogenous ADH.

DIFFERENTIAL DIAGNOSIS

Other causes of polyuria/polydipsia, including chronic renal disease, diabetes mellitus, hyperadrenocorticism, hypercalcemia, hyperthyroidism, hypoadrenocorticism, hypokalemia, liver disease, primary hyperaldosteronism (rare), primary renal glycosuria (rare), psychogenic polydipsia, pyelonephritis, and pyometra (see p. 902).

INITIAL DATABASE

- CBC: usually normal; mild hemoconcentration may be present if the animal is dehydrated.
- Serum biochemical profile
- Urea may be decreased due to increased renal loss, or mildly increased in dehydrated patients.
- Mild hyponatremia or hypokalemia occasionally seen
- Urinalysis: usually hyposthenuria (urine specific gravity <1.008) but can concentrate up to 1.015 in cases with partial ADH deficiency
- Other tests to rule out causes of secondary NDI usually include urine culture, abdominal ultrasound, and testing for hyperadrenocorticism (see p. 548).

ADVANCED OR CONFIRMATORY TESTING

- Endogenous creatinine clearance testing or nuclear scintigraphy to estimate glomerular filtration rate: considered if persistent isosthenuria is present, to rule out renal insufficiency.
- Random plasma osmolality:
  - A large overlap can occur between results from patients with a primary polyuric disorder (e.g., CDI or NDI) and a primary polydipsic disorder (i.e., psychogenic polydipsia).
  - Plasma osmolality <280 mOsm/kg is suggestive of psychogenic polydipsia.
  - Plasma osmolality >280 mOsm/kg can be seen with CDI, NDI, or psychogenic polydipsia.
- Modified water deprivation test:
  - Used for differentiating between diabetes insipidus and psychogenic polydipsia
  - Causes of secondary NDI should be ruled out before performing this test.
  - Should not be performed if renal disease or dehydration is present.
  - The patient must be monitored throughout the test.
  - Procedure:
    - Slowly decrease the patient's water intake to 70-100 mL/kg/d over 3-5 days before starting the test to help correct any secondary renal medullary solute washout.
    - Fast the patient for 12 hours before the test.
    - At the start of water deprivation, empty the patient's bladder, and determine the patient's weight, blood urea nitrogen (BUN) (via an Azostick is sufficient), urine specific gravity (USG), and urine osmolality (if readily available).
    - Withhold water and monitor clinical demeanor, weight (after emptying bladder), and USG (± urine osmolality) q 1 h. Assess BUN every few hours.
    - This portion of the test is stopped when 3% of the body weight has been lost, USG increases to >1.030, azotemia occurs, or the pet becomes clinically dehydrated or depressed.
    - If 3% of the body weight has been lost, urine concentration is <1.030, and the pet is still clinically normal, administer ADH (aqueous vasopressin: 0.55 U/kg IM to a maximum of 5 U) and reassess USG at 30, 60, and 120 minutes.
    - Slowly reintroduce water when the test is completed.
  - Interpretation:
    - USG in patients with psychogenic polydipsia should slowly increase to >1.030 with water deprivation alone.
    - Patients with complete CDI will show little or no increase in urine concentration (still <1.015-1.020) with fluid loss of 3%-5% of body weight, but will then show a >50% increase in USG after ADH administration.
    - Patients with partial CDI will show little increase in urine concentration by the time they have lost 3%-5% of body weight but will show an increase in USG of >15% but <50% after ADH administration.
    - Patients with NDI will show little increase in USG even with ADH administration.
  - Possible complications of the test: hypernatremia/hypertonic dehydration (irritability, weakness, ataxia, stupor, coma)
- CT or MRI of the brain can be used to image a potential underlying cranial mass in older patients with CDI.

TREATMENT

TREATMENT OVERVIEW

Therapy is aimed at improving patient and owner quality of life through reduction or resolution of polyuria and polydipsia. Treatment is expected to be lifelong unless an underlying cause can be identified and resolved.

ACUTE GENERAL TREATMENT

None generally required

CHRONIC TREATMENT

- Exogenous ADH administration (desmopressin acetate [DDAVP]: either as tablets [0.1 mg/dog PO q 8 h or 0.025-0.05 mg/cat q 8-12 h; increase dose if no response within 1 week] or intranasal drops administered into the conjunctival sac [1-4 drops/patient q 12 h]) is the treatment of choice for CDI. Patients with NDI are unresponsive to DDAVP therapy.
- Thiazide diuretics can be used in cases of primary NDI or partial CDI to reduce total body sodium concentrations, thereby increasing renal sodium and water resorption and reducing urine volume. Chlorothiazide (20-40 mg/kg PO q 12 h) or hydrochlorothiazide (1-2 mg/kg PO q 12 h) should be used in conjunction with a low-sodium diet.
- Chlorpropamide is an oral hypoglycemic agent that potentiates renal ADH action and may be useful in cases of partial CDI. Doses of 10-40 mg/kg PO q 24 h have been suggested, but clinical responses in cats and dogs have been variable.
- If the polyuria/polydipsia is not disruptive to the owners, and the animal has free access to water, therapy for CDI or NDI may not be required.

NUTRITION/DIET

A sodium-restricted diet alone may be useful at reducing urine volume in patients with CDI and NDI.

DRUG INTERACTIONS

Chlorpropamide may enhance the antidiuretic effects of desmopressin and displaces nonsteroidal antiinflammatory drugs, warfarin, and many others from circulating protein-binding sites, elevating their serum levels.

POSSIBLE COMPLICATIONS

- Cellular overhydration can theoretically occur in patients that consume large volumes of water shortly after receiving DDAVP, owing to a decreased ability to excrete the free water once DDAVP reaches therapeutic effect. Neurologic signs (ataxia, depression, tremors) can occur as a consequence of cerebral edema. It is recommended that pets not have free access to water immediately after each dose.
- Conjunctival irritation is occasionally seen with conjunctival administration of DDAVP but is usually mild.
- Thiazide diuretics may cause hypokalemia and, if given to a patient with primary polydipsia, could lead to cellular overhydration due to decreased free water excretion.
- Hypoglycemia is the most common complication of chlorpropamide therapy.

RECOMMENDED MONITORING

- Clinical response should be monitored in those patients receiving DDAVP therapy.
- Serum electrolytes should be periodically monitored if thiazide diuretics are used, as should blood glucose levels if chlorpropamide is used.

PROGNOSIS AND OUTCOME

- In patients with congenital or idiopathic CDI, clinical signs generally resolve completely with DDAVP therapy, and patients can have a normal life expectancy. The expense of DDAVP therapy, however, can make lifelong treatment not feasible for some pet owners.
- CDI secondary to an underlying cranial tumor has a very guarded prognosis, as progressive neurologic signs often develop in the ensuing months.
- The polyuria/polydipsia of primary NDI is often difficult to manage medically and therefore is associated with a guarded prognosis.

PEARLS & CONSIDERATIONS

COMMENTS

- Response to exogenous DDAVP therapy can be used as a less arduous and less hazardous alternative to the water deprivation test to diagnose CDI, once the differential diagnosis has been narrowed down to CDI, NDI, or psychogenic polydipsia. Daily water consumption and USG should be measured before the administration of DDAVP and after a 5- to 7-day course of exogenous therapy. A marked reduction in water consumption and increase in urine concentrating ability occurs in patients with CDI. Patients with NDI or psychogenic polydipsia do not have a clinical response to DDAVP.
- Hyperadrenocorticism is a likely differential in a patient that initially responds to exogenous DDAVP therapy but later has recurrence of polyuria and polydipsia.

TECHNICIAN TIP

- The water deprivation test requires extremely diligent hourly monitoring for the entire duration of the test, without which there is a risk of rapidly progressive life-threatening dehydration in these patients.

CLIENT EDUCATION

Patients with diabetes insipidus must always have free access to water.

SUGGESTED READING

Feldman EC, Nelson RW: Water metabolism and diabetes insipidus. In Feldman EC, Nelson RW, editors: Canine and feline endocrinology and reproduction, ed 3, St Louis, 2004, Saunders, pp 2–41.

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Dermatophytosis

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Dermatophytosis is a well-recognized contagious infection of the skin, hair, and/or claw with one of several species of superficial fungi (i.e., dermatophytes).

SYNONYMS

Ringworm; tinea (Latin term used by physicians)

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Any animal species may contract dermatophytosis, though it is particularly important in cats. It is most commonly a disease of young animals, owing to immaturity of their defense mechanisms.
    - In dogs, the incidence is low. Circular, scaling patches in dogs are more likely to be superficial staphylococcal pyoderma or demodicosis rather than dermatophytosis.
    - In cats, the incidence is higher; it tends to be underdiagnosed in part because of the polymorphic nature of lesions.

GENETICS & BREED PREDISPOSITION

Some breeds or lines of long-haired cats (Persians, Himalayans) appear to be predisposed to infection; some individuals of these breeds are more difficult to treat effectively.

RISK FACTORS

- Any condition that results in debilitation or immunocompromise can serve as a predisposing factor. Examples include cancer, immunosuppressive therapy, metabolic disease.
- Incidence is higher with inadequate husbandry conditions (some shelters, catteries, pet stores, stray/feral cat populations), where high population density, stress (pregnancy, lactation), poor nutrition, concurrent parasitisms, viral infections, and other diseases may make dermatophytosis endemic.

CONTAGION & ZOONOSIS

Dermatophytosis is a contagious zoonotic disease. Humans, dogs, and cats exposed to an infected animal are at risk. Transmission occurs by direct contact, contact with contaminated fomites (carpeting, bedding, grooming implements) or with infected soil. Unaffected animals in the household may serve as “fomites” by innocently transporting spores on their haircoats, though such individuals are actually not infected and should not be termed “carriers.” Fungal spores remain viable for years under ideal conditions.

GEOGRAPHY AND SEASONALITY

Incidence is higher in warmer tropical or subtropical geographic regions, particularly in locales with large stray cat populations.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Beyond the typical grossly visible superficial infection, other forms include:
    - *Subclinical infection:* some infected cats have subtle hair loss and scaling, even appearing grossly normal (particularly if long-haired). These normal-appearing yet infected cats pose a special risk in multianimal facilities, where their unaffected appearance may lead to lack of treatment.
    - *Kerion:* an uncommon, overly exuberant immunologic/inflammatory response to the organism leads to thickened plaquelike to smooth, nodular growths or masses.
    - *Mycetoma or pseudomycetoma:* rare formation of pyogranulomatous draining nodules as a result of deeper extension

of the infection in an immunocompromised host.

HISTORY, CHIEF COMPLAINT

Often a young patient, sometimes from a multianimal environment, presenting with one or more patchy areas of alopecia, scaling, or poor haircoat. There may be a history of contagion to the owner.

PHYSICAL EXAM FINDINGS

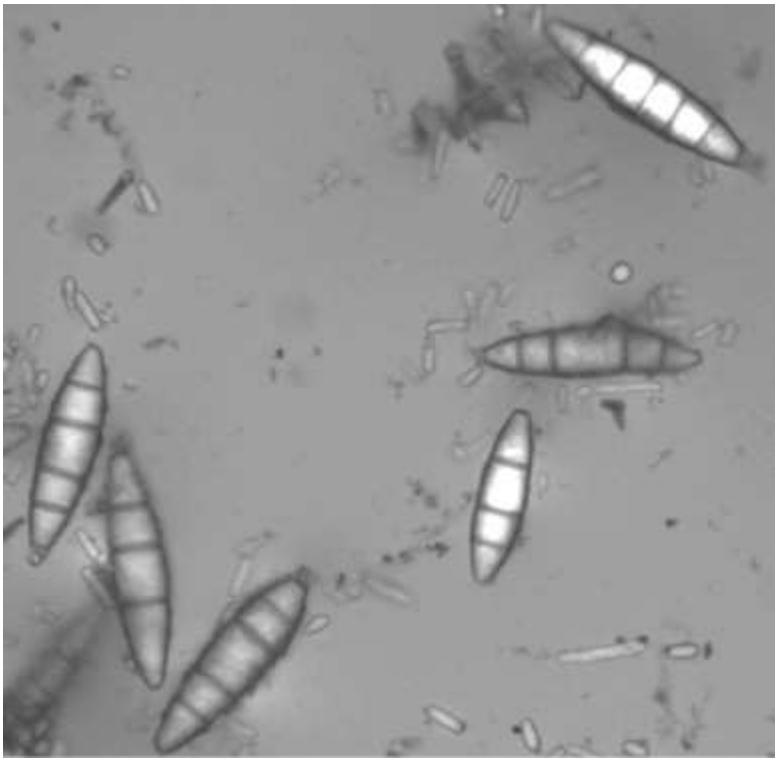
- The classical appearance is focal or multifocal areas of alopecia and scaling or crusting of varying severity, most commonly occurring on the face and forelimbs. The lesions can be circular or ringlike, or more diffuse, and are associated with variable degrees of inflammation and pruritus.
- In cats, dermatophytosis creates an especially large range of clinical signs, including (less commonly) miliary dermatitis, chin acne, or generalized scaling.
- Uncommonly, follicular infection and rupture may produce a pustular appearance.
- Uncommonly, infections on the facial and nasal areas may produce severe alopecia, crusting, weeping, and inflammation that clinically and histologically resemble pemphigus.

DERMATOPHYTOSIS Macroconidia of *Microsporum canis*.

(Copyright Dr. Manon Paradis.)

ETIOLOGY AND PATHOPHYSIOLOGY

- In order of prevalence, causative fungal species include *Microsporum canis*, *Microsporum gypseum*, and the *Trichophyton* group (the latter also known as *Arthroderma*). Feline infections with *M. gypseum* and *Trichophyton* appear to be on the rise, especially in animal shelters; other species such as *M. persicolor* are reported rarely.
- Under usual circumstances, dermatophytes live in nonviable, cornified tissue (superficial epidermis, actively growing hairs, nails); invasion into living tissue implies a compromised host.
- The presence of the fungus alone will not necessarily result in infection. Whether infection ensues depends on host factors (youth, debility, genetics) ; host immunity (natural and acquired); husbandry (stress, nutrition, concurrent disease); number of spores; trauma to the skin (as with scratching); and presence of occlusive conditions on the skin.
- In most normal individuals, after infection, cell-mediated immunity develops against the fungus, eventually resulting in spontaneous cure (typically 12-20 weeks). Animals that fail to develop the appropriate immune response may remain persistently infected until treated.



DERMATOPHYTOSIS Macroconidia of *Microsporum gypseum*.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is suspected based upon history and clinical signs and confirmed with the gold standard of fungal culture; other diagnostic tests are helpful but not reliable.

DIFFERENTIAL DIAGNOSIS

- In dogs, superficial staphylococcal pyoderma and demodicosis have a similar clinical appearance and are more common; therefore, these disorders should be suspected first.
- In cats, miliary dermatitis due to other causes such as flea allergy, mite infestation, or other allergy should be considered, as well as other causes of generalized scaling and pruritus.

INITIAL DATABASE

Following initial clinical suspicion, the following tests can be used to help confirm infection:

- *Trichogram:* the finding of ectothrix spores and/or hyphal elements within hair shafts upon microscopic examination; difficult and insensitive.
    - Hairs are plucked from the edges of lesions and wet mounted in 10% potassium hydroxide or chlorphenolac clearing solution. Plucking fluorescing hairs (see below) may increase the chances of finding spores. This technique is insensitive, requires considerable experience to avoid artifact, and is not recommended for routine use.
- *Wood's lamp*: about 50% of strains of *M. canis* will fluoresce a bright "apple green" color upon exposure to UV light of wavelength 320-400 nm; a reasonable screen but not dependable.
    - This technique is inexact and prone to misinterpretation, because many strains of *M. canis* (and other dermatophyte species) do not fluoresce. Other materials such as keratin scale and topical products may fluoresce, leading to false-positive results.
    - Fluorescence is due to a fungal metabolite produced only when the organism is growing on hair shaft material. A true positive thus appears as bright green fluorescence along the length of the *hairs only*, never in scale, claw, or culture.
    - It is helpful to allow the lamp to warm up for 5 minutes before use to produce maximum fluorescence. Suspected fluorescing hairs should *always* be examined microscopically and/or cultured to confirm the presence of a

dermatophyte.
    - A Wood's lamp is a useful aid to monitor infection status in an animal shelter experiencing endemic infection, if the infection is with a fluorescing strain.
- *Fungal culture:* a highly reliable method if done properly. Requires some skill and experience; therefore submission to a reference laboratory is a valid consideration.
    - To collect a sample for culture, the toothbrush technique is preferred. A new inexpensive toothbrush is vigorously combed over the lesions (or all parts of the haircoat if lesions are not obvious or cat appears “normal”) for 2-3 minutes; wrap in plastic and submit.
    - In-clinic cultures can be carried out using dermatophyte test medium (DTM), available in several formats (vial, round, or square plate). All are equally useful, though the plate formats are easier to inoculate. Some plate formats include a separate compartment with a different medium (Sabouraud's dextrose agar or rapid sporulation medium), which is marginally useful in practice. To inoculate the medium, touch all sides of the toothbrush bristles lightly onto the DTM multiple times.
    - Cover plates, but do not seal with tape. Incubate at warm room temperature (ideally, 28°C/80°F); light conditions do not matter. Growth occurs typically within 7-14 days, though plates are kept for 21 days before deeming them negative.
    - Examine the plates *daily* for growth. Look for a white to off-white, fluffy to powdery colony, with a red color change in the medium *at the same time* that the colony is first visible. Dermatophyte colonies are never black, grey, green, or multicolored.
    - DTM is not infallible. All fungi will eventually cause a red color change; some nonpathogenic saprophytes cause rapid color change. Thus, suspect colonies must be examined microscopically for confirmation: brush a strip of clear cellophane tape over the colony, and mount the tape sticky side down onto a drop of lactophenol cotton blue stain (or methylene blue) on a microscope slide. Examine at 100× to 400× total magnification for typical appearance of dermatophyte macroconidia (see figures). The appearance of these macroconidia varies with fungal species; consult a reference text.
    - When working with an infected multianimal facility, it is convenient to sample each cat with a separate toothbrush and place each in a separate zip-lock plastic bag labeled with identification information.

ADVANCED OR CONFIRMATORY TESTING

Skin biopsy: dermatophytes may be visible on histopathologic examination of skin biopsy specimens, though they are sometimes difficult to find; a negative result does not preclude dermatophytosis. Advising the pathologist that dermatophytosis is suspected will prompt special stains to facilitate identification of fungal elements.

TREATMENT

TREATMENT OVERVIEW

Treatment is strongly advised to accelerate recovery and help minimize spread. The best treatment protocol combines 3 elements: topical, systemic, and environmental treatment. All treatments are continued until clinical (and preferably, mycologic) cure is effected, typically 8-16 weeks.

ACUTE GENERAL TREATMENT

- Topical therapy: kills infective material on the haircoat, but by itself may not speed resolution. Whole-body treatment (dip or rinse) is greatly preferred to spot treatment, which will miss areas of active infection. Any of the following whole-body treatments is recommended and applied twice weekly:
    - Lime-sulfur solution, 1/16 dilution (8 oz in 1 gal water; 30 mL in 480 mL water); do not rinse. Towel dry. In some countries, agricultural products are used. They are labeled 23% calcium polysulfide or 23% sulfur sulfide, which is equivalent to 76.9% lime sulfur solution. Therefore, the same dilution (1/16) is required to obtain a ~5 % solution.
    - Enilconazole topical solution, 0.2% (dilute per label instructions); in cats, prevent grooming with Elizabethan collar until dry.
    - Chlorhexidine + miconazole or chlorhexidine + ketoconazole shampoo or rinse (rinse preferred, use per label instructions).
    - Products based on chlorhexidine or miconazole alone are less effective and not recommended.
- Systemic therapy: shortens the disease course in each animal:
    - Itraconazole is the systemic drug of choice for cats; cost limits its use in dogs. Administer 5-10 mg/kg PO q 24 h for 7 days, then stop drug for 7 days, then treat again for 7 days, then stop for 7 days, then treat for a final 7 days. This week-on/week-off “pulse regimen” saves cost and is effective because the drug accumulates in hair and skin tissue. Animals unresponsive to this protocol may benefit from use of 10 mg/kg PO daily without pulse dosing.
    - Ketoconazole is a reasonable and often inexpensive choice for dogs (5-10 mg/kg PO q 24 h) but should not be used in cats because of frequent hepatotoxicity in this species.
    - Fluconazole may be less effective than other drugs but is rarely hepatotoxic. Administer to dogs or cats at 5-10 mg/kg

PO q 24 h.
    - Terbinafine is much less studied and may have adverse effects, but use is increasing owing to the recent appearance of inexpensive generic formulations. For cats, administer 30-40 mg/kg PO q 24 h; malaise and elevated ALT may occur in up to a third of animals. Terbinafine has been successful in some cats initially unresponsive to azole therapy; unstudied for use in canine dermatophytosis.
    - Griseofulvin: microsize formulation, 25 mg/kg/d (cats); 50-100 mg/kg/d (dogs). Ultramicrosize in PEG base formulation, 5-10 mg/kg/d (cats); 10-30 mg/kg/d (dogs). Teratogenic; do not administer to pregnant animals. Idiosyncratic myelosuppression may be seen in cats, especially those positive for FeLV or FIV.
    - Lufenuron, despite early reports to the contrary, is not effective in treatment or prevention of dermatophytosis in cats.
- Environmental treatment: helps prevent recurrence and spread to other individuals in the household. Effective disinfectants include diluted chlorine laundry bleach (final concentration 0.05% sodium hypochlorite; consult label, but this is most often 1/100 dilution); enilconazole environmental products are effective in countries where licensed. Other disinfectants labeled as effective against dermatophytes often have limited or no effectiveness under field conditions.
    - Typical household with one or a few cats: disinfection not critical; vacuum thoroughly, wipe down hard surfaces with disinfectant if possible.
    - Multianimal facility: *critical* to disinfect entire premises monthly during eradication efforts; see further reading below.
- Treatment of *kerion* is as listed above; *mycetoma* or *pseudomycetoma* require very long-term systemic treatment often combined with surgical debulking.

RECOMMENDED MONITORING

- Fungal culture: repeat after 2 months of treatment, then once monthly until culture is negative twice.
- Serum ALT: once monthly for all cats receiving terbinafine
- CBC: for all cats receiving griseofulvin; after 2 weeks of treatment, then once monthly.

PROGNOSIS AND OUTCOME

- Prognosis for most cases is good, except in immunocompromised animals.
- Especially in long-haired cats, a few animals require more intensive treatment and may take several years to resolve completely.

PEARLS & CONSIDERATIONS

COMMENTS

- Clipping of haircoat: necessity is controversial; it facilitates treatment but is unnecessary in most household situations.
- Eradication of dermatophytosis from an animal shelter or cattery is possible, but expensive and time consuming. Consult references (below and online) for detailed protocols.

TECHNICIAN TIPS

- Remember the potential both for zoonosis and contagion. Basic hygiene (gloves, handwashing) is important to prevent spread.
- Dermatophytosis is common in cats and often does not produce the classic “ring” lesion, whereas it is uncommon in dogs. Appropriate precautions should be implemented accordingly.

CLIENT EDUCATION

Clients should always be advised of the zoonotic nature of this disease, and prompted to seek medical advice if they have concerns or develop lesions.

SUGGESTED READING

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Dermatomyositis

BASIC INFORMATION

DEFINITION

Familial canine dermatomyositis is a hereditary, idiopathic inflammatory skin disease producing alopecia, erosions, and crusting, predominantly over bony prominences, tip of the tail, and pinnae in collies and Shetland sheepdogs. Histologically, myositis and vasculitis may be noted as the disease progresses. Acquired dermatomyositis may be rarely noted in other breeds.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs: primarily young dogs (<6 months old). The full extent of the disease is usually noted by 1 year. Number of lesions and severity usually decreases from then on.
- Cats: do not appear to get dermatomyositis.

GENETICS & BREED PREDISPOSITION

- Dermatomyositis is classically overrepresented in collies and Shetland sheepdogs, Beauceron shepherds, and their crossbreeds.
- Acquired dermatomyositis has been reported in Welsh corgis, Lakeland terriers, chow chows, German shepherds, Kuvasz, and Australian cattle dogs but has an unproven familial basis.

RISK FACTORS

Mechanical trauma and sunlight (UV) and reproductive stress (estrus, parturition, lactation) may worsen the lesions.

ASSOCIATED CONDITIONS & DISORDERS

Myositis and muscle atrophy may lead to dysphagia, megaesophagus with subsequent aspiration pneumonia, skeletal muscle weakness, and lameness.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Owner generally presents a young collie or Shetland sheepdog puppy with skin lesions over bony prominences, face, pinnae, and tip of the tail.
- Puppies may be painful or inappetent, the latter being directly related to the degree of myositis affecting pharyngeal muscles.

PHYSICAL EXAM FINDINGS

- Clinical signs wax and wane and vary from minor skin lesions (papules/rarely vesicles) to severe ulceration of the skin, with a generalized debilitating myositis affecting the head and distal limbs.
- Skin lesions are generally characterized by erosion and crusting around the eyes, on the bridge of the nose, lips, ear, bony prominences (elbows, hocks, digits), and the tail tip. Vesicles are occasionally noted.
- Pruritus is not normally present unless complicated by another condition such as pyoderma.
- Some dogs present with onychodystrophy (abnormal claw formation). Ulcers of the footpads are rarely noted.
- Healing may lead to scarring alopecia.
- Megaesophagus and aspiration pneumonia are occasionally noted.
- Stunted growth, lameness, and muscle wasting may occur as the disease progresses.
- Littermates may be affected to different degrees.

ETIOLOGY AND PATHOPHYSIOLOGY

- The condition is thought to be associated with a hereditary autosomal dominant trait of variable expression in affected collies and Shetland sheepdogs (chromosome 35 in the Shetland sheepdog).

- Most researchers believe the condition has an immune-mediated or autoimmune basis, although others have suggested that a viral or environmental trigger could be important.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A young collie or Shetland sheepdog presenting with facial, ear, and tail tip alopecia and erosion is strongly suggestive of dermatomyositis. This clinical picture should prompt clinician to perform a skin biopsy. Electrodiagnostic testing and muscle biopsy are used when signs of muscle dysfunction predominate (no skin lesions).

DIFFERENTIAL DIAGNOSIS

- Demodicosis
- Dermatophytosis
- Bacterial folliculitis
- *Malassezia* dermatitis
- Discoid lupus erythematosus
- Vasculitis

INITIAL DATABASE

- Skin cytologic preparations: no abnormal findings
- Skin scraping to rule out demodicosis
- Skin biopsy for histopathologic evaluation (may be nondiagnostic in mild cases). Characteristic hydropic degeneration in the basal cell layer, with a mild perivascular to interstitial dermatitis. Follicular atrophy may be noted in chronic lesions. Vasculitis is occasionally noted.
- CBC, serum biochemistry profile, urinalysis: usually within normal limits

ADVANCED OR CONFIRMATORY TESTING

- Electromyograms (see online chapter: Electromyography) are abnormal in cases with subclinical or clinical myositis.
- Muscle biopsy (see p. 1305) reveals myofibrillar degeneration and atrophy, with accumulations of mixed inflammatory cells.
- Neurologic examination is usually normal.

TREATMENT

TREATMENT OVERVIEW

The therapeutic goal is to minimize scarring of facial skin and debilitating myositis. Specific approaches vary, with some dermatologists using several drugs initially and tapering, while others begin with one or two and increase if needed.

ACUTE AND CHRONIC GENERAL TREATMENT

- Therapeutic options include the following drugs, which may be used alone or in combination, depending on the severity of the disease:
  - Pentoxifylline, 15-25 mg/kg PO q 8-12 h
  - Tetracycline and niacinamide *(adult dogs only):* given for minimum 3 months, weaning down based on a favorable response
    - >10 kg: 500 mg of each drug PO q 8 h
    - <10 kg: 250 mg of each drug PO q 8 h
- Vitamin E, 400-800 IU per day PO for minimum 1-2 months
- Omega-3 EFA (Derm Caps)
- Also used often, though with consideration given to risk of side effects (especially prednisone) and cost (cyclosporine):
  - Prednisone, 1-2 mg/kg PO q 12-24 h, weaning down to an alternate-day regimen based on a favorable response.
  - Cyclosporine (Atopica, Neoral): 5 mg/kg PO q 12-24 h
- Supportive care should be considered for all cases and can include controlling secondary infection with appropriate therapy and avoiding mechanical trauma to the face (avoid “gentle leaders”–type muzzle collars), aggressive bathing, or harsh shampoos.
- Soften dry foods and raise bowls to minimize dysphagia.

- Avoid intense sunlight.

POSSIBLE COMPLICATIONS

- Chronic prednisone use can cause iatrogenic hyperadrenocorticism and immune suppression.
- Pentoxifylline can cause gastric irritation, elevated coagulation times, and nervous irritability.
- Cyclosporine: diarrhea, vomiting, anorexia, gingival hyperplasia, and gingivitis are possible. Monitor for tumors.

RECOMMENDED MONITORING

Cyclosporine: check trough cyclosporine levels if adverse reactions are noted, particularly in collies; many are homozygous mutant for the ABCB1 (MDR1) gene, which may cause a marked increase in cyclosporine blood level (see p. 706).

PROGNOSIS AND OUTCOME

Prognosis is variable depending on severity. Mild cases may resolve without further problems, although scarring of the skin may be noted. Dogs with more severe skin lesions may be prone to recurrent skin problems. Cases with severe myositis have a poor prognosis for long-term survival.

PEARLS & CONSIDERATIONS

COMMENTS

- Facial skin lesions in a young Sheltie or collie are very evocative of demodicosis, whereas involvement of the tip of the tail and pinnae is much more suggestive of dermatomyositis.
- The waxing and waning nature of lesions renders evaluation of the efficacy of different drugs very difficult.

PREVENTION

- Do not breed affected individuals.
- Minimize exposure to UV light for affected individuals.

CLIENT EDUCATION

Affected individuals will likely require a higher level of skin care than unaffected dogs.

SUGGESTED READING

Clark LA, Credille KM, Murphy KE, et al: Linkage of dermatomyositis in the Shetland sheepdog to chromosome 35. Vet Dermatol 16:392–394, 2005.

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Demodicosis

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Demodicosis is a common inflammatory disease associated with an increase in the number of *Demodex* mites found on the skin.

SYNONYM

Demodectic mange

EPIDEMIOLOGY

SPECIES, AGE, SEX

- *Demodex canis* mites are present in small numbers on the skin of most healthy dogs. Transmission occurs from bitch to pups within 3 days of birth.
- Juvenile demodicosis is often first noted by 3-6 months of age.
- Adult-onset demodicosis usually occurs in middle-aged to old dogs and is associated with internal disease and immunosuppression.

GENETICS & BREED PREDISPOSITION

- Dogs affected with juvenile-onset generalized demodicosis, their siblings, and their parents should not be bred; hereditary predisposition is likely.
- Purebred dogs are predisposed for juvenile-onset demodicosis; overrepresented dog breeds may include short-coated dogs such as American Staffordshire terriers, boxers, pit bull terriers, and shar peis.

RISK FACTORS

Poorly characterized immunologic factors influenced by genetics. Concurrent immunosuppressive diseases, states, or treatments.

CONTAGION & ZOONOSIS

Canine demodicosis not considered contagious to immunocompetent animals. *Demodex gatoi*, however, is transmissible to normal in-contact cats.

GEOGRAPHY AND SEASONALITY

D. gatoi is common in the southeastern United States but very rare in many other parts of North America.

ASSOCIATED CONDITIONS & DISORDERS

Canine demodicosis is very frequently complicated by pyoderma.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Canine:

- Juvenile demodicosis: *D. canis* (usually <18 months of age)
  - Localized: one to several small areas of alopecia, most commonly on face and forelegs
  - Generalized: entire body region, complete involvement of two or more feet, or more than six lesions. Often more severe skin lesions and secondary pyoderma.
- Adult-onset demodicosis: *D. canis* (usually >4 years of age)
  - Usually generalized
- Other:

- *Demodex injai:* large follicular mite, often present in low numbers and associated with pruritus and greasy skin on the dorsal trunk of terriers, particularly West Highland white terriers and fox terriers
- A short-bodied *Demodex* mite (tentatively named *D. cornei* because of its likely residence in the stratum corneum) is reported to coinfect the skin of some dogs with *D. canis*.

Feline:

- *Demodex cati:* often associated with immunosuppressive disease, may also cause ceruminous otitis externa
- *D. gatoi:* pruritic, contagious

HISTORY, CHIEF COMPLAINT

- Chief complaint is typically hair loss, but may be pruritus or other skin lesions.
- Pruritus may be absent in canine demodicosis but is very common if secondary pyoderma is present.
- Pruritus is a major feature of *D. gatoi* infestation in cats and of *D. injai* infestation in dogs.
- Malaise may accompany severe cases of generalized canine demodicosis, likely due to severe secondary pyoderma.
- In adult-onset demodicosis, signs caused by underlying disease (e.g., hyperadrenocorticism) or history of immunosuppressive treatment may be present.

PHYSICAL EXAM FINDINGS

Canine:

- Localized demodicosis: several small areas of patchy alopecia, mild erythema, scaling, and variable hyperpigmentation on the face or forelimbs.
- Generalized demodicosis: lesions may be similar but are usually more severe and extensive and complicated by pyoderma. Comedones, papules, pustules, follicular casts, plaques, crusts, edema, and deep folliculitis/furunculosis are common. Peripheral lymphadenopathy, pain, pruritus, and malaise may also be present. In adult-onset cases, physical changes associated with underlying disease (e.g., hyperadrenocorticism, neoplasia) may be found.
- *D. injai:* greasy skin and pruritus on dorsal trunk

Feline:

- *D. cati:* patchy alopecia or ceruminous otitis
- *D. gatoi:* excoriations, symmetrical self-induced alopecia

ETIOLOGY AND PATHOPHYSIOLOGY

- The immune system defect in demodicosis is still poorly understood (likely a mite-specific deficiency in T-lymphocyte function).
- In adult dogs, changes in the immune system relating to internal systemic disease or drug therapy allow the mites to proliferate. Previous corticosteroid administration is a common cause. Less common are spontaneous hyperadrenocorticism, hypothyroidism, concurrent parasites, and neoplasia.
- Poor nutrition, estrus, parturition, and stress also contribute.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

In most cases, canine demodicosis is a straightforward diagnosis, so long as skin scrapings are not overlooked. Diagnostic cornerstones are the presence of cutaneous lesions and associated mites demonstrated on skin scrapings. Al though *D. canis* is a normal skin inhabitant, it is rare to find mites unless there is overgrowth.

DIFFERENTIAL DIAGNOSIS

Uncomplicated demodicosis resembles many other skin disorders, which emphasizes the value of skin scrapings.

Dogs:

- Bacterial folliculitis
- Dermatophytosis

- Dermatomyositis
- Pemphigus foliaceus and other immune-mediated diseases
- Sebaceous adenitis

Cats:

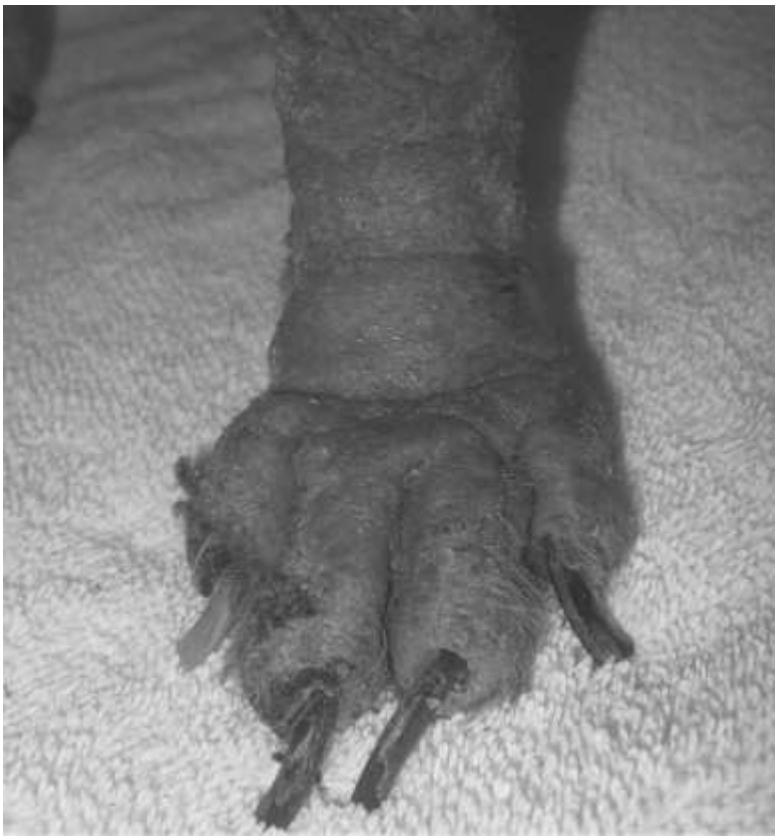
- Hypersensitivity disorders and other ectoparasites *(D. gatoi)*
- Psychogenic (symmetrical) alopecia *(D. gatoi)*
- Dermatophytosis *(D. cati)*

INITIAL DATABASE

- Deep skin scrapings from at least three sites for most species of *Demodex* mites.
    - Skin should be squeezed to express mites from the hair follicles immediately before and/or during scraping, and scraping should continue until mild capillary bleeding is seen.
    - A subjective assessment of mite numbers (0-4+) and the proportion of live mites as well as juvenile mites is important for baseline and subsequent monitoring of therapy.
- In sensitive areas, a trichogram (forceful hair pluck) can reveal the mites but is generally less rewarding than skin scrapings.
- If trichography is negative, skin scrapings should be collected using sedation.

ADVANCED OR CONFIRMATORY TESTING

- Skin biopsies may be needed to find mites when extensive scarring is present (particularly with pedal involvement). Always scrape before collecting biopsies, as histopathologic evaluation usually is not necessary to diagnose this disease.
- Adult-onset demodicosis cases warrant a full diagnostic workup for internal disease as deemed appropriate, including CBC, chemistry profile, urinalysis, imaging, screening tests for endocrinopathies, and FeLV/FIV evaluation in cats.
- In cats suspected of *D. gatoi* infestation, mites are easy to miss owing to removal by licking. If broad superficial skin scrapings, acetate tape preparations, and fecal flotation are negative, a series of weekly lime sulfur dips is used in endemic areas.



DEMODICOSIS Pododemodicosis can resemble many other conditions. Skin scrapings and trichograms should be collected in dogs of any age presenting with pedal lesions.

TREATMENT

TREATMENT OVERVIEW

- Generalized demodicosis requires miticidal therapy and can be a challenging condition to treat.
- Most cases of localized demodicosis will resolve spontaneously as the immune system matures.
- Treatment for underlying or concurrent disease, or discontinuation of immunosuppressive therapy in adult patients.
- Concurrent pyoderma must be treated, and this component of therapy is often most important in restoring normal skin appearance.
- A "cure" means that there is no relapse within 1 year.

ACUTE AND CHRONIC TREATMENT

- Localized demodicosis does not require treatment; topical antimicrobial agents such as benzoyl peroxide gel or mupirocin may be used.
- Therapy for generalized canine demodicosis requires several months and commitment on the part of the owner. All treatments should continue until two consecutive sets of skin scrapings are negative, or for at least 1 month beyond a set of negative skin scrapings.
- Response to therapy is monitored by clinical improvement and monthly skin scrapings.

Options include:

- Amitraz dips:
  - Used in dogs
  - Approved for canine demodicosis, but side effects and the risk to the handler are of concern (see Possible Complications)
  - Labeled for use as a 0.025% dip every 14 days in dogs >4 months of age
  - Increasing the concentration and frequency is associated with a higher success rate.
  - Environmental Protection Agency (EPA)-registered pesticide, so a violation of U.S. federal law to use it in a manner inconsistent with labeling
  - In very small dogs, treat only half the body at a time to minimize the risk of side effects.
  - Clip long-haired dogs and shampoo all dogs (benzoyl peroxide) prior to dipping
- Oral ivermectin (e.g., 10 mg/mL bovine injectable solution):
  - Used off-label in dogs
  - Best studied of the oral treatments
  - Effective at 0.3-0.6 mg/kg PO q 24 h
  - Incrementally increase to full dose over 7-10 days
  - Contraindicated in certain dogs (see Possible Complications)
- Oral milbemycin (oral monthly heartworm preventative):
  - Used off-label in dogs
  - Acceptable alternative at 0.5-2 mg/kg PO q 24 h; greater success at higher end of dose
  - Must be used with caution in certain dogs (see Possible Complications)
- Oral moxidectin (e.g., 10 mg/mL bovine injectable solution):
  - Used off-label in dogs
  - Effective at 0.4 mg/kg PO q 24 h
  - Same contraindications as ivermectin (see Possible Complications)
- Injectable doramectin (e.g., 10 mg/mL bovine/swine injectable solution)
  - Used to a limited degree off-label in dogs and cats (for *D. cati*)
  - Dosed at 0.6 mg/kg SQ once weekly
  - Same contraindications as ivermectin (see Possible Complications)
- Topical metaflumizone and amitraz (ProMeris)
  - Labeled in the United States for dogs with demodicosis
  - Promising results in preliminary studies
  - Monthly topical application (EPA-registered pesticide, so adhere to label)
- Topical imidacloprid and moxidectin (Advantage Multi, Advocate)
  - Labeled for dogs with demodicosis in several countries (not United States)
  - Studies suggest that monthly topical application (as labeled) is insufficient.
- Lime sulfur dips
  - Weekly for 4-6 weeks; treatment of choice for *D. gatoi* infestation and also used for *D. cati*
- Pyoderma may be a substantial secondary problem in dogs; antibiotic therapy should be continued until hair is regrowing.
- In adult-onset cases, strive for control of the underlying disease.

POSSIBLE COMPLICATIONS

- Macrocyclic lactones (ivermectin, oral moxidectin, doramectin, milbemycin [see p. 625]): monitor carefully for neurotoxicity, and educate clients about potential signs. All patients should be heartworm negative. Oral ivermectin and moxidectin can be started at a low dose (e.g., 1/10 of intended volume) and incrementally increased over 7-10 days to avoid the most severe side effects. Listed doses of oral ivermectin, moxidectin, and injectable doramectin should not be used in dogs homozygous for the MDR-1 mutation. However, these patients may tolerate topical moxidectin (Advantage Multi, Advocate) at labelled doses and may tolerate low-dose oral milbemycin (0.5 mg/kg PO q 24 hr, use with caution). See MDR1 Mutation (p. 706).
- Chronic toxicosis (several weeks into therapy) is generally less severe and not associated with MDR-1 mutations.
- Macrocyclic lactone toxicity can be induced in normal dogs by coadministration with p-glycoprotein inhibitors such as ketoconazole and cyclosporine. Coadministration of spinosad is also contraindicated.
- Side effects of amitraz are due to its monoamine oxidase (MAO) inhibitor or alpha-2 adrenergic agonist properties. They include sedation, depression, bradycardia, pruritus, vomiting/diarrhea, and hyperglycemia (avoid in diabetics). Atipamezole can be used as an antidote at 50 mcg/kg IM. Coadministration of MAO inhibitors, including some sedatives, antidepressants, and deprenyl, should be avoided. The dip must be applied in a well-ventilated area using gloves and should be avoided by people with Parkinson's disease, diabetes, respiratory disease, or those taking interacting medications.

RECOMMENDED MONITORING

Skin scrapings are performed every 2-4 weeks during therapy. At this time, score the approximate numbers of mites, the proportion of live mites, the proportion of adults versus immature mites, and the numbers of eggs. Adjust therapy if parameters are not improving.

PROGNOSIS AND OUTCOME

- For most cases of localized juvenile demodicosis, the prognosis is excellent. The prognosis for generalized juvenile cases is good, but a small proportion cannot be cured and require long-term treatment.
- In all cases of adult-onset demodicosis, the prognosis is guarded.

PEARLS & CONSIDERATIONS

COMMENTS

- MDR-1 (ABCB1) testing is available from the Washington State University College of Veterinary Medicine Clinical Pharmacology Laboratory (www.vetmed.wsu.edu/depts-VCPL/test.aspx).
- Remember hair plucks (trichography) as an alternate way of looking for *Demodex* in dogs.
- Scrape greasy terriers, even if alopecia is not a feature, to look for *D. injai*.
- Do not discontinue antibiotic therapy prematurely.
- In *D. gatoi*–endemic areas, weekly lime sulfur dips are part of the workup for pruritic cats.
- *D. canis* mites are usually easy to find, so skin scrapings should be part of the workup of most dermatology patients. Do not miss this important step.

TECHNICIAN TIPS

- For a skin scraping to be considered negative, it must demonstrate no mites whatsoever. Finding dead mites, or just mite segments, is still a positive scraping.
- When assessing skin scrapings, methodically scan the entire slide.
- *Demodex* mite eggs are fusiform (spindle- or lemon-shaped) and are important to note, as they indicate an actively reproducing population.
- Counsel owners on risks of therapy to their pets (all treatments) and themselves (amitraz dips).

SUGGESTED READING

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Dehydration

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Dehydration occurs when fluid losses (sensible loss [renal] and insensible loss [normally daily gastrointestinal, respiratory]) exceed fluid intake.

SYNONYMS

Decreased circulating blood volume, negative fluid balance

EPIDEMIOLOGY

SPECIES, AGE, SEX

All animals are susceptible to dehydration, depending on the underlying disease process. Due to a high body surface area–to-volume ratio, smaller animals (<10 kg) are more prone to dehydration.

RISK FACTORS

- Diseases and toxins that affect appetite, decreased water ingestion, decreased renal and intestinal conservation of water, and poor vascular integrity predispose to dehydration.
- Infectious diseases such as parvoviral enteritis and coccidiosis; metabolic disturbances resulting from diseases, such as renal failure or hypoadrenocorticism; endocrinopathies such as diabetes mellitus or insipidus; intoxications with substances such as ethylene glycol; and any cause of decreased water and food intake can all result in dehydration.

CONTAGION & ZOONOSIS

Some of the diseases that cause dehydration (such as parvoviral enteritis and leptospirosis) can be contagious to other pets and/or have zoonotic potential.

GEOGRAPHY AND SEASONALITY

- Hotter weather in the summer may make a sick animal become dehydrated more rapidly.
- Frozen water bowls in the winter may cause pets to become dehydrated.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Hypertonic dehydration, isotonic dehydration, hypotonic dehydration

HISTORY, CHIEF COMPLAINT

Anorexia, vomiting, diarrhea, lethargy, weakness, panting

PHYSICAL EXAM FINDINGS

Lethargy, dry/tacky mucous membranes, tachycardia, poor pulse quality, skin tenting, sunken eyes/enophthalmos, and weight loss. The approximate level of dehydration is estimated based on the following physical exam findings: 5% = dry/tacky mucous membranes; 6%-8% = dry mucous membranes and delayed skin tent test, 10%-12% = the patient is in hypovolemic shock, and signs include all of the above plus bilaterally symmetric enophthalmos, tachycardia (dogs), weakness, slow capillary refill time, poor pulse, and lethargy or obtundation.

ETIOLOGY AND PATHOPHYSIOLOGY

Etiology:

- Lack of intake; no access to water
- Gastroenteritis (clostridial, parvoviral, parasitic, foreign body-induced, obstruction-induced)
- Renal failure (acute, chronic)
- Endocrine disease (hypoadrenocorticism, diabetes mellitus or insipidus)
- Intoxication (ethylene glycol, salt water ingestion, or any other toxin that causes vomiting, diarrhea, or renal failure)

Mechanism:

Regardless of cause, dehydration results in a decrease in circulating blood volume, which directly affects perfusion and oxygen delivery to essential tissues/organs. Mild cases may be clinically insignificant, but in moderate or severe dehydration, the metabolic processes in hypoperfused tissues must then rely on anaerobic pathways to produce adenosine triphosphate, which is a less efficient process. Furthermore, a byproduct of anaerobic metabolic pathways is lactic acid, which accumulates in states of decreased perfusion and results in metabolic acidosis.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Since dehydration is unlikely to be a primary problem, a diagnostic search for an underlying cause or syndrome is always warranted. Many of the possible causes of dehydration can be ruled out simply with history and physical examination.

DIFFERENTIAL DIAGNOSIS

- Skin tent: old age, thin/emaciated body condition (false increase), obesity (false decrease)
- Tacky mucous membranes: may occur in healthy individuals

INITIAL DATABASE

CBC, serum biochemical profile, urinalysis, fecal exam

ADVANCED OR CONFIRMATORY TESTING

Urine/fecal culture, thoracic and abdominal radiographs, abdominal ultrasound, adrenocorticotropic hormone stimulation testing, ethylene glycol testing, parvoviral fecal antigen testing, *Giardia* antigen testing gastrointestinal barium series—all as dictated by initial diagnostic information and case evolution.

TREATMENT

TREATMENT OVERVIEW

- Fluid replacement
- Correction of electrolyte abnormalities
- Treatment of underlying disease

ACUTE GENERAL TREATMENT

- Fluid replacement with an isotonic crystalloid such as lactated Ringer's solution, Normosol-R, or 0.9% sodium chloride
- Maintenance rate and dehydration replacement must be calculated.
- Dehydration volume is delivered over 24-48 hours and is added to maintenance rates.
- Maintenance rate = 40 mL/kg/24 hours for large dogs (>10 kg), 60 mL/kg/24 hours for cats and small dogs (<10 kg)
- Dehydration replacement volume (mL) = % dehydration as a decimal (e.g., 10% is 0.1) × body weight in kg × 1000
- Adjustment of fluid rate and frequent, close monitoring of respiratory rate and comfort if heart disease, renal disease, or systemic hypertension is present
- Electrolyte replacement:
    - Do not supplement potassium at a rate of >0.5 mEq/kg/h.
    - Do not raise or lower serum sodium at a rate of >1 mEq/L/h.

NUTRITION/DIET

If vomiting has resolved, gradual access to water for oral intake is recommended.

CHRONIC TREATMENT

Depends on underlying disease process

DRUG INTERACTIONS

Do not add sodium bicarbonate to calcium-containing fluids (precipitation reaction).

POSSIBLE COMPLICATIONS

Overhydration: pulmonary edema, pleural or peritoneal effusion, hemodilution, cerebral edema, peripheral edema. Monitor more closely if heart or renal disease; consider colloidal therapy (plasma, albumin, hetastarch) if hypoalbuminemia is present.

RECOMMENDED MONITORING

Body weight, urine output, heart rate, pulse quality, capillary refill time, skin turgor, blood pressure, packed cell volume/total solids, blood urea nitrogen, creatinine

PROGNOSIS AND OUTCOME

Prognosis is good if the underlying disease process is identified and can be corrected.

PEARLS & CONSIDERATIONS

COMMENTS

Recheck electrolyte (sodium, potassium, chloride, and phosphorus) imbalances and acid-base status frequently (every 4-8 hours) during the first 24 hours of therapy to ensure treatment goals are being achieved. Body weight and urine output are among the easiest and most accurate ways to gauge the level of hydration.

PREVENTION

See specific disease information.

TECHNICIAN TIP

Assessing hydration status by skin turgor alone can be misleading, especially in cachectic patients, as the decreased fat content in their subcutaneous tissues will make them appear dehydrated no matter what their hydration status is. The conjunctival mucous membranes are often most reliable (barring ocular disease) because oral mucous membranes are prone to drying (open-mouth breathing/panting in dogs) or coating with mucus (vomiting).

CLIENT EDUCATION

Anorexic animals or those vomiting and having diarrhea (especially very young or very old) can become dehydrated quickly and should be examined by a veterinarian as soon as possible.

SUGGESTED READING

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Degenerative Myelopathy

Additional Images Available on Website

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Canine degenerative myelopathy is an inherited degenerative disease, most severely affecting the thoracolumbar spinal cord.

SYNONYMS

Canine degenerative radiculomyelopathy, German shepherd dog myelopathy

EPIDEMIOLOGY

SPECIES, AGE, SEX

Canine; age usually 8 years or older; mean age 9 years

GENETICS & BREED PREDISPOSITION

- Presumed autosomal recessive with a mutation discovered in the canine superoxide dismutase 1 *(SOD1)* gene
- The genetic mutation is similar to some forms of human amyotrophic lateral sclerosis (Lou Gehrig's disease)
- Breed predisposition: purebred dogs—German shepherd, Pembroke and Cardigan Welsh corgi, standard poodle, Rhodesian ridgeback, collie, boxer, Chesapeake Bay retriever, Irish setter, Bernese Mountain dog, mixed breed, wire fox terrier, Kerry blue terrier

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Progressive weakness of pelvic limbs
- Initially, affected dogs will drag nails and show pelvic limb ataxia.
- Difficulty jumping
- The disease results in a progressive paraparesis to paraplegia over 6-12 months from time of suspected diagnosis.
- If signs are allowed to progress, the thoracic limbs will eventually become affected.

PHYSICAL EXAM FINDINGS

- Pelvic limb tremors
- Asymmetric truncal general proprioceptive (GP) ataxia to severe paraparesis and paraplegia
- Upper motor neuron spastic paraparesis (long stride length)
- Postural reaction deficits (e.g., toe dragging, absent conscious proprioception)
- Spinal reflexes present or exaggerated
- Patellar reflex may be decreased to absent
- Variable presence of crossed extensor reflex in pelvic limbs
- Disuse muscle atrophy of pelvic limbs which progresses to neurogenic muscle atrophy
- Absence of paraspinal hyperesthesia
- Urinary and fecal incontinence in later disease stage
- If euthanasia is delayed, the clinical signs will ascend, causing flaccid tetra-paresis and other lower motor neuron signs.
- Dogs at end stage may also have swallowing and respiratory dysfunction.

ETIOLOGY AND PATHOPHYSIOLOGY

- The etiology of degenerative myelopathy is a genetic mutation in the superoxide dismutase 1 *(SOD1)* gene, resulting in a toxic gain of function (the mutation results in misfolding of *SOD1*, causing abnormal accumulations of aggregates in the neuron).
- Dogs homozygous for the mutation are at risk for development of degenerative myelopathy.
- Neuropathologic lesion distribution in the CNS involves axons and myelin in all funiculi of the spinal cord; most severe in the dorsal funiculus and dorsal portion of the lateral funiculus of the thoracolumbar spinal cord.

- Neurons in degenerative myelopathy–affected dogs contain cytoplasmic aggregates that stain with anti-*SOD1* antibodies.
- Some studies have shown degenerative changes in some neurons of the brainstem.
- Peripheral nerves show nerve fiber loss reflective of axonal degeneration and secondary demyelination.
- Muscle specimens show excessive variability in myofiber size, with large and small groups of atrophic fibers.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis of degenerative myelopathy is based on exclusion of other disorders that mimic it. The genetic test may assist with interpretation of clinical signs and diagnostic testing toward a presumptive diagnosis of degenerative myelopathy.

DIFFERENTIAL DIAGNOSIS

Other spinal cord disorders mimic signs of degenerative myelopathy:

- Intervertebral disk disease: Hansen type II
- Inflammatory disease of the spinal cord: myelitis
- Spinal cord neoplasia
- Degenerative lumbosacral stenosis
- Hip dysplasia
- Other coexisting orthopedic diseases

INITIAL DATABASE

- Neurologic examination (see p. 1311).
  - See Physical Exam Findings above for clinical findings.
    - Nonpainful progressive myelopathy
  - Neuroanatomic localization: initial disease stage—upper motor neuron signs (T3 to L3 spinal cord segments); later disease stage involves lower motor neuron signs to the pelvic limbs; end stage—generalized lower motor neuron signs.
- Clinical pathologic tests: generally unremarkable
- Thoracic radiography
  - Screening for metastatic neoplasia (central nervous system neoplasia differential diagnosis)
- Genetic testing
  - Dogs that test homozygous for the mutation are AT RISK for developing degenerative myelopathy. Not all dogs that test AT RISK will develop degenerative myelopathy
  - A direct mutation test for a susceptibility gene is offered. For recessive diseases, the results are expressed as follows:
    - Normal—homozygous for the normal gene
    - Carrier—heterozygous with one copy of the normal and mutated gene
    - AT RISK—homozygous for the mutated gene

ADVANCED OR CONFIRMATORY TESTING

- Clinical working diagnosis is based on ruling out other diseases that cause progressive myelopathy.
- Cerebrospinal fluid analysis: may show increased protein concentration.
- Electrophysiologic testing
  - Electromyography and nerve conduction studies (see p. 1253)
  - Used for ruling out other neuropathic disorders
  - In later disease stage, dogs with degenerative myelopathy will show evidence of axonopathy.
- Survey spinal radiography
- Myelography: no evidence of a compressive myelopathy
- Advanced imaging: no evidence of a compressive myelopathy
  - CT combined with myelography
  - MRI
- Definitive diagnosis is only ever determined postmortem by histopathologic examination of the spinal cord.

TREATMENT

TREATMENT OVERVIEW

There are no proven effective therapies for degenerative myelopathy. Supportive and palliative care are provided to maintain quality of life.

ACUTE AND CHRONIC TREATMENT

Exercise, vitamin supplementation (B12, E, and C), and protease inhibitors (aminocaproic acid) have been advocated as potential therapies. Disclaimer: Although the following drugs have been recommended as supplements in dogs with degenerative myelopathy, efficacy still remains to be proven.

- Aminocaproic acid (500 mg/dog; 15 mg/kg PO q 8 h)
- Vitamin E (1000-2000 IU/dog PO q 24 h)
- Vitamin B12 (100-200 mcg/dog PO q 24 h)
- Encourage exercise and physical rehabilitation to slow onset of disuse muscle atrophy
- Assistive walking devices enable ambulation support and may improve quality of life.
- Monitor for urinary and fecal incontinence:
    - Basic nursing care and hygiene if incontinence occurs, to prevent the onset of urine scald, infected decubital ulcers, or similar skin lesions
- When patient becomes nonambulatory, keep on a well-padded surface.

POSSIBLE COMPLICATIONS

- Urinary tract infections
- Decubital ulcer formation (see p. 174)

RECOMMENDED MONITORING

- Monitor for secondary urinary tract infection
- Monitor for proper nursing care

PROGNOSIS AND OUTCOME

- Long-term prognosis is considered poor.
- Dogs often lose their ability to ambulate in the pelvic within 6-12 months from time of diagnosis.
- The disease eventually will progress to affect the thoracic limbs.
- Owners of large-breed dogs often will elect for euthanasia when their dog needs ambulatory assistance.

PEARLS & CONSIDERATIONS

COMMENTS

- Lack of paraspinal hyperesthesia is a key clinical feature of degenerative myelopathy.
- A suspected diagnosis is based on exclusion of other spinal cord disorders.

TECHNICIAN TIPS

- Physical rehabilitation (see p. 1329) using light exercise may improve the patient's quality of life.
- The patient will need to be closely monitored for urine scald and decubitus ulceration when the disease progresses to lower motor neuron involvement.

CLIENT EDUCATION

- Meticulous nursing care is essential in the recumbent patient.
    - Keep patient clean and dry to prevent urine scald.
    - Keep patient on a protective surface (optimize padding, traction, and ease of cleaning).
- A sling with wheels or a cart may assist with patient mobility.
- Physical therapy using range-of-motion and isometric exercises will help maintain joint flexibility and muscle strength (see p. 1329).

SUGGESTED READING

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Decongestant Toxicosis

BASIC INFORMATION

DEFINITION

Common decongestants are pseudoephedrine, ephedrine, phenylephrine, and imidazoline derivatives (oxymetazoline, naphazoline, tetrahydrozoline, xylometazoline). They are active ingredients in over-the-counter (OTC) human medications used for the treatment of cold, flu, sinusitis, and allergies. Toxicosis from other active ingredients is discussed separately ().

EPIDEMIOLOGY

SPECIES, AGE, SEX

All species, breeds, and both sexes are susceptible; dogs are more likely to be involved, based on their predilection for dietary indiscretion.

RISK FACTORS

Preexisting cardiac disease, systemic hypertension, and seizure disorders may exacerbate signs of toxicosis.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Direct observation or indirect evidence of exposure
- Pseudoephedrine: rapid onset (within 15-30 minutes with immediate release products; 3-6 hours with extended-release medications) of agitation, hyperactivity, restlessness, panting, mydriasis, shaking, circling or head bobbing
- Phenylephrine: less likely to result in clinical effects, owing to enterohepatic degradation by monoamine oxidases and resultant poor bioavailability (38%) and lack of norepinephrine release (hyperactivity, pacing, shaking)
- Imidazoline decongestants: rapid onset (within 60 minutes; not expected after 3-4 hours) of vomiting, weakness, collapse

PHYSICAL EXAM FINDINGS

- Pseudoephedrine/phenylephrine: as above, plus injected mucous membranes, hyperthermia, tachycardia or reflex bradycardia; less commonly lethargy and staring
- Phenylephrine: as above, plus tachycardia, mydriasis
- Imidazoline: weakness, lethargy, bradycardia, hypotension, prolonged capillary refill time; less commonly hypertension, panting, nervousness, hyperactivity, and shaking

ETIOLOGY AND PATHOPHYSIOLOGY

Source:

- Toxicosis can occur either when animals accidentally ingest OTC medications or are mistakenly given the medication.
- Decongestants stimulate alpha-adrenergic receptors, resulting in vasoconstriction of arterioles in the nasal passages, thus improving air flow.
    - Pseudoephedrine, ephedrine (stereoisomer), ma huang (a herbal form of ephedra). Pseudoephedrine is available as a hydrochloride or sulfate salt. It is found as a single ingredient (30-mg or 60-mg regular pill), or extended-release (120 mg as 12-hour pill or 240 mg as 24-hour pill) or as a liquid (varying concentration). It is more commonly available in combination with other ingredients (cough suppressants, antihistamines, acetaminophen, ibuprofen). Common brand names of products that contain pseudoephedrine include Sudafed, Afrin, Tylenol, Vicks, Alka-Seltzer, and Contac.
    - Phenylephrine is available for oral use (mostly 5- to 15-mg tablets), nasal sprays (0.25%-1%), or eye drops (0.1%). It is available in combination with other medications (antihistamines, cough suppressants, pain killers).
    - Imidazoline decongestant examples are oxymetazoline, tetrahydrozoline, naphazoline, and xylometazoline. These are available as nasal and ophthalmic solutions of varying concentrations (0.01%-0.1%).

Mechanism of Toxicosis:

- Adverse effects are dose-dependent and reflect excessive stimulation of the adrenergic nervous system.
- With pseudoephedrine, the release of norepinephrine increases the potential for central nervous system stimulation. Ingestion of >3 mg/kg in an otherwise healthy dog typically warrants decontamination of the patient and close monitoring.
- With imidazoline decongestants, overdoses cause excess stimulation of central alpha-2 receptors, which results in hypotension. The margin of safety is very narrow with these agents, with ingestion of even a small amount potentially resulting in toxicosis.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is suspected based on a combination of evidence of exposure along with presence of consistent signs. OTC urine drug-test kits can detect pseudoephedrine, or it can be detected in plasma at a diagnostic laboratory (can help determine exposure).

DIFFERENTIAL DIAGNOSIS

Toxicologic:

- Pseudoephedrine/ephedrine/phenylephrine: amphetamines, antihistamines, cocaine, metaldehyde, methylxanthines, phenylpropanolamine, strychnine
- Imidazoline: alcohols, amitraz, barbiturates, benzodiazepines, calcium channel blockers, clonidine, essential oils, medetomidine, xylazine

Spontaneous, nontoxicologic:

- Pseudoephedrine/phenylephrine: pheochromocytoma, renal disease, intracranial disease
- Imidazoline: hypoadrenocorticism, advanced cardiovascular disease/cardiogenic shock, sepsis, hypovolemic shock, trauma

INITIAL DATABASE

- CBC
- Serum biochemistry profile
- Arterial blood pressure
- ECG (heart rate and rhythm)
- Body temperature

ADVANCED OR CONFIRMATORY TESTING

Urine drug screening with OTC test kit (optional)

TREATMENT

TREATMENT OVERVIEW

Treatment is indicated based on clinical suspicion (history and physical examination), without urine test confirmation. Treatment may consist of patient decontamination alone (emesis and administration of activated charcoal) if clinical signs are absent, or decontamination and management of cardiovascular and CNS aberrations and thermoregulation if clinical signs are present.

ACUTE GENERAL TREATMENT

- Decontamination of patient:
  - Pseudoephedrine/ephedrine/phenylephrine:
    - Induction of emesis (see p. 1364) with 3% hydrogen peroxide, 2 mL/kg PO 1-2 times to effect, maximum of 45 mL; useful only in asymptomatic animals within 1 hour of ingestion of immediate-release products and within a couple of hours of extended-release products.
    - Activated charcoal (1-2 g/kg granules or 6.6-11 mL/kg of 10% solution with sorbitol or other cathartic PO). Repeat (3.3-5.5 mL/kg without cathartic PO) once 6-8 hours after initial administration if extended-release decongestant.
    - Acidification of urine (use only if facility to run blood gases available): ammonium chloride, 50 mg/kg PO q 6 h; or ascorbic acid, 30 mg/kg PO q 8 h to promote excretion (ion trapping).

        - Control CNS excitation (note: phenothiazines are drugs of choice for controlling CNS excitation: acepromazine, 0.02-0.05 mg/kg IV, IM, repeat as needed; useful for mild hypertension and CNS stimulatory signs; or chlorpromazine, 0.5-1 mg/kg IV.
        - Control tachycardia: propranolol, 0.02-0.04 mg/kg IV, repeat in 4-8 hours; or use esmolol, 0.2-0.5 mg/kg IV or 25-200 mcg/kg/min IV as constant rate infusion.
    - Imidazoline decongestants:
        - Due to the rapid onset of signs after imidazoline decongestant ingestion, emesis and charcoal are generally not recommended.
- Specific treatment:
    - Imidazoline decongestants:
        - Atipamezole (50 mcg/kg IM to effect for hypotension); may be repeated as needed for life-threatening hypotension and bradycardia. A quarter to a third of the dose may be given IV for rapid effect, and the remainder IM.
        - Yohimbine: 0.1 mg/kg IV; repeat in 2-3 hours if needed. Use if atipamezole is not available.
- Supportive care for all decongestant exposures:
    - Intravenous fluid therapy
    - Thermoregulation: cool fluids, external cooling measures as needed
    - Keep the patient calm and reduce external stimuli (quiet surroundings).

DRUG INTERACTIONS

- Diazepam: paradoxical response (when given at high doses or when given too fast) may add to stimulatory signs from pseudoephedrine/ephedrine/phenylephrine.
- Propranolol: contraindicated if systemic hypertension is present (beta-2 blockade in vessels may cause vasoconstriction and worsen the hypertension).
- Atropine: contraindicated for reflex bradycardia due to hypertension.

POSSIBLE COMPLICATIONS

- Disseminated intravascular coagulation (DIC) due to hyperthermia
- Permanent brain damage from prolonged stimulation
- Renal failure from systemic hypo- or hypertension and/or rhabdomyolysis

RECOMMENDED MONITORING

- Heart rate/rhythm
- Blood pressure
- Body temperature
- Mentation
- Serum biochemistry profile, including electrolytes
- Acid-base status if acidifying urine

PROGNOSIS AND OUTCOME

Generally favorable with prompt presentation and appropriate care. Presence of head bobbing, circling, or DIC carries a poor prognosis. Pseudoephedrine exposures exceeding 10 mg/kg are potentially lethal without treatment.

PEARLS & CONSIDERATIONS

COMMENTS

- The use and availability of pseudoephedrine in several U.S. states has been restricted because of alleged use of this medication in illegal amphetamine synthesis. Pseudoephedrine is being replaced by phenylephrine.
- Other agents (nonsteroidal antiinflammatory drugs [p. 768], antihistamines [p. 87], cough suppressants) may also cause toxicosis if a combination product was ingested; be sure to monitor for signs and treat accordingly.
- The signs of pseudoephedrine toxicosis are very similar to amphetamine toxicosis in dogs.
- Several weight-loss OTC products contain varying levels of ma huang, a natural source of ephedrine.

TECHNICIAN TIPS

The over-the-counter availability of these medications may give owners the wrong impression that they are harmless. Any casual mention by an owner of this type of medication is worth discussing with the veterinarian, especially if physical signs compatible with toxicosis are present.

PREVENTION

- Keep medications out of animal's reach.
- Awareness of where pets roam when unsupervised
- Never administer OTC medications to pets without consulting a veterinarian.

CLIENT EDUCATION

- Need to control or monitor pet's environment
- Location of nearest veterinary hospital at any time of day or night

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Deciduous Teeth, Persistent (“Retained”)

BASIC INFORMATION

DEFINITION

Deciduous teeth that failed to exfoliate

SYNONYM

Retained deciduous teeth: *retained* refers to failure to erupt (emerge through the gingival surface); *persistent* is more accurate because it refers to failure to exfoliate (cause shedding of the deciduous tooth).

EPIDEMIOLOGY

Dogs and cats. Permanent dentition eruption schedules dictate when a deciduous tooth is considered persistent (use table cautiously; breed and individual variation can be significant [±1 to 2 months]):

GENETICS & BREED PREDISPOSITION

High prevalence in toy dog breeds (Yorkshire terriers, miniature poodles, Pomeranians) suggests inheritance. Recent advances in the understanding of eruption and exfoliation suggest familial and/or genetic influence.

Permanent Dentition Eruption Times in the Dog and Cat

	Dog	Cat
Incisors	3-5 months	3-4 months
Canines	4-6 months	4-5 months
Premolars	4-6 months	4-6 months
Molars	5-7 months	4-5 months

ASSOCIATED CONDITIONS & DISORDERS

As a result of persistence of deciduous teeth:

- Periodontal disease
- Malocclusion
- Malposition, retarded eruption, impaction of permanent teeth
- Palatal/labial trauma

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

Teeth appear too numerous or are angled abnormally. A large percentage of persistent deciduous teeth are found on physical examination of adolescent dogs and cats presented for neutering.

PHYSICAL EXAM FINDINGS

A narrower deciduous tooth is observed alongside an erupting or fully erupted permanent tooth. The deciduous canine and incisor teeth are most commonly affected, though persistent deciduous premolars do occur (there are no deciduous molars or first premolars).

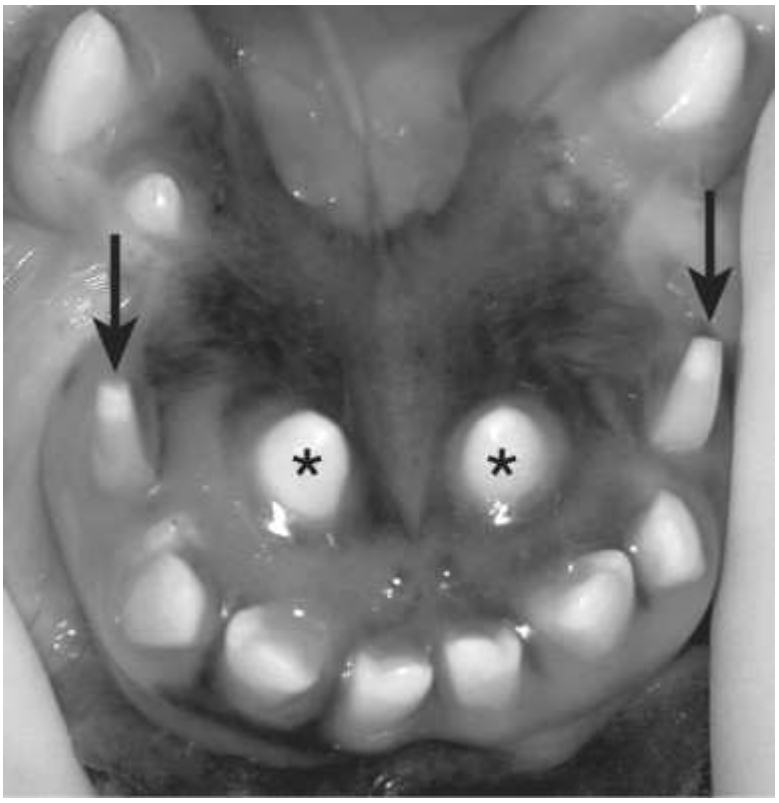
ETIOLOGY AND PATHOPHYSIOLOGY

- Commonly reported causes:
  - Lack of permanent successors
  - Dentoalveolar ankylosis of deciduous teeth
  - Failure of the erupting permanent crown to apply pressure to the deciduous tooth root
  - Hormonal abnormalities affecting growth or metabolism
- Pathophysiologically important information includes:
  - Persistent deciduous teeth may result in malpositioned permanent teeth.
  - Permanent mandibular incisors, canines, and premolars erupt lingual (i.e., toward the tongue) to persistent deciduous teeth; lingually deviated permanent mandibular canine teeth may cause palatal trauma.
  - Permanent maxillary incisors and premolars erupt palatal (i.e., toward the palate) to persistent deciduous teeth.
  - Permanent maxillary fourth premolars erupt buccal/labial (i.e., toward the cheek/lip) and distal (i.e., away from the midline of the dental arch) to persistent deciduous teeth.
  - Permanent maxillary canine teeth erupt mesial (i.e., toward the midline of the dental arch) to persistent deciduous teeth.
  - Food, debris, plaque, and calculus accumulating on and between deciduous and permanent teeth may cause periodontal disease even in young animals.

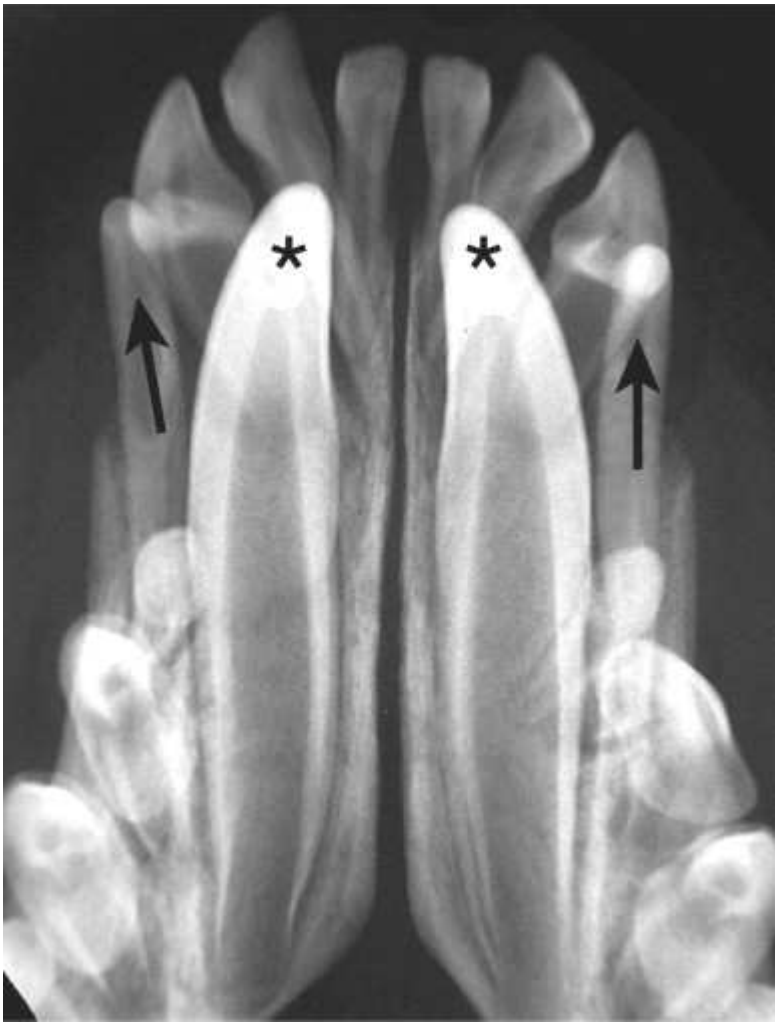
DIAGNOSIS

DIAGNOSTIC OVERVIEW

Physical exam is highly suggestive; presence of a deciduous tooth in a dog or cat with otherwise permanent dentition. Dental radiography is indicated prior to intervention.



DECIDUOUS TEETH, PERSISTENT (“RETAINED”) Bilateral persistent deciduous mandibular canine teeth in a dog *(arrows)*, causing permanent canines *(asterisks)* to be displaced lingually.



DECIDUOUS TEETH, PERSISTENT (“RETAINED”) Radiograph of lower jaw of same dog. Persistent deciduous canine teeth *(arrows)* block normal eruption pathway of permanent successors *(asterisks)*. Radiograph arranged in labial mounting; rostral is toward top of image, patient's left is on right of image.

DIFFERENTIAL DIAGNOSIS

- Missing, malformed, malpositioned or unerupted permanent tooth
- Supernumerary permanent tooth
- Malocclusion

INITIAL DATABASE

- CBC, serum chemistry panel, urinalysis: preoperative, generally unremarkable
- Full-mouth dental radiographs: evaluate root structures, confirm and document presence of healthy permanent teeth.

ADVANCED OR CONFIRMATORY TESTING

Hormone levels if metabolic/endocrine disease is suspected

TREATMENT

TREATMENT OVERVIEW

Extraction is indicated in virtually all cases (exception: no equivalent permanent tooth) to alleviate dental crowding, soft-tissue trauma, and/or dental interlock; prevent periodontal disease; prevent malpositioning of permanent teeth and malocclusion; and

correct existing malocclusion.

ACUTE GENERAL TREATMENT

- No treatment is needed for uncrowded, healthy persistent deciduous teeth that have no permanent counterpart.
- Extraction of all other persistent deciduous teeth is advised.
- Closed and open extraction techniques are acceptable, depending on tooth to be extracted and degree of root resorption.
    - Closed extraction for mobile teeth
    - Open extraction via creation of a mucoperiosteal flap and alveolar bone removal for solid teeth with complete root structures
    - Slow, steady pressure with a dental elevator is key for inducing periodontal ligament fatigue and successful extraction.
    - Be sure to keep all instrumentation away from the erupting permanent tooth.
- Extraction sites should be closed using rapidly absorbable synthetic suture material while avoiding placing sutures directly over an erupting tooth.
- Postoperative dental radiographs are recommended to ensure complete extraction, evaluate surrounding structures for damage, and provide documentation.
- Antibiotics are not usually necessary post extraction.
- Pain management: intraoperative nerve block (0.5% bupivacaine hydrochloride, 0.2 to 0.3 mL near middle mental, inferior alveolar, infraorbital or maxillary nerve) followed by oral nonsteroidal antiinflammatory medication (e.g., carprofen, 2 mg/kg PO q 12 h) for 2-3 days postoperatively.

POSSIBLE COMPLICATIONS

- Root fracture and retained root tips, leading to infection of the permanent tooth
- Retarded eruption, malpositioning, and/or mechanical damage to the permanent tooth
- Accidental extraction of permanent tooth

RECOMMENDED MONITORING

- Examination in 1-2 weeks to evaluate extraction sites
- Examination in 4-6 weeks to evaluate occlusion if necessary; if abnormalities persist, therapeutic recommendations are offered.

PROGNOSIS AND OUTCOME

Excellent for regional healing and reduction of risk of periodontal disease

PEARLS & CONSIDERATIONS

COMMENTS

- Early extraction (5-7 months of age) of persistent deciduous teeth is key to success.
- Deciduous teeth have a thin dentinal layer and long, spindly roots. They are difficult to extract and break easily. The first rule is to *go slow!*

PREVENTION

Selective breeding

TECHNICIAN TIPS

- One tooth in one place at one time is the general rule of thumb.
- If deciduous and permanent teeth of the same type are occupying the same space, the deciduous tooth is persistent.

CLIENT EDUCATION

Genetic counseling

SUGGESTED READING

Hobson P: Extraction of retained primary canine teeth in the dog. J Vet Dent 22:132, 2005.

AUTHOR: JENNIFER E. RAWLINSON

EDITOR: ALEXANDER M. REITER

Deafness

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

- *Deafness* is the inability to hear.
- *Sensorineural deafness* results from an abnormality in the inner ear and/or vestibulocochlear nerve and/or the auditory pathways in the brain.
- *Conduction deafness* results from a lesion in the outer ear and/or tympanum and/or middle ear.

SYNONYM

Hearing loss

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs and cats; any age, either gender

GENETICS & BREED PREDISPOSITION

- Congenital, inherited, sensorineural deafness is associated with coat and iris color.
  - Cats with white haircoats and blue irides are commonly affected by congenital deafness.
  - Dog breeds with white, spotted, merle, or dapple haircoats are predisposed to congenital deafness.
- Inherited sensorineural deafness is also seen in breeds not related to white, spotted, merle, or dapple coat colors (e.g., Doberman pinscher).
- Breeds with presumed inherited conditions involving the conduction portion of the ear (external and middle ears) are predisposed to developing hearing loss (e.g., Cavalier King Charles spaniels with secretory otitis media (see p. 807).

RISK FACTORS

- Genotype: white, piebald, extreme piebald, or merle genes
- Old age
- Repeated exposure to loud noises
- Breeds of cats or dogs susceptible to otitis externa and/or otitis media
- Exposure to high dosages of systemic ototoxic drugs, such as aminoglycosides, erythromycin, loop diuretics, cisplatin, nitrogen mustard, or topical chlorhexidine antiseptic. Topical drugs are potentially more ototoxic if the tympanum is not intact.

ASSOCIATED CONDITIONS & DISORDERS

- Otitis externa and/or media
- External or middle ear canal neoplasia
- Nasopharyngeal polyps (cats)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Described as:

- Congenital or adult-onset
- Inherited or noninherited
- Sensorineural or conduction deafness

HISTORY, CHIEF COMPLAINT

- Animals with bilateral congenital or adult-onset deafness:
  - Overly aggressive with other puppies in a litter (congenital deafness)
  - Nonresponsive to auditory stimuli (particular frequencies and/or magnitudes)

- Difficult to obedience train, or the adult animal becomes unresponsive to auditory commands to which it was previously responsive
- Tendency to startle when approached from a position out of visual field
- Increased tendency to sleep
- Not aroused from sleep with auditory stimuli

- Diagnosis of unilateral deafness is not possible with behavioral markers alone; electrodiagnostic evaluation is required to establish a diagnosis of unilateral deafness.

PHYSICAL EXAM FINDINGS

- Animals with normal hearing may not respond to loud sounds in the clinical setting; behavioral response to auditory stimuli is unreliable for evaluating deafness.
- Animals with peripheral sensorineural deafness typically have no abnormal physical examination findings.
- Animals with acquired conduction deafness may have one or all of the following clinical signs:
  - Abnormal aural examination
  - Head tilt
  - Facial droop
  - Horner's syndrome
  - Head shaking
  - Signs of pain upon manipulation of the ears
- Animals with deafness resulting from diseases affecting the vestibulocochlear nerve or central components of the auditory pathways will typically demonstrate other concurrent abnormal neurologic signs.

ETIOLOGY AND PATHOPHYSIOLOGY

- Acquired conduction deafness resulting from otitis externa/media
  - Impaired conduction of sound waves to the tympanic membrane from hyperplasia and exuberant cerumen production or the presence of pus in the external ear canal
  - Impaired transduction of sound waves to the otic ossicles due to stiffened, fibrotic, or ruptured tympanic membrane
  - Impaired mechanoelectrical transduction due to sclerosis of otic ossicles
- Acquired conduction deafness from external or middle ear masses
  - Obstruction of sound waves to the tympanic membrane
  - Destruction of middle ear structures
- Presbycusis (senile deafness)
  - Degeneration of the neural components of the inner ear
  - ± Stiffening of the tympanic membrane
  - ± Ankylosis of the otic ossicles
- Loud noise exposure
  - Damage to inner ear hair cells and/or ossicles and/or tympanic membrane
- Congenital hereditary deafness associated with coat color
  - Associated with coat-color genes
  - Abnormal migration of neural crest cells (precursor to melanocytes) to the inner ear (thought to provide nourishment to inner ear); associated with sacculocochlear-type degeneration

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

Bilateral complete deafness is apparent from lack of response to loud noises; diagnostic evaluation should consider history, neurologic exam findings, and otoscopic exam findings. Unilateral or partial bilateral deafness may only be apparent on auditory testing and is generally of interest in preventive medicine (breeders).

DIFFERENTIAL DIAGNOSIS

- Primary behavioral/psychological disorder
- Canine cognitive dysfunction syndrome (geriatric dogs)

INITIAL DATABASE

- Distant and proximal physical examinations
- Neurologic examination (see p. 1311)
- Thorough aural examination (see p. 1316)

ADVANCED OR CONFIRMATORY TESTING

Brainstem auditory evoked response/potential (BAER or BAEP) testing using air or bone-conducting stimuli (see p. 1216)

TREATMENT

TREATMENT OVERVIEW

- Prevent hearing loss from developing or progressing.
- Improve hearing ability.

ACUTE GENERAL TREATMENT

- No treatment for congenital inherited sensorineural deafness; careful selection of breeding animals by only using non-deaf animals for breeding (perform BAER tests on untested adults and all puppies).
- No practical treatments for animals with sensorineural deafness. Custom-fit hearing aids are offered by some specialty practices (consult with neurologist or audiologist).
- For acquired conduction deafness, treat the underlying cause of the disease.
- Use ototoxic drugs with caution or not at all (topically) if the tympanum is not known to be intact.

RECOMMENDED MONITORING

Repeated BAER testing to monitor response to therapy in animals with incomplete deafness

PROGNOSIS AND OUTCOME

- Inherited sensorineural deafness and deafness resulting from degeneration of inner ear is permanent.
- Variable prognosis for animals with conduction deafness (depends on chronicity and/or severity of the disease)

PEARLS & CONSIDERATIONS

COMMENTS

- Unilaterally deaf animals are as likely as bilaterally deaf animals to produce deaf offspring.
- Animals with bilateral deafness require special care, including:
  - Keeping animals on leash, especially when near traffic
  - Obedience training using hand signals
  - To minimize the risk of bite injury, prevent children from startling the animal.
- Animals with presbycusis may have concurrent cognitive decline, accounting for behavioral changes.

PREVENTION

- Use non-deaf animals for breeding.
- For breeds predisposed to congenital deafness, use animals with non-blue irides for breeding.

CLIENT EDUCATION

- For dog breeders:
  - Inherited sensorineural deafness is a multifactorial genetic condition and is not easily eliminated from particular breeds.
  - Breeding unilaterally or bilaterally deaf animals together increases the incidence of deafness in the offspring; conversely, the incidence of deafness decreases when two hearing dogs are bred together.
  - Breeding two hearing dogs together can still result in producing unilaterally or bilaterally deaf puppies (for inherited deafness).
  - Avoid producing animals homozygous for the merle gene.
- For owners:
  - Inform owners that the dog has special training needs.
  - Recommend Susan Cope Becker's book, *Living with a Deaf Dog: A Book of Advice, Facts and Experiences about*

Canine Deafness (Cincinnati, 1997, Susan Cope Becker).

SUGGESTED READING

Deafness in dogs and cats: Information on deafness prevalence, causes and management for owners, breeders and researchers © George M. Strain: http://www.lsu.edu/deafness/deaf.htm

Listing of worldwide BAER test sites © George M. Strain: http://www.lsu.edu/deafness/baersite.htm

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Dacryocystitis

BASIC INFORMATION

DEFINITION

Although *dacryocystitis* is technically inflammation of the lacrimal sac, the term is commonly used for describing inflammation anywhere along the tear drainage (i.e., nasolacrimal) system, including the lacrimal puncta, canaliculi, lacrimal sac, and nasolacrimal duct. Dacryocystitis is an acquired condition resulting in ocular discharge (see p. 777).

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs and cats; no age or sex predisposition

GENETICS & BREED PREDISPOSITION

- Brachycephalic breeds (lacrimal stasis): most common conformation associated with dacryocystitis
- Some extremely dolichocephalic breeds (Doberman pinschers, collies, etc.) also have poor tear drainage and stasis due to a small, deeply set eye and loss of eye-to-lid contact in the medial canthal area.

RISK FACTORS

- The most common causes of dacryocystitis in dogs and cats are foreign bodies (e.g., plant awns that become lodged in the nasolacrimal system) and descending infections due to poor conformation and subsequent lacrimal stasis.
- Animals that spend time outdoors are at increased risk.

GEOGRAPHY AND SEASONALITY

- Areas with an abundance of plants
- Increased incidence in spring and summer

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Ocular discharge (serous, mucoid, purulent, or a combination)
- Owner may report swelling and/or draining tract in skin ventral to medial canthus.

PHYSICAL EXAM FINDINGS

Ocular discharge in the form of tears, mucus, or pus, with any or all of the following:

- Conjunctivitis
- Lacrimal punctal foreign body
- Swelling and signs of pain in the medial canthal area
- If sufficiently chronic, fistulous tracts may be present in the medial canthal area.

ETIOLOGY AND PATHOPHYSIOLOGY

- Most common cause of dacryocystitis is migration of foreign bodies, most frequently plant material, into the nasolacrimal system.
- Descending infections from ocular surface flora, often associated with poor tear drainage and lacrimal stasis, also incriminated with initiating inflammation.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Suspicion for the diagnosis arises based on chief complaint and physical exam findings indicative of ocular abnormalities including ocular discharge. Determination of whether dacryocystitis involves an obstruction or is secondary to inflammation is the key to diagnosis and prompt treatment. This is accomplished by checking for nasolacrimal passage of fluorescein dye and nasolacrimal flushing.

DIFFERENTIAL DIAGNOSIS

- Other causes of blockage of the nasolacrimal system:
  - Congenital disorders, including micropunctum or imperforate lacrimal punctum
  - Acquired disorders, including traumatic lacerations or neoplastic invasion or compression of the nasolacrimal drainage apparatus
- Other causes of ocular discharge (see p. 777)

INITIAL DATABASE

- Complete ophthalmic examination (see p. 1313) including:
  - Schirmer tear test (rule out keratoconjunctivitis sicca [KCS; see p. 1406] as cause for ocular discharge). Normal >15 mm after 1 minute in dogs, variable in cats.
  - Fluorescein dye application
    - Rule out corneal ulceration as cause for ocular discharge.
    - Fluorescein dye application also tests for nasolacrimal system patency.
      - Dye normally traverses the nasolacrimal apparatus to exit the nares within 5 minutes (dogs and cats).
      - Visualization of the dye in the nares can be assisted with a Wood's lamp (dye fluoresces).
      - False-negative results may occur if animal licks dye from nares before dye is visualized, or dye may drain caudally into nasopharynx (mainly brachycephalic breeds).
- Nasolacrimal flushing if suspect complete or partial nasolacrimal duct blockage:
  - May be done under firm restraint with topical ocular anesthesia (e.g., proparacaine 0.5% [dogs]).
  - Resistant animals or signs of discomfort warrant routine preanesthetic evaluation and subsequent sedation or general anesthesia (cats have small lacrimal puncta).
  - Lacrimal puncta can be cannulated but not distal nasal puncta (dogs and cats), which are difficult to identify in many or most individuals irrespective of dacryocystitis.
  - Identify dorsal and ventral lacrimal puncta (oval in dog and round in cat, with or without circumferential pigment), 1 to 2 mm from eyelid margin in palpebral conjunctiva near medial canthus.
  - Gently insert cannula or intravenous catheter (stylet removed; 22 to 24 gauge, dogs; 24 to 26 gauge, cats), with 3-mL syringe filled with sterile saline or eyewash attached, approximately 3 mm into the dorsal lacrimal punctum.
  - Slowly inject the saline/eyewash until it flows from the ventral lacrimal punctum (confirms puncta, canaliculi, and lacrimal sac are patent).
  - Next, occlude ventral lacrimal punctum with digital pressure and flush 3-12 mL saline/eyewash through the nasolacrimal duct.
  - Collect fluid/discharge at naris in sterile basin.
- Culture and sensitivity testing of purulent discharge if present
- Consider referral to a veterinary ophthalmologist if unable to establish patency of nasolacrimal system.

ADVANCED OR CONFIRMATORY TESTING

- Dacryocystorhinography (contrast study of nasolacrimal system) with standard radiography can identify an obstruction site.
- Recently, CT-dacryocystorhinography has been demonstrated to allow highly accurate characterization of lesions obstructing the nasolacrimal duct.

TREATMENT

TREATMENT OVERVIEW

Determine character (i.e., plant material, inflammatory debris, etc.) and location of obstruction and relieve it.

ACUTE GENERAL TREATMENT

- If foreign body is lodged in canaliculi or lacrimal sac, it may be manually removed by flushing lacrimal punctum.
- If a foreign body is present in nasolacrimal duct, removal may be accomplished by dacryocystotomy (surgical incision of nasolacrimal duct; referable procedure).

CHRONIC TREATMENT

- Care after any of the preceding surgeries would include topical antibiotic/steroid combination medication (neomycin/polymyxin /dexamethasone suspension or ointment q 4-6 h) for the first 2-4 postoperative weeks.
- Dacryocystotomy requires placement and maintenance of a Silastic cannula and oral antibiotics for 3-4 weeks after surgery.

POSSIBLE COMPLICATIONS

If foreign bodies are left in the nasolacrimal drainage system, scarring, permanent occlusion, and chronic epiphora may result.

PROGNOSIS AND OUTCOME

- Depends on underlying cause
- Good prognosis with successful removal of foreign body

PEARLS & CONSIDERATIONS

COMMENTS

- Prompt retrieval of foreign bodies from the proximal portions of the nasolacrimal system is essential; surgical removal from the nasolacrimal duct is technically difficult and has many potential complications.
- False-negative results can occur when attempting nasolacrimal fluorescein dye passage in brachycephalic breeds, because fluorescein may drain into the back of the oral cavity, owing to the characteristic shape of a brachycephalic dog or cat's maxilla.

PREVENTION

Keep pets away from areas with tall grass, especially in the late summer.

SUGGESTED READING

Grahn BH: Diseases and surgery of the canine nasolacrimal system. In Gelatt KN, editor: Veterinary ophthalmology, ed 3, Philadelphia, 1999, Lippincott Williams & Wilkins, pp 569–581.

Miller PE: Lacrimal System. In: Slatter's fundamentals of veterinary ophthalmology, ed 4, St Louis, 2008, Saunders Elsevier, pp 157–174.

Nykamp SG, et al: Computed tomography dacryocystography evaluation of the naso-lacrimal apparatus. Vet Radiol Ultrasound 45:23, 2004.

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EDITOR: CHERYL L. CULLEN

Eyelid Defects: Trauma, Masses

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Eyelid trauma is associated with any external injury to the eyelid predisposing to inflammation or laceration. Eyelid masses are very common and are associated with neoplastic or inflammatory conditions.

SYNONYMS

- Chalazion: hordeolum, meibomian gland cyst
- Meibomian glands: tarsal glands, palpebral glands

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs and cats
- Eyelid trauma may occur at any age.
- Eyelid mass: average age 9-10 years (eyelid neoplasia, dogs) but depends on type of mass

GENETICS & BREED PREDISPOSITION

- Eyelid trauma: more common in young animals, outdoor animals, and sporting breeds of dogs
- Eyelid mass (dogs): more common in American cocker spaniel, boxer, poodle, golden retriever, Labrador retriever, English springer spaniel, beagle, collie, Siberian husky, and English setter

RISK FACTORS: Excessive sunlight and white hair in the periocular region both predispose to squamous cell carcinoma (SCC), the most common eyelid neoplasm in cats.

ASSOCIATED CONDITIONS & DISORDERS

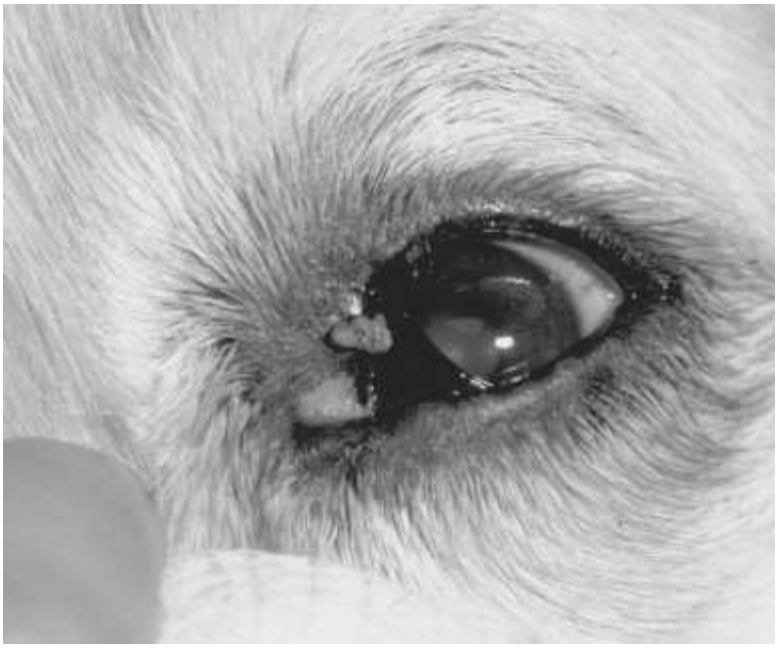
EYELID TRAUMA

- Corneal/scleral trauma (see p. 249)
- Uveitis (see p. 1151)
- Eyelid mass:
  - Blepharitis (eyelid inflammation)
  - Conjunctivitis (see pp. 239 and 237)
  - Corneal ulceration (see p. 250)

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Eyelid trauma:
  - Witnessed traumatic event
  - Swollen eyelid(s) (blepharoedema)
  - ± Eyelid laceration
- Eyelid mass:
  - Growth on eyelid and/or eyelid margin
  - Persistent or intermittent bleeding of eyelid
  - Signs of ocular pain if mass large and causing conjunctival and/or corneal irritation
  - Ocular discharge



EYELID DEFECTS Eyelid mass.

(Courtesy Dr. Phillip A. Moore.)

PHYSICAL EXAM FINDINGS

- Eyelid trauma (some or all of the following):
  - Blepharoedema
  - Eyelid laceration (partial- or full-thickness)
  - Blepharospasm
  - Ocular discharge
  - Conjunctival hyperemia/edema (chemosis)
  - Keratitis (ulcerative or nonulcerative)
- Eyelid mass (some or all of the following):
  - Mass located along eyelid margin or adjacent to margin of eyelid
  - Size, location, and appearance vary with type of mass:
    - Neoplasm associated with the meibomian gland appears as an irregular, raised, variably sized mass ± pigment.
    - SCC appears as an erosive, ulcerated mass along the eyelid, often near the medial canthus.
    - Chalazion (meibomian gland cyst) presents as smooth, raised, yellow to white mass associated with the meibomian gland.
  - Ocular discharge, blepharospasm, conjunctivitis, keratitis if mass irritating the eye
  - Eyelid hemorrhage
  - Lagophthalmos (incomplete closure of the eyelids)

ETIOLOGY AND PATHOPHYSIOLOGY

- Eyelid trauma is generally associated with blunt trauma, penetration by sharp objects, or self-mutilation (pawing at eye).
- Eyelid mass (neoplastic)
  - Common in dogs; most are benign.
  - Rare in cats; most are SCC (malignant).
  - Similar to those of the skin; arise from epithelial, mesenchymal, and melanogenic cells.
  - In dogs, 82% of eyelid neoplasms are sebaceous adenomas, papillomas, or melanomas.
  - Sebaceous gland tumors (sebaceous adenoma, sebaceous epithelioma, and sebaceous adenocarcinoma) arise from the meibomian glands.
- Focal eyelid inflammation: a chalazion is a pyogranuloma associated with retained meibomian gland secretions.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

- The diagnosis of eyelid trauma is suspected based on the presence of blepharoedema and/or blepharitis with or without ocular discharge.
- The diagnosis of an eyelid mass is suspected based on the presentation of a "mass"-type lesion or swelling adjacent to or along the lid margin; confirmation of the nature of the mass requires cytologic and/or histopathologic assessment.

DIFFERENTIAL DIAGNOSIS

Eyelid swelling:

- Anaphylaxis
- Conjunctival/subpalpebral foreign body

INITIAL DATABASE

Complete ophthalmic examination (see p. 1313) including:

- Schirmer tear test
- Fluorescein dye application
- Intraocular pressures
- Examination of periocular (e.g., conjunctiva) and intraocular structures, especially if trauma suspected
- Examination of eyelid margin for extent of laceration or extent and point of origin of mass

ADVANCED OR CONFIRMATORY TESTING

- Fine-needle aspiration and cytologic evaluation of eyelid masses
- Histopathologic evaluation of all surgically removed eyelid masses

TREATMENT

TREATMENT OVERVIEW

Treatment goals are to restore normal eyelid conformation, eliminate ocular irritation, and prevent recurrence of eyelid mass. Treatment for an eyelid mass should be initiated early in the course of the disease to ensure normal eyelid conformation.

ACUTE GENERAL TREATMENT

- Eyelid trauma:
  - Laceration requires primary/surgical closure of wound.
  - If full-thickness laceration, close in two layers (conjunctiva followed by skin) starting at eyelid margin to ensure accurate apposition of eyelid margin.
- Eyelid mass:
  - Neoplasia:
    - Surgical removal:
      - If involves eyelid margin and ≤⅓ length of eyelid, remove by a full-thickness V-shaped or "house"-shaped excision.
      - Close in two layers (see Eyelid Trauma under Acute General Treatment above).
      - Eyelid margin mass > ⅓ eyelid length requires a plasty procedure to ensure proper eyelid length (e.g., H-plasty). Consider referral to ophthalmologist or surgeon.
    - Cryosurgery:
      - Useful in treating benign eyelid mass in older animals
      - May be performed under sedation
      - Recurrence rate higher with cryotherapy than with full-thickness excision.
- Chalazion:
  - Surgical treatment:
    - Scalpel incision of overlying palpebral conjunctiva with curettage; heals by second intention
  - Topical antibiotic/corticosteroid (e.g., neomycin-polymyxin-dexamethasone suspension) q 8 h for 7 days after surgery; corticosteroid contraindicated if cornea is not intact.

POSSIBLE COMPLICATIONS

- Poor apposition of eyelid margin results in cicatrix (scar) formation, predisposing to entropion or ectropion, or "step" to eyelid margin, resulting in corneal irritation and ulceration.

- Improperly placed sutures at the eyelid margin can predispose to corneal ulceration.
- Local regrowth of eyelid mass, if mass not completely removed

RECOMMENDED MONITORING

Reevaluate apposition of eyelid margin, and remove skin sutures 10 days after surgery.

PROGNOSIS AND OUTCOME

- Eyelid laceration: prognosis good if apposition of eyelid margin is achieved.
- Removal of eyelid neoplasm: dogs, prognosis good, majority are benign; cats, prognosis guarded, majority are malignant.
- Local recurrence is possible if an eyelid mass is not completely excised.

PEARLS & CONSIDERATIONS

COMMENTS

- Eyelid lacerations are treated surgically, not as open wounds, to prevent eyelid scarring, contraction, and distortion of the eyelid margin.
- Eyelid masses should be removed early to prevent the need for plasty procedures.

PREVENTION

Limit actinic radiation (sunlight) exposure in white cats to decrease the potential for SCC.

CLIENT EDUCATION

Recurrence is possible after the removal of any eyelid mass.

SUGGESTED READING

Stades FC, Gelatt KN: Diseases and surgery of the canine eyelid. In Gelatt KN, editor: Veterinary ophthalmology, ed 4, Ames, 2007, Blackwell Publishing, p 563.

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EDITOR: CHERYL L. CULLEN

Exocrine Pancreatic Insufficiency

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

A syndrome caused by insufficient secretion of pancreatic digestive enzymes by the exocrine pancreas

SYNONYM

EPI

EPIDEMIOLOGY

SPECIES, AGE, SEX: Occurs more commonly in dogs than in cats; any age. In dog breeds that are affected by pancreatic acinar atrophy (PAA), exocrine pancreatic insufficiency (EPI) is most commonly diagnosed in young adults. In other dog breeds and cats, EPI can occur at any age.

GENETICS & BREED PREDISPOSITION: In dogs, EPI most commonly occurs in the German shepherd, for which an autosomal recessive inheritance has been proposed. A breed predilection has also been reported for rough coated collies and Eurasians. There is no known breed predilection in cats. See Etiology, below, regarding PAA.

RISK FACTORS

- Chronic pancreatitis can lead to destruction of exocrine pancreatic tissue and EPI.
- Pancreatic adenocarcinoma or surgery could lead to obstruction of the pancreatic duct, leading to lack of pancreatic enzyme secretion into the small intestine.

ASSOCIATED CONDITIONS & DISORDERS: Many canine and feline patients with EPI have other gastrointestinal disorders. Dogs with EPI due to PAA commonly have secondary small-intestinal bacterial overgrowth (also termed antibiotic-responsive diarrhea [see p. 81]); other dogs and cats often have concurrent inflammatory bowel disease (see p. 605).

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Weight loss is the most common clinical sign in both dogs and cats.
- Loose stools and less commonly diarrhea
- Ravenous appetite

PHYSICAL EXAM FINDINGS

- Poor body condition (Note: nowadays patients often are diagnosed much earlier in the disease process, and emaciated patients with EPI are rare.)
- Poor hair coat and sometimes in cats, greasy soiling of the hair coat

ETIOLOGY AND PATHOPHYSIOLOGY

- The most common cause of EPI in the dog is pancreatic acinar atrophy. This condition is mostly seen in German shepherds, rough coated collies, and Eurasians.
- The most common cause of EPI in the cat and the second most common cause of EPI in dogs is chronic pancreatitis.
- Other potential causes of EPI include obstruction of the pancreatic duct by a pancreatic adenocarcinoma and pancreatic aplasia or hypoplasia, but these have not yet been reported in dogs or cats. Surgical obstruction of the pancreatic duct, leading to EPI, has recently been described.
- Decreased secretion of exocrine pancreatic digestive enzymes leads to lack of digestive enzymes in the small intestine, which will lead to maldigestion and associated clinical signs.
- Secondary cobalamin deficiency is very common in dogs and occurs in almost all cats with EPI.
- In patients with EPI due to chronic pancreatitis, pancreatic inflammation may also lead to destruction of islets of Langerhans and cause concurrent diabetes mellitus.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The most reliable diagnostic test for EPI for both dogs and cats is serum trypsin-like immunoreactivity concentration (TLI), which is measured by a species-specific assay.

DIFFERENTIAL DIAGNOSIS

- Primary small intestinal disease (e.g., inflammatory or infiltrative bowel disease)
- Other secondary causes of chronic diarrhea and weight loss (i.e., hepatic failure, renal failure, hypoadrenocorticism, hyperthyroidism [cats])

INITIAL DATABASE

- CBC, serum chemistry profile, and urinalysis are usually within normal limits (including serum total protein concentration).
- Imaging studies are usually within normal limits.

ADVANCED OR CONFIRMATORY TESTING

- Serum TLI is the diagnostic test of choice for the diagnosis of EPI.
  - A severely decreased serum TLI concentration is diagnostic of EPI.
    - In dogs: ≤2.5 µg/L (canine TLI; reference range 5.7–45.2 µg/L)
    - In cats: ≤8.0 µg/L (feline TLI; reference range 12–82 µg/L)
  - Some patients with EPI may have a serum TLI concentration in the questionable range (>2.5 but <5.0 µg/L [dog]; >8.0 but <12.0 µg/L [cat]).
    - These patients most likely have chronic small-intestinal disease and should be evaluated accordingly and retested 4–6 weeks later.
- Other diagnostic tests are much less reliable and should *not* be used for the diagnosis of EPI:
  - Fecal proteolytic activity is only recommended in species for which a TLI assay is not available.
  - Fecal elastase concentration is only available in Europe. Positive test results must be confirmed with a cTLI test; the false-positive rate is high.

TREATMENT

TREATMENT OVERVIEW

- Pancreatic enzyme replacement is crucial.
- Cobalamin must be supplemented parenterally if cobalamin deficiency is present.

ACUTE GENERAL TREATMENT

- Oral enzyme replacement therapy
  - Starting dose: 1 tsp per 10 kg body weight with each meal
  - Tablets and capsules are not as effective as powder.
  - Premixing the pancreatic enzymes with the diet is not necessary.
- Parenteral cobalamin supplementation if the patient is cobalamin deficient (approximately 80% of dogs with EPI and virtually all cats with EPI are cobalamin deficient; see p. 220).

CHRONIC TREATMENT

- Oral enzyme replacement therapy:
  - Once patients have fully responded and gained back their original body weight, the amount of enzyme can be decreased to the lowest effective dose, titrated based on stool consistency and body weight.
- Oral antibiotic therapy (i.e., tylosin, 25 mg/kg PO q 12 h for 6 weeks) if canine patient does not respond to enzyme replacement therapy and is suspected of having antibiotic-responsive diarrhea
- Insulin therapy if patient has concurrent diabetes mellitus

NUTRITION/DIET

- Dietary fat restriction is not recommended.
- Several studies in dogs have failed to show any impact of diet on therapeutic response.
- Premium maintenance diet is sufficient.

POSSIBLE COMPLICATIONS

Enzyme supplementation can lead to oral bleeding in approximately 10% of patients:

- Most of these patients will normalize after reduction of the dose.
- Patients may rarely develop bleeding diathesis due to vitamin K deficiency, which must be treated with vitamin K supplementation.

RECOMMENDED MONITORING

Body weight, fecal quality, and serum cobalamin concentration after supplementation

PROGNOSIS AND OUTCOME

Most patients with EPI respond to therapy and have a normal life.

PEARLS & CONSIDERATIONS

COMMENTS

- Some patients may not respond to enzyme replacement therapy and cobalamin supplementation alone.
  - Many of these patients have concurrent small-intestinal disease (i.e., small-intestinal bacterial overgrowth/antibiotic-responsive enteritis, and/or inflammatory bowel disease).
  - If concurrent disease cannot be identified, gastric acid inhibition can be tried (i.e., omeprazole, 0.7 mg/kg PO q 12 h has been most useful).
- Fresh-frozen raw pancreas can also be used for enzyme replacement therapy (1–2 oz of ground raw pancreas equals about 1 tsp of powdered pancreatic extract).

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Ethylene Glycol Intoxication

BASIC INFORMATION

DEFINITION

Ethylene glycol (EG) intoxication manifests as the peracute onset of marked central nervous system (CNS) depression and progressive, dose-related metabolic acidosis and renal failure. Sources of EG are commonly found in automobile radiator fluid, aircraft and runway deicing products, home solar units, and portable basketball goal post bases, among others.

SYNONYMS

Ethylene alcohol poisoning, radiator antifreeze poisoning, 1,2-ethanediolmono-ethylene glycol poisoning, glycol alcohol poisoning, CAS 107-21-1 poisoning

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Animals of all ages, breeds, and both sexes are equally susceptible to EG poisoning.
- Cats are most sensitive to EG intoxication.
- Dogs are intermediate in sensitivity among the species.
- Dogs are more commonly exposed than cats. Intact young male dogs may be more likely to be involved.

RISK FACTORS

- Pets living outdoors or having free-range access to EG sources (e.g., garages)
- Northern climates or freezing temperatures provide increased opportunity, especially when water sources are limited (frozen), and antifreeze remains in the liquid state because of its low freezing point.
- Engine leak is the most common source of exposure in pets.
- In the home, the garage is one of the most common exposure locations.

GEOGRAPHY AND SEASONALITY

- EG poisoning cases can occur throughout the year; it is no longer considered a seasonal problem.
- Northern and colder climates are over-represented, but exposure can occur anywhere radiator fluid flushing is common. Summer automobile radiator flushing procedure is considered routine maintenance.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Indirect evidence of exposure:
  - Pet being near an automobile garage or work area
  - Roaming free in areas suspected or known to have EG sources
- Classic “drunken sailor” behavior (stupor, narcosis, stumbling, ataxia, falling, nausea) may be noted within 1-2 hours.
- Stupor phase gradually subsides over several hours.
  - Stupor phase may go unnoticed altogether, especially in outdoor pets.
  - Owner may note the pet “getting better.”
  - Patient is quiet, depressed, polydipsic, and polyuric.
- Patient gradually and steadily shows more weakness, depression, anorexia, and tachypnea/dyspnea as acute renal failure occurs (12–72 hours after ingestion).

PHYSICAL EXAM FINDINGS

- CNS depression, generalized weakness, hyporeflexia, knuckling, hypothermia, hypotension, tachycardia, vomiting, and polyuria
- Urinary bladder may be empty on palpation.
- Patient may have already progressed beyond the initial “drunk” phase and may not present as “classic,” thus potentially

confusing the picture.
    - Overt signs of acute renal failure (oliguria/anuria, anorexia, vomiting, renomegaly with signs of renal pain) begin 24–72 hours post ingestion.
- In severe intoxications, seizures, nystagmus, and tremors may occur in the first few hours post ingestion (grave prognosis).

ETIOLOGY AND PATHOPHYSIOLOGY

- Lethal dose of 95% ethylene glycol: 4.4 mL/kg (dog), 1.4 mL/kg (cat)
- Rapid oral absorption of EG
    - Blood levels detectable in <30 minutes
    - Initial CNS depression and narcosis, vasodilation, and hypotension with reflex tachycardia, diuretic effect
- Metabolism involves hepatic alcohol dehydrogenase oxidation of EG to the aldehyde (glycoaldehyde).
    - This oxidation is a saturable process; therefore it is the rate-limiting step.
    - Metabolic progression can be interrupted at this point with fomepizole or ethanol.
    - Glycoaldehyde is very toxic but quickly converts to glycolic acid.
    - Glycolic acid (30%–45% of metabolite load) is fairly stable, further oxidizes to glyoxylic acid, then further metabolism occurs along several paths to oxalic acid, glycine, formate, hippurate, CO2, and so on. Aldehyde and acid load create a high-anion-gap metabolic acidosis.
- Metabolites inhibit the citric acid cycle and substrate level phosphorylation, depress serotonin and pyruvate metabolism, and alter CNS amine levels.
- Secondary lactate accumulation, hypoperfusion, calcium oxalate formation, and precipitation in microvasculature and renal tubules occur.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A high index of suspicion should exist based on history alone (owner saw pet licking, or in the same room as, fluorescent green liquid). Treatment must be implemented early—prior to renal failure and possibly prior to definitive diagnostic confirmation in many cases—to avert toxic renal injury. The diagnosis is more straightforward, but the prognosis worse, >12–24 hours after ingestion when overt clinical signs emerge.

DIFFERENTIAL DIAGNOSIS

Rule out other causes of acute CNS depression, ataxia, acidosis, or acute renal failure: encephalitis, cranial trauma, intracranial neoplasia, diabetic ketoacidosis; or intoxication with barbiturates, aspirin, methanol, ethanol, isopropanol, propylene glycol, glycol ethers, vitamin D3, *Lilium* and *Hemerocallis* spp. (cats), nonsteroidal antiinflammatory drugs, grapes, or raisins.

INITIAL DATABASE

- Ethylene Glycol Test Kit screening tool (Allelic Biosystems: PRN Pharmacal Inc., Pensacola, Fla. [800-874-9764; www.prnpharmacal.com]). Recommended for use in dogs, not sensitive enough for cats (false negatives). Test can produce false-positive results with propylene glycol, glycerol, diethylene glycol (or other *cis*-1,2 diols), metaldehyde, and formaldehyde. Limited availability.
- React ethylene glycol test kit. PRN Pharmacal Inc., Pensacola, FL (800-874-9364; www.prnpharmacal.com). The React Test is fairly new in the market and its accuracy has not yet been determined.
- Serum chemistry panel including serum electrolytes (especially Ca^{++}, Mg^{++}, K^{+}, and P)
- Acid-base: blood pH, Pco2, Po2, serum bicarbonate
- Urinalysis: specific gravity, crystals, glucose, cellular debris
    - As in any cause of acute anuric renal failure, specific gravity will not necessarily be low.
    - Calcium oxalate monohydrate crystals (“picket fence boards,” flattened hexagon shapes: can be observed 18 hours after EG ingestion and are much more specific to ethylene glycol intoxication than calcium oxalate dihydrate crystals (“Maltese cross” or “square envelope” appearance:, which can occur from nutritional or laboratory artifactual causes as well as EG intoxication.
- Fluids: measure total input and output; body weight.
- Optional Wood's lamp examination (detects fluorescein dye in antifreeze); scan of muzzle, paws, vomitus, urine (excretes < 3–6 hours in humans) for fluorescence that subjectively supports exposure.

ADVANCED OR CONFIRMATORY TESTING

- EG and glycolic acid levels (serum, urine); requires STAT turnaround time to benefit early diagnosis in determining treatment approach

- Serum osmolality; requires colloid osmometer
  - Normal osmole gap: 5-10 mOsm/kg water (dogs and cats). Osmole gap = measured osmolality – calculated osmolality.
  - >20 mOsm/kg strongly suggestive of EG intoxication; parallels EG blood level. Significant increase within 1 hour of exposure.
- Anion gap
  - Normal anion gap: 10–25 mEq/L (dogs and cats)
  - >25 mEq/L is significant for diagnostic purposes
  - May note change by 3 hours, but may require 6 hours. Therefore, less preferred as an early diagnostic tool.
- Ultrasound: increased renal cortical echogenicity at 4-6 hours; late in the course, “halo sign” indicative of anuria, and grave prognosis.
  - *Note:* many normal, healthy cats have diffuse hyperechogenicity of renal cortices (avoid overinterpretation).
- Renal calcium level in postmortem tissue sample

TREATMENT

TREATMENT OVERVIEW

EG toxicosis is a medical emergency. Due to rapid progression and irreversibility of renal lesions, any patient suspected of consuming EG should be tested and decontaminated unless/until exposure has been ruled out; empirical treatment with fomepizole or ethanol is indicated if the index of suspicion is high and a confirmatory test is not available in time. The greatest window of opportunity for intervention is <8–12 hours post exposure in dogs, <2 hours post exposure in cats. Immediate decontamination of the patient (early induction of emesis and administration of activated charcoal) is indicated in all suspected or confirmed cases presented within 1 hour of exposure. Confirmed cases should also receive an antidote (fomepizole or ethanol) and be hospitalized for management of acid-base abnormalities, fluid diuresis for renal protection, and supportive care as dictated by progression of the case.

ACUTE GENERAL TREATMENT

- Induction of vomiting (see p. 1364) with hydrogen peroxide 3%: 0.25–0.5 mL/kg PO once; or apomorphine, 0.03 mg/kg IV or in conjunctival sac, then administration of activated charcoal (1–2 g/kg PO once). Can reduce absorption within 30–60 minutes; indicated if patient is a good risk. Some clinicians precede this by very rapidly feeding a tasty meal to provide a substrate for the vomiting if the pet has an otherwise empty stomach.
- Interrupt conversion to toxic metabolites with fomepizole (4-MP, 4-methylpyrazole, Antizol-Vet, Paladin Labs [www.antizol-vet.com]).
  - Loading dose: 20 mg/kg slow IV infusion
  - Then 15 mg/kg slow IV q 12 h × 3 treatments in the dog
  - Not effective in cats at labeled dose
- Off-label fomepizole: use in cats <3 hours after ingestion at 125 mg/kg slow IV infusion, then 31.25 mg/kg q 12 h × 3 treatments has shown significant success.
- Or interrupt conversion to toxic metabolites with 7% ethanol solution.
  - Loading dose: 8.6 mL/kg slow IV
  - Maintenance dose: 1.43-2.86 mL/kg/h constant rate infusion (CRI) to effect
    - Achieve serum ethanol concentrations of 100 mg/dL or lethargic/comatose state.
    - Duration: approximately 48 hours
  - Dogs treated with ethanol starting at 3 hours post ingestion of EG excrete 80% of EG intact.
- Hemodialysis (more effective) or peritoneal dialysis while on ethanol or fomepizole. Immediate dialysis on any patient showing clinical signs of toxicity will tend to increase the survival rate.
- Acid-base and perfusion management is critical to survival. Sodium bicarbonate CRI as needed for metabolic acidosis.
- Crystalloids: high infusion rate required to correct severe dehydration and hypoperfusion.
- Provide cofactors for metabolism of toxic compounds.
  - Pyridoxine, 1-2 mg/kg IV q 6 h
  - Thiamine, 50 mg slow IV q 6 h

CHRONIC TREATMENT

Dialysis to allow regeneration of damaged tubular basement membrane

POSSIBLE COMPLICATIONS

Renal compromise. May be salvageable, depending on degree of insult and response to intensive treatment.

RECOMMENDED MONITORING

Renal function (urinalysis, serum chemistry, biopsy, etc.) should be monitored as needed in surviving patients.

PROGNOSIS AND OUTCOME

- Dogs: fair to good if proper aggressive intervention within 8-12 hours; prognosis worsens by the hour if clinical signs are apparent and/or a large dose was ingested.
- Cats: guarded to poor at best in any case showing clinical signs. Aggressive intervention (interruption of metabolism with high doses of fomepizole, dialysis, acid-base management) within 3 hours of exposure may prove successful.

PEARLS & CONSIDERATIONS

COMMENTS

- Progression of irreversible, potentially life-threatening effects in patients that have ingested EG is rapid (hours); therefore, evaluation and treatment are urgent, even in animals without overt clinical signs.
- "Safe antifreeze" contains propylene glycol, which is less toxic compared to EG; much less risk of renal injury. Dogs would generally need to ingest 3–4 times more propylene glycol than EG to develop clinical signs.
- Use of injectable valium, phenobarbital, pentobarbital, or some commercial oral preparations of activated charcoal before using EG test kits can give a false-positive result due to presence of propylene glycol in them.

TECHNICIAN TIPS

- Calcium oxalate monohydrate urinary crystals (□) are strongly suggestive of ethylene glycol intoxication, whereas calcium oxalate dihydrate crystals (□) may also be caused by nutrition or refrigeration of the urine sample.
- Many human hospital laboratories have the capability of detecting and quantifying EG quickly in different body fluids and can be helpful if an EG test kit is not available on site.
- Antifreeze (ethylene glycol) is generally fluorescent green, viscous (like light syrup), and does not have a volatile odor; windshield washer fluid (not ethylene glycol) is generally translucent blue, pungent (volatile odor), and nonviscous (like water).

PREVENTION

Keep animals indoors and not in the garage, especially in freezing temperatures (frozen water sources, antifreeze remains in liquid state, thus is more attractive).

CLIENT EDUCATION

Lock antifreeze plastic containers away from chewing dogs. Use cat litter to clean up any spills, leaks. About 1 tsp (5 mL) of radiator antifreeze is lethal to an adult cat.

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Esophagitis

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Acute or chronic inflammation of the esophagus, often secondary to reflux of gastric acid, foreign bodies, or medications

SYNONYMS

Gastroesophageal reflux, reflux esophagitis

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs and cats of any age and either sex can be affected; females may be overrepresented.

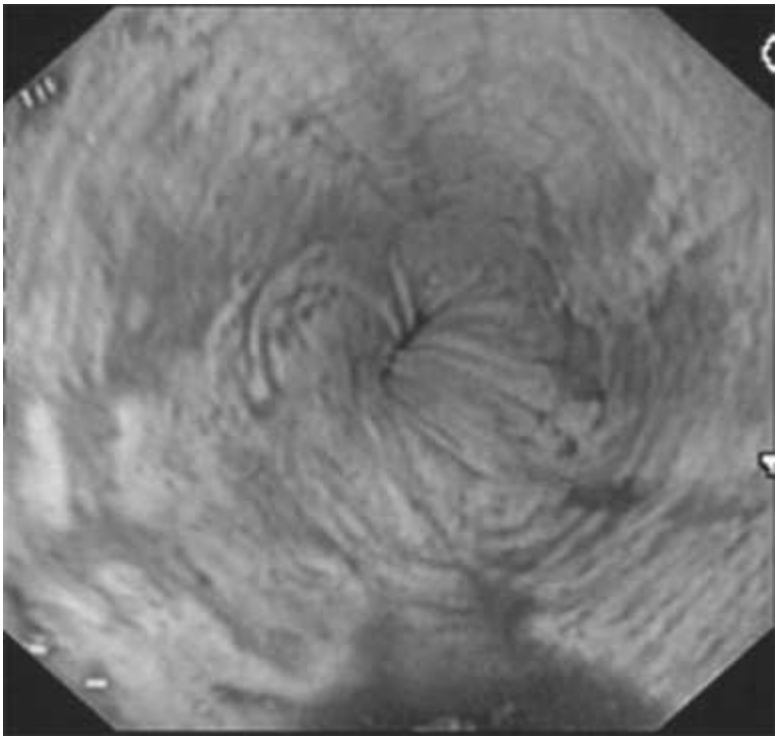
RISK FACTORS

- General anesthesia, even of short duration:
  - Most common cause of reflux esophagitis in the dog and cat
- Hiatal hernia or other causes of lower-esophageal sphincter dysfunction
- Esophageal foreign body
- Oral medications (e.g., tetracyclines, ciprofloxacin, NSAIDs) given without being followed by food or water administration
- Persistent vomiting
- Gastric hyperacidity (e.g., gastrinoma)

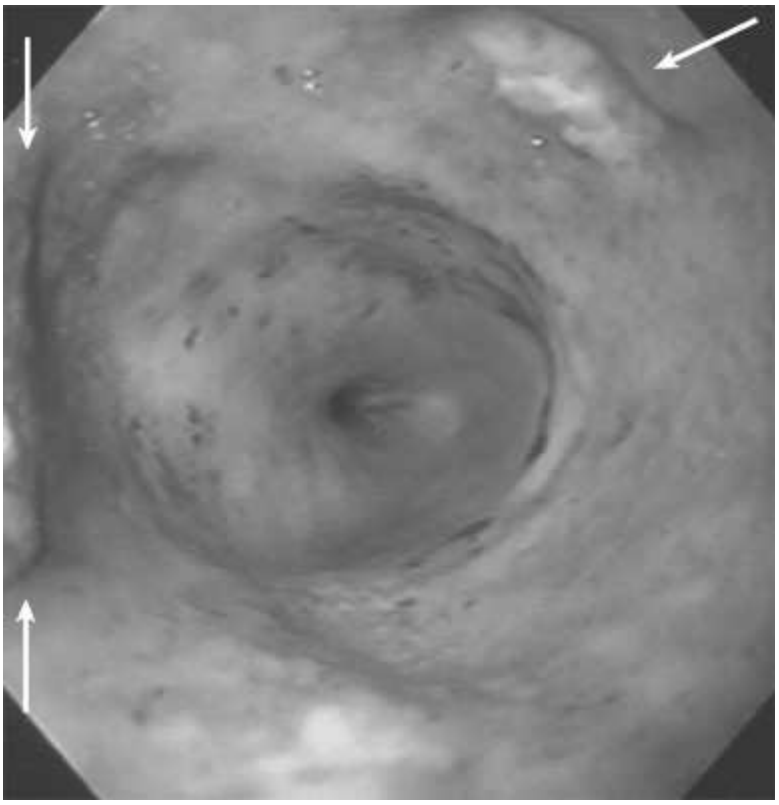
CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Mild esophagitis may be subclinical.
- Clinical signs may include:
  - Increased swallowing motions, ptyalism
  - Inappetence, anorexia, and/or odynophagia (discomfort when swallowing) due to pain
  - Regurgitation or vomiting
  - Reluctance to move or lie down
  - Cats may vocalize after eating as an indication of esophageal pain.
- Affected patients may have a history that reveals risk factors (above).



ESOPHAGITIS Endoscopic view of a patient with esophagitis. Note the longitudinal, darker patchy areas indicative of inflammation and mucosal erosion. Fluid pooling is apparent at the bottom of the image.



ESOPHAGITIS Endoscopic view of a patient with ulcerative esophagitis. Ulcers are apparent as deep depressions in the esophageal wall on the left edge of the image *(arrows)* and at the 1 o'clock position *(single arrow)*. Mucosal hemorrhages are also evident as darker, thin, circumferential streaks and pinpoint lesions on or near the gastroesophageal sphincter.

PHYSICAL EXAM FINDINGS: May be normal; abnormalities may include:

- Thin body condition
- Dehydration
- Ptyalism

- Pharyngitis
- Cranial abdominal/thoracic discomfort:
    - Hunched-up appearance
    - Guarding or pain on palpation

ETIOLOGY AND PATHOPHYSIOLOGY

- Etiology:
    - Premedicant drugs (atropine, benzodiazepines, phenothiazines, opioids) and anesthetic induction agents may decrease lower-esophageal sphincter tone, allowing gastroesophageal reflux.
    - Anatomic abnormalities (e.g., hiatal hernia) can increase risk of reflux esophagitis.
    - Ingested medications or chemicals can damage the esophagus because of their pH or osmolarity.
- Pathophysiology:
    - Esophageal mucosal contact with low-pH gastric fluid, pepsin, trypsin, bile salts, and/or alkaline fluid causes damage and inflammation, which may remain mucosal or involve all layers of the esophagus.
    - Caustic agent ingestion (e.g., detergents, alkalis, acids)
    - Volume, frequency, and duration of contact of material with esophagus affects the severity of esophageal damage.

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

The diagnosis can be suspected in two contexts: a suggestive history and/or chief complaint or a vague presentation with nonspecific clinical signs. In either situation, esophagitis may be confirmed by direct endoscopic visualization (rules out impostors but requires expertise and equipment) or by response flexible endoscopic equipment or it may be suspected based on response to treatment (but other diseases may respond to therapy for esophagitis).

DIFFERENTIAL DIAGNOSIS

- Thermal damage (e.g., gavage/tube feeding with excessively hot liquids)
- Esophageal foreign body
- Megaesophagus
- Vomiting
- Neoplasia or mass lesions (intrinsic or extrinsic)
- Vascular ring anomaly
- Hiatal hernia
- Gastroesophageal intussusception

INITIAL DATABASE

- CBC, serum biochemistry profile, urinalysis: often within normal limits
- Survey thoracic radiographs seldom diagnostic, but may show esophageal dilation
- Contrast esophagram sometimes demonstrates mucosal ulceration or hyperplasia, or decreased esophageal motility.

ADVANCED OR CONFIRMATORY TESTING

- Esophagoscopy typically allows definitive diagnosis, exclusion of other disorders, and evaluation of extent and severity based on gross appearance.
    - Biopsy of canine esophageal mucosa is difficult but occasionally reveals organisms (e.g., yeast *[Candida]* or hyphae *[Pythium]*).
    - Biopsy may be important in cats with chronic inflammation at lower-esophageal sphincter which may not be grossly obvious.
- Fluoroscopy often needed to detect lower esophageal sphincter dysfunction not due to hiatal hernia

TREATMENT 

TREATMENT OVERVIEW

Goals of therapy are to protect the esophageal mucosa from further damage, decrease the amount and frequency of reflux, and eliminate acid from reflux.

ACUTE GENERAL TREATMENT

- Lessen or eliminate gastric acid secretion.
  - H2 receptor antagonists (e.g., famotidine, 0.5–2 mg/kg PO or IV q 12–24 h): achieves maximal efficacy immediately but is not as effective as proton pump inhibitors
  - Proton pump inhibitors (e.g., omeprazole, 0.7–1 mg/kg PO q 12–24 h): most effective class of drugs but typically requires 2-5 days to reach maximal efficacy
- Minimize reflux by increasing lower-esophageal sphincter tone and keeping stomach empty
- Prokinetic drugs (e.g., metoclopramide, 0.2–0.5 mg/kg PO or SQ q 8 h; or cisapride, 0.1–0.25 mg/kg PO q 8–12 h).
- Sucralfate slurry (0.25–1 g/patient PO q 8 h):
  - Protects the esophageal mucosa from further damage

CHRONIC TREATMENT

- Treat until esophagitis resolves.
- Indefinite prokinetic and antacid therapy may be needed when lower-esophageal dysfunction is not amendable to surgical resolution.

NUTRITION/DIET

- Feed a moderate- to high-protein, low-fat diet; increases lower esophageal tone and encourages gastric emptying.
- If necessary, place gastrostomy tube to ensure nutrition and ability to medicate patient (see p. 1267).

POSSIBLE COMPLICATIONS

Esophageal stricture formation

RECOMMENDED MONITORING

- Normal eating without dysphagia, ptyalism, or regurgitation usually implies resolution.
- Hyporexia, dysphagia, ptyalism, or regurgitation necessitates reexamination for stricture or inflammation.
- Strictures may cause regurgitation beginning days to 4 weeks post injury.

PROGNOSIS AND OUTCOME

- If the cause can be eliminated, is not severe, and is recognized early and treated aggressively, prognosis is usually good.
- Prognosis is guarded if the cause cannot be resolved or if esophagitis is severe or patient develops long esophageal strictures.

PEARLS & CONSIDERATIONS

COMMENTS

- Decrease the risk of prolonged contact of medication with esophageal mucosa by administering water (e.g., 5-10 mL by syringe) following any dry oral medication (tablet or capsule) given without food.
- Consider reflux esophagitis in patients showing ptyalism, hyporexia, or regurgitation shortly after anesthesia.

PREVENTION

- Routine use of preanesthetic antacid drugs is of unknown efficacy and cost-effectiveness.
- Routine postanesthetic esophageal lavage and suction is of uncertain efficacy and cost-effectiveness.

CLIENT EDUCATION

Administer water (e.g., 5–10 mL by syringe trickled in the cheek pouch) following any dry oral medication (tablet or capsule) given without food.

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Esophageal Stricture

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

A circular band of scar tissue that forms after deep esophageal injury (foreign body or esophagitis resulting in inflammation that extends into the submucosal and muscular layers) and compromises food passage through the esophageal lumen (see pp. 406 and 367 for related information).

EPIDEMIOLOGY

SPECIES, AGE, SEX: Strictures due to foreign bodies (bones, fish hooks) are more common in dogs, and strictures due to chemical esophagitis (pills, caustic agents) are more common in cats.

RISK FACTORS

- Dogs: ingestion of bones, rocks, other foreign objects
- Cats: administration of medications not followed with water or food (capsules or uncoated tablets are the most common medications that lodge and cause esophagitis or stricture).
- Dogs or cats: gastroesophageal reflux due to anesthesia, persistent vomiting

ASSOCIATED CONDITIONS & DISORDERS

- Esophagitis (common)
- Esophageal foreign bodies (common)
- Esophageal neoplasia (rare)

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Regurgitation is the classic presenting sign (distinguish from vomiting: regurgitation involves no prodromal signs or active retching).
- Difficulty swallowing or pain associated with swallowing (repeated swallowing efforts)
- Ptyalism/hypersalivation
- Inappetence
- Lethargy
- Weight loss (if the condition is long-standing)
- Cough, increased respiratory rate or effort may be seen if the patient has concurrent aspiration pneumonia.

PHYSICAL EXAM FINDINGS

- May be normal
- Weight loss
- Ptyalism or gagging
- Coughing, fever, or increased bronchovesicular sounds if aspiration pneumonia has occurred

ETIOLOGY AND PATHOPHYSIOLOGY

- Some of the more frequently reported causes of stricture formation are esophagitis secondary to chronic persistent vomiting, foreign bodies that lodge in the esophagus, and ingestion of caustic substances (including medications that lodge in the esophagus).
- A commonly reported cause of esophagitis in dogs and cats is reflux esophagitis due to general anesthesia; however, the incidence of stricture secondary to this cause of esophagitis is much less frequent.
- Infrequently reported causes of stricture formation in dogs and cats are hiatal hernias, esophageal *Pythium* spp. infection, esophageal neoplasia (the most common cause of stricture formation in humans), and esophageal surgery (to remove foreign bodies, masses).
- Esophageal stricture formation requires substantial esophageal injury (usually chemical or mechanical) resulting in

penetration or inflammation that extends to the submucosa or muscular layers. The normal repair process that follows this injury results in formation of fibrous connective tissue, and many times this occurs in a circular band of scar tissue that narrows or closes the esophageal lumen.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

- Esophageal strictures are easy to diagnose (with endoscopy); the challenge is that there is a degree of clinical suspicion necessary to put the pieces together from the history and physical exam findings.
- History of regurgitation should prompt the consideration of esophageal disease and evaluation of thoracic radiographs. If no abnormality is seen and regurgitation is convincingly present, contrast radiography or esophageal endoscopy (confirmatory test of choice) is warranted.

DIFFERENTIAL DIAGNOSIS

Regurgitation:

- Esophagitis
- Esophageal foreign body
- Esophageal mass (granuloma, parasites, neoplasia)
- Esophageal motility disorders (megaesophagus, congenital or acquired)
- Esophageal diverticulum
- Persistent right aortic arch
- Gastroesophageal reflux during anesthesia (history of anesthesia is important)
- Gagging/dysphagia
- Oropharyngeal, nasopharyngeal disease

INITIAL DATABASE

- CBC, serum chemistry panel, urinalysis likely normal; changes are nonspecific.
  - Inflammatory leukogram present if aspiration pneumonia
  - Evidence of dehydration possible if stricture is severe
- Thoracic/abdominal radiographs are indicated in all regurgitating patients.
  - Plain thoracic films may be normal, may show evidence of megaesophagus (or air/food in esophagus cranial to the stricture), or may reveal signs of aspiration pneumonia.
  - Plain abdominal films are usually unremarkable unless there is an obvious gastric outflow obstruction that is causing persistent vomiting/gastroesophageal reflux.

ADVANCED OR CONFIRMATORY TESTING

- Endoscopy (see p. 1284) is the preferred diagnostic imaging tool of choice for definitive identification of esophagitis, other esophageal anomalies, and esophageal strictures. In addition, endoscopy can be used for facilitating balloon dilation of the stricture site—the best approach for long-term stricture management.
- Contrast films may reveal stricture site or esophageal motility defect if food or paste is used, but liquid barium or iodinated contrast agents may pass through the stricture undetected. Contrast studies are helpful if multiple strictures are suspected, because visualization with the endoscope will be limited to the first stricture site in many (see). Caution is advised when administration of contrast is contemplated; regurgitation of barium may result in aspiration.
- Fluoroscopy is often needed to identify a hiatal hernia or distal lower-esophageal sphincter defect leading to reflux.
- Abdominal ultrasound is indicated to rule out abdominal causes of persistent vomiting that may lead to reflux esophagitis.

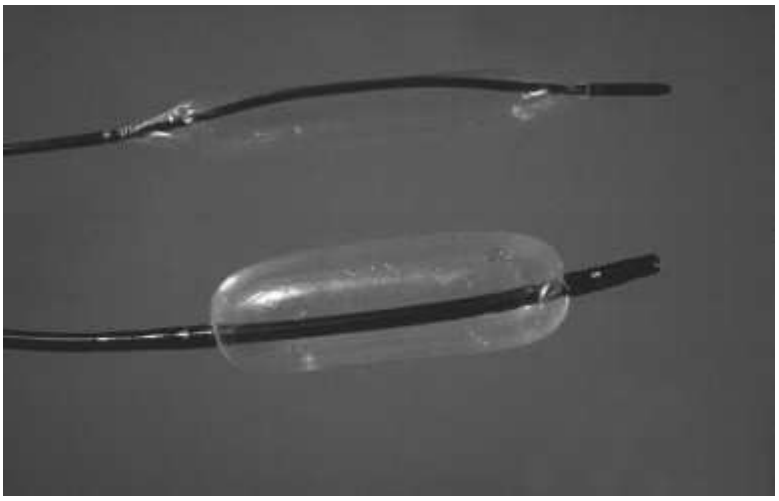
TREATMENT

TREATMENT OVERVIEW

Therapeutic goals are to protect the esophageal mucosa from additional injury, eliminate the underlying cause of the injury (if possible), adequately resolve regurgitation, and allow the patient to maintain nutrition and hydration by oral feeding.

ACUTE GENERAL TREATMENT

- Treatment of esophagitis if present (see p. 367) or other underlying causes of stricture (control vomiting, remove foreign body, etc.)
- If the stricture is mild (liquid or canned foods can pass through the stricture site with few or no clinical signs, and no weight loss is evident), management may be accomplished by dietary modifications (feeding liquid, gruel, or canned foods in frequent, small meals).
- In severe strictures refractory to such conservative management, the stricture must be dilated to allow liquids or gruels to pass. If this is not possible, a gastric feeding tube must be placed to allow maintenance of hydration and nutrition (see p. 1267).
- Dilation can be accomplished by balloon or by esophageal bougienage. Balloon dilation is the preferred means of dilation and entails passage of an inflatable balloon catheter into the stricture site, inflating the balloon to allow the pressure to tear/break down the scar tissue and thus increase the diameter of the esophageal lumen.
- Alternatively, bougienage involves the passage of rigid dilators of gradually increasing size through the stricture site. Both of these procedures are facilitated by concurrent use of endoscopic (or fluoroscopic) guidance to monitor the procedural success and identify complications (e.g., esophageal tear) early.
- Corticosteroids (e.g., prednisone, 0.5–1 mg/kg PO q 24 h × 5–10 days) may be considered in an attempt to delay fibrosis of recently dilated strictures. Delayed healing and the risk of immunosuppression are drawbacks that contraindicate higher dose or longer-term treatment.
- Lifelong dietary management is usually necessary. Complete resolution of the stricture and normalization of esophageal function are unlikely.



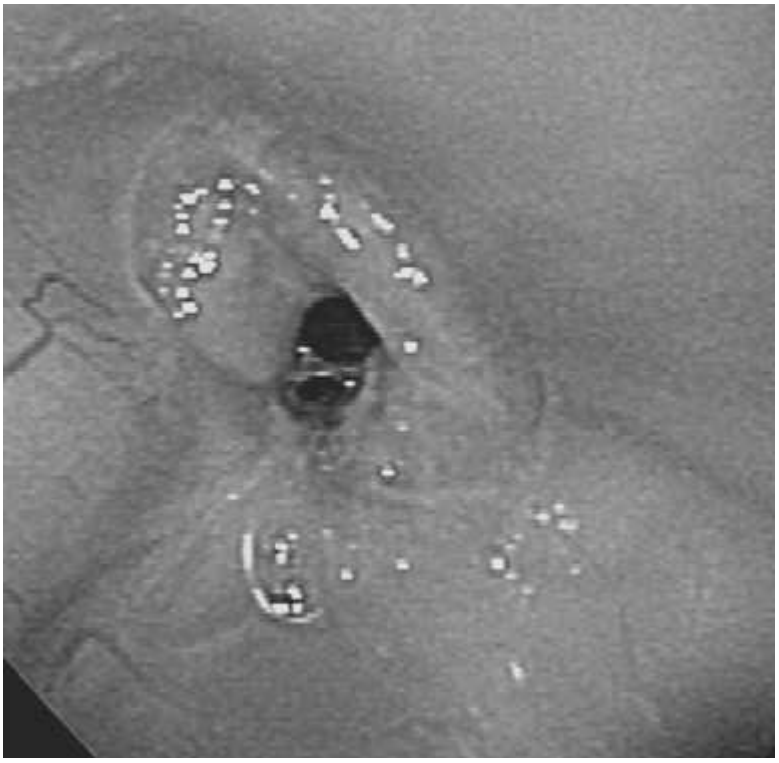
ESOPHAGEAL STRICTURE Photo illustration of a 180-cm, 15-mm outer diameter esophageal/pyloric balloon (CRE Wireguided balloon [Boston Scientific, Natick, Mass]). Upper balloon is undilated for comparison.

CHRONIC TREATMENT

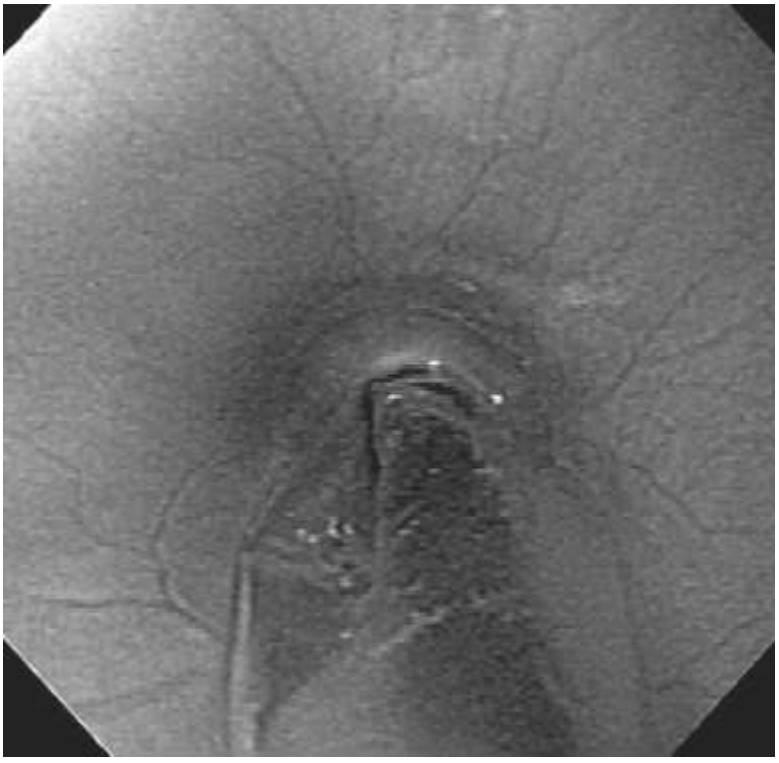
- Many animals require several dilation procedures to achieve an esophageal opening sufficiently large to accommodate liquid or gruel diets.
- As for animals with esophagitis, long-term therapy may be needed. A cornerstone of treatment is the avoidance of hard foods.

POSSIBLE COMPLICATIONS

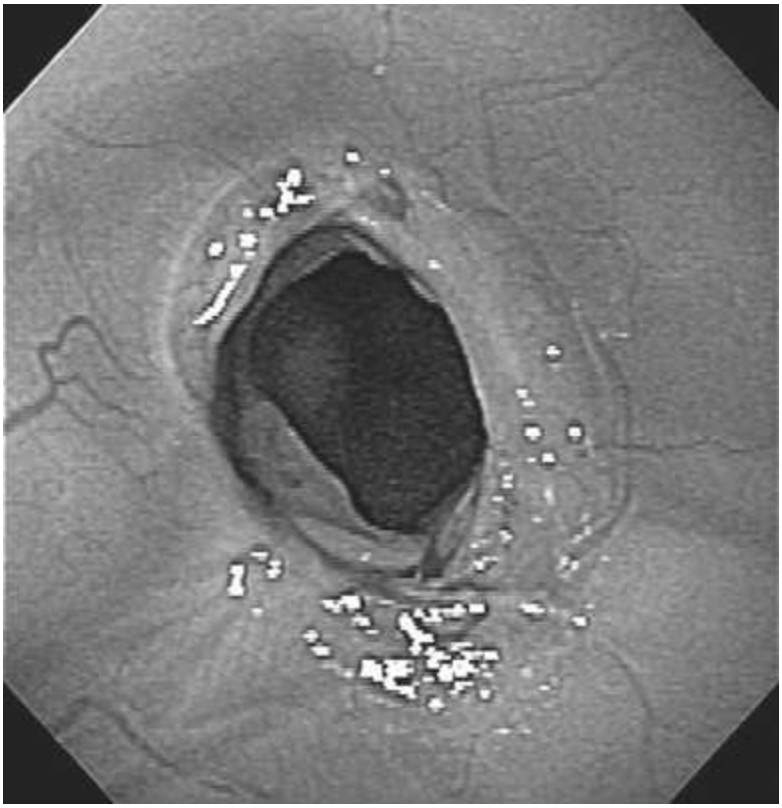
- The most important complication of esophageal stricture therapy is rupture or perforation of the esophagus during the ballooning or bougienage procedure.
- Complete recurrence of the stricture can occur if the dilation procedure is too aggressive, resulting in excessive inflammation.
- Aspiration pneumonia remains a possible complication if the stricture remains and the patient has episodes of regurgitation or does not have well-controlled dietary management (e.g., the dog gets into the garbage or is allowed to eat foods that will not pass).



ESOPHAGEAL STRICTURE Digital image obtained during esophagoscopy. A stricture site is apparent at center of image. Note that very little material (except small amounts of liquids) could pass through this opening.



ESOPHAGEAL STRICTURE Digital image obtained during esophagoscopy of same patient, illustrating placement of balloon in stricture site. Balloon is partially inflated and momentarily will be fully inflated for stretching the fibrous stricture, or cicatrix.



ESOPHAGEAL STRICTURE Digital image obtained during esophagoscopy after balloon dilation of esophageal stricture in same dog. Note degree of inflammation and bleeding at the site, but lumen diameter is markedly enlarged. Goal is to minimize degree of inflammation created to avoid stricture redevelopment post ballooning.

PROGNOSIS AND OUTCOME

- The prognosis for mild strictures is generally good.
- The prognosis for severe strictures requiring multiple balloon dilation procedures is guarded.
- If the patient can be managed on liquid or gruel diets, with minimal to no regurgitation, the treatment is considered successful. Most animals with severe strictures must consume a softened, semiliquid to liquid diet, as complete resolution of the stricture is not possible.

PEARLS & CONSIDERATIONS

COMMENTS

- Esophageal strictures should be viewed as a clinical problem with a favorable outcome, as long as appropriate dilation procedures are implemented and appropriate client expectations are achieved.

PREVENTION

- Prevent all dogs from eating bones, rocks, fish hooks, and other foreign objects.
- Oral medications should not be administered alone; they should be given with food or followed with food. If medication must be given on an empty stomach, it should be followed with water to prevent capsules or tablets from lodging in the esophagus.
- Do not tip surgical tables to a degree that will allow gastroesophageal reflux and esophagitis (a risk factor for iatrogenic strictures).

CLIENT EDUCATION

- The importance of giving water to a pet after administration of medications cannot be overstressed.
- The long-term successful management of dogs or cats with strictures requires strict, lifelong dietary management.

SUGGESTED READING

Adamama-Moraitou KK, et al: Benign esopha-geal stricture in the dog and cat: a retrospective study of 20 cases. Can J Vet Res 66:55–59, 2002.

Leib MS, et al: Endoscopic balloon dilation of benign esophageal strictures in dogs and cats. J Vet Intern Med 15:547–552, 2001.

AUTHOR & EDITOR: DEBRA L. ZORAN

Esophageal Perforation

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

An uncommon condition consisting of a full-thickness defect in the esophagus with leakage of esophageal contents into the mediastinum and potentially the pleural space (For related information, see Foreign Body, Esophageal, p. 406; Esophagitis, p. 367.)

SYNONYMS

Esophageal laceration, esophageal rupture

EPIDEMIOLOGY

SPECIES, AGE, SEX

- No age or sex predilection
- Perforation has been reported in more dogs than cats:
  - Attributed to the less discriminate feeding behavior of dogs

GENETICS & BREED PREDISPOSITION: 86% of esophageal foreign bodies reported in dogs weighing <12 kg (26 lb)

RISK FACTORS

- Foreign body ingestion (see p. 406)
- Esophageal strictures can be related to balloon dilatation procedures (see p. 365)

ASSOCIATED CONDITIONS & DISORDERS

- Mediastinal abscess
- Pneumothorax
- Pyothorax
- Bronchoesophageal fistula

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: History associated with esophageal perforation includes:

- Retching, regurgitation, vomiting, ptyalism, anorexia
- Coughing, dyspnea
- Restlessness
- Cervical swelling, subcutaneous emphysema

PHYSICAL EXAMINATION FINDINGS

- Physical findings may include:
  - Fever
  - Subcutaneous emphysema
  - Rapid, shallow respiration consistent with pneumothorax or pyothorax
  - Moist rales on auscultation if aspiration pneumonia is present
  - Dehydration
- The duration of clinical signs associated with esophageal perforation is reported to be longer than with esophageal foreign body alone.

ETIOLOGY AND PATHOPHYSIOLOGY

- Sharp edges of a foreign body may lacerate the esophagus and more rarely the great vessels.
- Large foreign bodies can result in pressure necrosis of the esophageal wall; the greatest damage is usually associated with

pressure points of the foreign body against the esophageal wall.
- The most common site of foreign body lodgment (and therefore perforation) is the distal esophagus just cranial to the gastroesophageal junction; other sites include the thoracic inlet, heart base, and less often the cervical esophagus.
- Esophageal perforation can also be associated with esophageal trauma or balloon dilation of esophageal strictures.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is suspected based on presenting history and physical examination findings. Survey cervical and thoracic radiographs and contrast esophagram +/− esophagoscopy are required to confirm the diagnosis.

DIFFERENTIAL DIAGNOSIS

- Megaesophagus
- Hiatal hernia or gastroesophageal intussusception
- Intrinsic or extrinsic esophageal masses
- Neoplasia
- Parasite infestation
- Esophagitis
- Esophageal diverticulum
- Vascular ring anomaly
- Abnormal pharyngeal or esophageal motility

INITIAL DATABASE

- CBC:
  - Neutrophilic leukocytosis
  - More immature neutrophils are present with a perforated esophagus than with esophageal foreign body alone.
- Diagnostic imaging:
  - Survey cervical and thoracic radiographs
    - Esophageal foreign body
    - Air within the periesophageal tissues
    - Pneumomediastinum
    - Pneumothorax
    - Pleural effusion/pyothorax
    - Increased lung density with concurrent aspiration pneumonia
  - Contrast esophagram (see p. 1205)
    - Should be performed with water-soluble contrast if perforation is suspected
    - Has a false-negative rate of 14.5%
- Esophagoscopy:
  - Performed with care
    - Do not create or worsen pneumothorax.
  - Evaluate integrity and viability of esophagus.
    - Identify site of perforation.
  - Possible foreign body removal
- Analysis of pleural effusion if present:
  - Cytology
  - Bacterial culture and susceptibility testing (both aerobic and anaerobic area required)

TREATMENT

TREATMENT OVERVIEW

Treatment depends on location of the perforation and severity of associated problems. Surgical intervention beyond abscess drainage may or may not be indicated for cervical perforations but is required for thoracic perforations to avoid life-threatening consequences associated with leakage of contents. Nutritional support that bypasses the damaged esophagus (PEG tube) is essential.

ACUTE GENERAL TREATMENT

- Correction of fluid and electrolyte deficits
- Antimicrobial therapy:
  - Empirical therapy using an antibiotic with a broad spectrum of aerobic activity
    - Cefazolin, 22 mg/kg IV q 6 h
  - Definitive antimicrobial therapy should be based on results of microbiological culture and susceptibility testing.
    - Pleural fluid
    - Mediastinal abscess
- Surgical intervention:
  - Removal of foreign body if underlying cause ○ Repair of perforation
    - Primary closure
    - Resection and anastomosis
  - Débridement and lavage
    - Mediastinal abscess
    - Pyothorax
- Treatment of esophagitis:
  - H^2 antagonists (e.g., famotidine, 0.5 mg/kg IV q 12-24 h) or antisecretory agents (e.g., omeprazole, 0.7 mg/kg via feeding tube q 24 h) to decrease gastric acid production
  - Motility agents (metoclopramide, 0.2–0.5 mg/kg SQ or PO q 6–12 h; or cisapride, 0.1–1 mg/kg PO q 8–12 h) to promote normal gastroesophageal sphincter tone (reduce gastroesophageal reflux and esophagitis) and gastric emptying

CHRONIC TREATMENT

Treatment of pyothorax (see p. 956):

- Long-term antibiotic therapy:
  - Based on accurate identification of organism(s) involved
  - Up to 3 months of therapy may be required.

NUTRITION/DIET

- Nutritional support is necessary until the esophagus has healed and normal function has returned:
  - Feeding tube (PEG) to bypass esophagus (see p. 1270)
  - Usually 10-14 days required to allow esophageal wall to heal

POSSIBLE COMPLICATIONS

- Dehiscence of esophageal repair: recurrent leakage
- Esophageal diverticulum formation: secondary to the presence of a foreign body
- Esophageal stricture formation: secondary to damage caused by foreign body, surgical technique, or esophagitis

RECOMMENDED MONITORING

- If PEG tube has been placed:
  - Removal may be possible in 10–14 days; 7- to 10-day requirement prior to removal to allow proper adhesion of the stomach to the abdominal wall.
- Ensure that normal esophageal function returns:
  - Esophageal stricture, if it occurs, usually becomes clinically apparent 3-4 weeks post injury (manifestation and consequence: increasing problem of regurgitation)

PROGNOSIS AND OUTCOME

Prognosis associated with esophageal perforation is guarded owing to multiple possible complications and is specifically influenced by the presence or absence of:

- Mediastinitis/mediastinal abscess formation
- Development of pyothorax
- Development of esophageal stricture

PEARLS & CONSIDERATIONS

COMMENTS

Endoscopic evaluation and removal of esophageal foreign bodies must be done carefully, with special attention paid to the patient's ventilatory pattern, oxygen saturation, heart rate, and blood pressure. Insufflation with air in the presence of an esophageal perforation can lead to tension pneumothorax and acute cardiopulmonary compromise of anesthetized patients.

PREVENTION

Do not let dogs and cats eat foreign objects that have the potential to become lodged in the esophagus.

TECHNICIAN TIPS

- Postoperative nutritional support (PEG tube feeding) is necessary for these patients while the damaged esophagus heals:
  - Be familiar with PEG tube use.
  - Ensure that patient is receiving correct amount of food and water.
- Knowledge of and experience in working with thoracostomy tubes is important in the postoperative management of patients who have undergone a thoracotomy.
- In-hospital care may include:
  - Flushing wound/abscess pocket as directed
  - Keeping drain/drainage site clean and free of discharge
  - Administration of antibiotics as directed
  - Ensuring adequate analgesia is provided

SUGGESTED READING

Houlton JF, et al: Thoracic oesophageal foreign bodies in the dog: a review of ninety cases. J Small Anim Pract 26:521,1985.

Parker NR, et al: Diagnosis and surgical management of esophageal perforation. J Am Anim Hosp Assoc 25:587, 1989.

Spielman BL, et al: Esophageal foreign body in dogs: a retrospective study of 23 cases. J Am Anim Hosp Assoc 28:570, 1992.

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Esophageal Neoplasia

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Benign or malignant tumor of the esophagus

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Rare in dogs and cats
- Older animals predisposed
- No sex predilection, although squamous cell carcinoma is more common in female cats

GENETICS & BREED PREDISPOSITION: No breed predilection

RISK FACTORS: *Spirocerca lupi* infection (see p. 1040), resulting in secondary sarcoma formation

GEOGRAPHY AND SEASONALITY: Areas where *S. lupi* is endemic, including the Middle East, Africa, and the southeastern United States

ASSOCIATED CONDITIONS & DISORDERS: Hypertrophic osteopathy has been reported, especially in *S. lupi*-induced sarcomas.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- The most common primary esophageal tumors are squamous cell carcinoma (cats), leiomyosarcoma (dogs), osteosarcoma, and fibrosarcoma; rarely, benign tumors such as leiomyoma or plasmacytomas may occur.
- Primary thyroid gland or mammary gland tumors may metastasize to the esophagus.
- Lymphoma may involve the esophagus, and generally when it does, multicentric lymphoma is present.
- Primary tumors arising from the thymus, heart base, or thyroid gland may extend directly into the esophagus.

HISTORY, CHIEF COMPLAINT

- Weight loss
- Discomfort with swallowing
- Dysphagia
- Regurgitation
- Lethargy, inappetence, dyspnea, cough (aspiration pneumonia)
- Less commonly, lameness or pain of the extremities associated with hypertrophic osteopathy

PHYSICAL EXAM FINDINGS

- Rarely, a palpable mass may be found in the ventral cervical region. Most often, however, no significant physical abnormalities are found.
- Thin body condition
- Melena
- Back pain from spondylitis of the caudal thoracic vertebrae caused by spirocercosis

ETIOLOGY AND PATHOPHYSIOLOGY

- Sarcoma formation has been correlated to infection with *S. lupi*.
- *S. lupi* causes persistent tissue irritation, resulting in aortic scarring and nodular esophageal granulomas, which can undergo neoplastic transformation.
- Metastasis to the esophagus from primary thyroid gland or mammary gland tumors is more common than primary esophageal neoplasia.

- Primary esophageal malignancies may metastasize to regional lymph nodes or lungs, less commonly to other organs.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Confirmation of diagnosis requires histopathology and often must be obtained surgically.

DIFFERENTIAL DIAGNOSIS

Any disease causing signs of partial esophageal obstruction (see p. 406) or megaesophagus (see p. 709)

INITIAL DATABASE

- Plain radiographs of the thorax (three views) and neck may show repeatable, excessive gas in the esophagus, presence of a mass, or megaesophagus, all proximal (orad) to the obstruction. Lung fields should be evaluated for metastases.
- Barium swallow (see p. 1205) to show an esophageal stricture or mass
- Esophagoscopy to visualize mass(es); often ulcerated, but leiomyomas are usually submucosal, well circumscribed, and not attached to overlying mucosa.
- Biopsy and histopathology, with samples usually obtained at the time of esophagoscopy
- CBC, serum biochemical profile, and urinalysis are usually normal, although some patients may be anemic due to chronic blood loss from friable esophageal tumors.
- Fecal flotation may show *S. lupi* ova, although a negative test does not rule out infection, as esophageal neoplasia may form long after initial exposure.
- Cytology of enlarged lymph nodes to differentiate reactive lymphadenopathy from metastasis

ADVANCED OR CONFIRMATORY TESTING

- CT or MRI to better delineate mass when radiographs are equivocal
- Exploratory surgery for histopathology when samples obtained during esophagoscopy are nondiagnostic

TREATMENT

TREATMENT OVERVIEW

Goals of treatment are relief of signs of partial esophageal obstruction and delay or prevention of disease progression.

ACUTE GENERAL TREATMENT

- Surgery when feasible; in general, difficult due to length of resection required in advanced cases and inability to obtain good exposure of the esophagus
- Placement of esophagostomy or gastrostomy tubes for feeding (see p. 1270)

CHRONIC TREATMENT

- Palliative radiation therapy for cervical esophageal masses
- Photodynamic therapy may be considered for superficial mucosal tumors, but efficacy is currently unknown.

NUTRITION/DIET

- Nutritional palliation with placement of feeding tubes
- Experimentation with a variety of food textures and elevated feedings may be necessary in dogs with megaesophagus.

BEHAVIOR/EXERCISE

No restrictions in activity are recommended.

POSSIBLE COMPLICATIONS

- Risk of short-term dehiscence or long-term stricture formation after esophageal surgery

- Risks associated with thoracotomy
- Risk of infection at site of feeding tube
- Palliative radiation usually not attempted for intrathoracic lesions, owing to relative intolerance of adjacent normal tissues such as the heart, lungs, and trachea

RECOMMENDED MONITORING

- Monitor body weight; ability to obtain adequate nutrition orally is often compromised.
- Thoracic radiographs and regional lymph nodes, looking for metastasis

PROGNOSIS AND OUTCOME

Long-term prognosis is usually very poor because of low likelihood of relieving clinical signs or preventing metastasis.

PEARLS & CONSIDERATIONS

COMMENTS

Little information is available about treating dogs with esophageal neoplasia, primarily because of the rarity of these tumors.

PREVENTION

Sarcoma formation may be prevented by avoiding *S. Iupi* infection.

TECHNICIAN TIPS

Clients may require in-depth counseling and training on how to optimally feed dogs with megaesophagus.

CLIENT EDUCATION

Quality of life is often very poor unless the tumor is benign and can be surgically excised.

SUGGESTED READING

Ranen E, et al: Partial esophagectomy with single layer closure for treatment of esopha-geal sarcomas in 6 dogs. Vet Surg 33:428, 2004.

Ranen E, et al: Oesophageal sarcomas in dogs: histological and clinical evaluation. Vet J 178:78, 2008.

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EDITOR: KENNETH M. RASSNICK

Esophageal Diverticulum

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

A rare disorder characterized by a pouchlike sacculation of the esophageal wall resulting in an area in which material can accumulate and remain

EPIDEMIOLOGY

SPECIES, AGE, SEX: Can happen in any age or sex, dog or cat

ASSOCIATED CONDITIONS & DISORDERS: Traction diverticula can be caused by tumors, infections, or scarring.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Congenital versus acquired
- Pulsion ("true diverticula") versus traction ("false diverticula")

HISTORY, CHIEF COMPLAINT

- Regurgitation may be seen, particularly with large diverticula.
- Prior thoracic inflammatory disease may be suggestive (opportunity for adhesion formation and therefore traction diverticulum), although diverticulum perforation or rupture with secondary pyothorax can occur with any type of diverticulum.

PHYSICAL EXAM FINDINGS

- Regurgitation may be noted in the exam room.
- No other findings are considered specific.

ETIOLOGY AND PATHOPHYSIOLOGY

- Pulsion diverticula are caused by herniation of the mucosa through the muscular wall of the esophagus, resulting in food retention within the diverticulum. This can be an acquired problem due to increased esophageal luminal pressure secondary to obstruction, esophagitis, stricture, foreign body, and similar problems; or it can be congenital, resulting from an inherent weakness in the esophageal wall or an abnormality of embryonic separation during development.
- Traction diverticula are caused by an extraesophageal lesion such as maturing fibrous connective tissue (typically an adhesion between the esophagus and another intrathoracic structure such as tracheal or hilar lymph nodes). This adhesion pulls a portion of the esophageal wall out of position as the connective tissue matures and contracts, creating a pouch. In dogs, it is suspected that the most likely cause of traction diverticula is a penetrating esophageal foreign body that results in adhesion formation outside the esophagus (see pp. 406 and).
- The main clinical utility of differentiating between these types is that surgery may correct a traction diverticulum (release adhesion), but pulsion diverticula are often due to an esophageal problem that may or may not be readily corrected surgically (e.g., vascular ring anomaly versus esophageal stricture, respectively).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Esophageal diverticulum may first be suspected based on clinical presentation (regurgitation) or based on incidentally found radiographic abnormalities. Confirmation generally occurs either during esophagoscopy with direct visualization of the lumen of the diverticulum, or with a barium contrast esophagram.

DIFFERENTIAL DIAGNOSIS

Regurgitation:

- Esophagitis
- Megaesophagus (idiopathic, secondary to systemic disease, or pediatric [transient or congenital]). In general, diverticula cause focal esophageal enlargement, whereas generalized esophageal enlargement should prompt the consideration of causes of megaesophagus (see 709). However, overlap exists between a true diverticulum and generalized or localized esophageal weakness (either congenital or acquired) when the latter is primarily represented by a large esophageal dilatation between the thoracic inlet and the base of the heart, somewhat similar to that seen with a vascular ring anomaly such as persistent right aortic arch. Such weakness is not a surgical lesion and is not a true diverticulum.
- Esophageal mass
- Esophageal stricture
- Vascular ring anomaly

INITIAL DATABASE

- CBC, serum chemistry profile, and urinalysis results are often normal unless there is systemic inflammatory disease (e.g., aspiration pneumonia).
- Plain thoracic radiographs:
  - Look for a localized density.
  - Distinguish focal from generalized esophageal disease (e.g., megaesophagus).
  - Assess for evidence of aspiration pneumonia.
  - Assess for evidence of mediastinitis or pleuritis (e.g., mediastinal widening, pleural effusion), as can occur with esophageal perforation.
- Contrast esophagram (see 1205):
  - Look for localized collection of contrast in a pouch outside the expected plane of the esophageal lumen.
  - Distinguish esophageal disease from pleural, mediastinal or pulmonary disease.
  - Distinguish from normal redundant esophagus seen in bulldogs and shar-peis.

ADVANCED OR CONFIRMATORY TESTING

- Esophagoscopy: find the outpouching, and distinguish traction from pulsion types.
- Histopathologic evaluation of resected pouch to look for cause of traction diverticulum

TREATMENT

TREATMENT OVERVIEW

- Try to resect pouch in animals that show clinical signs but do not have generalized esophageal weakness; however, there is substantial risk of dehiscence.
- Clinically silent diverticula should generally be left alone unless there appears to be substantial risk of perforation on endoscopy or contrast radiography.

ACUTE GENERAL TREATMENT

- Treat aspiration pneumonia if present (see p. 1419).
- Treat septic pleuritis/mediastinitis if present (see p. 956).
- Treat esophagitis or esophageal stricture as appropriate (see 367).
- Remove diverticulum surgically if appropriate.

CHRONIC TREATMENT

None unless esophageal stricture or esophageal hypomotility is present after diverticulectomy

NUTRITION/DIET

As for megaesophagus (see 709)

POSSIBLE COMPLICATIONS

- Perforation of diverticulum leading to pleural or mediastinal sepsis
- Aspiration pneumonia

PROGNOSIS AND OUTCOME

Guarded. Too few such cases have been identified and treated to produce objective prognostic information. No instances of self-resolution have been documented, however.

PEARLS & CONSIDERATIONS

COMMENTS

- A very rare condition in dogs and cats
- Must distinguish from the clinically insignificant redundant esophagus often seen in bulldogs and shar-peis.
- Can be difficult to recognize at esophagoscopy. If food is retained within them, diverticula can be seen easily during esophagoscopy. However, if the diverticulum is empty, it is just a fold of tissue that can be overlooked, especially if there is inadequate insufflation of the esophagus during the endoscopic examination. Adequate insufflation may require closing off the proximal esophagus manually to hold air in the esophageal lumen to facilitate evaluation.

SUGGESTED READING

Jergens AE: Diseases of the esophagus. In Ettinger SJ, Feldman EC, editors: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Elsevier Saunders, pp 1298–1310.

Woods CB, et al: Esophageal deviation in four English bulldogs. J Am Vet Med Assoc 172:934, 1978.

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EDITOR: DEBRA L. ZORAN

Erythema Multiforme and Toxic Epidermal Necrolysis

BASIC INFORMATION

DEFINITION

Spectrum of acute, potentially severe and fatal mucocutaneous diseases defined by distinctive clinical and histopathologic findings. Uncommon this diagnosis is considered if dermatologic findings include annular ("target") lesions, erythematous eruptions, and epidermal/mucosal detachment, with secondary ulcerations.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs and cats of any age and both sexes

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Based on clinical and histopathologic features, the erythema multiforme (EM)–toxic epidermal necrolysis (TEN) spectrum is divided into five different categories adapted from the Human International Consensus clinical classification: EM minor, EM major, Stevens Johnson syndrome (SJS), overlap syndrome (OS), and TEN. However, this classification should be considered a general guideline because it is not universally accepted. Furthermore, some cases can overlap these categories or present only a few clinical signs.

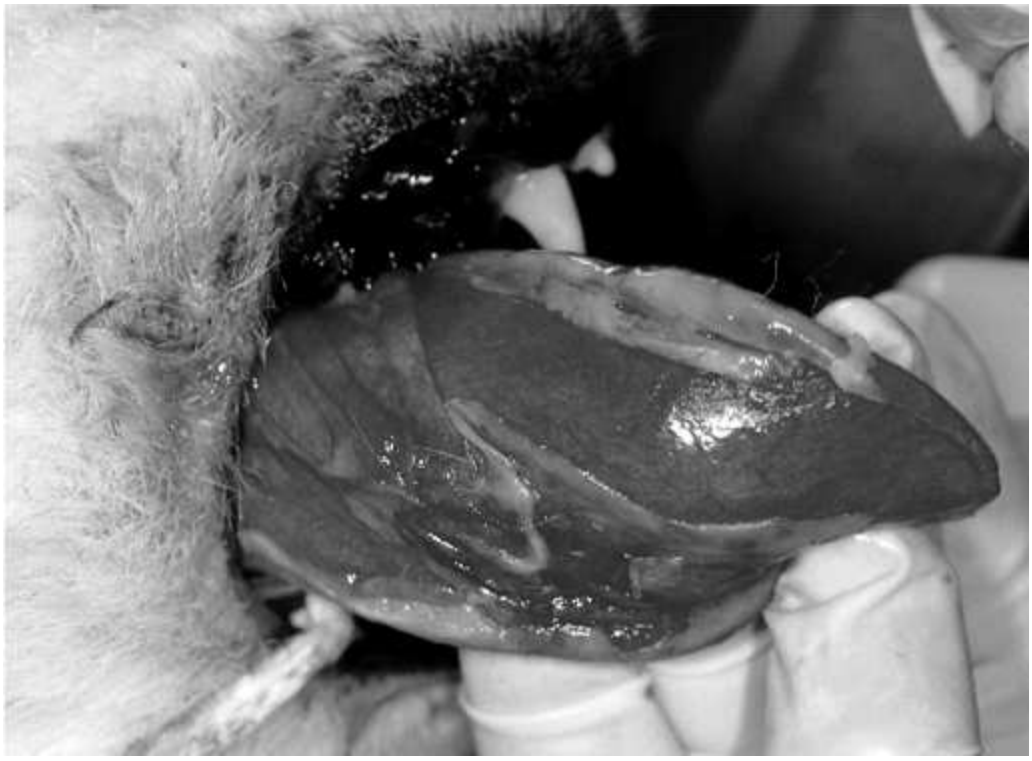
HISTORY, CHIEF COMPLAINT: A dermatosis with an acute onset and rapid deterioration. Systemic signs of illness and severe skin lesions are usually the main complaints. Therapeutic drug administration can be an important element of the history.

PHYSICAL EXAM FINDINGS

- The animal can be debilitated, especially with TEN. Fever precedes virtually all cases of TEN in humans.
- In more severe cases, internal organ function may be affected.

ETIOLOGY AND PATHOPHYSIOLOGY

- In dogs and cats, EM is usually associated with drug therapy or infections (herpesvirus, parvovirus) or is idiopathic.
- TEN is usually associated with drug therapy but can be idiopathic.
- The mechanism of the EM-TEN spectrum diseases seems to be immune mediated. A cell-mediated immune response directed toward various antigens is suspected in EM; a defective epidermal detoxification of drug byproducts, in addition to the cellular immune reaction, is proposed to explain TEN. Both processes lead to keratinocyte apoptosis via perforin/granzyme pathway and the ligation of Fas to its ligand FasL. Moreover, the overproduction of cytokines by cytotoxic T lymphocytes might play a major role by upregulating the adhesion molecules, recruiting lymphocytes, and contributing to keratinocyte apoptosis.



ERYTHEMA MULTIFORME AND TOXIC EPIDERMAL NECROLYSIS Idiopathic erythema multiforme in a Samoyed, showing lingual mucosa detachment.

(Courtesy Dr. Frédéric Sauvé.)

EM, Erythema multiforme; *SJS,* Stevens Johnson syndrome; *OS,* overlap syndrome; *TEN,* toxic epidermal necrolysis.

Dermatologic Examination	EM Minor	EM Major	SJS	OS	TEN
Flat or raised, focal or multifocal, target (concentric rings around a clear or crusty center) or polycyclic lesions	Yes	Yes	No	No	No
Number of mucosal surfaces involved	1 or fewer	>1	>1	>1	>1
Erythematous or purpuric, macular or patchy eruption (% of body surface affected)	<50	<50	>50	>50	>50
Epidermal detachment (vesicles, bullae, erosions, and ulcers) (% of body surface affected)	<10	<10	<10	10-30	>30

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The skin lesions are pleomorphic (varied in shape and appearance). Therefore, the differential diagnosis list is long. The presence of acute-onset skin lesions, particularly with epidermal detachment, signs of systemic illness, and a history of ongoing medication administration (or some combination of these features), should prompt the consideration of skin biopsies, which confirm the diagnosis.

DIFFERENTIAL DIAGNOSIS

Differentiation can be based on history (e.g., in contrast to burns), time course (EM-TEN typically worsens rapidly, unlike urticaria which tend to improve spontaneously and quickly), and ultimately histopathologic appearance.

- Superficial and deep infection (bacterial and fungal)

- Urticaria
- Systemic and cutaneous lupus erythematosus
- Cutaneous drug eruption
- Pemphigus vulgaris
- Vasculitis
- Bullous pemphigoid
- Epidermolysis bullosa
- Burns
- Ulcerative stomatitis
- Epitheliotropic lymphoma

INITIAL DATABASE

- No specific laboratory findings
- Routine dermatologic diagnostics tests should be performed as appropriate (skin scrapings, skin cytology, skin biopsy, fungal culture) based on differential diagnosis (see p. 1248).

ADVANCED OR CONFIRMATORY TESTING

- Hallmark histopathologic findings in skin biopsies include hydropic degeneration, single-cell apoptosis to full-thickness necrosis of the epidermis, dermal lymphohistiocytic cells infiltration, and subepidermal vesicles; hair follicles may be similarly affected. Skin biopsies also help by excluding other differential diagnoses.
- Since the histopathologic findings of EM and TEN might overlap, clinical classification (see table on preceding page) should be considered to differentiate these entities.

TREATMENT

TREATMENT OVERVIEW

- Goals are to stop the immunologic reactions causing the epidermal necrosis, prevent skin infection if the cutaneous barrier is ruptured, and provide supportive care if the animal is debilitated.

ACUTE GENERAL TREATMENT

- Try to find and correct the underlying cause. If any drug is being administered at the time of initial presentation, the first rule is to discontinue its use.
- May resolve spontaneously (EM)
- Severe cases of EM and TEN need supportive care:
  - Fluid therapy if fluid deficits/electrolyte imbalances/acid-base disturbances
  - Nutritional support
  - Maintain thermoregulation
  - Wound care (gentle washes with saline or chlorhexidine gluconate 0.05% solution, dermal protection to prevent infection or desiccation, and topical antibiotics)
- Necrotic epidermis, rich in cytokines, can help reepithelialization. Some authors recommend not to débride skin lesions unless infected.
- Systemic antibiotic therapy is warranted if there is evidence of bacteremia or sepsis; may be considered if cutaneous ulcerations are present.
- Use of glucocorticoids is controversial and usually not beneficial.
- Pentoxifylline (10 mg/kg PO q 8 h) has been useful in some cases.
- Intravenous immunoglobulin (Ig) therapy using human Ig (1 g/kg infused slowly IV over 4-6 hours) may be beneficial. A similar equine product is also available, but there are anecdotal reports of serious adverse effects.
- Severe oral ulcerations may require oral rinses with chlorhexidine 0.1%-0.2% solution or gel, or viscous lidocaine 2% application to the oral ulcers for comfort.

PROGNOSIS AND OUTCOME

- The prognosis is usually good in EM (except if the lesions are severe and extensive) and poor in TEN.
- The condition should improve within 3 weeks when the underlying cause is identified and eliminated.

PEARLS & CONSIDERATIONS

COMMENTS

- Ocular involvement has been reported.
- Some cases have been related to diet, so animals diagnosed with idiopathic disease should receive a hypoallergenic diet.

SUGGESTED READING

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EDITOR: MANON PARADIS

Epulides

BASIC INFORMATION

DEFINITION

- *Epulis* (plural *epulides)* is a nonspecific clinical descriptive term referring to a local, exophytic growth on the gingiva (e.g., focal fibrous hyperplasia, peripheral odontogenic fibroma, acanthomatous ameloblastoma, nonodontogenic tumors).
- This chapter focuses on peripheral odontogenic fibroma, giant cell epulis, and acanthomatous ameloblastoma, which are all benign tumors (that do not metastasize). Peripheral odontogenic fibromas and giant cell epulides do not invade bone, but acanthomatous ameloblastomas are locally invasive.

SYNONYMS

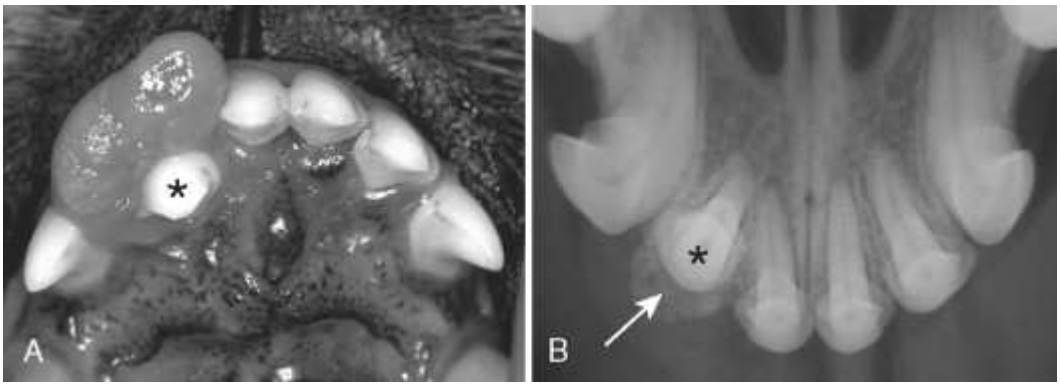
- *Peripheral odontogenic fibroma* replaces the terms *fibromatous* (or fibrous) *epulis* and *ossifying epulis.* Fibromatous epulis is distinguished from ossifying epulis by containing less bone or dental hard tissue within the tumor's soft tissue. Another synonym is *periodontal ligament tumor.*
- Giant cell epulis has also been called *giant cell tumor* or (peripheral) *giant cell granuloma.*
- *Acanthomatous ameloblastoma* replaces the terms *acanthomatous epulis* and *adamantinoma.*

EPIDEMIOLOGY

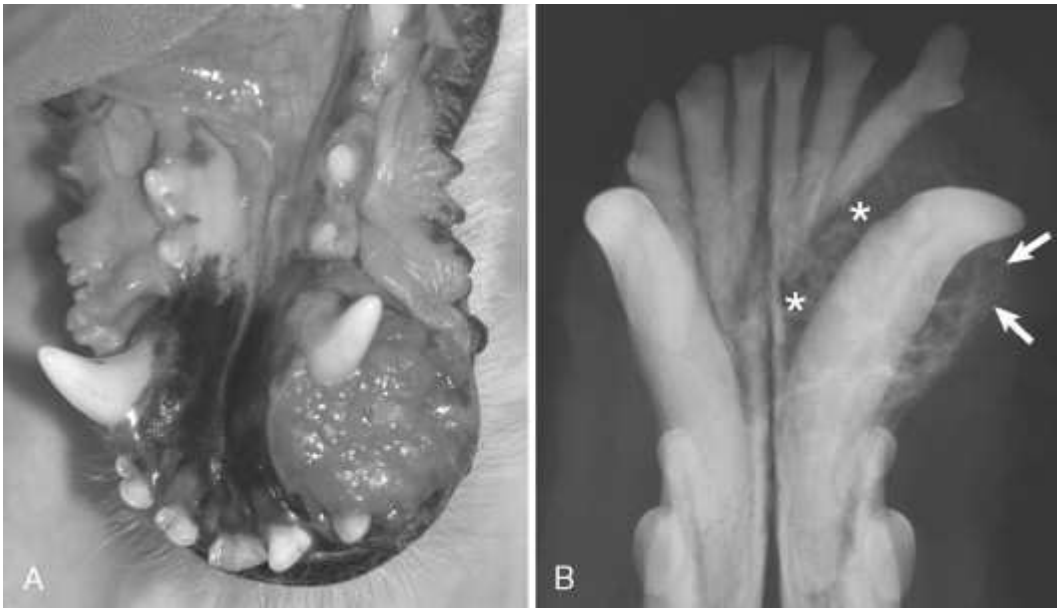
SPECIES, AGE, SEX

Dogs:

- Prevalence: common (except giant cell epulis, which is rare)
- Distribution: peripheral odontogenic fibroma ~80%, acanthomatous ameloblastoma ~18%, and giant cell epulis ~2%
- Breed: acanthomatous ameloblastoma more commonly noted in Shetland sheepdogs
- Age: unknown for giant cell epulis; dogs with peripheral odontogenic fibroma usually >5 years old; dogs with acanthomatous ameloblastoma usually >7 years old (but can affect dogs as young as 1 year of age)
- Sex: conflicting results; female dogs more often affected than males with acanthomatous ameloblastoma, male dogs more often affected than females with peripheral odontogenic fibroma and giant cell epulis



EPULIDES A, Clinical photograph of rostral upper jaw in a dog with peripheral odontogenic fibroma. Note smooth-surfaced and minimally ulcerated/inflamed gingival mass associated with palatally displaced right maxillary second incisor *(asterisk)*. **B,** Dental radiograph of rostral upper jaw in same patient (radiograph arranged in labial mounting; rostral toward bottom of image, and patient's right side is on left of image). Note displaced right maxillary second incisor *(asterisk)* and presence of hard tissue *(arrow)* within tumor's soft-tissue shadow.



EPULIDES A, Clinical photograph of rostral lower jaw in a Shetland sheepdog with acanthomatous ameloblastoma. Note red, cauliflower-like and easily bleeding mass located between left mandibular third incisor and canine tooth. **B,** Dental radiograph of rostral lower jaw in same patient (radiograph arranged in labial mounting; rostral toward the top of image, and patient's left side is on right of image). Note displacement of involved teeth, lysis of alveolar bone *(asterisks)*, and sunburst pattern at left lateral mandibular border *(arrows)*.

Cats:

- Prevalence: uncommon
- Distribution: Peripheral odontogenic fibroma ~63%, giant cell epulis ~29%, and acanthomatous ameloblastoma ~8%
- Breed: no predilection reported
- Age: cats with single peripheral odontogenic fibroma and giant cell epulis usually >7 years old; acanthomatous ameloblastoma and multiple feline epulides particularly in young-adult cats
- Sex: no predilection reported

ASSOCIATED CONDITIONS & DISORDERS: oral tumors, benign (see p. 786). Hypercalcemia of malignancy has been reported in some dogs with acanthomatous ameloblastomas (increased serum concentrations of ionized calcium, total calcium, and parathyroid hormone-related peptide).

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Peripheral odontogenic fibroma:
  - Slow growth; gingiva-like
  - Fibroblast is main component in mass.
  - Slow recurrence after incomplete excision
  - Multiple feline epulides may not originate from the periodontal ligament but may represent reactive lesions arising from the periosteum.
- Giant cell epulis:
  - Rapid growth; inflammatory and ulcerative changes ○ Multinucleated giant cell is main component in mass; osteoid and woven bone formation.
  - Rapid recurrence after incomplete excision
- Acanthomatous ameloblastoma:
  - Rapid growth; cauliflower-like
  - Basal cell is main component in mass.

HISTORY, CHIEF COMPLAINT

- Gingival mass noticed by owner or at routine oral examination
- Clinical complaints mostly absent with peripheral odontogenic fibromas; dysphagia, increased salivation, bloody oral

discharge, and halitosis occasionally reported with giant cell epulides and acanthomatous ameloblastomas.

PHYSICAL EXAM FINDINGS

- Peripheral odontogenic fibroma:
  - Firm, rarely ulcerated gingival mass that measures 0.5 to 3 cm in diameter
  - Located near canine, premolar, and molar teeth (less commonly in the incisor tooth area) and variably fixed to the gum line
  - Covered by oral epithelium; ulceration infrequent
- Giant cell epulis:
  - Soft, reddish purple
  - Ulcerated and inflamed
- Acanthomatous ameloblastoma:
  - Cauliflower-like, red, ulcerated, easily bleeding gingival mass that measures 0.5 to 10 cm in diameter
  - Most commonly located in the rostral lower jaw near incisor and canine teeth; less often in the rostral upper jaw (incisor and canine tooth area), caudal lower jaw (near first molar), and caudal upper jaw (near fourth premolar)

ETIOLOGY AND PATHOPHYSIOLOGY

- Peripheral odontogenic fibroma:
  - Mixed or mesenchymal (dependant on literature studied) odontogenic tumor
  - Arising from cells in the periodontal ligament
- Giant cell epulis: considered to be a variant of the peripheral odontogenic fibroma in which extensive ulceration and inflammation results in strongly increased osteoclastic activity, but the real origin remains unknown.
- Acanthomatous ameloblastoma:
  - Epithelial odontogenic tumor
  - Debatable whether arising from epithelial rests of Malassez in periodontal ligament (intraosseous/central ameloblastoma) or epithelial rests of Serres in gingival connective tissue (extraosseous/peripheral ameloblastoma)

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis requires staging, including oral examination under anesthesia, thoracic radiographs, regional diagnostic imaging (dental radiographs, computed tomography), lymph node palpation and aspiration, and biopsy of the gingival mass.

DIFFERENTIAL DIAGNOSIS

Dogs:

- Gingival hyperplasia (often generalized)
- Pyogenic granuloma (uncommon)
- Dentigerous cyst (around crown of an unerupted tooth)
- Odontoma (not a real tumor, but a hamartoma, i.e., accumulation of normal cells in an abnormal manner)
- Viral papillomatosis (usually in puppies or immunocompromised adults)
- Plasmacytoma (usually solitary, pink-red, well circumscribed)
- Osteoma (slow-growing)
- Malignant melanoma (most common malignant oral tumor)
- Squamous cell carcinoma (second most common oral malignant tumor)
- Fibrosarcoma (third most common malignant tumor)
- Peripheral nerve sheath tumor (along major nerves)
- Osteosarcoma (usually osteolytic type; variant: multilobular tumor of bone)
- Lymphosarcoma (also look for lesions on skin around mouth and nasal plane, bilateral enlargement of tonsils and regional lymph nodes)
- Amyloid-producing odontogenic tumor (rare)
- Erythema multiforme (also look for lesions on skin)
- Autoimmune diseases (bullous pemphigoid, lupus erythematosus)
- Eosinophilic granuloma (usually on soft palate and lateral edges of the tongue)

Cats:

- Gingival hyperplasia, osteoma, plasmacytoma

- Squamous cell carcinoma (most common malignant oral tumor)
- Fibrosarcoma (second most common oral malignant tumor)
- Inductive fibroameloblastoma (rare)
- Amyloid-producing odontogenic tumor (rare)
- Eosinophilic granuloma (usually on upper lip, tongue, sublingual tissues, and palate)

INITIAL DATABASE

- Physical examination, chemistry screen, CBC
- Dental and skull radiographs:
  - Peripheral odontogenic fibromas are not invasive, and radiographic changes to alveolar bone are unlikely.
  - Acanthomatous ameloblastomas are invasive, and changes to alveolar bone are often visible on dental radiographs.
- CT: considered to be superior to radiography, particularly for maxillary and caudally located mandibular lesions
- Biopsy
  - Cytologic techniques are less diagnostic. Biopsy for histopathologic examination is the only definitive test to establish an accurate diagnosis.
  - For small lesions, excisional biopsy can be performed during the initial oral examination, which may be curative.
  - For larger lesions, an incisional biopsy should be performed. Confirmation of the tumor type will allow the clinician to properly plan for future definitive surgery.

ADVANCED OR CONFIRMATORY TESTING

CT is valuable to determine local disease extension and bony invasion in dogs with maxillary or caudal mandibular acanthomatous ameloblastoma. This facilitates achieving wide surgical margins and allows for radiation therapy planning.

TREATMENT

TREATMENT OVERVIEW

The primary goal of treatment is complete tumor removal with minimal functional and cosmetic compromise.

ACUTE GENERAL TREATMENT

- Surgery: conservative and radical
  - Peripheral odontogenic fibroma: gingival excision with conservative margins, extraction of the associated tooth (or teeth in case pinpointing the lesion to one tooth is difficult), and curettage of the alveolar socket(s) to remove the periodontal ligament; local excision without tooth extraction and socket curettage is rarely curative (recurrence is likely, as these tumors arise from cells in the periodontal ligament).
  - Acanthomatous ameloblastoma: mandibulectomy and maxillectomy with at least 1 cm margins (depending on location of the tumor)
- Radiation therapy: considered for nonresectable masses, incomplete resections, and recurrent tumors
  - Peripheral odontogenic fibroma: effective but rarely required, as surgical resection typically results in complete cure.
  - Acanthomatous ameloblastoma: effective, with tumor control achieved in about 90% of dogs, especially for smaller tumors; larger tumors (>4 cm) are more likely to recur (only about 30% tumor control); higher radiation doses may be required to improve control rates.
  - Acute and late side effects can occur, most notably radiation-induced tumors (many years after radiation therapy in about 3.5%–12.5% of dogs with acanthomatous ameloblastoma) and bone necrosis.
- Cryosurgery: causes cellular death after controlled freezing and thawing of the tumor.
  - Best for low-grade tumors <2 cm in diameter and adherent to or minimally invasive into one cortex; tumor should first be debulked and biopsied, followed by cryosurgery applied to underlying bone.
  - Inadequate for tumors with extensive fixation to or invasion into bone; full-thickness freezing of maxillofacial bones (such as the maxilla or mandible) can lead to bone necrosis, bone fracture, or oronasal fistula.
  - Despite maintenance of the bony framework and preservation of oral function, recurrence is more common than with surgical excision.

NUTRITION/DIET

Soft food and avoidance of chew treats/toys for 2 weeks after tooth extraction or radical resection (mandibulectomy, maxillectomy)

POSSIBLE COMPLICATIONS

- Wound dehiscence

- Incomplete resection and tumor recurrence
- Bone necrosis after cryosurgery or radiation therapy

RECOMMENDED MONITORING

- Clinical reexamination 2 weeks, 6 and 12 months, and then once yearly after definitive treatment
- Radiographic reexamination (for acanthomatous ameloblastoma) once yearly

PROGNOSIS AND OUTCOME

- Peripheral odontogenic fibroma and giant cell epulis: excellent prognosis (after complete gingival resection, tooth extraction and curettage of the alveolus); cats with multiple fibromas may have higher recurrence rates.
- Acanthomatous ameloblastoma: excellent prognosis (after mandibulectomy and maxillectomy procedures when clean histopathologic margins can be accomplished); smaller tumors and rostral location are positive prognostic factors because these masses are detected earlier and are easier to remove; postoperative radiation therapy may occasionally be required for tumor control.

PEARLS & CONSIDERATIONS

COMMENTS

- Because peripheral odontogenic fibromas and giant cell epulides arise from the periodontal ligament, excision limited to the gingiva will be inadequate, resulting in tumor recurrence. Gingival excision, extraction of the involved tooth and curettage of the alveolar sockets to remove any remaining periodontal ligament will usually be curative.
- Aggressive surgical excision (mandibulectomy, maxillectomy) is usually curative in dogs with acanthomatous ameloblastoma.
- Radiation therapy offers excellent long-term control for treatment of acanthomatous ameloblastoma, but malignant tumor development in the irradiated area several years later has been reported in some dogs.

PREVENTION

Early tumor detection (daily home oral hygiene and oral examination at every patient visit).

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McEntee MC, et al: Malignant tumor formation in dogs previously irradiated for acanthoma-tous epulis. Vet Radiol Ultrasound 45:357, 2004.

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Epistaxis

BASIC INFORMATION

DEFINITION

Bleeding from the nasal cavity

SYNONYMS

Hemorrhagic nasal discharge, nosebleed

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dependent on underlying cause:

- Young purebred animals: coagulopathies
- Young to middle-aged animals: infectious diseases, trauma
- Middle-aged animals: acquired immune-mediated diseases
- Older animals: neoplasia

GENETICS, BREED PREDISPOSITION, AND RISK FACTORS

- Immune-mediated thrombocytopenia: young to middle-aged, small to medium female dogs
- Rickettsial disease: dogs living or traveling to endemic areas
- Thrombasthenia: otter hounds
- Thrombopathia (see p. 881): basset hounds
- von Willebrand disease: Doberman pinscher, Airedale, German shepherd, Scottish terrier, Chesapeake Bay retriever, and many other breeds; cats: Himalayan
- Hemophilia A: German shepherd and many other breeds; cats
- Hemophilia B: Cairn terrier, coon-hounds, Saint Bernard, and other breeds; cats
- Nasal lesions:
    - Aspergillosis: German shepherd, dolichocephalic breeds
    - Neoplasia: dolichocephalic breeds

CONTAGION & ZOONOSIS: Fungal infections (transmission potential appears low).

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: (Some or all may be present.)

- Nasal hemorrhage
- Sneezing
- Pawing at mouth and/or nose
- With coagulopathy: hematochezia, melena, hematuria, or hemorrhage
- Blindness, central nervous system (CNS) deficits possible with systemic hypertension

PHYSICAL EXAM FINDINGS

- Melena: from swallowing blood
- Nasal hemorrhage
- With coagulopathy: petechia, ecchymosis, hematomas, hematochezia, melena, and hematuria
- With coagulopathy or hypertension: retinal hemorrhages or detachment, CNS deficits

ETIOLOGY AND PATHOPHYSIOLOGY

Bleeding disorder:

- Thrombocytopenia:

    - Immune-mediated disease: idiopathic disease, systemic lupus erythematosus (SLE), drug reaction
    - Rickettsial disease: ehrlichiosis, Rocky Mountain spotted fever
    - Bone marrow disease: neoplasia, aplastic anemia, infectious (fungal, rickettsial, or viral)
    - Disseminated intravascular coagulopathy (DIC)
- Thrombopathia:
    - Congenital: von Willebrand disease, thrombasthenia, thrombopathia
    - Acquired: nonsteroidal antiinflammatory drugs (NSAIDs), hyperglobulinemia (ehrlichiosis, multiple myeloma), uremia, DIC
- Coagulation factor defect:
    - Congenital: hemophilia A (factor VIIIc deficiency) and hemophilia B (factor IX deficiency)
    - Acquired: anticoagulant rodenticide (warfarin) intoxication, liver disease, DIC

Nasal disease:

- Foreign body
- Trauma
- Infection: fungal *(Aspergillus, Cryptococcus, Rhinosporidium),* viral, or bacterial
- Inflammation: lymphoplasmacytic rhinitis
- Neoplasia
- Vascular malformations

Systemic disease:

- Hypertension: renal disease; hyperthyroidism; hyperadrenocorticism; idiopathic
- Hyperviscosity: multiple myeloma, ehrlichiosis, polycythemia
- Vasculitis: immune-mediated and rickettsial diseases

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is apparent on physical examination. Diagnostic testing first must evaluate the possibility of a systemic disorder (bleeding disorder, systemic hypertension). If none, evaluation of the nasal cavities consists of diagnostic imaging and biopsies.

DIFFERENTIAL DIAGNOSIS

See Etiology and Pathophysiology above.

INITIAL DATABASE

- CBC:
    - Anemia if sufficient hemorrhage has occurred
    - Thrombocytopenia or thrombocytosis
    - Neutrophilia: infection; neoplasia
    - Pancytopenia: bone marrow disease
- Urinalysis:
    - Usually normal
    - Hematuria (coagulopathy), isosthenuria with renal failure, proteinuria
- Serum biochemistry profile:
    - Hypoproteinemia if sufficient hemorrhage has occurred
    - Elevated urea with normal creatinine: gastrointestinal blood
    - Hyperglobulinemia: ehrlichiosis, multiple myeloma
    - Azotemia (with isosthenuria): renal failure–induced systemic hypertension
    - Elevated liver enzymes and total bilirubin: severe hepatic disease causing coagulopathy

ADVANCED OR CONFIRMATORY TESTING

- Other laboratory tests:
    - Coagulation profile: prolonged times with coagulation factor defects; normal with thrombocytopenia and thrombopathia
    - Antinuclear antibody test for SLE
    - Platelet function testing (bleeding time, von Willebrand factor analysis)
    - *Ehrlichia* and Rocky Mountain spotted fever titers/PCR

- Thyroid hormone assay in middle aged to old cats
- Diagnostic imaging:
  - Thoracic radiograph: metastatic neoplasia
  - Nasal series: open mouth and frontal sinus views
  - CT scan: more sensitive than radiographs for many nasal diseases
- Other diagnostic procedures:
  - Rhinoscopy, nasal flush, nasal biopsy indicated for suspected space-occupying disease, removing foreign bodies, and sampling nasal tissue
  - Cytologic and histopathologic examination
  - Bacterial and fungal culture and sensitivity testing
  - Bone marrow aspiration and cytology (± core biopsy) with pancytopenia
  - Blood pressure evaluation

TREATMENT

TREATMENT OVERVIEW

- Stop epistaxis
- Treat primary cause

ACUTE GENERAL TREATMENT

- Minimize activity or stimuli that precipitate hemorrhage episodes:
  - Environment
  - Consider tranquilization (e.g., opiates)
- Whole blood or packed red blood cell (RBC) transfusion; may be needed with severe anemia.
- In life-threatening cases of refractory, exuberant arterial epistaxis, both carotid arteries may be ligated without adversely affecting perfusion of the head (vertebral artery collaterals).

SPECIFIC TREATMENT

Coagulopathy:

- von Willebrand disease: plasma or cryoprecipitate for acute bleeding
- Hemophilia: plasma or cryoprecipitate for acute bleeding; no long-term treatment
- Anticoagulant rodenticide intoxication: plasma for acute bleeding and vitamin K supplementation
- Liver disease and DIC; treat underlying cause; plasma may be beneficial.
- Discontinue all NSAIDs.
- Hyperglobulinemia: plasmapheresis

Nasal disease:

- Radiotherapy: nasal tumors
- Topical clotrimazole therapy for fungal disease
- Surgery: if foreign body irremovable by rhinoscopy; fungal rhinitis *(Aspergillus* and *Rhinosporidium),* neoplasia

Systemic disease:

- Hyperviscosity: treat underlying disease (e.g., ehrlichiosis and multiple myeloma); plasmapheresis
- Vasculitis: doxycycline for rickettsial disease; prednisone for immune-mediated disease
- Hypertension: treat underlying disease (e.g., renal disease, hyperthyroidism, and hyperadrenocorticism); reduce weight if obesity is present; restrict sodium; antihypertensive medication.

POSSIBLE COMPLICATIONS

Anemia and collapsed state

RECOMMENDED MONITORING

- Platelet count with thrombocytopenia
- Coagulation profile with coagulation factor defects
- Blood pressure with hypertension

- Monitor clinical signs

PROGNOSIS AND OUTCOME

Dependent on cause

PEARLS & CONSIDERATIONS

COMMENTS

- Remember that epistaxis may indicate a systemic coagulopathy; use care when deciding which vein to use for blood sampling (prefer limb to jugular for compression), whether to perform centeses, and so forth.
- Epistaxis is not a diagnosis but a clinical sign.
- A systemic bleeding disorder may present as unilateral epistaxis.
- Rule out systemic diseases and coagulopathy before focusing on nasal disease.

CLIENT EDUCATION

Monitor for recurrence of presenting signs.

RECOMMENDED READING

Madden SN: Diseases of the nasal cavity and paranasal sinuses. In Morgan RV, Bright RN, Swartout MS, editors: Handbook of small animal practice, ed 4, Philadelphia, 2003, WB Saunders, pp 136–143.

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EDITOR: ETIENNE CÔTÉ

Episcleritis/Scleritis

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

- Episcleritis: focal or diffuse inflammation of the episclera, a thin collagenous and vascular membrane that makes up the superficial layer of the sclera
- Scleritis: inflammation and thickening of the anterior and posterior sclera, involving cornea, uvea, and retina in advanced cases

SYNONYMS

Collie granuloma, fibrous histiocytoma, necrotizing scleritis, nodular fasciitis, proliferative keratoconjunctivitis, limbal granuloma, nodular granulomatous episcleritis/episclerokeratitis (NGE), nonnecrotizing deep scleritis, nonnecrotizing superficial scleritis

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs; no age or sex predisposition

GENETICS & BREED PREDISPOSITION: Spaniel breeds, especially American cocker spaniel (episcleritis, scleritis), collie, Shetland sheepdog (NGE).

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Episcleritis: primary (simple, nodular) or secondary
- Scleritis: necrotizing granulomatous or nonnecrotizing granulomatous

HISTORY, CHIEF COMPLAINT

- Episcleritis:
  - Pinkish-red growth on eye (nodular)
  - “Red eye” (diffuse)
  - Typically painless
- Scleritis:
  - Signs of ocular pain noted by owner: photophobia, blepharospasm, excessive tearing, inktan colored sector lesions near the limbus

PHYSICAL EXAM FINDINGS

- Episcleritis:
  - Conjunctival hyperemia
  - Engorgement of episcleral vessels
  - Thickening of episclera (partial or diffuse)
  - With nodular forms, multiple or single raised, pinkish-red mass(es) may be apparent at limbus; typically bilateral
  - ± Perilimbal keratitis with corneal vascularization and edema (e.g., nodular granulomatous episclerokeratitis)
- Scleritis:
  - Conjunctival hyperemia
  - Engorgement of episcleral vessels
  - Typically bilateral, mildly elevated, red lesions in the anterior sclera
  - Peripheral corneal vascularization and edema
  - Nongranulomatous anterior uveitis, (see p. 1151)
- Advanced scleritis: presence of signs of scleritis and any or all of the following:
  - Stromal keratitis (see Corneal Discoloration, p. 245)
  - Inflammation of the vitreous
  - Secondary glaucoma (see p. 448)
  - Retinochoroidal degeneration (see p. 983)
  - Cystic retinal detachment (see p. 985)

- Scleral thinning, which may cause subconjunctival iris prolapse

ETIOLOGY AND PATHOPHYSIOLOGY

- Episcleritis/scleritis:
  - Often idiopathic; immune-mediated disease
  - Association with positive *Toxoplasma* titers has been found.
- Episcleritis:
  - Primary:
    - Simple (uncommon): not associated with systemic disease; usually responsive to therapy; often self-limiting
    - Nodular (common): proposed pathogenesis of nodular granulomatous episcleritis involves production of inflammatory mediators by T lymphocytes and subsequent chemotaxis of histiocytes.
  - Secondary:
    - Develops as a result of inflammation extending to episclera from severe intraocular diseases including panophthalmitis/endophthalmitis (see Hypopyon, p. 583), chronic glaucoma, or ocular trauma
- Scleritis:
  - Nonnecrotizing granulomatous:
    - Characterized by infiltration of lymphocytes, plasma cells, and macrophages
    - Granulomatous response seen in cornea with corneal extension
    - ± Secondary uveitis
    - Damaged sclera replaced by fibrous tissue and/or cystic spaces, causing scleral thinning after several episodes
  - Necrotizing granulomatous (rare):
    - Aggressive disease causing necrosis of scleral collagen
    - Typically affects both anterior and posterior segments of the eye
    - Commonly associated with secondary uveitis, glaucoma, and retinal detachment
    - *Ehrlichia canis* infection reported in certain cases

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Episcleritis/scleritis should be strongly suspected on the clinical appearance of the affected globe(s), ruling out other causes of red eye, and response to treatment. If the ocular disease does not respond to medical therapy as expected, episcleral biopsy (usually referable procedure) for a histologic diagnosis is warranted.

DIFFERENTIAL DIAGNOSIS

- Nodular episcleritis; other pinkish, raised lesions:
  - Neoplasia:
    - Conjunctival neoplasia (e.g., mast cell tumor; hemangiosarcoma; histiocytoma)
    - Extension of intraocular tumor
- Granuloma (e.g., foreign body; parasitic—*Onchocerca* spp.)
- Granulation tissue
- Diffuse episcleritis/scleritis; other causes of red eye:
  - Conjunctivitis
  - Glaucoma
  - Uveitis

INITIAL DATABASE

- Complete ophthalmic examination (see p. 1313), including:
  - Schirmer tear test (normal >15 mm in 1 minute in dogs)
  - Fluorescein dye application
  - Intraocular pressures (normal >15 mm Hg and <25 mm Hg)
  - Examination of the anterior and posterior segments of the eye
- Cytologic examination of nodular lesion; may help differentiate neoplasia from inflammation (see Differential Diagnosis)

ADVANCED OR CONFIRMATORY TESTING

- Episcleral biopsy and histopathologic evaluation (nodular granulomatous episcleritis characterized by histiocytes, plasma cells, lymphocytes, and fibroblasts)

- Serologic titers for infectious diseases if supportive systemic signs (e.g., *T. gondii; E. canis)*
- Laboratory testing: canine rheumatoid factor, antinuclear antibody, lupus erythematosus cell identification negative in most cases
- Ocular ultrasound if ocular media opaque, compromising evaluation of deeper ocular structures; useful for ruling out concurrent ocular abnormalities (i.e., retinal detachment)

TREATMENT

TREATMENT OVERVIEW

Many forms of episcleritis respond well to topical corticosteroid application, tapered gradually to the lowest effective frequency. Therapeutic goals are to promote regression of disease, eliminate ocular pain, and keep disease in remission with maintenance therapy. Treatment of NGE and scleritis often requires topical and systemic therapies, including oral prednisone ± azathioprine.

ACUTE GENERAL TREATMENT

To be implemented only if fluorescein staining has ruled out corneal ulceration:

- Topical corticosteroids (e.g., 0.1% dexamethasone solution or ointment or 1% prednisolone acetate) q 6-8 h for 2-3 weeks then gradually tapered
- ± Topical cyclosporine (0.2%–2%) q 12 h; used in addition to corticosteroids in refractory cases.

CHRONIC TREATMENT

NGE and scleritis often require topical (see Acute General Treatment) and systemic therapy(ies) including:

- Prednisone 1-2 mg/kg PO q 24 h until clinical improvement then gradually tapered over 3-4 weeks until maintenance dose reached
- ± Azathioprine 1.5-2 mg/kg PO q 24 h until clinical improvement then gradually tapered to as low a dose as possible (e.g., 0.75-1 mg/kg PO q 24 h, then q 48 h, then once weekly for maintenance.
- Options if medical management ineffective:
    - Cryosurgery
    - Surgical excision

Alternative medical treatment includes tetracycline combined with niacinamide (PO q 8 h): 250 mg of each for dogs 10 kg; 500 mg of each for dogs >10 kg; clinical response may take 1-2 months; occasional gastrointestinal side effects from niacinamide.

POSSIBLE COMPLICATIONS

- Chronic ocular pain
- Uveitis
- Secondary glaucoma
- Blindness
- Azathioprine may cause severe life-threatening myelosuppression; potentially hepatotoxic.

RECOMMENDED MONITORING

- Monitor for regression of disease every 2–3 weeks until clinical signs resolve, then as needed depending on response to therapy.
- In animals receiving azathioprine therapy, CBC and liver enzymes should be assessed every 1–2 weeks for the first 2 months then regularly (e.g., monthly) once clinically stable.

PROGNOSIS AND OUTCOME

- Variable depending on underlying condition and cause
- Episcleritis: prognosis usually good
- Recurrence possible

PEARLS & CONSIDERATIONS

COMMENTS

Lifelong treatment is typically required.

TECHNICIAN TIP

Some ophthalmic drugs have virtually identical names for their formulations with and without corticosteroids. This similarity presents a risk of using the wrong drug. Prior to topical application, it is extremely useful for technicians to carefully read the label of the tube/vial and identify whether it contains corticosteroids and to check the medical record for consistency. Substitution error (especially administering corticosteroids when they are contraindicated) can be devastating and has been made by veterinarians, technicians, and clients.

SUGGESTED READING

Grahn BH, Sandmeyer LS: Canine episcleritis, nodular episclerokeratitis, scleritis and necrotic scleritis. Vet Clin North Am Small Anim Pract 38:291–308, 2008.

AUTHOR: URSULA M. DIETRICH

EDITOR: CHERYL L. CULLEN

Epilepsy, Idiopathic

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

A syndrome characterized by chronic recurrent seizures for which there is no identifiable cause. Other terms:

- Status epilepticus: a seizure lasting more than 5 minutes, or two or more seizures in which there is incomplete recovery of consciousness.
- Cluster seizures (also called *serial* or *acute repetitive seizures*): three or more isolated seizures occurring within a short period of time.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs: commonly affected, 1-5 years old, slightly more common in males
- Cats: uncommonly affected compared with dogs, but not rare in this species

GENETICS & BREED PREDISPOSITION

- More common in large-breed dogs, but any breed can be affected.
- Inherited in beagle, Belgian Tervuren, keeshond, dachshund, British Alsatian, Labrador retriever, golden retriever, Shetland sheepdog, Irish wolfhound, Viszla, Bernese mountain dog, English springer spaniel, and probably others

ASSOCIATED CONDITIONS & DISORDERS: During status epilepticus, hyperthermia can occur secondary to muscle activity.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- One or more seizures
- Most common are generalized tonic-clonic seizures characterized by loss of consciousness and sustained contraction of all muscles, followed by paddling motions of the limbs or rhythmic muscle contractions, especially of the limbs and masticatory muscles.
- Also possible are milder generalized tonic-clonic seizures in which consciousness is maintained, and focal seizures in which only part of the body is involved (e.g., fly-biting movements).
- With idiopathic epilepsy, the interictal period (period between seizures, after recovery) is normal, and owners do not report evidence of ongoing neurologic deficits.
- An effort should be made to clarify any possible sources of intoxication (e.g., lead, ethylene glycol, organophosphate, carbamate, metaldehyde).

PHYSICAL EXAM FINDINGS

- Normal unless examined immediately after a seizure when temporary postictal deficits are possible, including generalized ataxia, abnormal behavior, and blindness that proceed to resolve over minutes to hours.
- Persistent neurologic deficits such as hemiparesis, abnormal behavior, or visual deficits are inconsistent with idiopathic epilepsy and suggest an underlying structural neurologic lesion.
- Persistent fontanelle may or may not be associated with hydrocephalus; however, it offers an acoustic window for ultrasonography to pursue this diagnosis.
- A fundic examination is essential. Uveal, retinal, or optic disk diseases that may correlate with causes of seizures and are inconsistent with idiopathic epilepsy include optic neuritis, feline infectious peritonitis, toxoplasmosis/neosporosis, systemic mycoses, rickettsial diseases, systemic hypertension, lymphoma, and metastatic neoplasia.

ETIOLOGY AND PATHOPHYSIOLOGY

Theories include inborn abnormalities in neuronal excitability, neurotransmitter, or receptor function.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Idiopathic epilepsy is a clinical diagnosis based on the typical age of onset, lack of persistent neurologic deficits, and exclusion of other potential causes based on laboratory testing. A presumptive diagnosis of idiopathic epilepsy may be made without comprehensive diagnostic testing when the patient's signalment and history are consistent with epilepsy, and physical and neurologic examination findings and initial database results are normal. In such cases, further testing may be pursued if deterioration or failure to respond to medication is noted. By declining a comprehensive evaluation, the patient's owner must assume the responsibility that an underlying progressive lesion, rather than epilepsy, may be present.

DIFFERENTIAL DIAGNOSIS

- Metabolic disorders: hepatic encephalopathy including portosystemic shunt, hypoglycemia, polycythemia, hypocalcemia
- Toxins: lead, ethylene glycol, organophosphate, carbamate, metaldehyde
- Brain malformations: hydrocephalus, lissencephaly
- Inherited degenerative diseases such as lysosomal storage diseases
- Encephalitis: granulomatous meningoencephalitis, necrotizing encephalitis, distemper, tickborne infections, fungal encephalitis, *Neospora caninum, Toxoplasma gondii*, feline infectious peritonitis
- Neoplasia: primary and metastatic brain tumor
- Vascular lesions: infarct, hemorrhage
- Head injury
- Also consider nonepileptic episodes such as syncope, narcolepsy, exercise-induced weakness, vestibular dysfunction, and episodes of pain.

INITIAL DATABASE

- CBC: generally unremarkable. Nucleated red blood cells and/or basophilic stippling suggest lead toxicosis rather than epilepsy; acanthocytes nonspecifically suggest hepatic disease.
- Serum chemistry profile, urinalysis: help identify hypoglycemia, hepatic encephalopathy, and renal failure (uremic encephalopathy) as possible causes of seizures instead of idiopathic epilepsy. Fasting hypercholesterolemia may suggest hypothyroidism and attendant central nervous system effects if hyperlipidemia is severe. Hypocalcemia can produce intense muscle tremors that may be misinterpreted as seizures. Hyperglobulinemia in cats raises the possibility of feline infectious peritonitis–based encephalitis as the cause of seizures rather than epilepsy.
- Serum bile acids (preprandial and postprandial):
    - Elevation of either or both suggests hepatic encephalopathy (portosystemic shunt, cirrhotic/fibrosing liver disease, other) rather than idiopathic epilepsy.
    - However, moderate elevations in bile acids routinely may occur soon after a seizure of any cause. In these cases, it is warranted to recheck bile acids 2-4 weeks later to see if the abnormality persists.
- Blood lead concentration if potential exposure

ADVANCED OR CONFIRMATORY TESTING

- Brain CT/MRI and cerebrospinal fluid (CSF) analysis are indicated in the following patients presenting with seizures and no identifiable systemic cause: dogs <1 year or <5 years, dogs with persistent neurologic deficits, and cats. Results of these imaging procedures and CSF analysis are normal with idiopathic epilepsy (diagnosis of exclusion).
- Electroencephalography (EEG) may show abnormalities that confirm seizure activity but are not pathognomonic for idiopathic epilepsy.

TREATMENT

TREATMENT OVERVIEW

Status epilepticus and cluster seizures require emergency treatment because they can lead to life-threatening complications such as hyperthermia and brain damage; prolonged seizures become progressively refractory to treatment. Long-term treatment with anticonvulsant drugs is instituted if seizures are severe and/or frequent. Daily medication is not indicated in patients with a single seizure, seizures caused by a transient condition (e.g., acute intoxication), or isolated seizures separated by a long period of time. Daily medication is indicated in patients with more than one isolated seizure per month, clusters of multiple seizures per day, or a clear pattern of increasing frequency or severity of seizures.

ACUTE GENERAL TREATMENT

- To stop an active seizure: diazepam 0.5–1 mg/kg IV to effect
- If the seizure does not stop with three doses of diazepam, administer:
  - Pentobarbital 3–15 mg/kg, slow IV; *or*
  - Propofol 1–8 mg/kg IV to effect followed by continuous infusion at 0.1 mg/kg/min titrated to effect.
- If the seizure stops with the above therapy but recurs soon after, there are several options:
  - Load with phenobarbital: 12-24 mg/kg slow IV or IM, single dose, followed by maintenance doses of 2-3 mg/kg slow IV, IM, or PO q 12 h; *or*
  - Diazepam continuous rate infusion: 0.5–1 mg/kg/h in 2.5% dextrose + 0.45% saline. Titrate based on seizure control and sedation.

CHRONIC TREATMENT

- Initial therapy with either phenobarbital (dog, cat) or bromide (dog)
  - Phenobarbital:
    - Initial dose: 2-3 mg/kg PO q 12 h (dog, cat) subsequently adjusted based on clinical effects and therapeutic monitoring
    - Steady-state serum concentrations are reached about 10 days after starting therapy or changing the dose.
    - Common side effects: polyuria/polyphagia, sedation, ataxia
  - Potassium bromide:
    - Initial dose: 20-30 mg/kg PO q 24 h (dog), subsequently changed based on clinical effects and therapeutic monitoring
    - Cats: substantial risk of pneumonitis
    - Steady-state serum concentrations are reached 2-3 months after starting therapy or changing the dose.
    - For more rapid control of seizures in dogs with frequent, severe seizures, administer a loading dose: 50–66 mg/kg PO q 6-8 h × 48 hours.
    - Common side effects: polyuria/polyphagia, sedation, ataxia
- If seizures are not adequately controlled despite target serum concentrations of the first drug, adding a second drug while continuing the first drug may be effective. If the seizures become well controlled, it may be possible to gradually wean the first drug.
- Other drugs:
  - Zonisamide (5 mg/kg if used alone, or 10 mg/kg in combination with phenobarbital PO q 12 h [dog]; or 5–10 mg/kg PO q 24 h [cat]; higher dose as combination due to hepatic enzyme induction by phenobarbital). Add-on therapy when seizures are not controlled with initial drug. Initial therapy to avoid side effects of phenobarbital or bromide.
  - Levetiracetam (20 mg/kg PO q 8 h; dog, cat). Add-on therapy with bromide. Initial therapy to avoid side effects of phenobarbital or bromide.
  - Gabapentin (100–300 mg PO total q 8 h; dog, cat). Add-on therapy when seizures are not controlled with initial drug.
  - Clorazepate (0.5–1 mg/kg PO q 8 h; dog, cat). Add-on therapy when seizures are not controlled with initial drug.
  - Felbamate (15–45 mg/kg PO q 8 h, dog). Add-on therapy when seizures are not controlled with initial drug.
  - Pregabalin (2–4 mg/kg PO, q 12 h, dog). Add-on therapy when seizures are not controlled with initial drug. Start at low end of dose to minimize sedation.
- For dogs that suffer clusters of multiple seizures despite daily medication, at-home administration of diazepam per rectum can decrease the need for emergency veterinary care. The client administers 2 mg/kg of parenteral diazepam solution per rectum using a syringe and urinary catheter or teat cannula, repeated for a maximum total of 3 doses within 24 hours.

DRUG INTERACTIONS

- Phenobarbital may decrease the effect of chloramphenicol, corticosteroids, doxycycline, propranolol, and metronidazole. Other depressants and chloramphenicol may increase the effect of phenobarbital.
- Bromide: higher chloride intake increases bromide elimination, which increases the dose requirement; lower chloride decreases bromide elimination.

POSSIBLE COMPLICATIONS

- Phenobarbital-induced hepatotoxicity (see p. 871):
  - Minimized by avoiding serum concentrations <35 mcg/mL
  - Evidence of hepatotoxicity: increases in bile acid concentrations; proportionally larger increases of ALT compared to alkaline phosphatase; icterus, weight loss, ascites if very severe and advanced
  - Potentially reversible if phenobarbital is stopped early enough
- Phenobarbital rarely causes hematologic abnormalities, including neutropenia, anemia, and thrombocytopenia; the drug must be stopped if these abnormalities occur.
- Bromide increases the risk of pancreatitis and may be associated with megaesophagus.

RECOMMENDED MONITORING

- Phenobarbital:
  - Measure serum concentrations 14 days after starting therapy or changing dose, when seizures are not adequately controlled, when signs of dose-related toxicosis occur, and every 6–12 months.
  - Blood sample is obtained immediately before the next dose is due (trough serum level), namely 8–12 hours after preceding dose was given.
  - Blood should *not* be drawn into serum separator tubes, as the separator material may artifactually reduce phenobarbital concentrations in vitro.
  - Target range: 20–35 mcg/mL (85-150 mmol/L).
  - Measure bile acids every 6–12 months to screen for hepatotoxicity.
- Bromide:
  - Measure serum concentrations 1 month and 3–4 months after starting therapy or changing dose, when seizures are not adequately controlled, when signs of dose-related toxicity occur, and every 6-12 months.
  - Because of the drug's extremely long elimination half-life, blood samples need not be drawn a certain number of hours after dosing.
  - Target range: 1–2 mg/mL (100–200 mg/dL; 1000–2000 µg/mL) when used concurrently with phenobarbital and 2–3 mg/mL (200–300 mg/dL; 2000-3000 µg/mL) when used as monotherapy

PROGNOSIS AND OUTCOME

- About 70% of dogs with idiopathic epilepsy can be adequately treated with phenobarbital and/or bromide and enjoy a good quality of life.
- In general, dogs with idiopathic epilepsy have a normal lifespan. However, some dogs with recurrent episodes of status epilepticus requiring emergency treatment have a decreased expected lifespan (≈8 years, versus ≈11 years).

PEARLS & CONSIDERATIONS

COMMENTS

- A common cause of poor seizure control is failure to reach target serum concentrations before switching to a second drug.
- Referral to a neurologist is considered if the diagnosis is uncertain or if the seizures are not adequately controlled within 3 months.

PREVENTION

- Animals with idiopathic epilepsy should not be bred because of potential genetic factors.
- Females should be spayed because estrus tends to increase seizures.

CLIENT EDUCATION

Client education is vital; the client must understand the goal of treatment, potential side effects, and need for periodic monitoring and dose adjustment. The client must agree that the benefits of treatment outweigh the side effects and must not alter treatment without consulting the attending veterinarian.

SUGGESTED READING

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Podell M: The use of diazepam per rectum at home for the acute management of cluster seizures in dogs. J Vet Int Med 9:68, 1995.

Thomas WB, Dewey CW: Seizures and narcolepsy. In Dewey CW, editor: A practical guide to canine and feline neurology, ed 2, Ames, 2008, Wiley-Blackwell, pp 237–259.

AUTHOR: WILLIAM B. THOMAS

EDITOR: CURTIS W. DEWEY

Eosinophilic Granuloma Complex

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

- Cats: several conditions affecting the oral cavity, lips, and skin, grouped together based on typical clinical presentation and an eosinophilic infiltrate histopathologically.
- Dogs: rare disease process characterized by single or multiple ulcerated lesions in oral cavity.

SYNONYMS

- Eosinophilic granuloma (cutaneous or oral): collagenolytic granuloma, linear granuloma
- Eosinophilic ulcer (oral): indolent ulcer, rodent ulcer
- Feline eosinophilic skin diseases (dermatoses)

EPIDEMIOLOGY

SPECIES, AGE, SEX: Lesions are more common in young animals, female cats, and male dogs.

GENETICS & BREED PREDISPOSITION

- Cats: no breed predisposition; genetic predisposition hypothesized (from a colony of related pathogen-free cats)
- Dogs: Siberian huskies, Alaskan malamutes, Cavalier King Charles spaniels (CKCS); unknown hereditary basis

RISK FACTORS: In one publication, 90% of cats with eosinophilic ulcers were feline leukemia virus (FeLV) positive.

CONTAGION & ZOONOSIS: Multiple cases in multicat households and experimental transmission from one area of a cat to another suggest an infectious or allergic etiology.

GEOGRAPHY AND SEASONALITY: Worldwide; warm weather seasonality may be observed.

ASSOCIATED CONDITIONS & DISORDERS: Miliary dermatitis or symmetric alopecia may be noted concurrently in cats.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Lesions may be insidious in onset.

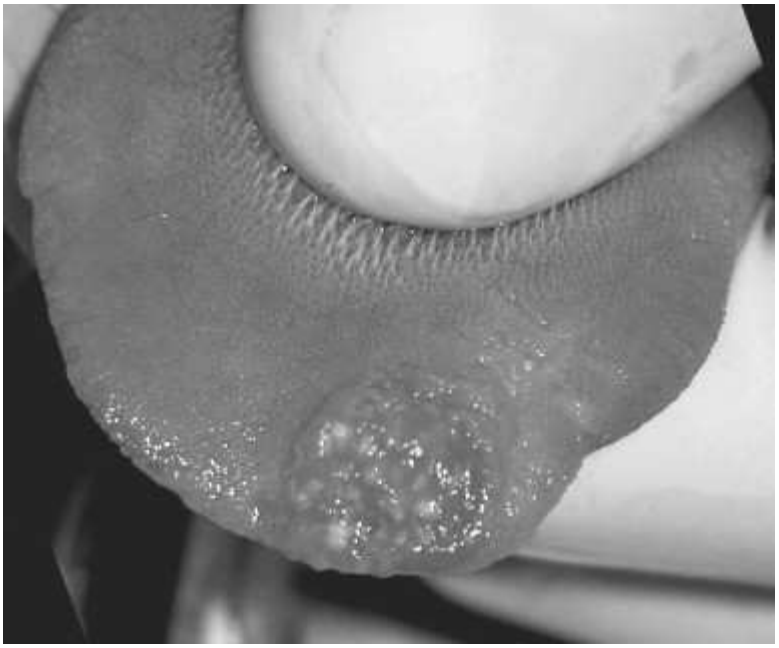
- Skin lesions associated with pruritus, pain
- Oral lesions associated with dysphagia, ptyalism, halitosis, inappetence

PHYSICAL EXAM FINDINGS: Three major forms in cats (all three forms may be observed in the same patient):

- Eosinophilic granuloma
  - Erythematous, alopecic, raised, linear skin lesions on lateral thorax, lateral shoulder, or caudal aspect of thighs; variable pruritus and pain
  - Nodules in oral cavity (dorsal and lateral tongue surfaces, hard and soft palate, glossopharyngeal folds) or at chin; surface often is speckled with small, dense white areas.
- Eosinophilic ulcer
  - Well-demarcated ulcer (raised edges surround a pink-yellow ulcerated surface) on the upper lip (midline or adjacent to the maxillary canine tooth); may also affect the philtrum; nonpruritic, apparently painless
- Eosinophilic plaque
  - Erythematous, raised plaquelike skin lesions, commonly on the ventral abdomen, perianal region and medial thighs; variable pruritus and pain

Two major forms in dogs:

- Single or multiple (often confluent) ulcerated lesions on soft palate and lateral pharyngeal mucosa; especially noted in CKCS
- Firm, raised, yellowish to brownish-pink, irregular, ulcerated lesions with well-demarcated edges on lateral or ventral tongue surfaces or lingual frenulum; especially noted in Siberian huskies and Alaskan malamutes



EOSINOPHILIC GRANULOMA COMPLEX Eosinophilic granuloma near the tip of the tongue in a cat.

(Courtesy Dr. Alexander M. Reiter, University of Pennsylvania.)

EOSINOPHILIC GRANULOMA COMPLEX Eosinophilic ulcer of the upper lip and philtrum in a cat.

(Courtesy Dr. Edmund J. Rosser, Michigan State University.)

ETIOLOGY AND PATHOPHYSIOLOGY

- Different forms may be regarded as different reaction patterns to underlying antigenic stimulation (hypersensitivity reaction), most commonly arthropods (fleas, mosquitoes), food, and contact or environmental (house dust mites, pollens) allergies.
- Other reported causes include viral and bacterial infections, chronic trauma, poor oral hygiene, genetic heritable eosinophilic dysregulation and autoimmune reaction.

DIAGNOSIS

OVERVIEW STATEMENT

The diagnosis is primarily visual and is confirmed by biopsy.

DIFFERENTIAL DIAGNOSIS

- Eosinophilic granuloma and plaque: cutaneous lymphoma, mast cell tumor, squamous cell carcinoma, demodicosis, dermatophytosis, bacterial pyoderma, mycobacterial infection
- Eosinophilic ulcer: squamous cell carcinoma, dermatophytosis, herpesvirus, calicivirus, FeLV, and *Cryptococcus*
- Lip/oral cavity lesions: squamous cell carcinoma, fibrosarcoma, focal inflammation due to a foreign body, trauma, or an infectious agent
- All forms: some cases are idiopathic.

INITIAL DATABASE

- Microscopic examination of plucked hair (trichogram), acetate tape preparation, skin scraping and flea-combing samples to rule out ectoparasites; alternatively, an improvement following appropriate empirical ectoparasiticidal therapy also supports parasitosis.
- Woods lamp examination/bacterial, fungal, mycobacterial cultures: negative
- Cytologic examination of the surface of lesions may reveal large numbers of eosinophils and bacterial or *Malassezia* overgrowth.
- Mild to moderate eosinophilia may occasionally be noted on CBC (rare in cats and inconsistent in dogs with oral lesions).
- Feline immunodeficiency virus/FeLV testing

ADVANCED OR CONFIRMATORY TESTING

- Skin biopsies reveal a superficial to deep to interstitial to diffuse predominantly eosinophilic dermal infiltrate +/− flame figures (collagen fibers surrounded by eosinophilic material).
- Oral biopsy is indicated to rule out neoplasia such as squamous cell carcinoma and fibrosarcoma and establish a diagnosis.
- Adverse food reaction: improvement with 8–10 weeks of elimination diet trial; relapse upon oral challenge

TREATMENT

TREATMENT OVERVIEW

- Treatment of choice consists of early and aggressive glucocorticosteroid therapy.
- Treat secondary infection and underlying cause where appropriate.
- Surgical excision and laser therapy can be attempted for single oral lesions.

ACUTE GENERAL TREATMENT

- Oral glucocorticosteroids: 1–2 mg/kg prednisone or prednisolone PO q 12 h initially, then taper to lowest effective dose. Prednisolone is a superior choice in cats (unpredictable absorption or metabolism of prednisone).
- Injectable glucocorticosteroids: 4 mg/kg methylprednisolone (maximum 20 mg, Depo-Medrol) can be given 2-3 times, 2 weeks apart. This should not be a standard therapy. Side effects include induction of congestive heart failure, diabetes mellitus, and hyperadrenocorticism (alopecia, thin or inelastic skin, skin fragility syndrome, hyperpigmentation, medially curled pinnae, bruising, poor hair coat, demodicosis, dermatophytosis, weight gain, steroid hepatopathy).
- Oral clavulanic acid–potentiated amoxicillin (Clavamox) at an average dose of 13.6 mg/kg q 12 h for 3 weeks has been shown to significantly decrease the size of eosinophilic cutaneous plaques in cats.
- Oral cyclosporine (5 mg/kg PO q 24 h initially, then taper to q 48 h) is an effective alternative to corticosteroids in cats with presumed or confirmed atopic dermatitis. This medication is available in a capsule and a liquid form. The liquid allows more flexible dosing but is bitter tasting. Main side effects include vomiting, diarrhea, soft stools, and very rarely, fatal acute toxoplasmosis.

CHRONIC TREATMENT

- If fleas are present, a rigorous flea control program should be started.
- Allergen-specific immunotherapy (desensitization) for the treatment of atopic dermatitis based on the results of intradermal test and/or aeroallergen-specific immunoglobulin E serum test.

NUTRITION/DIET

Strict elimination diet in proven cases of adverse food reaction

POSSIBLE COMPLICATIONS

- Inadequate initial therapy may result in refractory lesions.
- Oronasal communication may result after surgical excision of palatal lesions.

PROGNOSIS AND OUTCOME

Good

PEARLS & CONSIDERATIONS

COMMENTS

- Feline eosinophilic granuloma complex is not a specific diagnosis. A primary underlying cause is likely to be present and should be investigated.
- Squamous cell carcinoma and eosinophilic granuloma of the tongue and sublingual tissues can clinically appear very similar. Biopsy and histopathologic examination are essential to obtain an accurate diagnosis.

PREVENTION

If an underlying allergic cause can be determined and controlled, the problem can be prevented from reoccurring.

CLIENT EDUCATION

- Skin lesions tend to wax and wane, so reoccurrence is unpredictable except in seasonal cases.
- Since glucocorticosteroids mask the problem rather than eliminating it, an effort should be made to identify the cause and possibly use other types of treatment if effective.
- Cats can (rarely) outgrow the disease over time.

SUGGESTED READING

Bloom PB, et al: Canine and feline eosino-philic skin diseases. Vet Clin North Am Small Anim Pract 36:141, 2006.

AUTHORS: VINCENT E. DEFALQUE, JAMIE G. ANDERSON

EDITORS: ALEXANDER M. REITER, MANON PARADIS

Eosinophilic Bronchopneumopathy

BASIC INFORMATION

DEFINITION

Idiopathic infiltration of airways, interstitium, and sometimes alveoli and/or nasal cavities with inflammatory infiltrates characterized by a high proportion of eosinophils. The disease is well recognized but not common.

SYNONYMS

Pulmonary infiltrates with eosinophils (PIE), canine idiopathic eosinophilic bronchopneumopathy (EBP; the most current term), eosinophilic pneumonia, eosinophilic bronchitis

EPIDEMIOLOGY

SPECIES, AGE, SEX: Primarily a disease of dogs of any age with no sex predilection. Cats are not affected.

GENETICS & BREED PREDISPOSITION

Any breed can be affected, although Siberian huskies have been suggested as a breed predisposed to the disease.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Animals that have EBP most often present with a chronic cough that is unresponsive or poorly responsive to antimicrobial therapy. Cough may be intermittent, frequent, or persistent and is usually accompanied by a terminal gag/retch. Affected animals may have very productive coughing to the point of expectoration of respiratory secretions onto the floor or may experience gagging and retching.
- Nasal discharge, which can be serous or mucopurulent, may also be a presenting complaint.
- Exercise intolerance
- Depression (uncommon)
- Weight loss in affected dogs is rare.

PHYSICAL EXAM FINDINGS

- Cough
- Crackles, wheezes, and increased bronchovesicular sounds heard during thoracic auscultation
- Tachypnea
- Hyperpnea/dyspnea
- Fever
- Bronchospastic reactions, such as expiratory dyspnea and wheezes, are rarely observed.

ETIOLOGY AND PATHOPHYSIOLOGY

- A hypersensitivity reaction is suspected as the main pathophysiologic process underlying the disease.
- The precipitating cause is rarely identified.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Clinical presentation is no different from many other causes of chronic cough. Peripheral eosinophilia may be seen on a CBC, and nonspecific changes are typical on thoracic radiographs. A functional clinical diagnosis rests on identifying sterile eosinophilic inflammation in the airways on bronchoscopy.

DIFFERENTIAL DIAGNOSIS

Other diseases associated with eosinophilic respiratory inflammation:

- Respiratory parasites (*Oslerus* and *Capillaria* spp., others)
- Respiratory infection (bacterial, fungal)
- Pulmonary neoplasia (primary or metastatic)
- Heartworm infection
- Eosinophilic granulomatosis, which on radiographs appears more as a nodular pulmonary disease

INITIAL DATABASE

- CBC:
  - Inflammatory leukogram
  - Peripheral eosinophilia is not always present.
- Serum biochemical profile and urinalysis results are usually normal.
- Thoracic radiographs commonly show bronchial and peribronchiolar patterns; increases in interstitial markings, alveolar patterns, and lobar consolidation or bronchiectasis may also be observed.
- Heartworm test results are negative.
- Fecal examinations (flotation, sedimentation techniques) will be negative for parasites and ova.

ADVANCED OR CONFIRMATORY TESTING

- Bronchoscopic abnormalities:
  - A common finding is green to yellow-green mucus, often abundant, in airways.
  - Airway mucosa may appear reddened, thickened, nodular, or polypoid; airway collapse may be evident during expiration.
- Examination of respiratory washes or brush cytologic examination shows a mix primarily of neutrophils and eosinophils. Infectious agents, neoplastic cells, or evidence of respiratory parasites are not expected with this disease.
- Culture of respiratory washes will be negative for pathogens in some cases; in those that have positive culture results, clinical signs persist in the face of antimicrobial therapy.

TREATMENT

TREATMENT OVERVIEW

Most dogs with EBP will require glucocorticoids to resolve clinical signs and eosinophilic inflammation.

ACUTE GENERAL TREATMENT

Immunosuppressive dosage of glucocorticoids (e.g., prednisone, 1-2 mg/kg PO q 24 h) initially.

CHRONIC TREATMENT

Glucocorticoids on a slowly tapering (weeks to months) dosage schedule are often needed for control of clinical signs:

- Clinical signs are likely to recur if glucocorticoids are administered inconsistently or if tapering occurs too quickly.
- Low-dose glucocorticoid therapy may be needed in some animals. Administer the lowest dose q 24-48 h to control clinical signs.
- Inhaled corticosteroids can manage the disease and may have the advantage of reducing side effects associated with oral corticosteroids.

POSSIBLE COMPLICATIONS

- Side effects of glucocorticoid therapy such as polyuria, polydipsia, and polyphagia are expected in treated animals.
- Untreated or inadequately treated patients may develop bronchiectasis (an irreversible airway change).

RECOMMENDED MONITORING

- Clinical signs
- Thoracic radiographs

PROGNOSIS AND OUTCOME

- Prognosis is generally good with appropriate doses of glucocorticoids for appropriate periods of time. Some animals may be able to be completely weaned from glucocorticoids.
- Excessively rapid cessation of glucocorticoids may provoke a relapse of clinical signs.

PEARLS & CONSIDERATIONS

COMMENTS

Hyposensitization against antigens identified by allergy testing has been associated with alleviation of clinical signs or control of clinical signs with smaller doses of glucocorticoids in a small number of reported animals. The amount of clinical benefit derived from hyposensitization and the role of hyposensitization in long-term management need additional investigation; hyposensitization may be a consideration for animals in which side effects of glucocorticoids are unacceptable or intolerable to owners.

PREVENTION

There is no reliable means of preventing this disease.

TECHNICIAN TIPS

Stained slides of sputum from dogs with EBP have high numbers of eosinophils that are easily recognized with rapid staining methods, so making slides of fresh sputum, even that obtained from the floor or ground, can be quite informative in these patients.

CLIENT EDUCATION

Clients should understand the importance of consistent treatment with glucocorticoids, particularly during the initial stages of treatment.

SUGGESTED READING

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AUTHORS: CÉCILE CLERCX

EDITOR: RANCE K. SELLON

Entropion/Ectropion

BASIC INFORMATION

DEFINITION

- *Entropion* is a common condition that consists of the inversion of part or the entire eyelid margin toward the eye; may be developmental or acquired.
- *Ectropion* is a well-recognized condition that consists of the eversion of part or the entire eyelid margin away from the eye; may be developmental or acquired.

SYNONYMS

Inrolled eyelid (entropion); everted eyelid (ectropion)

EPIDEMIOLOGY

SPECIES, AGE, SEX

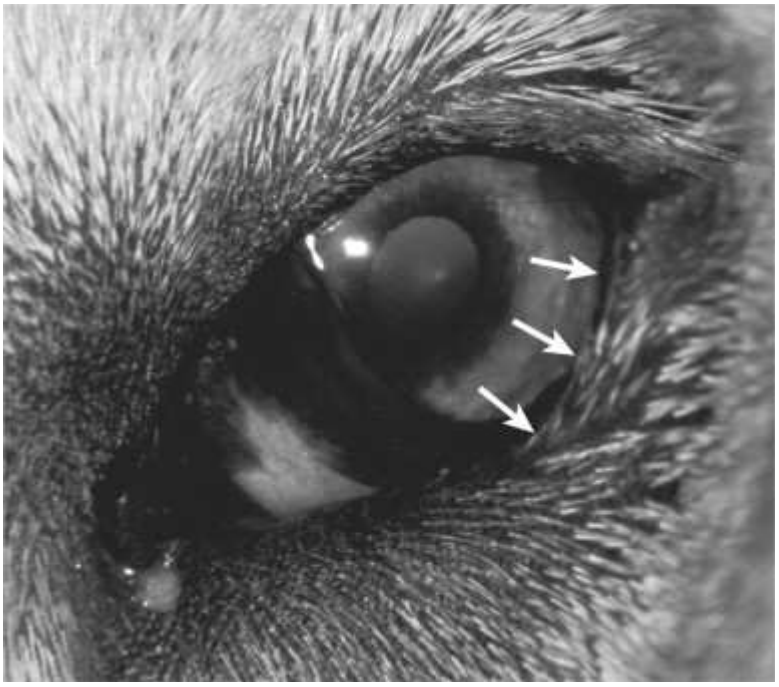
- Entropion:
  - Dogs common; cats less common
  - Can occur at any age; developmental entropion usually develops in dogs <1 year of age
- Ectropion:
  - Dogs
  - Age variable, depends on cause

GENETICS & BREED PREDISPOSITION

- Developmental entropion:
  - Lateral entropion: English bulldog, chow chow, shar-pei, Saint Bernard, boxer, rottweiler, pointers, spaniels, and all retrievers
  - Medial canthal entropion: miniature and toy poodles, English bulldog, Cavalier King Charles spaniel, Maltese, and brachycephalic breeds including Pekingese, pug, and shih tzu; brachycephalic cats
  - Genetic basis not fully understood; considered inherited as a simple dominant trait, with complete penetrance in some breeds of dogs
- Developmental ectropion: bloodhound, Saint Bernard, Great Dane, bullmastiff, Newfoundland, and some spaniel breeds
- Combination entropion-ectropion affecting the same lid: bloodhound, Saint Bernard, and English bulldog

RISK FACTORS

- Developmental entropion and ectropion: breed predisposition
- Acquired entropion: ocular conditions that stimulate blepharospasm (e.g., see Conjunctivitis: Dogs, p. 239, Cats, p. 237; Corneal Ulceration, p. 250)
  - Eyelid trauma (see p. 373)
  - Blepharitis
  - Old age and associated loss of orbicularis oculi muscle tone
  - Phthisis bulbi (see Ocular Size Abnormalities, p. 778)
  - Enophthalmos (see Orbital Disease, p. 790)
- Acquired ectropion:
  - Eyelid trauma
  - Blepharitis
  - Old age and associated loss of orbicularis oculi muscle tone
  - Facial nerve paralysis



ENTROPION/ECTROPION Entropion of ventrolateral eyelid in a dog (*arrows*). Note prolapse of third eyelid and mild mucoid ocular discharge at the medial canthus, which are common concurrent findings.

ASSOCIATED CONDITIONS & DISORDERS

- Conjunctivitis
- Keratitis (ulcerative and nonulcerative)
- See Risk Factors above.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Developmental and acquired forms.

HISTORY, CHIEF COMPLAINT

- Entropion:
  - Ocular discharge
  - Blepharospasm
  - "Red eye"
  - Visible inrolling of eyelid
  - ± Vision impairment in severe cases
- Ectropion:
  - Ocular discharge
  - "Red eye"
  - Droopy/long lower eyelid

PHYSICAL EXAM FINDINGS

- Entropion:
  - Inversion of the eyelid (see figure) and some or all of the following:
    - Conjunctivitis (cats, see p. 237; dogs, see p. 239)
    - Epiphora or mucoid to mucopurulent ocular discharge
    - Blepharospasm
    - Protrusion of the third eyelid (see figure)
    - Nonulcerative keratitis (see Corneal Pigmentation, p. 246; Corneal Vascularization, p. 254)
    - Ulcerative keratitis (see Corneal Ulceration, p. 250)
- Ectropion:
  - Eversion of the lower eyelid and some or all of the following:
    - Conjunctivitis
    - Lagophthalmos (incomplete closure of the eyelids)

ETIOLOGY AND PATHOPHYSIOLOGY

Dogs:

- Developmental entropion:
  - Related to abnormal skull and palpebral fissure (eyelid opening) conformation
  - Associated with misdirection of the lateral canthal ligament in mesaticephalic (intermediate facial somato-type; neither brachycephalic nor dolichocephalic) breeds
  - Upper eyelid entropion can be associated with ptosis and weight from excessive dorsal skinfolds
  - Associated with microblepharon (small eyelids)
- Acquired entropion:
  - Decreased orbital support (decreased orbital mass, phthisis bulbi, or retractor bulbi muscle contraction) predisposes to loss of lid support (see Orbital Disease, p. 790).
  - Secondary to blepharospasm
  - Secondary to scarring and contraction of the eyelid from a previous eyelid injury and/or inflammation
- Developmental ectropion:
  - Mild ectropion is a desired feature in some breeds (i.e., hounds).
  - Related to abnormal skull and palpebral fissure conformation
  - Associated with laxity of the palpebral fissure related to macroblepharon
- Acquired ectropion:
  - Transient ectropion results from laxity of the eyelid from relaxation or following excessive exercise in breeds with long lower eyelids.
  - Scarring and contraction of the eyelid from a previous eyelid injury and/or inflammation
  - Facial nerve paralysis

Cats:

- Developmental entropion:
  - Medial canthal entropion in brachycephalic breeds
- Acquired entropion:
  - Decreased orbital support associated with loss of orbital and periorbital fat predisposes to loss of eyelid support.
  - Secondary to blepharospasm
  - Associated with scarring and contraction from chronic conjunctival and/or eyelid inflammation

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis of entropion is suspected based on the presence of ocular irritation (epiphora, conjunctivitis, or keratitis) and is confirmed based on identification of abnormal lid conformation (inversion of part or all of the eyelid). Ectropion is diagnosed on physical examination: eversion of the lower eyelid. For both disorders, an ophthalmic examination is indicated to identify lesions caused by the eyelid malformation.

DIFFERENTIAL DIAGNOSIS

- Entropion:
  - Usually readily diagnosed on clinical examination; must be differentiated from:
    - Distichiasis (see Distichiasis/Ectopic Cilia/Trichiasis, p. 319): one or more cilia emerge from the meibomian glands instead of the normal peripheral lid margin.
    - Trichiasis (see Distichiasis/Ectopic Cilia/Trichiasis, p. 319): normal eyelid or facial hair directed toward, and contacting, the conjunctiva or cornea
- Ectropion:
  - Usually readily diagnosed on clinical examination: apparent even before handling the patient

INITIAL DATABASE

Complete ophthalmic examination (see p. 1313) including:

- Schirmer tear test (normal >15 mm after 1 minute in dogs, variable in cats)
- Fluorescein dye application
- Intraocular pressures
- Careful examination of conformation of eyelid margins, conjunctiva, and cornea

ADVANCED OR CONFIRMATORY TESTING

- Variable depending on underlying cause of acquired entropion and/or ectropion
- With entropion, apply topical anesthetic (e.g., proparacaine 0.5%) to eye to evaluate degree of spastic entropion (i.e., entropion secondary to ocular pain versus developmental entropion or entropion from primary ocular disease such as ulcerative or nonulcerative keratitis). Spastic entropion temporarily resolves or decreases in severity within a few minutes of proparacaine application.
- Examine animal in a relaxed state to determine extent of entropion and/or ectropion and to select most appropriate corrective surgical technique; restraining the animal or manipulation of the head at examination can increase the severity of blepharospasm and exaggerate the degree of entropion.

TREATMENT

TREATMENT OVERVIEW

- The treatment goals for entropion are to resolve any underlying painful ocular disease (e.g., conjunctivitis, keratitis) and restore normal lid conformation (temporary versus permanent repair).
- The treatment goals for ectropion are to restore normal lid conformation only if severe and predisposing to chronic ocular irritation. Mild ectropion is normal for some larger-breed dogs.

ACUTE GENERAL TREATMENT

Entropion:

- Treat underlying condition(s)
- Temporary correction until adult conformation reached (i.e., in puppies), or until underlying condition resolved:
    - Roll eyelids away from eye by placing temporary tacking or temporary tarsorrhaphy sutures to prevent chronic ocular pain and blepharospasm and to prevent corneal pigmentation, vascularization, ulceration, and scarring.
    - If successful, may not require permanent repair
- Permanent correction once adult conformation reached (increases success) and no other underlying condition (see Chronic Treatment)

CHRONIC TREATMENT

- Chronic *entropion* in mature animal requires some form of surgery to evert the eyelid margin.
    - Cases of mild entropion:
        - Consider Hotz-Celsus procedure (surgical procedure involving excision of an elliptical section of skin adjacent to the lid margin).
    - Lateral canthal entropion:
        - Creation or cutting of the lateral canthal ligament (modified Wyman's lateral canthoplasty or lateral canthal tenotomy, respectively)
        - Hotz-Celsus procedure and eyelid shortening procedure may be needed.
    - Medial canthal entropion:
        - Medial canthoplasty procedure (e.g., pocket flap or Wyman technique)
        - Localized Hotz-Celsus procedure
    - Ptosis and upper eyelid entropion:
        - Stades procedure to evert upper eyelid margin
- Ectropion:
    - Surgery rarely needed unless severe or if concurrent with entropion elsewhere on the lid
    - Cases of severe ectropion:
        - Consider modified Kuhnt-Szymanowski technique (lid-shortening procedure)
    - Cicatricial (scar-induced) ectropion
        - V-Y blepharoplasty may be used

POSSIBLE COMPLICATIONS

- Temporary tacking sutures may pull through skin, necessitating repeat procedure(s) until animal is mature or until underlying condition is resolved.
- Undercorrection or overcorrection of entropion
- Correction of subclinical ectropion predisposing to entropion

RECOMMENDED MONITORING

- Leave the temporary tacking sutures or temporary tarsorrhaphy in place until adult conformation reached or for 2–3 weeks until concurrent ocular disease resolves.
- Permanent entropion and/or ectropion repairs require suture removal approximately 10-14 days after surgery.

PROGNOSIS AND OUTCOME

- Prognosis for restoring normal eyelid conformation is good.
- Recurrence of entropion is possible, depending on underlying cause and surgical treatment.

PEARLS & CONSIDERATIONS

COMMENTS

- Treat any concurrent ocular disease before surgically correcting entropion.
- No single surgical procedure is effective for correction of all forms of entropion and/or ectropion (see Chronic Treatment above for some options).
- Err on the side of undercorrection when performing entropion surgery; further future correction is much easier to manage than the other extreme (overcorrection causing ectropion).
- Correction of naturally occurring ectropion is rarely needed unless severe or occurs in conjunction with entropion on the same eyelid.

PREVENTION

Avoid breeding affected or closely related dogs with developmental entropion or clinically significant developmental ectropion.

CLIENT EDUCATION

If the initial repair is ineffective, additional surgical procedures may be needed.

SUGGESTED READING

Read RA, Broun HC: Entropion correction in dogs and cats using a combination Hotz-Celsus and lateral eyelid wedge resection: results in 311 eyes. Vet Ophthalmol 10(1):6, 2007.

Stades FC, Gelatt KN: Diseases and surgery of the canine eyelid. In Gelatt KN, editor: Veterinary ophthalmology, ed 4, Ames, 2007, Blackwell Publishing, p. 563.

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Endocarditis, Infective

BASIC INFORMATION

DEFINITION

Endocarditis is inflammation of the endocardial surface of the heart (endocardium). *Infective endocarditis* is microbial infection of the endocardium. *Vegetative endocarditis* is a specific form of endocarditis where structures (vegetations) composed of platelets, fibrin, microorganisms, and inflammatory cells adhere to heart valves or cling to septal defects, chordae tendineae, or the mural endocardium. Endocarditis (both the term and the disease) is unrelated to the most common form of chronic valvular heart disease in dogs, myxomatous valve disease or *endocardiosis*.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Endocarditis is uncommon in dogs and rare in cats.
- Dogs: male > female, large breeds > small breeds.
- In the dog, the left-sided heart valves (aortic and mitral) are by far the most frequently affected.

RISK FACTORS

- Congenital aortic valve disease (e.g., subaortic stenosis) and other congenital heart diseases that cause disturbances of blood flow and subsequent changes in the endocardium
- Glucocorticoid use predisposes to endocarditis, and many cases appear to have a nosocomial origin. Infected intravenous catheters, prosthetic heart valves, heart surgery, and interventional cardiac catheterization all enhance the risk.
- Infection with potentially immunosuppressive organisms (e.g., *Bartonella* spp., *Ehrlichia* spp.) enhances the risk of endocarditis.
- Predisposing factors for endocarditis in dogs include sources of chronic bacteremia (e.g., urinary tract infection, discospondylitis) and systemic illnesses that facilitate bacterial infection (e.g., diabetes mellitus, hyperadrenocorticism/Cushing's disease).

GEOGRAPHY AND SEASONALITY:

Infective endocarditis is recognized more in warmer climates (e.g., southern and western United States).

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Endocarditis is classified as acute or subacute-chronic based on the duration, rate of progression, and severity of clinical signs.

HISTORY, CHIEF COMPLAINT

- Extracardiac manifestations of systemic infection and inflammation are the source of most of the historic complaints.
- Manifestations of fever (e.g., lethargy, anorexia) are the most common sign, although they may be intermittent, minimal, or even absent in patients with less virulent organisms (e.g., *Bartonella* spp., some gram-positive organisms) or severe debilitation.
- Weight loss
- Reluctance to move (back pain, polyarthritis)
- Intermittent lameness (muscle embolization, polyarthritis)

PHYSICAL EXAM FINDINGS: Most patients diagnosed with endocarditis have a heart murmur:

- The murmur may be newly recognized or may have changed in intensity, quality, timing, or duration. Many animals with endocarditis have a preexisting heart murmur (e.g., from subaortic stenosis).
- The presence of a diastolic murmur in a systemically ill animal dramatically raises the index of suspicion for infective endocarditis.
- Aortic insufficiency often causes a soft, blowing murmur with a distant quality that is difficult to hear.

ETIOLOGY AND PATHOPHYSIOLOGY

- *Staphylococcus* spp., *Streptococcus* spp., *Erysipelothrix* spp., *Corynebacterium* spp., and *Escherichia coli* have been the most common bacterial isolates in canine infective endocarditis.
- *Bartonella* spp. is being isolated with increasing frequency and appears to have a tropism for the aortic valve.
- A wide variety of other organisms has been cultured from individual cases, with many nosocomial cases involving *Pseudomonas* spp., *Proteus* spp., or other antibiotic-resistant isolates. Anaerobic bacteria (e.g., *Bacteroides* spp.) are occasionally found.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Endocarditis is suspected based on clinical signs and the presence of a heart murmur on physical exam. The index of suspicion may increase substantially based on echocardiographic findings, but a positive bacterial blood culture is required to establish the clinical diagnosis.

DIFFERENTIAL DIAGNOSIS

- Presenting complaints of animals with infective endocarditis tend to be vague and associated with some aspect of systemic illness (e.g., fever, lameness).
- Endocarditis should be included in the differential diagnosis of any persistent fever of unknown origin, especially in the presence of a heart murmur.

INITIAL DATABASE

- Definitive diagnosis requires the synthesis of clinical, laboratory (microbiologic), and echocardiographic data.
- CBC or serum biochemical changes are not specific.
- Echocardiography reveals an oscillating mass at a site of endocardial injury (i.e., a mass near but separate from the valve, whose movements are distinct from those of the valve; it is important to note that this excludes valves that are merely thickened, as in myxomatous valve disease/endocardiosis).
- Two separate blood cultures must be positive for a typical organism and obtained by separate venipunctures an hour apart (three cultures are recommended if time, money, and patient size permit; at least two must be positive).
- In acutely ill patients with apparent sepsis syndrome, three blood cultures 5-10 minutes apart should be obtained if the patient's size permits, followed by empirical antibiotic therapy.

ADVANCED OR CONFIRMATORY TESTING

- Patients with suspected or definite endocarditis should have electrocardiograms recorded (and repeated regularly during their clinical course), because the onset of AV or bundle-branch block suggests perivalvular extension of the infection.
- When blood cultures from suspected infective endocarditis patients remain sterile after 72 hours of incubation, the laboratory should intensify efforts to grow fastidious organisms such as *Bartonella* spp., and the clinician should initiate alternative (e.g., serologic, PCR) assessment.
- Panbacterial PCR amplification of the 16s ribosomal bacterial DNA from patients with suspected or definite endocarditis is available. Currently, the sensitivity of this technique is equivalent to standard blood culture techniques.

TREATMENT

TREATMENT OVERVIEW

- Provide effective antiinfective therapy to minimize valve damage.
- Manage complications (e.g., heart failure).

ACUTE GENERAL TREATMENT

- Treatment is usually begun with parenteral antibiotic combinations in hospitalized dogs, but once the fever has resolved and clinical improvement (e.g., return of appetite) is evident (generally not more than 3-5 days), treatment is completed on an outpatient basis with oral antibiotics.
- Treatment is based on blood culture and sensitivity results; these results are not available for the first critical hours or days of therapy.

- Empirical antibiotic therapy for dogs with a clinical history and echocardiographic findings compatible with endocarditis is started with a combination of fluoroquinolone and penicillin-based antibiotics. Parenteral enrofloxacin (5 mg/kg IV q 12 h) and amoxicillin (20 mg/kg IV q 8 h) are most often chosen.
- Although discussed by some veterinary authors, anticoagulation does not appear to diminish the risk of bacterial embolization in humans and is not generally recommended.

CHRONIC TREATMENT

- Therapy is generally continued for 12 weeks, and blood cultures are ideally obtained after 10-14 days (on antibiotics) and then again 1 week after stopping antibiotics.
- If *Bartonella* spp. is identified by culture or serology, azithromycin, 5–10 mg/kg PO q 24 h is recommended for the first 7 days, then every other day for 6–12 weeks.

POSSIBLE COMPLICATIONS

Congestive heart failure, renal failure, or neurologic events are the complications that appear to have the greatest influence on prognosis.

PROGNOSIS AND OUTCOME

- Prognosis at the time of diagnosis is guarded, owing to the future possibilities of embolic complications and/or congestive heart failure.
- Factors negatively associated with short-term survival include thrombocytopenia, renal complications, and thromboembolism.
- Long-term prognosis depends primarily on the valve damage that has been done at the time of diagnosis, as well as the response to antibiotic therapy.
- Recurrence or treatment failure is likely with inadequate duration of therapy, inappropriate antibiotic selection, or owner noncompliance.
- Despite optimal therapy and therapeutic monitoring, cure rates for endocarditis do not appear to be especially promising in dogs, and heart failure or deteriorations due to recurrent embolic events is often the long-term result.

PEARLS & CONSIDERATIONS

COMMENTS

- Although both can cause valve thickening and heart murmurs, taking a broader perspective of the case can more clearly demonstrate the differences between acute bacterial endocarditis (typically medium- to large-breed dogs of any age, overt clinical signs of recurrent infection/sepsis, new-onset heart murmur; overall, occurs uncommonly) and endocardiosis (medium- to small-breed dog, generally older adult, no link to overt signs of infection, murmur may be new in onset or long standing; common).
- The murmur of aortic insufficiency is often heard best by placing the diaphragm of the stethoscope in the animal's left armpit, with the animal lying on its left side (on top of the stethoscope).
- A high index of suspicion for endocarditis is warranted in cases of disco-spondylitis and in any animal with fever and a diastolic murmur.
- With appropriate therapy, prognosis appears to be better for animals with less aggressive organisms such as *Bartonella* spp. if valve damage is not too severe at time of diagnosis.

PREVENTION

Animals with subaortic stenosis, animals with cardiac implants (e.g., transvenous pacemakers), and animals that have undergone balloon valvuloplasty should receive routine antibiotic prophylaxis for all procedures that are likely to induce transient bacteremia.

CLIENT EDUCATION

Owner compliance is perhaps an even bigger issue in the treatment of endocarditis than it is with other heart diseases, and effective explanation of the rationale for extended (often expensive) antibiotic treatment and a guarded prognosis is therefore critical.

SUGGESTED READING

Wall M, Calvert CA: Cardiovascular infections. In Greene CE, editor: Infectious diseases of the dog and cat, ed 3, St Louis, 2006, Elsevier Saunders, pp 841–865.

AUTHORS: ANDREA C. LANTIS, BRUCE W. KEENE

EDITOR: ETIENNE CÔTÉ

Encephalopathy, Vascular

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Brain dysfunction caused by ischemia, or lack of oxygen delivery. These are most commonly focal events (i.e., infarcts or strokes) but occasionally manifest as widespread brain ischemia (i.e., global ischemia).

SYNONYMS

Infarct, ischemic encephalopathy, stroke, cerebrovascular accident

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs and cats of any age and either sex

GENETICS & BREED PREDISPOSITION:

Cavalier King Charles spaniels may be predisposed to cerebellar infarcts; this may be related to local pressure abnormalities due to caudal occipital malformation syndrome in this breed. Greyhounds may also be predisposed to brain infarction, possibly related to their relatively high resting blood pressure. Brachycephalic breeds may be predisposed to developing global brain ischemia.

RISK FACTORS: Focal ischemic events (strokes): hypertension, hypercoagulability, and hyperviscosity. The most prevalent diseases that cause these disturbances in patients with vascular encephalopathy are chronic kidney disease and hyperadrenocorticism. Other conditions include diabetes mellitus, hypothyroidism, hyperthyroidism, hepatic failure, pheochromocytoma, and infectious diseases. Feline ischemic encephalopathy has been linked to intracranial migration of *Cuterebra* larvae. Risk factors for global brain ischemia include inadequate anesthetic monitoring, cardiac arrest, severe hypoxemia, and the use of ketamine in anesthetic protocols (especially in brachycephalic breeds).

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Focal brain ischemic events (strokes, infarcts) can be small (lacunar) or large (territorial) and either hemorrhagic or nonhemorrhagic (the latter are more common). Global brain ischemia usually involves some degree of diffuse oxygen deprivation in the brain and is much less common than focal brain ischemia.

HISTORY, CHIEF COMPLAINT

- The characteristic historic feature of both focal and global ischemic encephalopathy is acute to peracute onset of brain dysfunction, which is nonprogressive after the first 24 hours.
- Typical chief complaints include sudden-onset, mentation change, vocalizing/crying, or seizures.

PHYSICAL EXAM FINDINGS

- Physical and neurologic examination findings depend primarily on the underlying disorder leading to the ischemic event (physical examination findings) and the region of the brain affected by the ischemic event.
- Strokes affecting the cerebrum (e.g., propulsive pacing, disorientation, seizures), diencephalon/midbrain (e.g., depression, obtundation/coma), or cerebellum (hypermetria, intention tremor) are seen with some frequency in affected dogs.

ETIOLOGY AND PATHOPHYSIOLOGY

- Interruption of oxygen delivery to brain tissue
- Disruption of cellular energy metabolism (i.e., ATP production)
- Brain necrosis and edema
- Generation of cytotoxic mediators of secondary brain injury

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on a history of sudden-onset neurologic deficits that are typically nonprogressive and asymmetric. Suspicion is heightened when a procoagulable state or other possible inciting factor is identified. Confirmation requires intracranial imaging (e.g., MRI).

DIFFERENTIAL DIAGNOSIS

- Brain neoplasm
- Inflammatory brain disease: sterile or infectious encephalitides
- Trauma (suggested at outset if history unknown, or supportive of trauma)

INITIAL DATABASE

- CBC, serum biochemistry profile: abnormalities depend on underlying cause (e.g., polycythemia or hyperglobulinemia with hyperviscosity syndrome); changes consistent with kidney disease if hypertension; hypoalbuminemia with hypercoagulability due to loss of antithrombin III (protein-losing nephropathy or enteropathy).
- Neurologic examination (see p. 1311): deficits according to site of ischemia; symmetric deficits with global ischemia, asymmetric with focal ischemia
- Serial blood pressure measurement (see p. 1209): rule out systemic hypertension.
- Urinalysis: pathologic proteinuria in cases of hypercoagulability due to protein-losing nephropathy

ADVANCED OR CONFIRMATORY TESTING

- MRI of brain (see p. 1302): diagnostic test of choice
  - Helps differentiate focal from global ischemia, but this distinction should be apparent from the history and neurologic exam alone.
- Cerebrospinal fluid examination (see p. 1228): may be unremarkable or show nonspecific changes.

TREATMENT

TREATMENT OVERVIEW

Therapeutic goals include:

- Minimize secondary brain swelling and tissue damage
- Treat underlying cause of brain ischemia
- Physical rehabilitation (see p. 1329)

ACUTE GENERAL TREATMENT

- Mannitol, 0.5–1 g/kg body weight slowly IV over 10-15 minutes
- Oxygen supplementation

CHRONIC TREATMENT

- Treat underlying condition (e.g., antihypertensive drugs if hypertension is documented).
- Physical rehabilitation

POSSIBLE COMPLICATIONS

- Recumbency-associated pneumonia
- Pressure sores (see p. 174)
- Recurrent stroke
- Exacerbation of underlying condition leading to ischemic event

RECOMMENDED MONITORING

- Serial neurologic examinations
- Blood pressure (if hypertension documented)
- Progression or regression of underlying condition (e.g., diabetes control, control of hyperadrenocorticism)

PROGNOSIS AND OUTCOME

- Most patients recover fully from focal ischemic events.
- Prognosis for stroke is more closely associated with the underlying cause than the stroke event itself
- Global brain ischemia is associated with a more guarded prognosis than focal brain ischemia.

PEARLS & CONSIDERATIONS

COMMENTS

- Recovery from vascular encephalopathy may take several weeks to several months.
- Aggressive physical therapy and nursing care are essential to a positive outcome.
- History and symmetry versus asymmetry of neurologic deficits are the main elements that allow the differentiation of global versus focal ischemia, respectively.
- Although dogs and cats can develop vascular encephalopathy (a true stroke) as described previously, overall this disorder occurs much less commonly than acute vestibular syndrome, which is an acute disorder that does not involve the brain (peripheral vestibular disease), does not involve infarction, and yet is often referred to inaccurately as a “stroke.”

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AUTHOR & EDITOR: CURTIS W. DEWEY

Emphysema and Pulmonary Bullae

BASIC INFORMATION

DEFINITION

- *Emphysema:* pathologic accumulation of air within an organ or tissue
- *Bulla:* an air-filled space within the pulmonary parenchyma that arises from alveolar distention or destruction of alveolar walls
- *Bleb:* an accumulation of air within the mesothelial covering and layers of elastic fibers and connective tissue cells that comprise the visceral pleura

SYNONYM

Bullous emphysema

EPIDEMIOLOGY

SPECIES, AGE, SEX

Reported most commonly in dogs of middle age, although dogs of any age can be affected. Cats are rarely affected.

GENETICS & BREED PREDISPOSITION

- A familial or genetic predisposition has not been demonstrated.
- Large, deep-chested dog breeds are considered at greater risk of pulmonary blebs and bullae.

RISK FACTORS

- Congenital bronchial hypoplasia (uncommon) reported in both dogs and cats.
- Chronic obstructive pulmonary diseases are a recognized risk factor in people and could be so in dogs (e.g., chronic sterile bronchitis).

ASSOCIATED CONDITIONS & DISORDERS

- Congenital bronchial hypoplasia
- Congenital bronchial cartilage hypoplasia/dysplasia
- Spontaneous pneumothorax
- Pneumomediastinum (uncommon)
- Subcutaneous emphysema (uncommon)
- Pneumopericardium (uncommon)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Congenital forms of bullous lung disease have been described, usually secondary to bronchial hypoplasia or bronchial cartilage defects.

HISTORY, CHIEF COMPLAINT

- Animals may be clinically normal:
  - A pulmonary bleb or bulla may be found incidentally during thoracotomy or thoracoscopy.
- Clinical signs, when present, can be acute, intermittent, or slowly progressive:
  - Anorexia
  - Lethargy
  - Respiratory distress
    - The rupture of a bleb or bulla, causing spontaneous pneumothorax, is typically associated with acute dyspnea.
  - Cough

- Exercise intolerance

PHYSICAL EXAM FINDINGS

- Respiratory distress
- Increased inspiratory effort (pneumothorax from ruptured bleb or bulla)
- Increased expiratory effort (pulmonary emphysema without pneumothorax)
- Tachypnea
- Tachycardia
- Diminished heart and lung sounds on one or both sides if pneumothorax
- Subcutaneous emphysema in occasional patients

ETIOLOGY AND PATHOPHYSIOLOGY

- Histopathologic assessment of resected tissues classifies lesions as blebs or bullae.
- Exact mechanisms leading to bulla or bleb formation are not defined:
  - Suspected to reflect the effects of distensile or traction forces on the lung surface, or the effects of inflammation or degradative enzymes in the alveoli to break down alveolar walls.
  - Increased alveolar pressure relative to transpleural pressure may also contribute.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Definitive diagnosis usually depends on exclusion of other causes of pneumothorax after evaluation of patient history, physical examination, and radiographic imaging, and then surgical observation of typical lesions.

DIFFERENTIAL DIAGNOSIS

- Other causes of pneumothorax:
  - Trauma, either blunt or penetrating, to the thoracic wall, trachea, esophagus, or pulmonary parenchyma
- Inflammatory lung disease
- Neoplastic lung disease
- Parasitic lung disease, especially *Paragonimus kellicotti* and *Dirofilaria immitis*
- Obstructive airway disease
- Migrating foreign bodies

INITIAL DATABASE

- Thoracic radiographs:
  - May demonstrate the features of pneumothorax (see p. 889)
  - Often unremarkable; observation of a bleb or bulla is uncommon.
  - Animals with paragonimiasis may have thick-walled bullae evident, even with pneumothorax.
  - Thoracic radiographs may in some cases show air-filled dilations within the parenchyma.
  - Occasional animals may have pneumomediastinum, pneumopericardium, or subcutaneous emphysema evident.
- Results of a CBC, biochemical profile, and urinalysis are typically unaffected by the disease.
- Hypoxemia will be the most consistently present abnormality on arterial blood gas analysis.
- Fecal examinations (flotation and sedimentation techniques) to rule out respiratory parasites

ADVANCED OR CONFIRMATORY TESTING

- Definitive diagnosis is usually made by detection of bullae, blebs, or air leaking from the lung surface during thoracotomy or thoracoscopy and confirmed with histopathologic examination of resected tissue.
  - Median sternotomy is the preferred approach in patients with spontaneous pneumothorax.
  - Cranial lung lobes are most commonly affected, although other lung lobes can also have lesions.
- Tracheoscopy, bronchoscopy, and esophagoscopy are usually normal in patients with bullous lung disease unless airway hypoplasia is present.
- In a small number of reported cases, CT scans of the thorax have proved more sensitive than plain thoracic radiographs for the detection of bullous lung lesions in dogs with spontaneous pneumothorax.

TREATMENT

TREATMENT OVERVIEW

- Improve respiratory function and oxygenation in patients with respiratory distress, typically by thoracocentesis, as most such patients will have pneumothorax.
- Remove bullae or blebs.
- Treat underlying obstructive disease, if present

ACUTE GENERAL TREATMENT

- Thoracocentesis if pneumothorax is present (see p. 1338):
  - Thoracostomy tubes with continuous suction may be needed in some patients for management of persistent air accumulation.
- Oxygen provided by mask, nasal catheter, oxygen cage
- Cage rest

CHRONIC TREATMENT

- Long-term resolution of spontaneous pneumothorax from rupture of blebs or bullous lung lesions, if not from parasitic diseases, is most reliably achieved with surgical resection of the affected lung tissue by either partial or complete lung lobectomy.
  - Persistence or recurrence of clinical signs is more likely if the patient is managed nonsurgically.
  - Partial or complete lung lobectomy may be accomplished via thoracotomy or thoracoscopy.
- Treat underlying obstructive disease, if present

POSSIBLE COMPLICATIONS

- Pneumothorax from leakage at suture or staple site of a lobectomy
- Postoperative complications of infection, wound dehiscence

RECOMMENDED MONITORING

- Clinical signs
- Thoracic radiographs

PROGNOSIS AND OUTCOME

Prognosis is good with surgical resection of bullous lung lesions.

PEARLS & CONSIDERATIONS

COMMENTS

- Often in patients with spontaneous pneumothorax of uncertain origin and no history of trauma, bleb or bulla rupture ultimately is found to be the underlying cause.
- Some animals can be successfully managed with nonsurgical methods (thoracocentesis, thoracostomy tubes), but the literature supports early lung lobectomy for the best long-term outcomes.
- Affected animals can have multiple lesions scattered over different lung lobes, and lung lobes on both sides of the thoracic cavity can be affected. It is thus imperative to examine the entirety of both lungs during thoracotomy or thoracoscopy.

PREVENTION

There is no means of preventing the disease. Animals with congenital bronchial hypoplasia should probably not be bred.

TECHNICIAN TIPS

- Thoracocentesis is most often done at around the 7th or 8th intercostal space, so these areas should be clipped in

preparation for the procedure.
- When the goal of thoracocentesis is to remove air, preferred recumbency is that in which the patient is most comfortable.

CLIENT EDUCATION

Nonsurgical treatment approaches are more likely to be associated with persistence or recurrence of clinical signs. Postsurgical outcomes are usually excellent.

SUGGESTED READING

Au JJ, et al: Use of computed tomography for evaluation of lung lesions associated with spontaneous pneumothorax in dogs: 12 cases (1999-2002). J Am Vet Med Assoc 228:733, 2006.

Brissot HN, et al: Thoracoscopic treatment of bullous emphysema in 3 dogs. Vet Surg 32:524, 2003.

Lipscomb VJ, et al: Spontaneous pneumotho-rax caused by pulmonary blebs and bullae in 12 dogs. J Am Anim Hosp Assoc 39:435, 2003.

Puerto DA, et al: Surgical and nonsurgical management of and selected risk factors for spontaneous pneumothorax in dogs: 64 cases (1986-1999). J Am Vet Med Assoc 220:1670, 2002.

AUTHOR & EDITOR: RANCE K. SELLON

Electrocution

BASIC INFORMATION

DEFINITION

The passage of electricity through tissue, resulting in electrophysiologic disruption of the tissue

EPIDEMIOLOGY

SPECIES, AGE, SEX

Most common in young cats and dogs (5 weeks to 1.5 years of age), with no sex predilection

RISK FACTORS

Young age and environmental access

GEOGRAPHY AND SEASONALITY

Seasonal associations: Christmas holidays (decorative holiday lights) or perhaps most often from late spring to early autumn, when owners are likely to operate electrical devices (e.g., fans), and there may be an increase in acquisition of puppies and kittens.

ASSOCIATED CONDITIONS & DISORDERS

Noncardiogenic pulmonary edema, cardiac arrhythmias, oral burns, and seizures

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

High-voltage injury versus low-voltage injury, based on the nature and intensity of the current. The most severe injuries result from a high-current and high-voltage situation and thus produce a worse clinical outcome. Electrical sources can produce energy levels that range from relatively low (e.g., 9-volt battery) to intermediate (e.g., household outlets) to very high (e.g., electrical metal utility cover). Household current is the most common.

HISTORY, CHIEF COMPLAINT

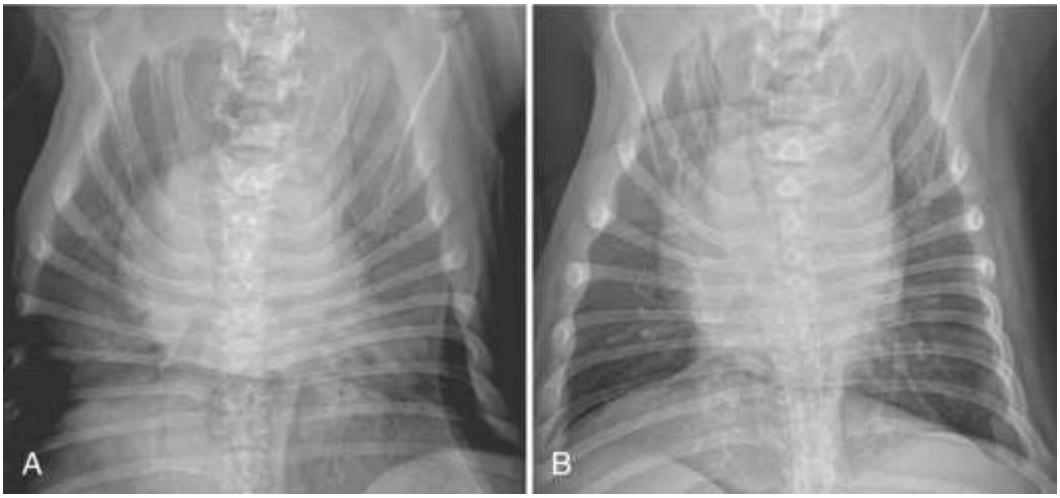
Sometimes witnessed; other times the owner reports sudden onset of dyspnea, collapse, or dysphagia.

PHYSICAL EXAM FINDINGS

- Oral burns: to the tongue, palate, and commissures of the lips
- Respiratory problems: dyspnea (harsh lung sounds, upper airway edema), cyanosis, coughing
- Cardiac problems: arrhythmias (ventricular fibrillation), asystole
- Neurologic abnormalities: loss of consciousness, focal muscle tremors, seizures

ETIOLOGY AND PATHOPHYSIOLOGY

- Electricity (usually 60 Hz of alternating current and 120 volts is found in most households in North and much of South America; in most of the rest of the world, it is usually 50-60 Hz of alternating current and 220 volts) disrupts the electrophysiologic activity of tissue, causing muscle spasms, ventricular arrhythmias, and vasomotor changes in the central nervous system, resulting in acute pulmonary edema. The electric energy is also transformed into heat, which can cause coagulation of tissue proteins. Sudden death may result from these processes.
- Electrocution is almost always accidental, typically with a young pet chewing on an electric cord.



ELECTROCUTION A, Dorsoventral thoracic radiograph of a 4-month-old male English bulldog that chewed on an electrical cord and was presented for evaluation of severe dyspnea. Heavy interstitial infiltrate is distributed caudally and symmetrically *(left-right)*. **B,** Same dog 2 weeks later after making a complete recovery. Infiltrate has resolved.

(Courtesy Dr. Julio Lopez, California Animal Hospital.)

DIAGNOSIS

DIAGNOSTIC OVERVIEW

If unwitnessed, the diagnosis is suspected if it is a young pet with the presence of oral burns and dyspnea. Thoracic radiographs classically show noncardiogenic edema (interstitial/alveolar pattern with a caudodorsal distribution).

DIFFERENTIAL DIAGNOSIS

Chemical or thermal burns, exposure to fire, and smoke inhalation

INITIAL DATABASE

Initial database is dependent on the severity of injury. In some cases, if the animal has no physical exam abnormalities, no testing is required. In other cases, if the pet is dyspneic or pulmonary crackles are auscultated, chest radiographs are warranted. In severely affected animals, CBC, serum biochemistry profile, coagulation profile, and urinalysis are warranted.

ADVANCED OR CONFIRMATORY TESTING

Pulse oximetry or arterial blood gas analysis may be useful to document hypoxemia. However, in young or small animals, the stress of arterial sample collection should be weighed against the potential benefits.

TREATMENT

TREATMENT OVERVIEW

Treatment mainly consists of supportive care, but the degree of intervention depends on the severity of the case. Burns should be cleaned; if severe, surgical débridement is indicated when the patient is stable. Noncardiogenic pulmonary edema is treated with supplemental oxygen administration. If severe or if pharyngeal edema is present, intubation and ventilation may be necessary.

ACUTE GENERAL TREATMENT

Noncardiogenic pulmonary edema is treated with rest and supplemental oxygen (see pp. 1318 and p. 1362).

CHRONIC TREATMENT

Treat burns with antibiotics, wound cleaning, soft food/feeding tube if burns are in the mouth, surgical débridement, and closure. Puppies in particular will commonly eat despite severe oral injury.

NUTRITION/DIET

If oral burns are severe and the patient will not eat, enteral nutrition may be instituted via placement of a nasoesophageal (see p. 1267) or esophagostomy (see p. 1269) tube.

POSSIBLE COMPLICATIONS

Infection of nonhealing burns, acute lung injury, acute respiratory distress syndrome. A rare but possible long-term complication is cataract formation.

RECOMMENDED MONITORING

Respiratory rate and effort, as well as the healing of any burns, should be monitored.

PROGNOSIS AND OUTCOME 

Depends on the degree of noncardiogenic pulmonary edema. Cats appear to do better than dogs in overall survival. Critical period is the first 24-48 hours after electrical shock; if the animal survives this period, he/she will likely survive to discharge with minimal/no permanent aftereffects.

PEARLS & CONSIDERATIONS 

COMMENTS

Noncardiogenic pulmonary edema can be difficult to treat. There are no known specific treatment recommendations.

PREVENTION

- When left unobserved, puppies and kittens should be crated or otherwise confined so access to electrical cords in use can be avoided.
- Remove access to wires that are plugged into outlets.

TECHNICIAN TIPS

When administering treatments to these pets, stress should be minimized, and treatments should be conducted in a stepwise manner.

CLIENT EDUCATION

Education about reexposure, removal of damaged or faulty electrical cords

SUGGESTED READING

Drobatz KJ, et al: Noncardiogenic pulmonary edema in dogs and cats: 26 cases (1987-1993). J Am Vet Med Assoc 206:1732–1736, 1995.

AUTHOR: MEGAN WHELAN

EDITOR: ELIZABETH ROZANSKI

Elbow Luxation

BASIC INFORMATION

DEFINITION

Dislocation between brachium (humerus) and antebrachium (radius and ulna)

SYNONYM

Elbow dislocation

EPIDEMIOLOGY

SPECIES/AGE/SEX

- Uncommon in dogs; rare in cats
- Any breed, age, or sex for traumatic luxations
- Juvenile dogs for congenital luxations

GENETIC & BREED PREDISPOSITION

- Congenital luxations generally more common in small breeds of dogs, but radial head luxation specifically occurs more frequently in larger breeds.
- Suspected hereditary predisposition
- Chondrodystrophic breeds are prone to asynchronous growth between radius and ulna, thereby resulting in subluxation.

RISK FACTORS

Forelimb trauma

ASSOCIATED CONDITIONS & DISORDERS

Some forms of congenital luxation may be associated with more generalized joint laxity syndromes.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Traumatic
- Congenital, complete
- Congenital, partial (radial head luxation only)

HISTORY, CHIEF COMPLAINT

- Forelimb trauma secondary to motor vehicle accident, fall, or rough play/fighting
- Spontaneous lameness/deformity in young dog

PHYSICAL EXAM FINDINGS

- Traumatic: non-weight-bearing lameness with antebrachium and paw abducted, elbow flexed, and severe elbow swelling and pain
- Congenital: partial weight-bearing lameness and joint thickening; discomfort during range-of-motion maneuvers

ETIOLOGY AND PATHOPHYSIOLOGY

- Majority of traumatic luxations are lateral (proximal radius/ulna are lateral to distal humerus).
- Medial luxations are associated with severe soft-tissue derangements.
- Traumatic injuries may cause avulsion fracture(s) of collateral ligament(s).

- Congenital/developmental luxations and subluxations may be associated with asynchronous growth of the radius and ulna.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is based on history, physical exam, and radiographs (sedated patient) of the affected limb, to include carpus, elbow, and shoulder joints.

DIFFERENTIAL DIAGNOSIS

- Distal humeral fracture
- Monteggia fracture (cranial displacement of radial head and proximal ulna fracture)
- Elbow neoplasia

INITIAL DATABASE

- Craniocaudal and mediolateral radiographs of the elbow
- Survey radiographs for other traumatic injuries, especially thoracic cavity
- Radiographs of the contralateral elbow in patients with congenital or developmental luxations
- Assess for neurologic injury: check for limb withdrawal and pain sensation.

TREATMENT

TREATMENT OVERVIEW

Goal of therapy is to achieve anatomic reduction of joint surfaces so normal joint mobility is restored, with eventual return to full weight bearing and elimination of discomfort.

ACUTE GENERAL TREATMENT

- Traumatic elbow luxations are best managed via early closed reduction before muscle contraction makes manipulations difficult (see Pearls, below, and for closed reduction procedure).
- Patient must be anesthetized for reduction.
- Concurrent injuries may result in postponement of anesthesia and early reduction.
- If closed reduction is not achieved, open reduction and reconstruction of the collateral ligaments are indicated.
- If open reduction is needed, the limb should be bandaged to reduce patient discomfort and tissue swelling before surgery.
- Appropriate analgesics should be administered.
- Congenital/developmental luxations do not require “acute” treatment, but intervention is preferred to help slow progression of secondary osteoarthritis.
- Congenital luxations are less amenable to closed reduction.
- Congenital luxations may require osteotomies or ostectomies for treatment.

CHRONIC TREATMENT

- Immobilization with elbow bandaged in extension for 1–2 weeks
- Initially, a heavy padded bandage (or more rigid splint for open reductions and those with severe collateral ligament damage), with gradual reduction in bandage thickness/stiffness as swelling subsides and stability increases
- Gentle, passive range-of-motion (flexion/extension) physiotherapy instituted after bandage removal
- Continued use of analgesic/antiinflammatory agents as needed for patient comfort

POSSIBLE COMPLICATIONS

- Recurrent luxation/instability
- Articular cartilage damage and secondary osteoarthritis
- Ligament damage
- Reduced range of motion from pericapsular fibrosis
- Chronic lameness

RECOMMENDED MONITORING

- Postreduction radiographs to confirm restoration of joint congruency
- Weekly bandage check/change until removal
- Lameness evaluations 2, 4, and 8 weeks after surgery; radiographs at 2 weeks, also at 6-8 weeks if open reduction/implants

PROGNOSIS AND OUTCOME

- Good if mild articular cartilage or ligamentous lesions
- Chronic fibrosis will result in a permanently thickened elbow.
- Most dogs with properly treated traumatic luxations will return to normal or near-normal function.
- More guarded prognosis for congenital/developmental luxations
- Severe complications/failures might necessitate salvage surgery (arthrodesis, total joint arthroplasty, or amputation).

PEARLS & CONSIDERATIONS

COMMENTS

- Early diagnosis is critical for promoting successful closed reduction.
- Closed reduction achieved by flexing elbow (moves anconeal process caudally), followed by abduction of the antebrachium, with the paw flexed (moves anconeal process medially, attempting to “hook” anconeal process medial to lateral epicondylar crest of the humerus), followed by adduction and pronation of the antebrachium (attempting to “snap” the radial head medially to its proper location under the capitulum of the humerus as the anconeal process acts as a fulcrum).
- Can consider paralyzing the patient pharmacologically (requires ventilation of patient for gas exchange) to achieve greater muscle relaxation to facilitate reduction maneuvers.

CLIENT EDUCATION

- Bandage/splint care
- Controlled activity (kennel/leash)
- Passive range-of-motion physiotherapy after removal
- Neuter dogs with congenital luxations, owing to potential heritability.

SUGGESTED READING

Dassler C, Vasseur PB: Elbow luxation. In Slatter DH, editor: Textbook of small animal surgery, ed 3, Philadelphia, 2003, WB Saun-ders, pp 1919–1927.

AUTHOR: MARY SOMERVILLE

EDITOR: JOSEPH HARARI

Elbow Hygroma

BASIC INFORMATION

DEFINITION

Fluid-filled (serum) cavity between skin and bony prominence (olecranon)

SYNONYMS

Elbow seroma, olecranon bursitis (incorrect term, as tendon bursa is not involved)

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs: any age, either sex

GENETICS & BREED PREDISPOSITION

Large-breed, heavy dogs

RISK FACTORS

- Insufficient callus over elbow
- Thin skin
- Small amount of subcutaneous fat
- Chronic pressure trauma to elbow
- Lying on hard surfaces

ASSOCIATED CONDITIONS & DISORDERS

Orthopedic problems (hip dysplasia) that increase trauma to skin and other soft tissues overlying the elbows as dog rises or lies down

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Gradually enlarging, fluid-filled swelling over point of elbow
  - Initially soft, then more turgid as fluid accumulates
- Ulceration of overlying skin may develop if continued trauma

PHYSICAL EXAM FINDINGS

Fluid-filled, fluctuant to turgid swelling over the point of the elbow. Unilateral or bilateral.

ETIOLOGY AND PATHOPHYSIOLOGY

- Caused by chronic repetitive pressure and trauma to the elbow
- Serum accumulates in subcutaneous space superficial to triceps fascia over the olecranon.
- Over time, fibrous proliferation occurs, causing nonpitting, nonpainful thickening of skin and subcutis.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on patient signalment, presenting history, and physical examination findings. Confirmation requires fine-needle aspiration cytology of the fluid-filled swelling.

DIFFERENTIAL DIAGNOSIS

- Abscess
- Neoplasia

INITIAL DATABASE

- If indicated, presurgical CBC, serum chemistry profile, urinalysis
- Fine-needle aspiration cytologic evaluation with or without bacterial culture and sensitivity: rule out abscess, neoplasia.
- Radiographs of elbow: rule out underlying orthopedic problems (degenerative joint disease, olecranon fracture).

TREATMENT 

TREATMENT OVERVIEW

Successful treatment of this problem requires:

- Complete drainage of fluid from the cavity and prevention of its reaccumulation
- Apposition and subsequent healing of fibrous tissue surfaces of the cavity together to obliterate the cavity and prevent reformation Prevention of continued trauma to the elbows and therefore recurrence of the problem

ACUTE GENERAL TREATMENT

Three suggested methods of treatment:

- Aseptic aspiration of fluid and pressure coaptation bandage
  - Rarely successful for larger or chronic hygromas
- Penrose drainage and padded bandage
- Suture obliteration and padded bandage

CHRONIC TREATMENT

- Padded bandage must remain in place for at least 4 weeks to allow the fibrous tissue surfaces to heal together and thereby obliterate the subcutaneous space in which fluid could accumulate.
- Dog should be restricted from lying on hard surfaces.
  - Suitable padded bedding should be provided.
- Elbow(s) should be padded until healing and adequate protective callus have developed.

POSSIBLE COMPLICATIONS

- Recurrence
  - Penrose drain removed too soon
  - Inadequate period of bandaging to allow fibrous healing to occur
  - Suitable padded bedding not provided after bandages have been removed
- Infection
  - Repeated needle drainage
  - Inadequate sterile surgical technique
  - Inadequate protective bandage over Penrose drains
- Development of a chronic nonhealing ulcer over olecranon
  - Infected hygroma
  - Dehiscence of suture line after surgery
  - Continued trauma to hygroma

RECOMMENDED MONITORING

- See Chronic Treatment above
- Observe elbow area for evidence of:
  - Recurrence of the hygroma

  - Infection of the overlying skin
  - Development of necrosis/ulceration of the overlying skin
- Be aware that problem may develop on other elbow if preventive measures are not taken.

PROGNOSIS AND OUTCOME

- Good with appropriate treatment
- Poor if:
  - Hygroma becomes infected
  - Dehiscence of suture line occurs
  - Nonhealing ulcer develops
- May require extensive reconstructive surgery to correct these problems

PEARLS & CONSIDERATIONS

COMMENTS

- *Do not* attempt surgical excision of the hygroma.
- Successful primary closure is difficult to achieve with excision, owing to tension and motion at surgical site; high risk of complications.

PREVENTION

- Dog should be restricted from lying on hard surfaces:
  - Especially if other orthopedic problems are present that restrict the dog's ability to rise and lie down
  - Suitable padded bedding should be provided.
- Elbow(s) should be padded until adequate protective callus has developed.

TECHNICIAN TIPS

In-hospital care:

- Ensure adequate bedding is provided to reduce pressure trauma to elbow(s).
- Ensure that bandage(s) remain securely in place and are clean and dry.
- Assist patient in getting up and down and ambulating as needed, to prevent additional elbow trauma.
- Client education before and at time of patient discharge: correct bandage care including being aware of potential problems/complications. Advise clients on home management/prevention:
  - Assisting dog getting up and down and ambulating while leg(s) bandaged
  - Appropriate bedding, avoiding hard surfaces
  - Purchase of custom-made elbow pads

CLIENT EDUCATION

Seek veterinary care and advise as soon as hygroma develops: easier to treat and less risk of complications if treated early (e.g., before infection).

SUGGESTED READING

Johnston DE: Hygroma of the elbow in dogs. J Am Vet Med Assoc 167:213, 1975.

Swaim SF, Henderson RA: Wounds on the limbs. In Small animal wound management. Philadelphia, 1990, Lea & Febiger, pp 181–188.

AUTHOR & EDITOR: RICHARD WALSHAW

Elbow Dysplasia

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

- A common group of developmental disorders including fragmented medial coronoid process (FCP), ununited anconeal process (UAP), osteochondritis dissecans (OCD), and elbow incongruity (uneven radial head and medial coronoid surfaces) that cause degenerative joint disease in the elbow
- FCP is a separation of the medial aspect of the coronoid process from the ulna.
- UAP is a failure of the anconeal process to fuse to the ulna.
- Osteochondrosis is an abnormality of endochondral ossification, whereas OCD implies separation of the diseased cartilage from the subchondral bone.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Primarily in dogs between 6 and 9 months old
- FCP may be present in older dogs with degenerative joint disease.

GENETICS & BREED PREDISPOSITION

Elbow dysplasia is hereditary but also is associated with rapid growth and high-energy diet.

- UAP is found primarily in German shepherds, basset hounds, and Saint Bernards.
- FCP and OCD affect primarily retriever breeds, Bernese mountain dogs, and rottweilers.

Other large breed dogs may be affected by elbow dysplasia, including the Newfoundland, mastiff, and Australian shepherd; however, elbow displasia is also becoming more prevalent in smaller breeds.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- History of lameness on one or both forelimbs, often worse after exercise
- Reluctance to play or take long walks

PHYSICAL EXAM FINDINGS

- Lameness on one or both forelimbs
- Pain on manipulation of the elbow, especially on extension
- If osteoarthrosis is advanced, crepitation or effusion may be palpable along with a decreased amount of flexion to the joint (reduced range of motion).

ETIOLOGY AND PATHOPHYSIOLOGY

- OCD occurs when there is osteochondrosis (a failure of endochondral ossification), which leads to cartilage thickening and fissure formation.
    - Factors such as diet, rapid growth, hormonal imbalance, trauma, and genetics may lead to the development of OCD as well as FCP and UAP.
- Joint incongruity, leading to increased pressure on the anconeus, has been implicated as a cause for UAP.
    - UAP may also be a form of osteochondrosis with abnormal thickened cartilage, leading to failure of unification.
- The underlying pathophysiology of FCP is unknown but is believed to be secondary to elbow incongruity or a form of osteochondrosis.
    - Incongruity of the joint, especially an increase in length of the ulna in relation to the radius, can lead to increased weight-bearing load on the medial aspect of the coronoid process, leading to fissuring and fragmentation.
    - Osteochondrosis may lead to a delay in ossification of the coronoid region and subject the joint to fragmentation when weight bearing.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

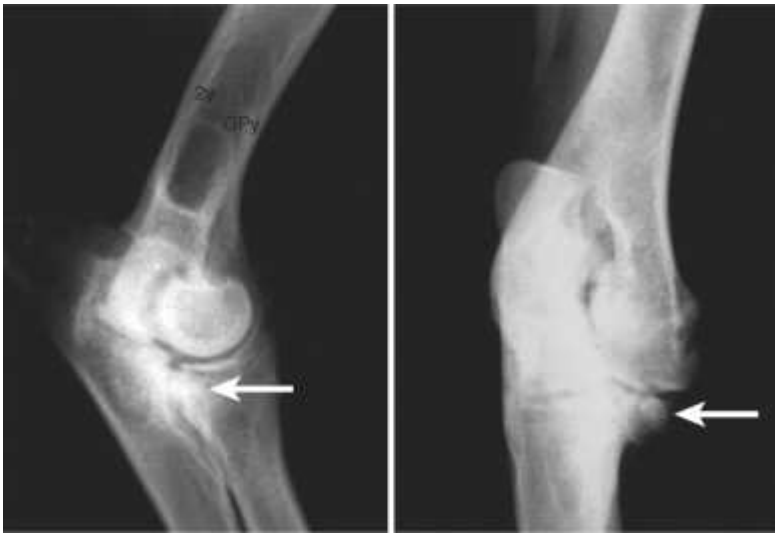
Radiography is the standard means of diagnosing elbow dysplasia. However, canine elbow dysplasia can be present without radiographic signs, and advanced imaging (nuclear scintigraphy, ultrasonography, CT, and MRI) or arthroscopy may help diagnose subtle lesions.

DIFFERENTIAL DIAGNOSIS

- Panosteitis
- OCD of the shoulder
- Elbow luxation

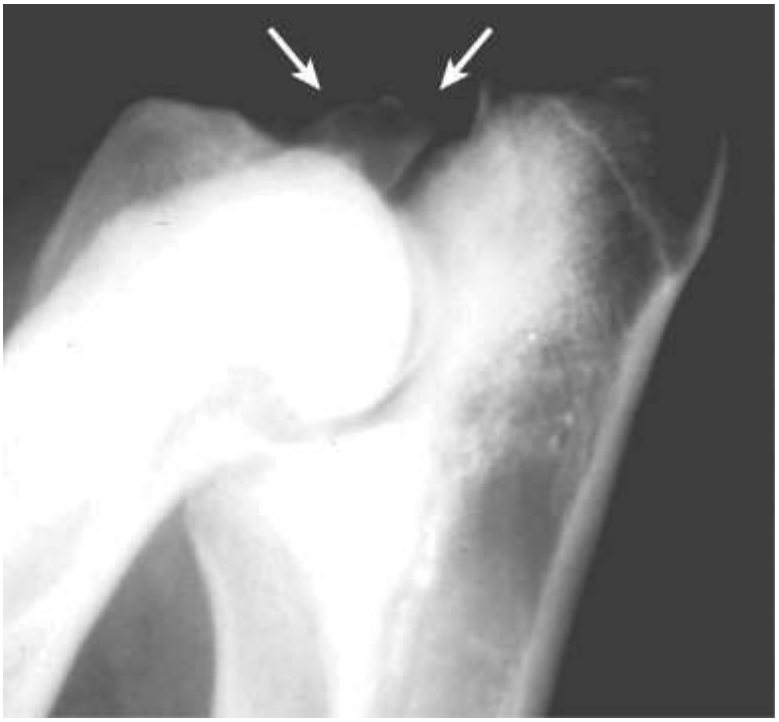
INITIAL DATABASE

- CBC and serum chemistry panel based on signalment:
  - Consider before treatment or sedation/anesthesia
  - Generally unremarkable for elbow dysplasia alone
- Mediolateral, craniocaudal, and flexed lateral radiographs of both elbows:
  - An oblique craniocaudal view with the elbow flexed 30° and rotated medially 15° may help to assess the medial coronoid process.
  - The flexed lateral is the best radiographic view to identify a UAP.
  - OCD is seen on the medial condyle of the humerus, primarily on the craniocaudal view.
  - Elbow congruity is best assessed on the mediolateral view, and the beam should be centered on the elbow joint.



ELBOW DYSPLASIA Mediolateral *(left panel)* and craniocaudal *(right panel)* projections of a canine elbow with fragmented medial coronoid process *(arrows)*.

(Courtesy Dr. J. Harari; reproduced with permission.)



ELBOW DYSPLASIA Mediolateral projection of a flexed canine elbow joint with an ununited anconeal process *(arrowheads).*

(Courtesy Dr. J. Harari; reproduced with permission.)

ADVANCED OR CONFIRMATORY TESTING

- A bone scan can be used for localizing the lameness if a complete orthopedic examination and radiographs are inconclusive.
- CT or MRI can be used for characterizing and delineating the elbow lesion.
- Arthroscopy can be used to confirm abnormalities in the elbow joint found with imaging modalities.
- Arthrocentesis may be performed to rule out other causes of joint effusion.

TREATMENT

TREATMENT OVERVIEW

In persistently lame dogs with elbow dysplasia, treatment involves removal of the FCP, OCD, or UAP fragment, which will result in an improvement in limb function. In dogs with elbow incongruity, surgery to improve congruity will minimize ongoing degenerative changes to the joint. However, degenerative joint disease is still expected to progress in most cases of elbow dysplasia.

ACUTE GENERAL TREATMENT

- Elbow arthroscopy via a medial portal is used for treatment of FCP and OCD and to assess elbow incongruity.
  - The FCP is identified and removed with grasping forceps or a motorized shaver.
  - Curettage or removal of the medial coronoid process via a subtotal coronoid ostectomy can be used when fissuring or chondromalacia of the coronoid is present without gross fragmentation.
  - OCD lesion is identified and the cartilage flap removed. A motorized shaver is used for removing fragments and to treat the underlying subchondral bone. Osteochondral autograft transfer is being researched as a treatment option for OCD lesions.
- A sliding humeral osteotomy has been proposed to redistribute forces within the medial compartment of the elbow, thereby decreasing pain associated with medial coronoid disease.
- In skeletally mature dogs, a UAP is often surgically removed via a lateral approach.
  - Various other surgical procedures have been described, such as lag screw fixation. However, these approaches result in no better success and have a higher complication rate related to the implants.
- In skeletally immature dogs, a dynamic ulnar osteotomy may be used for removing the pressure on the anconeal process and allowing bone or fibrous union of the fragment.
  - This may be used simultaneously with lag screw fixation of the anconeal process. Lag screw fixation causes compression of the anconeal process to the ulna and leads to bone fusion.
- If elbow incongruity exists, a dynamic ulnar osteotomy is performed to allow proximal movement (triceps muscles pull) of the

ulna to improve joint congruency.
    - An intramedullary pin is placed in the ulna by some surgeons to provide stabilization and reduce callus formation.
- Total elbow replacement or elbow arthrodesis may be performed in dogs with moderate to severe elbow osteoarthritis secondary to elbow dysplasia.

CHRONIC TREATMENT

- If an ulnar osteotomy is performed, postoperative placement of a soft padded bandage for 2-4 weeks is used for support.
- Exercise should be restricted to short leash walks for 4-6 weeks after surgery.
- Physical therapy may be useful to maintain range of motion within the elbow joint after surgery.
- Medical therapy may be necessary after surgery if a significant amount of degenerative joint disease is present.
    - Nonsteroidal antiinflammatory drugs (NSAIDs):
        - Aspirin, 10–25 mg/kg PO q 8-24 h; *or*
        - Carprofen, 2 mg/kg PO q 12 h; *or*
        - Etodolac, 10–15 mg/kg PO q 24 h *or*
        - Deracoxib, 1–2 mg/kg PO q 24 h (may use 3-4 mg/kg PO q 24 h for first 7 days only); *or*
        - Meloxicam, 0.1 mg/kg PO q 24 h; *or*
        - Meclofenamic acid, 1.1 mg/kg PO q 24 h after eating, 5 days maximum; *or*
        - Tepoxalin, 10 mg/kg PO q 24 h (new product, objective data pending); *or*
        - Others
    - Chondroprotective agents:
        - Polysulfated glycosaminoglycan, 5 mg/kg IM once weekly × 4–6 weeks; *or*
        - Pentosan polysulfate (from beech-wood hemicellulose) 3 mg/kg SQ once weekly; *or*
        - Oral formulations (glucosamine, chondroitin sulfate, hyaluronan): according to formulation/labeled instructions

POSSIBLE COMPLICATIONS

- Infection
- Implant failure if performing lag screw fixation

RECOMMENDED MONITORING

- Suture removal and recheck 2 postoperative weeks
- Repeat radiographs 6 postoperative weeks if an ulnar osteotomy, lag screw fixation of the anconeal process, sliding humeral osteotomy, or total elbow replacement was performed.

PROGNOSIS AND OUTCOME

- Surgery will help alleviate lameness for OCD, FCP, and UAP, but most affected dogs will continue to have progressive DJD and need medical therapy.
- Prognosis for return to full function depends on the degree of preexisting DJD.
- Medical treatment consisting of weight control, exercise restriction, NSAIDs, and polysulfated glycosaminoglycan therapy is reported to have a similar outcome to surgical treatment of OCD and FCP.

PEARLS & CONSIDERATIONS

COMMENTS

- Clinical signs of FCP may not correlate with radiographic evidence of disease.
    - Initial radiographic change will be mild osteophytosis on the anconeal process.
    - Some dogs may show mild or no radiographic changes, yet be profoundly lame; such a patient needs MRI, CT, or arthroscopy.
    - Conversely, some dogs are not lame, yet have radiographic evidence of DJD.
    - Hence, treatment is directed toward the patient and not the radiograph.
- Unilateral forelimb lameness may not be detectable if bilateral forelimb disease is present.
- Because of the prevalence of bilateral disease, both elbows may undergo arthroscopy with one anesthetic episode if clinically indicated.
- The anconeal process does not fuse until 4-5 months of age and cannot be diagnosed radiographically as ununited before that time.
- When manipulating the elbow to check for pain, avoid movement of the shoulder, which may obscure localization of the

discomfort.

CLIENT EDUCATION

Because of the hereditary component of elbow dysplasia, affected dogs should not be used for breeding.

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Eisenmenger's Syndrome

BASIC INFORMATION

DEFINITION

Uncommon syndrome involving any large communication between the left and right sides of the heart, in association with severe pulmonary hypertension, which results in right-to-left shunting of blood.

SYNONYMS

- Eisenmenger's physiology or reaction
- Eisenmenger's complex (large, nonrestrictive ventricular septal defect [VSD] plus pulmonary hypertension causing right-to-left shunting with or without dextroposition of the aorta)
- The term *cyanotic congenital heart disease* includes Eisenmenger's syndrome as well as right-to-left cardiac shunts without pulmonary hypertension (i.e., VSD with concurrent pulmonic stenosis).

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs and cats
- Young animals
- Female dogs more predisposed to patent ductus arteriosus (PDA); 15% of dogs with PDA may develop severe pulmonary hypertension.

GENETICS & BREED PREDISPOSITION

Dependent on the underlying cause:

- PDA: quasi-continuous or threshold trait with high degree of heritability. Miniature and toy poodles, collie, Pomeranian, Shetland sheepdog, American cocker spaniel, German shepherd, Maltese, keeshond, Yorkshire terrier.
- VSD: autosomal-dominant trait with incomplete penetrance or a polygenic trait. English springer spaniel, English bulldog.

RISK FACTORS

Living at high altitude

ASSOCIATED CONDITIONS & DISORDERS

Eisenmenger's syndrome can originate from an isolated cardiac defect (i.e., PDA) or from a combination of VSD or ASD and PDA.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Dyspnea (most common sign in cats)
- Exercise intolerance
- Syncope
- Lethargy
- Cough
- Cyanosis
- Hind limb collapse

PHYSICAL EXAM FINDINGS

- Heart murmur (timing and location determined by defect[s] present)
- Right or left apical systolic murmurs (inconsistent)
- Tachycardia

- Tachypnea
- Generalized or regional cyanosis, depending on underlying cause
- Loud second heart sound
- Split second heart sound

ETIOLOGY AND PATHOPHYSIOLOGY

- Size of the defect and severity of pulmonary hypertension determine the degree of shunting and thus the occurrence and extent of clinical signs.
    - Hypoxemia from shunting of venous blood into the arterial circulation leads to erythropoietin production and polycythemia.
    - Polycythemia, if severe, can produce hyperviscosity and pulmonary embolism, central neurologic signs, and/or coagulopathies.
- Congenital:
    - High pulmonary vascular resistance is maintained after birth.
    - Abnormal maturation of the pulmonary vasculature
- Acquired:
    - Large systemic-pulmonary communication (left-to-right shunt) offers minimal resistance to systolic flow.
    - Relative flows are determined by systemic and pulmonary vascular resistance.
    - Prolonged pulmonary hypertension leads to pulmonary vascular disease, an abnormal maturation of the pulmonary vasculature, and right ventricular hypertrophy.
    - Pulmonary arterial histologic features: medial muscular hypertrophy, laminar intimal fibrosis, necrotizing arteritis, plexiform lesions.
    - With progression, pulmonary vascular resistance may increase to a value greater than the systemic vascular resistance, causing right-to-left or bidirectional shunting (mixing of venous and arterial blood).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected in a young patient presenting with dyspnea, cyanosis, and collapsing episodes. Polycythemia and right heart enlargement are usually present. An echocardiogram with contrast is required for confirmation.

DIFFERENTIAL DIAGNOSIS

- Radiographic/electrocardiographic:
    - Right heart enlargement: other types of cardiac disease (pulmonic stenosis, tetralogy of Fallot, heartworm disease, tricuspid valve dysplasia, atrial septal defect), cor pulmonale
- Echocardiographic:
    - Pulmonic stenosis
    - Tetralogy of Fallot
    - Heartworm disease

INITIAL DATABASE

- CBC: polycythemia (usually progressive with age)
- Heartworm test: antigen, antibody (cats), and microfilaria tests
- Thoracic radiographs: right heart enlargement, enlarged main pulmonary artery, normal to mildly enlarged pulmonary vasculature
- Systemic arterial blood pressure measurement: hypotension contraindicates performing phlebotomy without fluid replacement
- Electrocardiogram: tall P waves in lead II, deep S waves in lead II, right axis deviation; arrhythmias are uncommon
- Echocardiogram:
    - 2D: right ventricular hypertrophy, enlarged main pulmonary artery, identification of structural defects
    - M mode: right ventricular free wall and septal hypertrophy, septal flattening, paradoxical septal motion
    - Color flow Doppler: aliased or laminar flow across the congeni-tal defect, tricuspid regurgitation (uncommon)
    - Spectral Doppler: tricuspid regurgitant velocity > 3.5 m/s, pulmonic insufficiency velocity > 3 m/s, reversed E/A ratio of mitral valve inflow profile, midsystolic notching of the pulmonary flow profile (severe cases)
    - Contrast echo: contrast appears in the left heart (intracardiac shunt) or in the abdominal aorta (extracardiac shunt).

ADVANCED OR CONFIRMATORY TESTING

- Cardiac catheterization: used for confirming diagnosis and to assess degree of shunting

- Angiogram: outlines the congenital defect(s) (PDA, VSD, ASD or aorticopulmonary communication)
- Pressure measurements: increased pulmonary artery pressures. With large defects, right and left ventricular pressures have a tendency to equalize.
- Oximetry: decreased aortic Po2
- Transesophageal echocardiography: better identification of the congenital defect

TREATMENT

TREATMENT OVERVIEW

Initial control of polycythemia and signs of hyperviscosity can be achieved with periodic phlebotomies. Hydroxyurea and a phosphodiesterase-V inhibitor (to reduce severity of pulmonary hypertension) may be started if clinical signs persist. Consider referral to cardiologist for diagnosis and advice on treatment plan.

ACUTE GENERAL TREATMENT

- Phlebotomy: if PCV > 60%. Withdrawal of 10%-20% of circulating blood volume (= 1-2 mL/kg) with or without intravenous fluid replacement. Repeated as needed (typically every several weeks) based on recurrence of clinical signs.
- Calcium channel blocker (e.g., amlodipine), phosphodiesterase V inhibitors (e.g., sildenafil): reduce pulmonary hypertension (see 935)

CHRONIC TREATMENT

Medical therapy:

- Hydroxyurea, 20-25 mg/kg PO q 12-24 h until hematocrit is lower; then 25-50 mg/kg PO q 48 h as needed to maintain stable hematocrit. Recommended when patient requires frequent phlebotomies.
- Diuretics, ACE inhibitors, and antiarrhythmics following the treatment guidelines. See Heart Failure, Acute/ Decompensated, 468; Heart Failure, Chronic, 470; Ventricular Arrhythmias (Premature Ventricular Complexes, Ventricular Tachycardia), .

BEHAVIOR/EXERCISE

Restrict exercise and excitement in patients with collapsing or syncopal episodes.

DRUG INTERACTIONS

Hydroxyurea: reversible bone marrow suppression (pancytopenia), anorexia, vomiting and diarrhea, sloughing of nails are possible.

RECOMMENDED MONITORING

Recheck examinations should include: CBC, serum renal profile, and systolic blood pressure measurement.

PROGNOSIS AND OUTCOME

Long-term prognosis is guarded to poor, depending on severity of pulmonary hypertension.

PEARLS & CONSIDERATIONS

COMMENTS

- Large systemic-pulmonary communications are uncommon in dogs and cats.
- Surgery is contraindicated, owing to severe pulmonary hypertension.

PREVENTION

Do not breed affected animals.

TECHNICIAN TIPS

- Check mucous membranes for cyanosis. The jugular vein is usually the best phlebotomy site; when administering fluids, use a different vein (e.g., cephalic vein)

CLIENT EDUCATION

- Monitor respiratory rate at rest, exercise tolerance, and appetite.
- Advise client not to breed affected animals.

SUGGESTED READING

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Ehrlichiosis, Canine Monocytic

BASIC INFORMATION

DEFINITION

Tick-transmitted disease caused by *Ehrlichia canis* or *Ehrlichia chaffeensis* infection. These organisms predominantly infect circulating monocytes, macrophages, and lymphocytes, causing nonspecific signs (fever, anorexia, lethargy, inappetence), bleeding, anemia, and cytopenias. Chronically, *E. canis* infection can cause bone marrow suppression, pancytopenia, glomerulonephritis, and death.

SYNONYMS

Canine monocytotropic ehrlichiosis *(E. canis),* human monocytic ehrlichiosis *(E. chaffeensis),* tropical pancytopenia

EPIDEMIOLOGY

SPECIES, AGE, SEX

Ehrlichiosis is most commonly seen in dogs; rarely in cats.

GENETICS & BREED PREDISPOSITION

German shepherd dogs have a more fulminant illness, owing to reduced cellular immune response.

RISK FACTORS

E. canis is transmitted by *Rhipicephalus sanguineus* (brown dog tick), whereas *E. chaffeensis* is transmitted by *Amblyomma americanum* (lone star tick) or *Dermacentor variabilis* (American dog tick). *R. sanguineus* is an urban tick capable of completing its entire life cycle indoors (exposure risk when boarding, pet stores, etc.) Therefore, access to wooded areas, outdoor activities, and tick season are risk factors for *E. chaffeensis* infection but not for *E. canis* infection.

CONTAGION & ZOONOSIS

Most *Ehrlichia* spp. may be infectious to humans, but there is no direct dog-to-dog or dog-to-human transmission. Personal protective equipment (gloves and safety glasses) should be used when handling biological samples (inoculation risk).

GEOGRAPHY AND SEASONALITY

E. canis infection has been found in most tropical and subtropical regions in the world, based on distribution of the vector. Because of different disease forms (acute, subacute, and chronic), there is no true seasonality. *E. chaffeensis* has been described predominantly in the United States, with emergence in South Korea, southern China, and Cameroon.

ASSOCIATED CONDITIONS & DISORDERS

Other tickborne diseases (Rocky Mountain spotted fever, cyclic thrombocytopenia, babesiosis, bartonellosis, hepatozoonosis) may occur concurrently.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Acute phase: onset 8-20 days post infection; signs last 2-4 weeks and may resolve spontaneously.
- Subclinical phase: onset 6-9 weeks post infection; clinically inapparent cytopenias
    - The infection may be cleared spontaneously at this time (uncommon) but if not, the chronic phase ensues.
- Chronic phase: onset is weeks to months after infection; signs are variable in severity, ranging from mild illness to a life-threatening syndrome.

HISTORY, CHIEF COMPLAINT

- History may include tick exposure weeks/months earlier; not always recalled by pet owners.
- Overt signs: depression, anorexia, weight loss, ocular or nasal discharge, bleeding tendencies, lameness.
- Clinical signs of the chronic phase may include overt bleeding, cachexia, lameness, ocular, and neurologic abnormalities.

PHYSICAL EXAM FINDINGS

- Fever may be present but is not always detected.
- Joint pain and shifting leg lameness
- Hepatomegaly, splenomegaly, peripheral lymphadenopathy, increased vesicular breath sounds
- Bleeding disorders: cutaneous and/or mucosal petechiae, ecchymoses, unilateral or bilateral epistaxis, melena, retinal hemorrhage, hyphema
- Signs of uveitis: blepharospasm, photophobia, excessive lacrimation, hyperemia of scleral vessels, and decreased intraocular pressure. Blindness due to retinal detachment can occur.
- Neurologic signs: ataxia, seizures, vestibular signs, anisocoria, and hyperesthesia (severe cases)
- Subcutaneous edema due to chronic protein-losing nephropathy (chronic cases) or vasculitis
- Arrhythmias due to vasculitis and myocardial injury may occur in severe cases.
- Mild cases may have unremarkable clinical findings.

ETIOLOGY AND PATHOPHYSIOLOGY

- Ticks acquire the organism by feeding as either larvae or nymphs on infected animals. No transovarial transmission occurs in the tick (i.e., life cycle requires the mammal).
- When an infected tick ingests a blood meal, the organism is transmitted via saliva to the vertebrate host.
- Infection leads to multiplication in mononuclear cells and tissues (spleen, liver, and lymph nodes).
- Infected cells attach to vascular endothelium in lungs, kidneys, joints, myocardium, and meninges, leading to vasculitis and subendothelial tissue infection and the acute phase of disease initially.
- Thrombocytopenia occurs secondary to increased platelet consumption and decreased platelet half-life, as a result of antiplatelet antibodies production, platelet migration-inhibition factor production, and splenic sequestration.
- Dysfunction of remaining platelets (thrombocytopathy) may occur secondary to antiplatelet antibodies binding to platelet receptors.
- Systemic inflammation may occur, with varying degrees of thrombosis, hyperviscosity, and red cell destruction.
- Subclinical phase is a result of ongoing bone marrow effects.
- Those unable to clear the infection in the subclinical phase develop chronic disease with hyperglobulinemia and immune complex formation, as well as bone marrow suppression, possibly leading to pancytopenia.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on the presence of anorexia, fever, lethargy, and/or bleeding tendencies in a dog with tick exposure, hematologic and clinical chemistry abnormalities, and response to therapy. Presumptive diagnosis is often based on specific antibody detection. Definitive diagnosis depends upon visualization of the organisms, microbial DNA amplification and genetic sequencing, or a fourfold change in antibody titers between acute and convalescent samples, but treatment often is indicated in patients showing overt clinical signs of ehrlichiosis before such results are available.

DIFFERENTIAL DIAGNOSIS

- Acute phase is similar to Rocky Mountain spotted fever (see p. 994).
- Chronic disease differentials include immune-mediated diseases, myeloma, lymphoma, hepatozoonosis, malignant histiocytosis, leukemia, myelodysplasia, leptospirosis, bartonellosis, and babesiosis.

INITIAL DATABASE

- CBC, serum biochemistry profile, urinalysis
  - Thrombocytopenia (mild to severe) is the typical finding in all stages of illness, but absence does not rule out ehrlichiosis.
  - Neutropenia, nonregenerative anemia, lymphocytosis (sometimes marked), monocytosis, and eosinophilia may be observed.
  - Hyperglobulinemia is common; polyclonal gammopathy is typical, but in rare cases a monoclonal gammopathy is present.
  - Increase in alanine aminotransferase (ALT) and alkaline phosphatase (ALP) activities.
  - Pathologic proteinuria (e.g., elevated urine protein/creatinine ratio in the absence of urinary tract infection) occurs

secondary to glomerulonephritis.
- Fundic examination: retinal hemorrhages/detachment may be seen.
- Abdominal imaging if splenomegaly/signs of abdominal pain
- Lymph node aspirates if lymphadenopathy
- Arthrocentesis and limb radiography if signs of polyarthritis. Sterile, nonerosive polyarthritis with predominance of nondegenerate neutrophils may occur.
- Bone marrow aspirate if pancytopenia is present
- Cerebrospinal fluid tap if neurologic signs are present
- Antinuclear antibody and Coombs' tests: to help identify primary or secondary immune-mediated disease. Coombs' test may be positive in *Ehrlichia* infection.

ADVANCED OR CONFIRMATORY TESTING

- Buffy coat, blood smear evaluation: rarely identify morulae in mononuclear cells (many false-negative results)
- Serologic titers: IFA or ELISA (antibody tests):
  - Negative results may occur in acute cases. Confirmation with a convalescent titer (2–4 weeks later; ≥fourfold increase) is necessary for definitive diagnosis.
  - Positive results suggest exposure, not infection. Antibody titers can persist from months to more than a year.
  - Antibodies from dogs infected with *E. canis* cross-react with *E. chaffeensis* antigens and occasionally with *E. ewingii* (IFA only) but do not cross-react with *Anaplasma phagocytophilum* antigens.
- PCR amplification: may be applied to tissue or whole blood. It provides definitive diagnosis, since it can differentiate between *A. phagocytophilum*, *A. platys*, *E. canis*, *E. chaffeensis*, *E. ewingii*, and other bacteria from the Anaplasmataceae family. False-negative PCR tests can occur if low numbers of circulating organisms.

TREATMENT

TREATMENT OVERVIEW

- The treatment of choice for both *E.canis* and *E. chaffeensis* infection is doxycycline or tetracycline, with rapid clinical improvement (beginning within 24-48 hours) in the majority of cases. Dogs with slow or partial recovery might be coinfected with other tickborne organisms. There is no consensus whether or not the antibiotic therapy clears these organisms from infected dogs, and chronic subclinical infections may be possible. Some manifestations such as glomerulonephritis may persist after treatment, but progression should be halted.

ACUTE GENERAL TREATMENT

- Clear organism:
  - Doxycycline, 5–10 mg/kg PO or IV q 12 h for 28 days (treatment of choice); *or*
  - Tetracycline, 22 mg/kg PO q 8 h for 21 days (alternative treatment)
  - For puppies under 1 year of age: chloramphenicol, 15-25 mg/kg PO (or IV, SQ) q 8 h for 14-21 days (to avoid discoloration of the teeth)
- Supportive care depends on clinical manifestation (i.e., transfusions for anemia, analgesics for polyarthritis pain).
- The authors do not routinely use corticosteroids for the treatment of ehrlichiosis. Reduction of ehrlichial antigens through appropriate antibiotic therapy should reduce secondary immune-mediated pathology. Despite being controversial, some clinicians have used corticosteroids at immunosuppressive doses (e.g., prednisone, 2–4 mg/kg PO q 24 h during first 2–7 days of acute stage).

CHRONIC TREATMENT

Chronic infections can occur with *E. canis;* however, response to doxycycline after 28 days of treatment is expected.

DRUG INTERACTIONS

- Imidocarb dipropionate or enrofloxacin are not effective against *Ehrlichia canis*.
- Tetracycline derivatives should not be used in the last half of pregnancy. Oral doxycycline should be given with food to avoid GI effects (nausea and vomiting). Tetracycline derivatives should not be given concomitant with oral antacids, cathartics, or other GI products containing cations (aluminum, calcium, magnesium, zinc, or bismuth).

POSSIBLE COMPLICATIONS

- Hemorrhage from severe thrombocytopenia or disseminated intravascular coagulation (DIC)

- Protein-losing glomerular disease
- Blindness associated with retinal hemorrhages and detachment
- Immune-mediated diseases
- Medullary aplasia and persistent pancytopenia
- Sudden death due to organ failure may occur in chronic cases.
- Dogs receiving incomplete or inadequate treatment may enter the subclinical phase.

RECOMMENDED MONITORING

- Resolution of clinical, hematologic, and biochemical abnormalities should be used to assess the response to therapy.
- Antibody titers may persist for months to years despite the absence of infection, so serologic testing is unreliable as a monitoring tool.
- PCR may aid in monitoring the response to treatment: a positive PCR test post treatment would be consistent with a treatment failure or reinfection.

PROGNOSIS AND OUTCOME

- Good prognosis with quick improvement in acute and mild chronic cases. Expect dramatic positive response to doxycycline or tetracycline beginning within 24-48 hours.
- Severely pancytopenic patients with hemorrhagic complications or concurrent infections have a guarded to poor prognosis.

PEARLS & CONSIDERATIONS

COMMENTS

- *E. canis* infection occurs in some cats, with clinical signs resembling acute canine monocytic ehrlichiosis.
- *E. canis* has been detected in at least six sick humans in Venezuela. Human *E. canis* cases have not been described from other countries.
- *E. chaffeensis* is the most frequent *Anaplasma*/*Ehrlichia* infection in humans in the United States, with 1137 cases reported in 2008.
- *E. chaffeensis* may produce similar but less severe signs in dogs than *E. canis*, although as a result of cross-reactivity, the true incidence of *E. chaffeensis* in dogs is poorly defined.

PREVENTION

Adequate tick control is the best prevention.

TECHNICIAN TIPS

- Low platelet numbers might increase bleeding time after blood sample collection.
- Despite a relatively low risk of infection, handling biological samples from animals suspected of *Ehrlichia* spp. or *Anaplasma* spp. infection should always be performed with precautions and with adequate personal protective equipment.

CLIENT EDUCATION

- Infected dogs pose little to no hazard to humans, so long as ticks are well controlled.
- Dogs are sentinels of human exposure to the pathogen in the shared environment; therefore owners should take proper actions to prevent tick bites.

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Edema, Subcutaneous

BASIC INFORMATION

DEFINITION

Subcutaneous edema is the local or generalized observable swelling from excessive fluid accumulation within the interstitial tissue spaces under the skin. Under normal circumstances, only a small amount of fluid leaks from vessels to form interstitial fluid, which is then removed by lymphatic vessels.

SYNONYMS

Peripheral edema (edema of the paws and legs), anasarca (generalized, massive subcutaneous edema)

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs and cats: any age, either sex

RISK FACTORS

Severe hypoproteinemia (from kidney, liver, or gastrointestinal disease), right-sided heart failure, systemic inflammation/vasculitis, extensive trauma or heat, hereditary or congenital malformation of the lymphatic system

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Pitting edema versus nonpitting edema

HISTORY, CHIEF COMPLAINT

Limb swelling or a swollen appearance may be historical findings suggestive of subcutaneous edema.

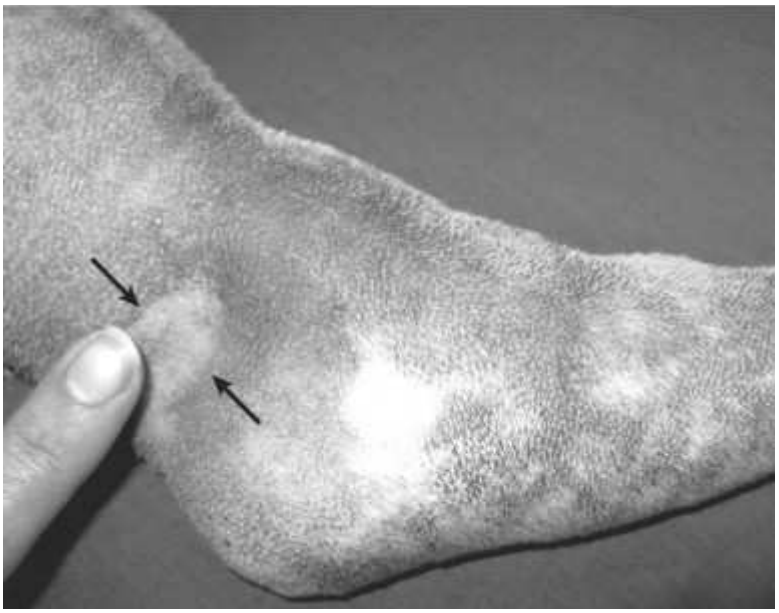
PHYSICAL EXAM FINDINGS

- The subcutaneous tissues appear locally or diffusely swollen.
- The hock with its lateral saphenous vein, the Achilles tendons, and the bony prominence of the mandible are useful to evaluate for subcutaneous edema; these areas are well defined even in obese animals.
    - With edema, these areas are less defined and have a “jelly-like” appearance of the skin.
- Edema is by definition nonpainful and neither very warm nor very cool to the touch unless secondary infection is present.
- Edema tends to accumulate where gravity draws it, where lymphatic obstruction or insufficiency is greatest, or a combination of both. Therefore, the pattern of edema distribution can be variable.
- It may be possible to “pit” edema: digital pressure exerted on edematous skin may leave a depression, or pit, for several seconds after the pressure is released. Pitting edema represents interstitial fluid accumulation, whereas nonpitting edema is formed by intra-cellular swelling (e.g., a wheal). In dogs and cats, pitting edema is more common than nonpitting edema.
- Hyperemia, or the reddening of the subcutaneous tissue due to engorgement of oxygenated blood, indicates an active process causing arteriolar dilation. Congestion, or the cyanotic (“blue-red”) appearance of the subcutaneous tissue, is a passive process that occurs as worsening congestion leads to accumulation of deoxygenated hemoglobin. Capillary bleeding can occur uncommonly as a result of chronic congestion and may appear as petechiae, purpura, ecchymosis, or hematoma.

ETIOLOGY AND PATHOPHYSIOLOGY

- More fluid leaves the capillaries than enters:
    - Increased hydrostatic pressure in vessels
        - Right-sided congestive heart failure
        - Impaired venous flow
        - Iatrogenic fluid overload

    - Decreased plasma oncotic pressure
        - Hypoalbuminemia due to increased loss (protein-losing nephropathy/enteropathy, nephrotic syndrome) or decreased production (cirrhosis, malnutrition)
    - Increased vascular permeability
        - Allergic response causing increased histamine
        - Acute inflammation
        - Burn injury
- Normal volume of interstitial fluid not reabsorbed by the lymphatic system:
    - Lymphatic obstruction (usually localized)
        - Neoplasia
        - Inflammation
        - Trauma



EDEMA, SUBCUTANEOUS Subcutaneous edema in the hindlimb of a dog. In this image, the clinician just removed her index finger after applying digital pressure for several seconds, revealing the depression or pit *(arrows)* that characterizes pitting edema.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Subcutaneous edema can be identified on physical exam (readily if it is very pronounced but less easily if it is mild in degree). The presence of subcutaneous edema warrants assessing the serum albumin concentration and also ruling out heart disease (thoracic radiographs, echocardiogram).

DIFFERENTIAL DIAGNOSIS

When edema affects only one leg, local factors such as neoplasia, trauma, or phlebitis should be considered. Swollen extremities and ventral edema are uncommonly seen with congestive heart failure. In the rare instance (in small animals) where subcutaneous edema is present secondary to congestive heart failure, the edema is usually symmetric in distribution.

INITIAL DATABASE

- CBC: evaluate for hypoalbuminemia, anemia, or inflammation.
- Serum biochemistry profile: evaluate for electrolyte abnormalities.

ADVANCED OR CONFIRMATORY TESTING

Thoracic radiographs, echocardiography, and electrocardiography: evaluate for right-sided congestive heart failure.

TREATMENT

TREATMENT OVERVIEW

The therapeutic goal is to identify the cause and reverse it if possible.

ACUTE AND CHRONIC TREATMENT

- Management of subcutaneous edema is typically nonemergent and is primarily achieved by treatment of the underlying condition while considering specific therapies to restore water balance within the body.
- Patients with decreased oncotic pressure (hypoproteinemia), decreased osmotic balance (anemia), or increased endothelial permeability (inflammation) may benefit from plasma products, hetastarch, or dextran 70 to increase intravascular volume and favor water retention within the vasculature.
- Patients with increased hydrostatic pressure secondary to severe right-sided heart failure can benefit from potent loop diuretics such as furosemide. Furosemide causes increased sodium excretion by the kidneys, with resultant water loss and edema mobilization from the interstitial tissues.
- Trauma, inflammation, or neoplasia causing subcutaneous edema should be addressed primarily.

PROGNOSIS AND OUTCOME 

The prognosis for patients with subcutaneous edema depends on the underlying condition and the ability to treat and resolve this primary disease. Edema due to inflammation or infection, congestive heart failure, or hypoproteinemia can often be successfully managed or resolved. Treatment response for lymphatic obstruction is variable; lymph-edema (see p. 667) can be challenging to manage long term, and there is no curative therapy.

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Eclampsia

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Moderate to severe hypocalcemia of the lactating female, most often occurring in the first four weeks postpartum.

SYNONYMS

Lactation tetany, periparturient hypocalcemia, puerperal tetany

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs: younger, postparturient bitches
- Cats: rare in queens

GENETICS & BREED PREDISPOSITION

More likely to occur in small-breed dogs, although any lactating bitch may be affected

RISK FACTORS

- Primiparous bitches may be at greater risk.
- Decreased nutrition in the periparturient period as a result of stress or underlying illness.
- Excess dietary calcium during gestation
- Large litter size is thought to be a risk factor.

ASSOCIATED CONDITIONS & DISORDERS

Hypoglycemia can arise secondarily due to energy demands of tetany.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- *Prepartum* eclampsia
- *Intrapartum* eclampsia
- *Postpartum* eclampsia (most common)

HISTORY, CHIEF COMPLAINT

Lactating bitch with signs of aberrant behavior, ataxia, muscle tremors, seizures, and/or tetany

PHYSICAL EXAM FINDINGS

In approximate order of disease progression/severity:

- Anxiety, restlessness, pacing, whining, disinterest in pups
- Pruritus and biting at feet
- Ataxia, staggering, and muscle stiffness
- Panting; respiration eventually becomes labored as the condition progresses.
- Mydriasis and diminished pupillary light reflexes
- Tachycardia or bradycardia
- Muscle tremors, collapse, clonic spasms (tetany), and seizures (musculoskeletal signs are often exaggerated with tactile stimulus).
- Hyperthermia secondary to tetanic muscle contractions

- Arrhythmias: premature ventricular complexes

ETIOLOGY AND PATHOPHYSIOLOGY

- Circulating ionized calcium is depleted due to lactation and fetal development, possibly in conjunction with underlying nutritional imbalance.
- Decreased circulating ionized calcium alters cellular membrane potentials and allows for spontaneous discharge of nerve fibers to induce contraction of skeletal muscles and alteration of central nervous system function.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A presumptive diagnosis (based on history, clinical signs, and physical exam) warrants immediate treatment. Response to therapy is the most reliable diagnostic aid.

DIFFERENTIAL DIAGNOSIS

- Hypocalcemia of alternate origin
- Hypoglycemia (may be concurrent)
- Cerebral edema (possibly secondary in eclampsia ± hypoglycemia)
- Toxin ingestion

INITIAL DATABASE

- Total serum calcium < 6–7 mg/dL (<1.5–1.74 mmol/L) is the characteristic biochemical finding of eclampsia.
    - Calculated ionized calcium < 3.5-4 mg/dL (<0.87-1 mmol/L)

ADVANCED OR CONFIRMATORY TESTING

Blood glucose should be evaluated to rule out hypoglycemia as a primary or secondary contributor to clinical signs.

TREATMENT

TREATMENT OVERVIEW

Treatment is primarily aimed at alleviating clinical signs of hypocalcemia via parenteral calcium therapy while monitoring for bradycardia and/or arrhythmias. Secondary hypoglycemia and hyperthermia must also be addressed in the seizuring animal.

ACUTE GENERAL TREATMENT

- Intravenous (IV) administration of a 10% calcium gluconate or calcium borogluconate solution *slowly*, at a rate of 1-1.5 mL/kg over 10-30 minutes or until resolution of clinical signs.
    - Calcium chloride solutions are not recommended; risk of perivascular corrosive effects if the solution extravasates.
    - Electrocardiographic (ECG) monitoring is warranted during administration (see Recommended Monitoring below).
- IV calcium gluconate administration may be repeated in the event of a relapse; refractory cases should be reevaluated for hypoglycemia.
- The IV dose of calcium gluconate required to resolve clinical signs can be diluted 1:1 in saline for subcutaneous administration in 3 equal doses over 24-48 hours to prevent immediate relapse.
- Severe hyperthermia > 104°F should be controlled with ice packs or alcohol baths (see p. 480).

CHRONIC TREATMENT

- Remove puppies for 24-36 hours to reduce maternal calcium loss through lactation; in the event of recurrence, remove puppies permanently.
- Puppies can be fed milk replacer every other day to decrease lactation demand on the bitch until weaning at age 3 weeks.
- In high-risk cases, lactation can be ceased using a prolactin inhibitor.
    - Cabergoline, 5 mcg/kg PO q 24 h for 7 days

NUTRITION/DIET

- Oral calcium replacement therapy for the bitch is recommended until weaning.
  - 20 mg/kg calcium carbonate PO q 8 h
  - Calcium carbonate antacid tablets available over the counter (e.g., Titralac, Tums) typically contain 500-750 mg calcium carbonate per tablet. See label for exact content.
  - Vitamin D^3 supplementation aids in calcium absorption and homeostasis.
    - Over-the-counter products: 50 IU/kg PO q 24 h

BEHAVIOR/EXERCISE

If puppies are weaned to stop lactation, monitor dam for self-milking (licking own mammary glands, which can induce milk letdown).

DRUG INTERACTIONS

- Avoid tetracyclines or other potential calcium chelators.
- Use of calcium carbonate antacids will affect absorption of oral medications.
  - Administer calcium carbonate at least 1 hour before or after other medications.
  - Consult product labels for potential interactions.

POSSIBLE COMPLICATIONS

Overly rapid or unmonitored IV calcium administration can lead to severe bradycardia, ventricular arrhythmias, hypotension, and death.

RECOMMENDED MONITORING

- Cardiac monitoring by auscultation and/or ECG is required during IV calcium therapy. If severe bradycardia and/or arrhythmias develop, discontinue IV calcium until heart rate and rhythm normalize, then readminister at a decreased rate.
- Rectal temperature should be monitored until hyperthermia has resolved.

PROGNOSIS AND OUTCOME

Prognosis is good to excellent with immediate treatment and subsequent management.

PEARLS & CONSIDERATIONS

COMMENTS

- Treatment should be initiated immediately based on signalment, history, and physical examination.
- Recurrence is possible up to the end of lactation.
- Preventive *prepartum* calcium supplementation is *not* recommended, as it may promote the development of eclampsia.
- Preventative *postpartum* calcium supplementation is recommended, as it may prevent recurrence during a subsequent lactation.
- Hypoglycemia is a common concurrent disorder.

PREVENTION

Bitches should be maintained on a high-quality food during pregnancy.

TECHNICIAN TIPS

Knowing the signs of hypocalcemia (Physical Exam, above) helps technicians quickly identify a patient in need of calcium.

CLIENT EDUCATION

Owners are to be cautioned that affected bitches may develop eclampsia in subsequent litters, and nutritional management and careful attention to early clinical signs are required.

SUGGESTED READING

Drobatz KJ, Casey KK: Eclampsia in dogs: 31 cases (1995-1998). J Am Vet Med Assoc 217(2):216–219, 2000.

Feldman EC, Nelson RW: Canine and feline endocrinology and reproduction, ed 3, Philadelphia, 2004, WB Saunders, pp 829–831.

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Echinococcosis

BASIC INFORMATION

DEFINITION

- Cestode (tapeworm) infection with larval stages (hydatid cysts) that causes hydatid disease, primarily in humans:
  - Cystic echinococcosis is caused by *Echinococcus granulosus*.
  - Alveolar echinococcosis is caused by *E. multilocularis*.
  - Polycystic echinococcosis is caused by *E. vogelii* or *E. oligarthrus*.
- *Hydatid cyst disease* refers to the clinical condition in which intermediate hosts have multiple, often large intraparenchymal cysts containing brood capsules that in turn contain protoscolices in serous fluid.
- When ingested by the canine or feline definitive host, *protoscolices* will develop to adult tapeworms within the host's small intestine.

SYNONYMS

Hydatid disease; hydatidosis

EPIDEMIOLOGY

SPECIES, AGE, SEX

- *E. granulosus* definitive hosts are dogs and other canids; intermediate hosts are sheep, goats, swine, cattle, horses, camels, and humans.
- *E. multilocularis* definitive hosts are foxes and less frequently dogs, cats, coyotes, and wolves. Intermediate hosts are small rodents.
- *E. vogelii* definitive hosts are bush dogs and dogs; intermediate hosts are rodents.
- *E. oligarthrus* definitive hosts are wild felids; rodents are intermediate hosts.

RISK FACTORS

Exposure and ingestion of intermediate hosts (rodents, cattle, sheep) harboring the hydatid cysts

CONTAGION & ZOONOSIS

- Highly zoonotic
- Humans (and other suitable intermediate hosts) become infected by ingestion of eggs from the feces of definitive hosts.
- Once ingested, the organism spreads, and cysts may develop in various organs.

GEOGRAPHY AND SEASONALITY

- *E. granulosus* occurs worldwide; more frequent in rural, grazing areas.
- *E. multilocularis*: northern hemisphere
- *E. vogelii* and *E. oligarthrus*: Central and South America

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Absence of clinical signs (definitive hosts, e.g., dogs and cats)
- Diarrhea (occasionally dogs and cats)
- Hydatid cyst disease (intermediate hosts, e.g., humans, sheep, cattle)

HISTORY, CHIEF COMPLAINT

- Clinical signs of hydatid disease in domesticated animals are uncommon; humans are most commonly affected by disease.
- Intermediate host's signs relate to location and size of cyst and the species of *Echinococcus* infecting the host.

- Definitive hosts with adult tapeworms may have enteritis.

PHYSICAL EXAM FINDINGS

- Generally unremarkable (dogs, cats)
- Adult tapeworms are small, ranging from 1.2-10 mm in length. These tapeworms have a limited number of proglottids (only 3 or 4), and even the gravid (most distal) proglottids would be very difficult to observe grossly.
- Respiratory signs, abdominal distension, and other signs of hydatid cyst disease are not expected in dogs or cats, because they are definitive hosts, not intermediate hosts.

ETIOLOGY AND PATHOPHYSIOLOGY

- *E. granulosus* adults reside in the small intestine of the definitive host (dogs, coyotes, wolves).
- Eggs are passed into the feces where they are ingested by an intermediate host (e.g., cattle, sheep, horses).
- In the intermediate host, the organism invades the small intestine and spreads through the circulatory system, entering organs of predilection. The organism develops into a thick-walled unilocular (single compartment) cyst that gradually enlarges.
    - Typically, liver, lungs, and other organs (central nervous system, bone, heart) are affected.
- Definitive host becomes infected by ingestion of raw hydatid cyst within the visceral organs of intermediate hosts.
- *E. multilocularis* larval growth remains in the proliferative stage, resulting in invasion of surrounding tissues. The liver is primarily affected, with occasional metastasis to the brain and lungs. The organism develops into a thin-walled multilocular (demonstrating many compartments) cyst that easily spreads, thus overtaking the affected organs.
- *E. vogelii* larvae have a predilection for the liver.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The main concern is zoonosis: this is an extremely pathogenic zoonotic parasite, so great care should be taken when handling any feces from a dog suspected of harboring adult *E. granulosus.* The diagnosis is confirmed in tissue (histopathologic analysis of a biopsy or necropsy specimen) or PCR.

DIFFERENTIAL DIAGNOSIS

Other taeniids, to include many tapeworms within the genera *Taenia* and *Multiceps*.

INITIAL DATABASE

Fecal examination may reveal eggs which are identical to other taeniids. Among the three genera (*Echinococcus*, *Taenia*, and *Multiceps*), the eggs of the taeniids are very similar in their structure. Each egg has a centralized portion that demonstrates 6 tiny hooklets. This central portion is surrounded by a striated egg shell that surrounds the egg. Latex gloves should be worn when handling suspect feces, and strict observance of lab biosafety is essential. All materials related to the fecal flotation procedure should be autoclaved prior to disposal. Feces should be disposed of with similar caution.

ADVANCED OR CONFIRMATORY TESTING

- Diagnosis in definitive hosts is by coproantigen or DNA detection.
- Hydatid cysts at necropsy, with accompanying histopathologic examination

TREATMENT

TREATMENT OVERVIEW

Due to the zoonotic nature of this parasite, appropriate anthelminthic therapy treatment is critical for eliminating the adult cestode.

TREATMENT

- Adult stages of the parasite may be treated with praziquantel, 2.5-7.5 mg/kg PO or SQ once.
- Hydatids require surgical removal from humans who serve as intermediate hosts. The thick-walled unilocular cysts of *E. granulosus* are less difficult to remove, but the thin-walled multilocular cysts of *E. multilocularis* are quite invasive and almost

impossible to remove. The organs infected by the hydatid cyst will also affect the prognosis.
- Epsiprantel (Cestex): dogs, 5.5 mg/kg PO once; cats, 2.75 mg/kg PO once. Single doses eliminate *E. multilocularis* in over 99% of animals, but there may be residual worm burdens in some animals.

POSSIBLE COMPLICATIONS

Gastrointestinal adverse effects may be seen with antiparasitics.

RECOMMENDED MONITORING

Regular fecal flotation. Again, use caution when handling suspect feces.

PROGNOSIS AND OUTCOME

- Definitive hosts may have enteritis.
- Prognosis for intermediate hosts, including humans, depends on location of cysts.

PEARLS & CONSIDERATIONS

COMMENTS

Echinococcosis does not cause hydatid cyst disease in definitive hosts such as dogs and cats. Therefore, its interest in small-animal medicine mainly revolves around the risk of zoonosis.

PREVENTION

- Vaccine available for intermediate hosts (sheep and cattle)
- Hygiene, to avoid human acquisition of the infection through fecal-oral contamination from dogs and cats
- Avoid consumption of raw or undercooked meat or viscera by humans, dogs, or cats.

TECHNICIAN TIPS

Think safety—use extreme caution! Due to the extreme pathogenicity of this parasite, all suspect feces should be collected and properly disposed. One cannot simply throw this feces away refuse or wash it down the drain; it should be incinerated.

CLIENT EDUCATION

Eggs can infect humans by contamination via the fecal/oral route: poor hygiene, dog licking anus or perineum and in turn licking the human's face, thus transferring infective eggs to the human's mouth.

SUGGESTED READING

Eckert J, Thompson RC, Bucklar H, Bilger B, Deplazes P: Efficacy evaluation of epsipran-tel (Cestex) against *Echinococcus multilocu-laris* in dogs and cats. Berl Munc Tierarztl Wochenchr 114(3-4):121–126, 2001.

Jenkins DJ, Romig T: Milbemycin oxime in a new formulation, combined with praziquan-tel, does not reduce the efficacy of praziqu-antel against *E. multilocularis* in cats. J Helminthol 77(4):367–370, 2003.

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1ST EDITION AUTHOR: LISA M. TIEBER NIELSON

Frostbite

BASIC INFORMATION

DEFINITION

Tissue damage caused by exposure to cold agents or temperatures; effects may be reversible with rewarming, or may be irreversible due to necrosis

SYNONYM

Hypothermic injury

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Any animal exposed to cold environmental temperatures, especially if the body temperature falls <34°C (<93°F). Young animals outdoors, or those in poor body condition, are at greater risk.
- Affected tissues often include the tail, testicles, and pinnae.

GENETICS AND BREED PREDISPOSITION: Hairless or shorthaired breeds of dogs and cats are predisposed.

RISK FACTORS: Low ambient temperatures

GEOGRAPHY AND SEASONALITY: Winter months in temperate to cold climates

ASSOCIATED CONDITIONS & DISORDERS: Hypothermia

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- History of exposure to cold temperatures or agents.
- Lesions visible to the owner will depend on the time course since the cold injury occurred.
- Animals may be presented for evaluation of acute injury (e.g., hit by car) and white, waxy, frostbitten skin, or injury may not be noticed until later stages when tissue sloughing is occurring.

PHYSICAL EXAM FINDINGS

- Dependent on extent of exposed parts of the body:
  - Mild cold injury to the extremities may go undetected (toe tips, ear tips, tail tip).
  - Very extensive regional cold injury may be evident as a frozen limb or other severe cold injury.
- Acutely affected animals have pale areas of skin that are cool to the touch, with or without freezing of deeper tissues.
- Affected body parts may appear either numb or hyperesthetic, and cyanosis may be evident.
- As the affected area thaws, the tissue may become reddened and swollen:
  - Depending on the extent of affected tissue, the thawing process may be associated with signs of intense pain.
- Affected skin may blister.
- Days after the frostbite has occurred, the tissues may appear shrunken and discolored and may begin to slough if necrotic. Days to weeks after injury, alopecia and sloughing may occur.

ETIOLOGY AND PATHOPHYSIOLOGY

- Cold induces vasoconstriction to affected tissue, as well as endothelial damage and thrombosis.
- Freezing results in crystallization of extracellular fluid that results in a fluid shift from the cell to the extracellular space. The change in electrolyte concentration within the cell then leads to change in cellular proteins.
- Lack of nutrients as well as direct cellular damage results in local tissue damage.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is entirely based on history of exposure to cold and physical examination findings. Patients may be prone to frostbite if debilitated by preexisting disorders (various metabolic or other diseases), and diagnostic testing for these as indicated by history and physical exam is appropriate.

DIFFERENTIAL DIAGNOSIS

Burn injuries may appear similar

INITIAL DATABASE

- None required
- Routine laboratory evaluation if systemic illness
- Imaging and further evaluation as dictated by other disorders or injuries (e.g., if frostbite is caused by cold exposure after the patient was hit by a car)

TREATMENT

TREATMENT OVERVIEW

Prevent further damage to tissues from continued cold exposure or self-trauma and secondary infection by using aseptic technique in handling wounds. Allow damaged tissue to declare itself prior to extensive débridement or amputation.

ACUTE GENERAL TREATMENT

- Prevent further contact with source of cold.
- Ensure further contact with source of cold is prevented.
- Gently apply warm compresses to the area.
    - Do not rub or massage, which could cause further tissue damage.
- Immerse affected areas if possible in warm (102°F-104°F or 39°C-40°C) water.
    - Avoid warmer temperatures that may potentiate tissue injury.
- Dry affected areas: apply light non-compressive bandages if integrity of skin is not intact.
- Administer prophylactic antibiotics if appropriate (e.g., cefazolin, 22 mg/kg IV q 8 h).
- Débride infected wound or sloughing tissue

CHRONIC TREATMENT

- Prevent further exposure of the tissue to freezing, particularly during the healing process.
- Assess necrotic tissue conservatively.
    - Do not amputate or débride large areas early on in the healing process unless signs of infection or sepsis are present.
    - Necrotic tissue can act as a protective covering; often, when necrotic tissue is removed, deeper tissue is healing.
- Tissue damaged by frostbite will likely be more susceptible to cold injury in the future.

POSSIBLE COMPLICATIONS

- Tissue necrosis
- Infection

PROGNOSIS AND OUTCOME

- Variable depending on amount of tissue affected:
    - Extremities (ear tips, toes, tail tip) may slough or require amputation without affecting quality of life or longevity.
    - More substantial frostbite (e.g., limbs) carries a greater risk of systemic complications such as infection and therefore a more guarded prognosis.
- Hypothermia may complicate frostbite and alter the prognosis, depending on severity.

PEARLS & CONSIDERATIONS

PREVENTION

- Avoid exposure to very low ambient temperature.
- Bring animals indoors during periods of low ambient temperature.

TECHNICIAN TIPS

Wear gloves when handling frostbitten regions to reduce the risk of infecting the patient.

SUGGESTED READING

Swaim SF: Trauma to the skin and subcutaneous tissues of dogs and cats. Vet Clin North Am Small Anim Pract 10(3):599-618, 1980.

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EDITOR: ELIZABETH ROZANSKI

Fractures, Abnormal Healing

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

- Delayed union: bone healing that is slower than expected
- Nonunion: failure of a fracture to heal or a fracture in which the fractured ends have stopped healing
- Malunion: fracture healing causing abnormal bone/limb alignment or function

EPIDEMIOLOGY

SPECIES, AGE, SEX: Older patients may take longer to heal.

GENETICS & BREED PREDISPOSITION

- Increased incidence of avascular nonunion with radius and ulna fractures in toy breed dogs
- Feline tibial fractures may be at greater risk of nonunions than those in dogs.

CLINICAL PRESENTATION

HISTORY/CHIEF COMPLAINT

- Continued lameness after fracture stabilization
- Abnormal limb angulation
- Decreased muscle mass of the affected limb

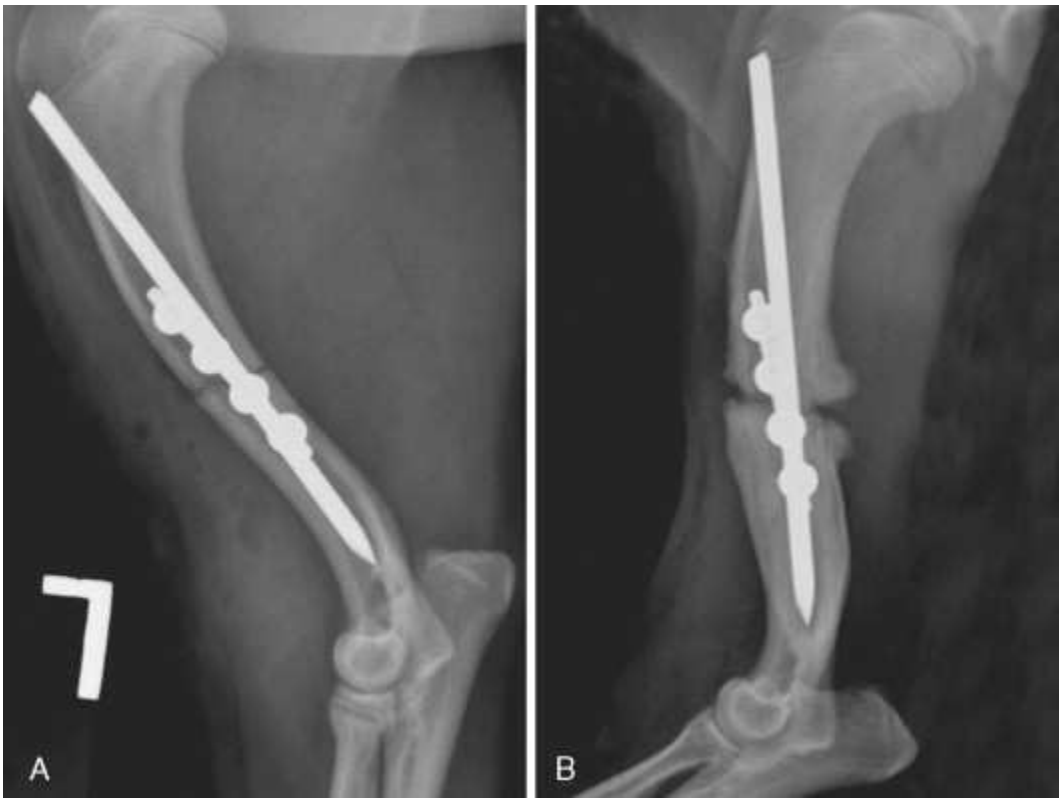
PHYSICAL EXAM FINDINGS

- Lameness
- Muscle atrophy
- Crepitus or obvious instability of the affected bone
- Palpably excessive callus formation in the face of physical instability
- Limited range of motion of the affected limb
- Discomfort on limb manipulation
    - Most animals with delayed union or nonunion experience only a moderate level of discomfort (worse with infection or sudden change in implant stability).
    - Draining tracts or warmth/evidence of inflammation over the fracture site possible with implant-associated osteomyelitis

ETIOLOGY AND PATHOPHYSIOLOGY

- Many factors affect fracture healing:
    - Fracture environment, patient's ability to heal, and veterinary decisions about case management
    - Other factors that can cause abnormal fracture healing:
        - Fracture site infection
        - Excessive fragmentation or bone loss results from open fractures where bone fragments are lost or from inappropriate surgical intervention when bone fragments are discarded or lost.
        - Inadequate fracture stabilization or immobilization
        - Poor vascular supply to the fracture site caused by the initial trauma, excessive or inappropriate surgical manipulation, or inappropriate selection of surgical implants
        - Inadequate fracture reduction and interposition of soft tissue in the fracture gap
        - Inappropriate or inadequate implant selection or application
- Fracture site stability is vital to decrease the risk of delayed union or fracture nonunion.
    - Motion at the fracture site increases interfragmentary strain, resulting in decreased healing.
- Other factors that may influence normal bone healing include:
    - Polytrauma
    - Metabolic diseases
- Lack of radiographic evidence supportive of bone healing (blurring of fracture lines, increased fracture gap opacity, callus

formation)
- Nuclear scintigraphy can be used to evaluate the fracture site for activity.



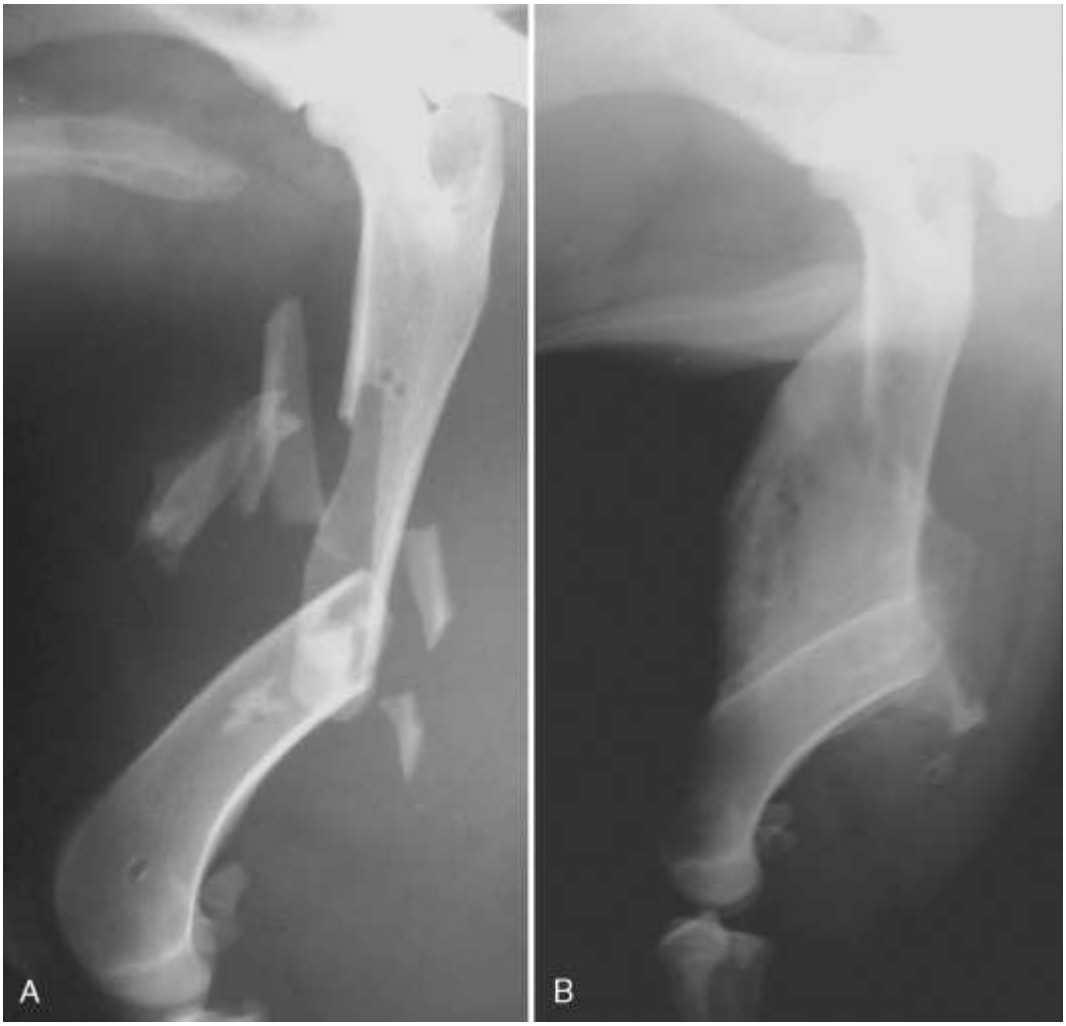
FRACTURES, ABNORMAL HEALING A,Midshaft humeral fracture following surgical stabilization. **B,** Same fracture at 8 weeks reexamination. The radiographic interpretation is a delayed union. There is a moderate amount of callus formation, a widening of the fracture gap, and increased intramedullary opacity. If the radiographic appearance is the same at 12-16 weeks, the diagnosis is changed to a nonunion.

(Courtesy Dr. John Hathcock, Auburn University.)

DIAGNOSIS

DIAGNOSTIC OVERVIEW

- Diagnosis of a delayed union or nonunion requires a complete history and is based on a quantitative judgment of radiographic evidence of healing.
- Clinical findings include decreased limb usage, sudden changes in limb usage, and increased bone pain.
  - Fracture stability is unaffected unless there is a failure of implants.
- Delayed unions and nonunions are normally identified during the routine follow-up examinations for fracture repair.
- Malunions may be present anytime.
  - Fracture malunion may involve animals that have changed owners, recently been adopted, or found as strays.
  - In some case, malunions may cause an idiopathic lameness.



FRACTURES, ABNORMAL HEALING A, Lateral radiograph of a comminuted femur fracture. **B,** Fracture healed as a malunion. Note lack of long-bone alignment and excessive callus formation. Opacity and smooth surface of fracture callus indicate a chronic malunion.

(Courtesy Dr. John Hathcock, Auburn University.)

DIFFERENTIAL DIAGNOSES

- Nonunions can be categorized as either viable or nonviable based on clinical signs and radiography of the fracture.
- Viable (active) nonunions are associated with nonbridging callus but still have potential to achieve bone union.
- With viable nonunions, the biological environment is generally adequate for fracture healing, and union is achieved by neutralization of uncontrolled fracture forces.
- Nonviable nonunions have minimal or no callus formation. There may be an increased fracture gap width or increased radiolucency at the fracture site.
- Nonviable nonunions are less common. It is more difficult to achieve clinical union in these patients.
- Some nonunions may form a pseudoarthrosis as the fracture ends stop trying to achieve osseous union and instead form a false joint between the fragments.
    - A pseudoarthrosis is caused by instability at the fracture site.
    - A true pseudoarthrosis may develop a true joint space and synovial cartilage within the space.
- Differential diagnoses for malunions include:
    - Congenital or breed-associated bone malformations
    - Abnormal growth patterns of bones due to soft-tissue abnormalities
    - Other osteoproliferative diseases or neoplasia should be considered when bone malformations are seen without history of previous fracture.

INITIAL DATABASE

Radiographs:

- Routine reexamination and radiographic evaluation is important to monitor all fracture healing.
- Radiographic interpretation indicates lack of progression or no bony healing over a period of months. This interpretation must be done with the understanding that animals of various ages will differ in healing time for clinical union.
    - Most young, skeletally immature animals demonstrate clinical union in less than 12 weeks. Older animals should have radiographic union by 4-6 months.
    - The time to union will also be influenced by the type of fracture fixation used to stabilize the fracture. Less rigid implants (e.g., intermedullary pins) normally have greater callus formation and are radiographically healed sooner than more rigid types of fixation (e.g., dynamic compression plate DCP).
- An appropriate radiographic schedule would be postoperative films 7-10 days to access fracture and implant stability, 30 days for progression, and 60 days to begin to evaluate for fracture union.
    - Good-quality, orthogonal views are essential to accurately evaluate the fracture.
    - Radiographic union may lag behind clinical union.
- Radiographs will contain evidence of malalignment of fracture fragments which may lead to malunion.

ADVANCED OR CONFIRMATORY TESTING

- Scintigraphy can be used to evaluate the fracture site for activity.
- Other advanced imaging techniques, such as CT or MRI, may aid in making the diagnosis and in monitoring healing.

TREATMENT

TREATMENT OVERVIEW

The goal of treatment for delayed union or nonunion is to achieve fracture union. This requires diagnosis and understanding of the reasons causing impaired fracture healing.

ACUTE AND CHRONIC TREATMENT

- Treatment for a *delayed union*is aimed at augmenting or continuing the original therapeutic plan rather than striking off in an entirely new direction.
    - The exception to this would be if the original plan was completely inadequate (e.g., external coaptation) for the fracture type.
    - If implant stability and blood supply to the fracture site are adequate (i.e., a delayed union), then patience and regular radiographic monitoring are warranted.
    - If the implants are stable but a poor biological environment exists, healing is promoted by bone grafting.
- Treatment for a *nonunion*requires the elimination of those factors that negatively affect healing and replacing Fractures, Abnormal Healing them with factors that would promote healing.
    - Goal is to alter the local fracture environment to promote healing of the fracture.
    - Identify the reason(s) for the nonunion:
        - Patient problems are uncommon as a cause for nonunion
            - Revision surgery
        - Correct implant problems:
            - Remove loose or broken plates, additional implants are needed for fracture stabilization
        - Improve fracture environment
            - Débridement of the fracture ends, removal of sequestra, addition of cancellous bone graft or other substances to promote bone healing (e.g., bone morphogenic protein, demineralized bone matrix)
            - Removal of excessive callus is not required but may allow for better plate contouring. Done with caution, since excessive débridement may further delay bone healing.
        - Atrophic nonunion will require resection of the fracture ends. This will shorten the limb length but should provide better fracture apposition and allow for compression across the fracture site. It will also expose adjacent medullary cavity to promote the in growth of vascular supply and mesenchymal cells.
- Important considerations for nonunions:
    - Bone grafting is critical for successful treatment of nonunions to fill in defects, promote osteogenesis, and hasten healing time.
    - Rigid fixation is essential
        - Stabilization with DCP plate is considered to be the fixation method of choice; plate/rod combination or interlocking nail may be alternative techniques.
        - Circular and linear fixators should be used by experienced surgeons for treatment of nonunions.
            - These can be used to promote distraction osteogenesis.
            - Open wound management may be required in patients that have traumatic injury or infected fracture sites.
    - Wound infections are treated based on culture and susceptibility testing.
    - Aggressive physical therapy is appropriate for the recovery period.

- Prognosis for eventually achieving fracture union is generally good, with exception of toy breeds.
- Many *malunions*don't require treatment. In cases where treatment is appropriate, practitioners should consider referral to an orthopedic specialist. Surgical restoration of malunions are complicated and difficult procedures.
- Use of corticosteroids may have a negative effect on bone healing.
- Cisplatin has been shown to effect bone healing, but these effects were not considered to be clinically relevant.

POSSIBLE COMPLICATIONS

- Intervention does have the potential to create further complication by continued selection of inappropriate implants, surgical destruction of a positive biological environment, surgical planning, or bacterial contamination of the fracture site.
- Complications (pain, donor-site infection, decreased limb use, donor-site fracture, inadvertent soft-tissue or neurologic damage, etc.) can rarely occur during bone graft harvesting.

RECOMMENDED MONITORING

- Postoperative care instructions require communication between the surgeon(s) and owner. There needs to be a clear understanding of expectations and follow-up requirements.
- All recommendations should be clearly written for owners.
- Additional fracture stabilization or increased restrictions on the animal's activity level may be required.

PROGNOSIS AND OUTCOME

- For delayed unions, the prognosis is generally good if the underlying conditions causing the delay in healing can be resolved.
- Nonunions have a more guarded prognosis for healing, especially in toy breeds.
- Malunions have a varied prognosis.
    - If the limb is functional but shortened, the animal will likely adapt to this by decreasing joint angles to compensate.
    - If the limb function is impaired, reconstructive procedures may be required to permit normal ambulation.
    - If joint angles are compromised by the malunion, the joint is prone to develop degenerative joint disease and osteoarthritis.

PEARLS & CONSIDERATIONS

COMMENTS

Delayed unions and nonunions are normally associated with poor decision making or technical failures on the part of the surgeon. Patient factors and owner compliance are less common as a reason for nonunions.

CLIENT EDUCATION

- Clients need to understand they are an important part of this process from the beginning.
- Owner compliance with postoperative instructions for exercise restriction, follow-up examinations, appropriate physical therapy, and consistent administration of all medications is critical to achieving a successful outcome.
- Owners of animals with a fracture malunion must understand restorative orthopedic procedures are not always effective, and complications can arise that affect bone healing or limb function.

SUGGESTED READING

Piermattei DL, Flo GL, DeCamp CE: Delayed union and nonunion. Handbook of small animal orthopedics and fracture repair, ed 4, St Louis, 2006, Elsevier.

AUTHOR: MICHAEL TILLSON, KATRIN SAILE

EDITOR: JOSEPH HARARI

Fractures of the Tibia and Fibula

BASIC INFORMATION

DEFINITION

Fractures of the tibia and fibula account for 20% of long-bone fractures and include avulsion of the tibial tuberosity, separation of the proximal or distal tibial physis, tibial shaft fractures, and fractures of the medial or lateral malleolus of the tibia.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Tuberosity avulsions and physeal fractures occur in immature animals.

RISK FACTORS

- Direct trauma
- Indirect trauma from muscle contraction (avulsion fractures)
- Torsional athletic injuries
- Bone tumors or metabolic bone disease

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Acute lameness, usually secondary to trauma

PHYSICAL EXAM FINDINGS

- Pain, swelling, and crepitus at the fracture site
- Stifle joint effusion with proximal physeal and tuberosity avulsion fractures
- Tarsocrural (hock) instability due to medial or lateral malleolar fractures

ETIOLOGY AND PATHOPHYSIOLOGY

- Because of sparse soft-tissue coverage, tibial fractures are often open.
- Most fibular fractures occur with tibial fractures and are not repaired unless stability of the stifle or hock is compromised.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

History and physical examination will identify most tibial and fibular fractures. Radiographs are used to confirm the diagnosis and determine the best method for repair.

DIFFERENTIAL DIAGNOSIS

- Osteochondrosis of the tibial tuberosity
- Primary or metastatic bone neoplasia
- Stifle or hock luxation

INITIAL DATABASE

- Craniocaudal and lateral radiographs, including both the stifle and hock
- Radiographs of the contralateral leg to help differentiate traumatic physeal separation from the normal appearance of an open physis (growth plate) in immature animals
- Stress radiography (general anesthesia) if a nondisplaced malleolar fracture or collateral ligament injury is suspected
- CBC, serum chemistry panel, and urinalysis based on patient stability and American Society of Anesthesiologists patient classification (see p. 1372).

TREATMENT

TREATMENT OVERVIEW

Fracture stabilization for rapid bone healing and early return to normal ambulation, without compromising bone growth

ACUTE GENERAL TREATMENT

- Nonsurgical treatment (if patient will tolerate splinting and exercise restriction; see p. 1336):
  - External coaptation (limb splinting) is used for minimally displaced, stable tibial physeal fractures. For adequate immobilization, the splint/cast must extend above the distal femur.
  - Minimally displaced tibial shaft fractures may be treated with external casting or splinting, especially if the fibula is intact and can act as an internal splint.
  - Incomplete or nondisplaced malleolar fractures usually heal with external splinting.
- Surgical treatment:
  - Tibial tuberosity avulsions are treated with a tension-band wire technique.
  - Displaced or unstable proximal tibial shaft or physeal fractures are treated with small cross pins, cancellous bone screws, or a small buttress plate.
  - Proximal fibular fractures are stabilized with a bone screw or tension-band band wire technique to preserve the insertion of the lateral collateral ligament.
  - For multiple or complex tibial shaft fractures, or for large and active dogs requiring more rigid support, treatments include intramedullary pinning, interlocking nails, bone plates, and external fixators.
  - In highly comminuted shaft fractures, rigid fixation (e.g., bone plating) is used for spanning the fracture site and providing spatial alignment of the fracture ends without disturbing their soft-tissue attachments (biological osteosynthesis). This preserves the vascular supply to the fracture bed and fosters new bone growth.
  - Displaced or unstable malleolar fractures require accurate fixation with a cancellous screw, two small cross pins, or a tension-band wire technique.

CHRONIC TREATMENT

- Casts and splints used in immature animals will require frequent monitoring and adjustment as the patient grows. They are removed once radiographic signs of healing are evident.
  - Usually 6-12 weeks depending on patient age
  - Younger patients heal more quickly.
  - Exercise restriction should be continued another 3-4 weeks.
- Bone plates are removed after bone union (5-12 months) in patients with discomfort or cold intolerance.
- Intramedullary pins are removed after healing to prevent later damage to the stifle articular cartilage.
- Implants used for stabilizing physeal fractures are removed after healing to avoid premature physeal closure.

POSSIBLE COMPLICATIONS

- Delayed union or nonunion
- Patellar luxation following poorly reduced tibial tuberosity avulsion fractures
- Degenerative joint disease (intraarticular fractures or implants)
- Osteomyelitis (open or highly comminuted fractures, or poor surgical asepsis)
- Growth disturbances causing limb shortening or angular limb deformity

RECOMMENDED MONITORING

Regular physical and radiographic examinations until clinical recovery (see p. 417)

PROGNOSIS AND OUTCOME

Physeal, simple shaft, and malleolar fractures in young, healthy patients heal by 1-3 months. Complex injuries in older patients heal more slowly, with increased risk of complications.

PEARLS & CONSIDERATIONS

COMMENTS

To avoid iatrogenic femoral condyle, cruciate ligament, or meniscal damage, nor-mograde intramedullary pinning of the tibia is preferred over retrograde pinning.

SUGGESTED READING

Piermattei DL, Flo GL, DeCamp CE: Fractures of the tibia and fibula. In Brinker, Piermat-tei, and Flo' s handbook of small animal orthopedics and fracture treatment, ed 4, Philadelphia, 2006, WB Saunders, pp 633–660.

Egger EL: Fractures of the tibia and fibula. In Birchard SJ, Sherding RG, editors: Saunders manual of small animal practice, ed 3, St Louis, 2006, Saunders Elsevier, pp 1144–1151.

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Fractures of the Spine/Luxations of the Spine

BASIC INFORMATION

DEFINITION

Well-recognized disorders primarily due to trauma and causing spinal instability, spinal cord damage, or spinal nerve damage

EPIDEMIOLOGY

SPECIES, AGE, SEX: Any dog or cat but most commonly younger animals

RISK FACTORS: Trauma; focal or diffuse bone demineralization due to vertebral column neoplasia (primary or secondary) infection, chronic phosphorus and calcium imbalances, osteoporosis, nutritional secondary hyperparathyroidism

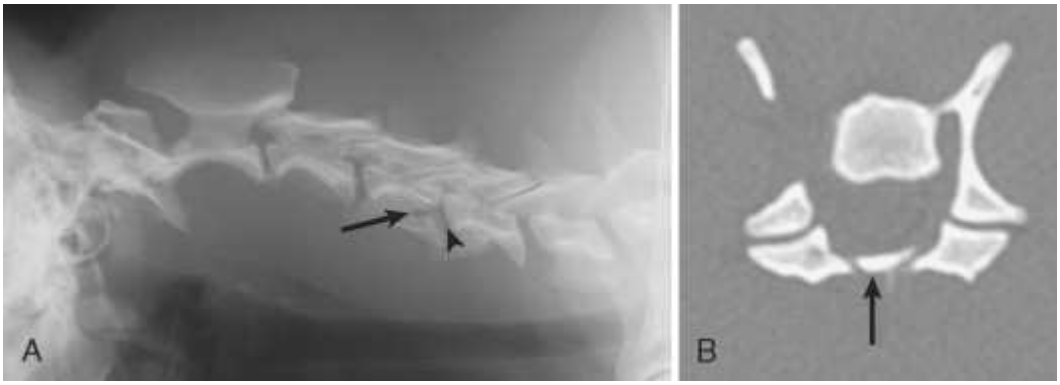
CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Trauma (most commonly vehicular trauma, less frequently falls, bite, and gunshot wounds)
- Spinal pain, swelling, or deformity
- Weakness or inability to stand/walk

PHYSICAL EXAM FINDINGS

- Signs of hypovolemic/hypotensive shock in acute trauma patients
- Guarding of neck, arched back, spinal hyperpathia and/or deformation
- Crepitus, excessive spinal movement in unstable fractures
- Neurologic deficits depend on localization and severity of lesion (proprioceptive, motor, or sensory deficits); monoparesis, paraparesis, or tetraparesis; upper motor neuron (UMN) or lower motor neuron (LMN) signs; loss of central recognition of pain; are-flexia; ipsilateral Horner's syndrome; enlarged UMN or LMN bladder.
- Spinal reflexes for fractures involving spinal cord segments:
  - C1-C5: UMN to the front and UMN to the hind limbs
  - C6-T2: LMN to the front and UMN to the hind limbs
  - T3-L3: Normoreflexia to the front and UMN to the hind limbs
  - L4-S3: Normoreflexia to the front and LMN to the hind limbs



FRACTURES OF THE SPINE/LUXATIONS OF THE SPINE Radiograph of canine cervical spine, lateral view **(A)** showing an oblique C4 vertebral body fracture through caudal endplate *(arrow),*with ventral displacement. Intervertebral disk space at C4-C5 is collapsed *(arrowhead).*CT of C4 vertebra, transverse view (**B**; dorsal is at the bottom of the image) showing a laminar fragment compressing the spinal cord *(arrow).* This lesion could not be detected with cervical radiographs.

ETIOLOGY AND PATHOPHYSIOLOGY

- Traumatic vertebral fractures result from forces causing spinal hyperextension, hyperflexion, compression, and/or rotation.
- Fractures occur most commonly at the craniocervical, cervicothoracic, thoracolumbar, and lumbosacral junctions.

- A decrease in spinal canal diameter may cause mechanical injury to nervous tissue.
- Secondary pathophysiologic events include ischemia, hemorrhage, alteration in blood flow to the spinal cord, and edema. These secondary effects are often more harmful than the initial mechanical injury.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is most commonly suspected based on the history of trauma associated with spinal hyperpathia and/or deformation and/or neurologic deficits associated with myelopathy; confirmation requires diagnostic imaging (spinal radiography, CT, and/or MRI).

DIFFERENTIAL DIAGNOSIS

Intervertebral disk disease, meningomyelitis, diskospondylitis, vertebral osteomyelitis, congenital malformations, spinal neoplasia

INITIAL DATABASE

- CBC, serum chemistry, urinalysis, thoracic and abdominal radiographs: generally unremarkable
- Spinal survey radiographs to detect discontinuity and fracture lines of vertebral column, malalignment of intervertebral space, and/or articular facets
- In cooperative patients, initial radiographs could be taken without sedation or anesthesia.

ADVANCED OR CONFIRMATORY TESTING

- Spinal radiographs of anesthetized, stable patients permit more accurate positioning and characterization of lesions (e.g., for surgical planning). Care must be taken to avoid iatrogenic exacerbation of injury when handling the anesthetized patient.
- CT or myelogram to exclude compression of spinal cord by herniated disk material or bone fragments
- MRI: superior for soft tissue (e.g., spinal cord)

TREATMENT

TREATMENT OVERVIEW

Initial treatment frequently requires stabilization of patients in shock. External coaptation may be needed for temporary and definitive fracture stabilization; pain management and physical rehabilitation are critical for recovery. Evaluation by a neurologic or orthopedic specialist is recommended.

ACUTE GENERAL TREATMENT

- Initial medical management:
  - Shock treatment in trauma patients
  - Tape thoracolumbar fracture patients to rigid board, and apply neck brace to patients with cervical fractures, to minimize further spinal cord damage. Sedate fractious or agitated patients.
  - Methylprednisolone sodium succinate: 30 mg/kg bodyweight once IV
  - Pain management with opiates or nonsteroidal antiinflammatory drugs
- Definitive treatment:
  - Decision of nonsurgical (strict confinement, neck or back brace, and pain management) versus surgical management (surgical spinal cord and nerve-root decompression, fracture reduction, and subsequent stabilization with implants) is based on initial neurologic status, serial reevaluations, spinal stability, and presence of concurrent injuries.
  - Unstable injuries result from lamina, pedicle, dorsal spinous process, and articular facet fractures and supra-spinous/interspinous ligament tears.
  - Stable injuries result from disk protrusion, ventral longitudinal ligament rupture, avulsion of ventral vertebral body.
- Nonsurgical management for patients with mild neurologic signs (pain, proprioceptive and motor deficits) and/or stable fractures that respond to medical management
- Surgery for patients with more severe neurologic signs (uncontrollable pain, minimal motor function, paresis or plegia), with unstable fractures or lesions not improving with medical management
  - Stabilization with internal implants: pins, wires, plates, or screws
  - Methylmethacrylate can be used for solidifying implants.
  - External fixators have been used less frequently.

CHRONIC TREATMENT

- Supportive care: appropriate bedding with traction for patients, bladder expressions in patients without bladder control
- Wheelchairs for patients with loss of hind limb function

NUTRITION/DIET

- Food and water needs to be placed near immobilized patients.
- Hand feeding in upright position for tetraplegic patients.

BEHAVIOR/EXERCISE

- Strict cage rest and short leash walks until radiographic evidence of healing
- Physical rehabilitation: assisted standing and walking, aquatherapy, gait and proprioceptive training

DRUG INTERACTIONS

Do not give steroidal and nonsteroidal antiinflammatory medications simultaneously.

POSSIBLE COMPLICATIONS

- Respiratory arrest due to cervical fractures
- Hemorrhage
- Neurologic deterioration
- Myelomalacia
- Infection
- Implant failure

RECOMMENDED MONITORING

- Serial neurologic evaluations
- Respiratory monitoring with cervical fractures and trauma patients

PROGNOSIS AND OUTCOME 

- Patients with pain sensation: good prognosis for functional recovery
- Patients with loss of pain sensation: fair to guarded prognosis
- Severed spinal cord or areflexia: grave prognosis
- Perioperative mortality for surgical stabilization of cervical vertebral fractures is up to 36%. Nonsurgical treatment often provides reasonable outcome.

PEARLS & CONSIDERATIONS 

COMMENTS

- Up to 20% of patients with traumatic spinal fractures have a second fracture.
- Radiographs may not reflect maximal spinal displacement. Therefore, neurologic evaluation is often more helpful than radiographic evaluation for prognosis.
- Radiographs have moderate sensitivity for spinal fractures and subluxations and low negative predictive values for canal narrowing or fragments within canal.

CLIENT EDUCATION

Care for paralyzed patients is laborious. It can take months until improvement is observed, and return to function cannot be guaranteed.

SUGGESTED READING

Bruce CW, Brisson BA, Gyselinck K: Spinal fracture and luxation in dogs and cats: a retrospective evaluation of 95 cases. Vet Comp

Orthop Traumatol 21:280–284, 2008.

Kube SA, Olby NJ: Managing acute spinal cord injuries. Compend Contin Educ Vet 30:496– 504, 2008.

Sturges BK, LeCouteur RA: Vertebral fractures and luxations. In Slatter D, editor: Textbook of small animal surgery. Philadelphia, 2003, Elsevier, pp 1244–1261.

AUTHOR: SUSANNE K. LAUER

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Fractures of the Scapula

BASIC INFORMATION

DEFINITION

Scapular fractures involve the spine, body, neck, or glenoid regions of the bone.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs and cats of either sex and any age

RISK FACTORS: Trauma to the proximal aspect of the forelimb

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Forelimb trauma secondary to motor vehicle/firearm accidents, falls, or fighting

PHYSICAL EXAM FINDINGS: Variable degree of lameness. Swelling, bruising, open wounds around scapula. Pain during palpation of shoulder joint.

ETIOLOGY AND PATHOPHYSIOLOGY

- Uncommon fractures representing 0.5%-2.5% of all fractures treated at referral hospitals
- Can be associated with regional injury to cervicothoracic spine, thoracic structures (pulmonary contusions, pneumothorax), and brachial plexus
- Extensive medial and lateral musculature provide soft-tissue support and extraosseous vascularity to fractured bone segments.
- Fractures are classified based on location: body, spine, neck, and glenoid *or*stable/unstable extraarticular versus intraarticular lesions.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Radiography is critical in establishing a diagnosis.

DIFFERENTIAL DIAGNOSIS

- Shoulder luxation
- Dorsal displacement of the scapula

INITIAL DATABASE

- Mediolateral and caudocranial radiographic projections of proximal aspect of limb
- CBC and serum chemistry panel based on American Society of Anesthesiologists patient classification (see p. 1372)
- Electrocardiogram and thoracic radiography

ADVANCED OR CONFIRMATORY TESTING

Distoproximal, axial radiographic projection with limb pulled caudally delineates occult lesions.

TREATMENT

TREATMENT OVERVIEW

Treatment goals are fracture stabilization for bone healing and maintenance of glenoid (joint) congruency.

ACUTE GENERAL TREATMENT

- Minimally displaced, nonarticular fractures can be stabilized for 1 month with external bandage support such as a Velpeau sling or spica splint (see p. 1336).
- Severely displaced, malaligned, nonarticular, or glenoid (joint) lesions require internal support with implants.
- Spine or body fractures are stabilized with orthopedic wire or bone plate/screws.
- Neck fractures are stabilized with small pins or bone plate/screws.
- Glenoid fractures require alignment of joint surface and are stabilized with screws or pins.
- Avulsions of the acromion process or supraglenoid tubercle require tension-band wiring to counteract distraction by the deltoideus and biceps muscles, respectively.

CHRONIC TREATMENT

- Bandage support for 4-6 weeks for comminuted lesions and tenuous fixations
- Controlled ambulation and passive flexion/extension exercises to maintain muscle tone and joint motion for 6 weeks until radiography confirms bone healing

POSSIBLE COMPLICATIONS

- Suprascapular nerve damage with neck fracture or surgical repair
- Malalignment of fractured bone segments
- Degenerative joint disease with glenoid fractures
- Infection
- Implant failure

RECOMMENDED MONITORING

- Lameness evaluation 1-3 months after injury and treatment
- Radiography at 6-10 weeks to evaluate fracture healing

PROGNOSIS AND OUTCOME

- Based on severity of injury
- Good to excellent for nonarticular lesions

PEARLS & CONSIDERATIONS

COMMENTS

- Scapular fractures can be missed if lameness is mild or ambulation is not evaluated at hospital admission (e.g., patient is carried in).
- Fractures are often identified during thoracic radiography of trauma patients.
- Suprascapular nerve damage is characterized by atrophy of supraspinatus and infraspinatus muscles.
- Scapular fractures tend to heal well because of abundant periosseous vascularity and cancellous bone supply distally.

SUGGESTED READING

Johnson AL: Scapular fractures. In Fossum TW, editor: Small animal surgery, ed 3, St Louis, 2007, Mosby, p 1029.

AUTHOR & EDITOR: JOSEPH HARARI

Fractures of the Radius and Ulna

BASIC INFORMATION

DEFINITION

Fractures of the radius involve the head, shaft, or medial styloid process; fractures of the ulna involve the olecranon, shaft, or lateral styloid process.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs and cats of either sex or any age

RISK FACTORS: Forelimb trauma

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Trauma from motor vehicle/firearm accidents, falls, and fights causing forelimb lameness

PHYSICAL EXAM FINDINGS: Variable degrees of lameness, soft-tissue swelling, bruising, and open wounds associated with an antebrachial injury

ETIOLOGY AND PATHOPHYSIOLOGY

- Nearly 20% of all fractures in dogs and cats involve the radius and ulna.
- The radius is the primary weight-bearing bone and is the most often stabilized; conversely, ulnar fractures can realign during repair of the radius and will heal in situ.
- The radius and ulna are a paired bone system connected by annular, collateral, and interosseous ligaments. Therefore growth-plate trauma and disturbed growth in either bone will cause a forelimb deformation (see Angular Limb Deformities, p. 78).
- Diminished vascularity in the distal aspect of the bones in small and toy breeds will cause impaired bone healing.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

In most cases, the diagnosis is grossly obvious on physical exam. Radiographs are confirmatory and help triage the fracture for optimal treatment.

DIFFERENTIAL DIAGNOSIS

- Elbow joint luxations
- Humeral condyle fractures
- Carpal luxations and fractures
- Radial nerve or brachial plexus injury

INITIAL DATABASE

- CBC, chemistry panel, electrocardiogram, thoracic radiography based on patient's American Society of Anesthesiologists patient classification (see p. 1372)
- Standard craniocaudal and mediolateral radiographic projections of forelimb

TREATMENT

TREATMENT OVERVIEW

- Initial external bandage and caudal splintage support are useful in reducing patient morbidity.
- Goals of treatment are:
    - Anatomic or functional realignment of fractures to maintain proximal and distal joint (elbow and carpus) congruency and parallelism
    - Tension-band stabilization (pins, wires, or bone plate/screws) of olecranon fractures to neutralize distraction by the triceps muscles
    - Tension-band pinning/wiring or screw fixation of styloid process fractures to provide collateral ligament support

ACUTE GENERAL TREATMENT

- First aid: external heavy bandage support to limit soft-tissue swelling, reduce bone fragment motion, provide limb support, and cover open wounds
- Lavage, débridement, and deep microbial culture and sensitivity assay of open, contaminated lesions
- Antibiotic (therapeutic or prophylactic), analgesic, and nonsteroidal antiinflammatory therapies as indicated
- Radial shaft fractures are stabilized with bone plate/screws applied cranially, or external skeletal fixation (ESF) with percutaneous pins applied mediolaterally (type 2) or angled craniocaudally (type 1b).
- Fresh autogenous cancellous graft tissue or commercially available allo-graft should be used for enhancing fracture healing (see p. 1212).
- Severely displaced ulnar fractures in large dogs can be stabilized with an intramedullary pin or bone plate/screws.
- Proximal ulnar fracture(s) with cranial displacement of the radial head (Monteggia fracture) requires reduction and stabilization of the bones with screws or small pins and suturing of the annular ligament.
- Casting of radius/ulnar fractures can only be recommended for minimally displaced, stable lesions in young, non–small-breed dogs.

CHRONIC TREATMENT

After surgical intervention: bandage support, sometimes with caudal splintage, and controlled exercise until radiographic and clinical evidence of bone union

POSSIBLE COMPLICATIONS

- Implant failure, stress protection (osteopenia), and cold conduction with the use of bone plate and screws for stabilization of radial fractures
- Pin tract sepsis and instability with ESF pins and frames
- Poor healing of distal radial and ulnar fractures in small, toy breeds
- Nonunion, delayed union, or malunion secondary to intramedullary (radial) pinning

RECOMMENDED MONITORING

Clinical and radiographic evaluations 4-6 and 10-12 weeks after surgery (see p. 417)

PROGNOSIS AND OUTCOME

- Bone plates/screws and ESF yield the most consistent clinical recoveries and return of limb functions.
- Casts are effective for minimally displaced fractures in young, healthy patients.
- Intramedullary pinning of the radius causes malunions and carpal joint damage and is rarely indicated.

PEARLS & CONSIDERATIONS

COMMENTS

- Irreparable proximal or distal lesions of the radius and ulna may require arthrodesis of the adjacent joint (elbow or carpus) to salvage the limb.
- ESF can be used in a minimally invasive or closed approach to preserve the soft tissues during a “biological” surgical approach.
- Patients with ESF require more intensive postoperative care than those treated with a bone plate/screws.
- Plate removal is infrequently required after bone union in dogs that are lame due to cold conduction or have radiographic evidence of osteopenia under the implant.
- Toy breed dogs with distal radial/ulnar fractures often have unsatisfactory healing without surgical intervention (i.e., plating).

SUGGESTED READING

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Larsen LJ, et al: Bone plate fixation of distal radius and ulna fractures in small and miniature breed dogs. J Am Anim Hosp Assoc 35:243, 1999.

Piermattei DL, Flo GL, DeCamp CE: Fractures of the radius and ulna. In Brinker, Piermat-tei, and Flo' s handbook of small animal orthopedics and fracture repair, ed 4, Philadelphia, 2006, WB Saunders, pp 359–381.

AUTHOR & EDITOR: JOSEPH HARARI

Fractures of the Pelvis

BASIC INFORMATION

DEFINITION

Pelvic fractures include ilial, ischial, pubic, and acetabular fractures; sacroiliac luxation and sacral fractures are also often included.

EPIDEMIOLOGY

SPECIES/AGE/SEX

Active, outdoor, sexually intact, roaming animals are most likely to be injured by motor vehicles. Dogs lying in driveways may be inadvertently run over.

RISK FACTORS

- Motor vehicle trauma and falling in juries (e.g., high-rise apartment buildings)
- Also can occur in racing dogs (greyhounds) as a spontaneous acetabular fracture

ASSOCIATED CONDITIONS & DISORDERS: Multisystemic polytrauma, especially urologic and neurologic

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Blunt force trauma in pets
- Racing injury (acetabular fracture) in greyhounds
- Occasional penetrating injuries (e.g., gunshot wounds)

HISTORY, CHIEF COMPLAINT: Severe hind limb trauma from motor vehicle accident or fall, inability to walk with one or both hind limbs pain

PHYSICAL EXAM FINDINGS

- Lameness in one or both pelvic limbs; possibly nonambulatory patient
- Palpable crepitus and/or pain on manipulation of leg(s)
- Palpable deformity of the pelvic canal during rectal examination
- Contusion (bruising) of skin overlying site(s) of injury

ETIOLOGY AND PATHOPHYSIOLOGY

- Very common sequela to blunt force trauma
- Normal boxlike pelvic structure accounts for frequency of injuries affecting two or more sites in the pelvis.
- Direct blows to the greater trochanter of the femur may cause an isolated impaction fracture of the adjacent acetabulum, with displacement of the femoral head through the medial acetabular wall into the pelvic canal.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is based on history and results of physical and radiographic examinations.

DIFFERENTIAL DIAGNOSIS

- Spinal fracture/luxation and spinal cord injury
- Long-bone fracture in pelvic limb

- Coxofemoral luxation(s)
- Concurrent orthopedic and soft-tissue injuries possible

INITIAL DATABASE

- Thoracic and abdominal radiographs; abdominal ultrasonography for visceral and abdominal wall injuries
- Neurologic examination
- CBC, serum biochemistry panel, and urinalysis (especially before sedation or anesthesia)
- Electrocardiogram to identify dysrhythmia due to traumatic myocarditis

ADVANCED OR CONFIRMATORY TESTING

- Multiple-view radiographs (lateral, oblique lateral(s), ventrodorsal) for assessment of the two hemipelves, sacroiliac joint, sacrum, tail, and distal lumbar spine. Narcotic sedation/general anesthesia usually required.
- CT to assess extent of injuries, identify sacral fractures, and for surgical planning (especially complex sacral fractures)
- Urinary tract imaging (e.g., contrast radiography) as needed to evaluate disrupted ureter(s), urinary bladder, or urethra

TREATMENT

TREATMENT OVERVIEW

- Elimination of pain
- Restoration of normal ambulation
- Restoration of pelvic canal diameter
- Prevention of secondary injuries to nerves from unstable or malunion of bone fragments

ACUTE GENERAL TREATMENT

- Analgesia compatible with other systemic injuries
- Ensure patent/functional urinary conduit.
- Surgery delayed until patient is adequately stabilized
- Injuries affecting the transmission of weight-bearing forces from the limb to the spine usually require surgery. These injuries involve acetabular, iliac, sacroiliac, and sacral disruptions.
    - Acetabular fractures are usually stabilized with plate/screws or pins/wires/screws, and methylmethacrylate bone cement.
    - Iliac fractures are usually stabilized with plate(s)/screws.
    - Sacroiliac and sacral body injuries are usually stabilized with screws/pins.
- External skeletal fixators sometimes employed for stabilization
- Patient size, degree of displacement, inherent stability, risk of secondary nerve injuries, and presence of other injuries help determine which injuries should be managed operatively versus conservatively (cage rest).

CHRONIC TREATMENT

- Confinement and sling support for 1-2 months, analgesics as needed
- Monitor for delayed signs of abdominal trauma (e.g., biliary disruption/leakage, delayed manifestations of lower urinary tract rupture) and cardiac complications (myocarditis/ventricular dysrhythmia).
- Protection of paw(s) if knuckling from sciatic neurapraxia

POSSIBLE COMPLICATIONS

- Malunions resulting in pelvic canal compromise, with secondary constipation/megacolon or dystocia
- Malunions or callus formation resulting in sciatic nerve impingement or entrapment, with neurapraxia
- Urethral damage or rupture
- Coxofemoral osteoarthritis (acetabular fractures)
- Persistent neuralogic deficits
- Persistent lameness or gait alteration
- Iatrogenic sciatic nerve injury during surgical manipulations
- Ventral abdominal hernia secondary to prepubic tendon avulsion or displaced pubic fracture

RECOMMENDED MONITORING

- Periodic radiographs to assess fracture healing
- Periodic clinical examinations including rectal palpation to assess improvement/resolution, function, and comfort
- Electromyography as needed in patients with peripheral nerve injuries/dysfunction

PROGNOSIS AND OUTCOME

- Increased risk for prolonged or persistent disability with fractures of the acetabulum or fractures associated with nerve injuries
- Improved prognosis for return to function when injuries that involve the sacrum, sacroiliac joint, ilium, or acetabulum are treated with anatomic reduction and rigid fixation of bone fragments.
- Intensive nursing care is involved for most patients and includes padded rest area, cleanliness following eliminations, pain management, nutrition, and physical therapy.

PEARLS & CONSIDERATIONS

COMMENTS

- Look for secondary injuries to the pelvic girdle (sacroiliac joints, sacral wings, and sacral body) with any diagnosis of pelvic fracture. Use oblique radiographic views to isolate the hemipelves. Always get at least two orthogonal radiographic views to avoid missing fractures where the bone ends overlap on one view.
- Acetabular fractures require accurate reconstruction of the articular surface to reduce the risk of osteoarthritis. Controversy exists as to whether fractures that involve only the caudal third of the acetabular articular surface require surgical treatment, but in general, all acetabular fractures would have a better prognosis with accurate anatomic reduction and stabilization.
- If acetabular repair cannot be achieved or if disabling osteoarthritis develops, a salvage surgery (hip replacement or femoral head/neck excision) usually is needed for a functional result.

PREVENTION

- Reduce free roaming by use of leashes, fences, neutering, and window screens to prevent falls from open windows.
- Counsel clients to always use precautions when backing up on driveways and in garages.

CLIENT EDUCATION

- Proper confinement/activity restriction during healing and recovery.
- Pets with acetabular fractures may require an acute or delayed salvage-type surgery (femoral head/neck resection).
- Acetabular fractures in particular might require revision surgery (hip replacement or excision arthroplasty) if the initial repair fails or disabling arthritis ensues.

SUGGESTED READING

Piermattei DL, Flo GL: Brinker, Piermattei and Flo's handbook of small animal orthopedics and fracture repair, ed 4, Philadelphia, 2007, WB Saunders, pp 395–421.

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Fractures of the Metacarpus and Metatarsus

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Metacarpal and metatarsal fractures account for 5% of long-bone fractures and may involve the proximal base, body, or distal head of the metacarpal or metatarsal bone.

SYNONYM

Fracture of the paw

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Young, athletic dogs are at increased risk.
- Male racing dogs have a greater incidence of injury (increased muscle mass and late growth plate closure).

RISK FACTORS

- Direct trauma
- Repetitive stress from racing (greyhounds) in a counterclockwise direction, causing fatigue fractures of the right medial and left lateral metacarpal bones. Poor training and nutritional deficiencies increase the risk and severity of these fractures.

ASSOCIATED CONDITIONS & DISORDERS: Carpal hyperextension (concurrent damage to the carpometacarpal ligaments). See also Shearing/Degloving Injuries, p. 1016.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Acute lameness
- Poor racing performance and subsequent lameness

PHYSICAL EXAM FINDINGS

- Pain, swelling, and crepitus of the affected foot
- Joint effusion, palpable dorsally, with intraarticular fractures
- Valgus (lateral) or varus (medial) displacement if the fracture involves the collateral ligament insertion on metacarpus (MC)/metatarsus (MT) II or V
- Luxation of the phalanx with distal condylar fractures

ETIOLOGY AND PATHOPHYSIOLOGY

- Proximal fractures usually involve MC II and IV in the front leg and MT III in the rear leg.
- The central metacarpals/metatarsals (MC/MT III and IV) are the major weight bearers, and these fractures cause significant lameness and loss of structural integrity.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Physical examination will usually identify most MC/MT fractures. Radiographs are used for better defining the extent of injury, to determine the best method of repair, and to monitor alignment post reduction.

DIFFERENTIAL DIAGNOSIS

- Joint luxation
- Sesamoid bone fracture
- Cellulitis, stress periostitis, or foreign body

INITIAL DATABASE

- Lateral and craniocaudal radiographs
- Stress radiographs of the carpus and digits, if an intraarticular fracture or collateral ligament damage is suspected
- CBC, serum biochemistry panel, and urinalysis based on the American Society of Anesthesiologists (see p. 1372) patient classification

ADVANCED OR CONFIRMATORY TESTING

Thermography, bone scintigraphy, or CT imaging for stress fractures or suspected lesions not identified with radiography

TREATMENT 

TREATMENT OVERVIEW

Fracture stabilization for bone healing and early return to normal ambulation and to minimize degenerative joint disease

ACUTE GENERAL TREATMENT

- A fitted cast or molded splint is recommended for:
  - Nondisplaced proximal fractures
  - Incomplete and acute stress fractures in greyhounds
  - Simple shaft fractures involving one or two bones, provided one of the central weight-bearing bones (III or IV) is intact
  - Minimally displaced multiple MC/MT fractures in cats and small dogs
- Surgical repair (internal fixation) is recommended for:
  - Displaced proximal fractures; lag screw or tension band wire fixation
  - Simple shaft fractures involving the weight bearing bones, especially in large breed or working dogs. Repair options include lag screw or cerclage wire, small intramedullary pins or K wires, or external fixators.
  - Comminuted, severely displaced, or nonunion shaft fractures are treated with a 1.5-to 2.5-mm bone plate.
  - Distal intraarticular fractures with instability of the metacarpophalangeal or metatarsophalangeal joint are treated with a lag screw or interfragmentary wire.

CHRONIC TREATMENT

Metacarpal and metatarsal fracture repairs are supported postoperatively with a molded splint or cast until radiographic signs of bone union.

- If a cast or splint is the primary method of fixation, it is removed after clinical union (6 weeks in young animals, longer in older patients).
- When used to supplement internal fixation, the splint may be removed in 3-4 weeks. Exercise is restricted for another 3-4 weeks.
- Bone plates and intramedullary pins penetrating the proximal or distal cortex should be removed after healing.
- Bone screws, wires, and toggled intramedullary pins may usually be left in place.

POSSIBLE COMPLICATIONS

- Healing may be delayed in unstable or highly comminuted fractures.
- Poor fracture alignment, inadequate fixation, and premature implant failure may result in a malunion or nonunion.
- Intraarticular fractures or incorrect pin placement can damage the articular cartilage and interfere with joint motion, resulting in degenerative joint disease and chronic lameness.

RECOMMENDED MONITORING

Regular (2-4 week intervals) physical and radiographic examinations until healing achieved

PROGNOSIS AND OUTCOME

- Good for simple fractures with adequate reduction and fixation
- Guarded for articular, highly displaced, or comminuted fractures

PEARLS & CONSIDERATIONS

COMMENTS

- External splints require diligent monitoring to prevent iatrogenic skin injury.
- Even with multiple MC/MT fractures, a good outcome is possible with external coaptation, provided adequate reduction and support is achieved.

SUGGESTED READING

Piermattei DL, Flo GL, DeCamp CE: Fractures of the carpus, metacarpus, and phalanges. In Brinker, Piermattei, and Flo's handbook of small animal orthopedics and fracture treatment, ed 4, Philadelphia, 2006, WB Saunders, pp 412–420.

AUTHOR: ELIZABETH J. LAING

EDITOR: JOSEPH HARARI

Fractures of the Mandible and Maxilla

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

- Mandibular fractures can involve either the horizontal body or vertical ramus of the mandible; separation of the mandibular symphysis also can occur. The *condyle*is the articular surface at the caudalmost aspect of the mandible has a condylar process that articulates with the mandibular fossa of the temporal bone in the temporomandibular joint.
- Maxillary fractures can involve the incisive, nasal, frontal, maxillary, palatine, zygomatic, or temporal bones.

SYNONYM(S)

Jaw fractures, maxillofacial fractures

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Traumatic jaw fractures are more likely to occur in younger animals; pathologic jaw fractures are more likely in older animals.
- Mandibular fractures are more common than maxillary fractures.
- In dogs, areas near the mandibular canine and caudal cheek teeth are often involved.
- In cats, the region of the mandibular symphysis and the condylar process are often involved.

GENETICS & BREED PREDISPOSITION: Mandibular fractures in dogs occur more often in smaller breeds.

RISK FACTORS

- Traumatic fracture: vehicular trauma, bites, kicks, hits, high-rise falls, gunshots, and secondary to tooth extraction
- Pathologic fracture: advanced periodontitis, neoplasia, metabolic disease

ASSOCIATED CONDITIONS & DISORDERS: Tooth fractures (see p. 1102), tooth displacement injuries (see p. 1000), temporomandibular joint luxation (see p. 1078), high-rise syndrome, craniofacial (see p. 529) and soft-tissue injuries to structures of the head

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Head trauma (e.g., hit by car)
- Malocclusion
- Recent dental procedure
- Oral/nasal bleeding
- Dropped lower jaw

PHYSICAL EXAM FINDINGS: Malocclusion, inability to close or open the mouth, swelling, bruising of face/oral cavity, tongue extrusion, nasal bleeding, stertor, dysphagia, oral bleeding, blood-tinged saliva, drooling, crepitus, palpable or visible fracture lines

ETIOLOGY AND PATHOPHYSIOLOGY

- Symphyseal separation/perisymphyseal fracture: most common mandibular injury in cats
- The most common sites for mandibular fracture in dogs are the areas near the last premolar (fourth premolar) and first and second molars, followed by the area just caudal to the canine tooth.
- Concurrent injuries to the head, thorax, or both are common and may require urgent treatment and delay surgical repair of maxillary/mandibular fractures.
- Surgical repair should avoid damage to mandibular canal, which contains the inferior alveolar nerve, artery and vein.
- In small dogs, tooth roots often reach into the ventral mandibular cortex and leave little bone farther ventrally.
- Favorable versus unfavorable mandibular fractures:
    - Favorable mandibular fracture: oblique fracture line running in a rostroventral direction; relatively stable (muscle

forces hold fracture segments in apposition)
- Unfavorable mandibular fracture: oblique fracture line running in a caudoventral direction; unstable (muscle forces lead to displacement of fracture segments)

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on history and physical examination; the fracture may be grossly apparent or may be subtle. Radiography under general anesthesia is often confirmatory and is indicated in all cases to determine optimal treatment. Note that nutritional support will be important if the patient cannot prehend and swallow food, and esophagostomy tube placement may be performed under general anesthesia prior to or immediately after jaw fracture management.

DIFFERENTIAL DIAGNOSIS

- Trigeminal neuritis/neuropathy (cranial nerve V)
- Temporomandibular joint luxation
- Open-mouth jaw locking
- Primary dental/periodontal disease
- Neoplasia

INITIAL DATABASE

- CBC/serum chemistry panel: generally unremarkable
- Head radiographs of stable, sedated patient can provide limited information.
- Open-mouth, oblique, lateral and ventrodorsal views, and intraoral dental radiographs are preferred, and general anesthesia is usually necessary (see p. 1246).
- Thoracic/abdominal radiographs to delineate other traumatic lesions
- Cranial nerve exam

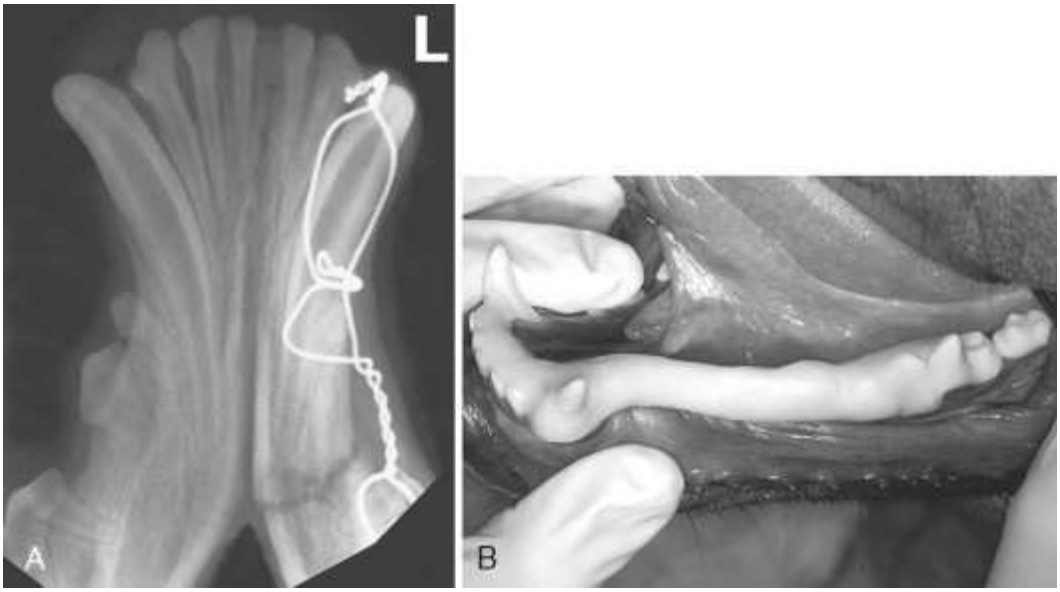
ADVANCED OR CONFIRMATORY TESTING

CT provides high resolution for maxillary and caudal mandibular fractures (however, a proper diagnosis can be obtained without CT in most cases).

TREATMENT

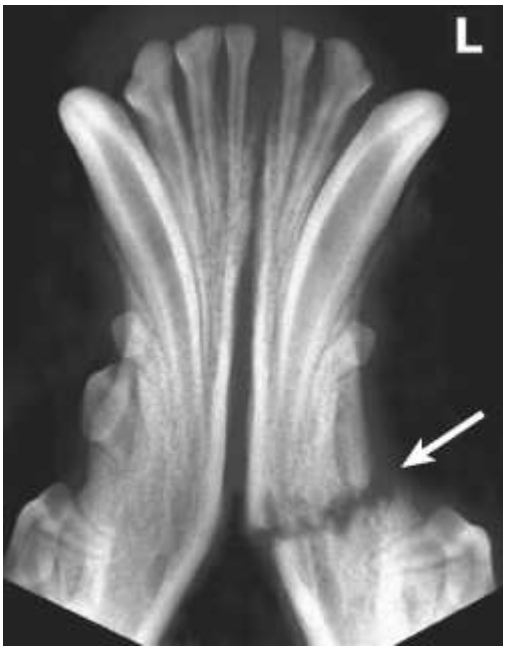
TREATMENT OVERVIEW

Acutely, all patients should receive adequate analgesia (systemic and/or local). Immediate fracture stabilization may be achieved with application of a custom-made muzzle. Long-term goals are to restore dental occlusion and restore oral functions.



FRACTURES, MANDIBLE AND MAXILLA An 8-month-old dog presented for evaluation and treatment of a left mandibular fracture between first premolar and third premolar *(arrow).*Second premolar is missing. Radiograph is arranged in labial mounting; rostral is toward top of image, and patient's left is on right of image.

(Copyright Dr. Alexander M. Reiter.)



FRACTURES, MANDIBLE AND MAXILLA A, Intraoperative radiograph of same patient. Fracture was first reduced with interdental wiring. **B,** Open-mouth view of same patient; rostral is to left. An intraoral splint was then fabricated covering the wire and tooth crowns.

(Copyright Dr. Alexander M. Reiter.)

ACUTE GENERAL TREATMENT

- Teeth may need to be removed to allow occlusion or closure of soft-tissue defects.
- Mandible:
  - Body:
    - Muzzling in stable or minimally displaced fracture. Muzzle should be flexible (nylon or white cotton hospital-type tape) and be sufficiently snug to immobilize fracture while still allowing the patient to drink water and lick liquid food. Favorable mandibular fractures in animals <6-8 months old often do not require treatment other than suturing of torn soft tissues and placing a tape muzzle for 2-3 weeks.
    - Interdental wiring and intraoral composite splint (preferred noninvasive technique of jaw fracture repair)

        - Intraosseous/interfragmentary wiring
        - Circumferential wire for symphyseal separation/perisymphyseal fracture
        - Percutaneous external fixation
        - Bone plating
    - Ramus:
        - Fractures rarely require any particular treatment beyond muzzling (snug tape muzzle through which the patient can still eat/drink). The muscle forces (temporal, masseter, and medial/lateral pterygoid muscles) hold the fracture segments in apposition.
        - If the mandible is displaced, resulting in malocclusion, treatment is required; noninvasive techniques first (maxillomandibular fixation, e.g., composite bridge between maxillary and mandibular canine teeth) before placing intraosseous wiring or bone plates.
        - Condylar process fractures may require condylectomy if there is progressive difficulty in opening the mouth (temporomandibular joint ankylosis).
- Maxilla:
    - Interdental wiring and intraoral composite splint, intraosseous wiring, bone plating
    - Midline palatal separation: primary (surgical) soft tissue closure if no tension; interquadrant wiring with or without composite splint if severe distraction
- Adjunctive treatment: broad-spectrum antibiotic therapy (e.g., amoxicillinclavulanate, 13.75 mg/kg PO q 12 h) for 1-2 weeks with open/contaminated fractures

CHRONIC TREATMENT

- Teeth causing mild malocclusion can be surgically reduced (without pulp exposure) or extracted.
- Tape muzzles are removed in 2-6 weeks, composite bridges in 5-8 weeks.
- Partial mandibulectomy possible for chronic nonunions
- Oronasal fistulas (see p. 795) may need secondary or delayed closure.
- Adjunctive treatment: oral instillation of dilute (0.12%) chlorhexidine solution or gel for 2-4 weeks; brushing of teeth and intraoral splints

NUTRITION/DIET

Nutritional support during healing. Blenderize food into liquid slurry, or place esophagostomy tube (see p. 1267) while patient is under general anesthesia.

POSSIBLE COMPLICATIONS

- Malocclusion
- Damage to dental structures
- Soft-tissue infection
- Osteomyelitis/sequestrum
- Implant failure
- Tongue and other soft-tissue trauma from exposed wires or plates
- Delayed union, nonunion
- Oronasal fistula
- Temporomandibular joint ankylosis
- Local pyoderma due to muzzle (transient)
- Malnutrition (very uncommon)

RECOMMENDED MONITORING

- Body weight (monitor adequate nutrition)
- Recheck at postoperative 2 weeks; remove skin sutures.
- Radiographs at 5-8 weeks and 6 months to evaluate bone healing
- Interdental wires, intraoral splints, and external fixators are removed after fracture healing (5-8 weeks). Bone implants may be left in place if soft-tissue damage and osseous abnormalities are absent.
- Teeth in fracture lines require radiographic monitoring in 6-12 months to determine pulp vitality.

PROGNOSIS AND OUTCOME

- Good to excellent if proper occlusion is established
- Fractures with tooth loss and severe periodontitis may heal slowly and by fibrous union only.

PEARLS & CONSIDERATIONS

COMMENTS

- Teeth in the fracture line should be preserved whenever possible, as they contribute to stability and alignment; should be removed if severely loose, fractured, or diseased.
- Administration of inhaled anesthetics via a pharyngostomy or temporary tracheostomy will aid with proper bone/teeth alignment during surgery.
- An esophagostomy feeding tube will reduce stress on repair(s), aid healing, and provide nutrition.
- Plates must have exact bone contour, or malocclusion will result.
- Minimally displaced maxillary fractures and fractures of the mandibular ramus may not require surgery beyond soft tissue closure.
- The mandible is a curved and small bone, containing neurovascular structures in its mandibular canal. Thus, intramedullary pinning is inappropriate, as it does not provide rotational stability and causes damage to nerves and vessels that supply teeth and lips.

TECHNICIAN TIPS

- Technicians should learn how to fabricate tape muzzles in cats and dogs and be able to give instructions to pet owners on the appropriate management of the patient at home.
- Patients with tape muzzles or composite bridges between maxillary and mandibular canine teeth may have compromised thermoregulation and should not be outdoors on warm or hot days. Restriction in mouth opening also bears the risk of aspiration in the regurgitating or vomiting patient.
- Tape muzzles may be removed during drinking and eating and put back in place once feeding is completed to reduce the possibility of local pyoderma from a soiled muzzle.

SUGGESTED READING

Kern DA, et al: Evaluation of three fixation techniques for repair of mandibular fractures in dogs. J Am Vet Med Assoc 206:1883, 1995.

Legendre L: Maxillofacial fracture repairs. Vet Clin North Am Small Anim Pract 35:985, 2005.

AUTHOR & EDITOR: ALEXANDER M. REITER

Fractures of the Humerus

BASIC INFORMATION

DEFINITION

Humeral fractures commonly involve the proximal physis, greater tubercle, metaphysis, diaphysis, supracondylar region, or condyle.

EPIDEMIOLOGY

GENETICS & BREED PREDISPOSITION: Spaniel breeds have a higher incidence of condylar fractures, possibly related to a reduced intraosseous blood supply.

RISK FACTORS

- Forelimb trauma from gunshot injuries, falls, or motor vehicle accidents
- Focal bone lesions (e.g., osteosarcoma or other bone neoplasm) or diffuse bone disease (e.g., nutritional, metabolic, or inherited) in cases of pathologic fractures

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Severe trauma to the forelimb

PHYSICAL EXAM FINDINGS: Non–weight-bearing lameness with swelling, pain, instability of the humerus

ETIOLOGY AND PATHOPHYSIOLOGY

- Thoracic wall, cardiopulmonary, and brachial plexus injuries may be present.
- Most fractures involve the middle-or distal-third segments.
- Condylar fractures involve the lateral portion more frequently than the medial; can be due to incomplete ossification in young dogs.
- Humeral fractures not caused by severe trauma may be pathologic fractures; these fractures are difficult to treat and may heal very slowly or not at all.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis of humeral fracture is suspected with acute non–weight-bearing lameness in a forelimb and confirmed with radiographs.

DIFFERENTIAL DIAGNOSIS

- Brachial plexus injury
- Pathologic fractures secondary to neoplasia
- Elbow or shoulder luxation
- Cervical spinal cord disease (disk herniation, tumor, etc.)

INITIAL DATABASE

- CBC and chemistry panel based on American Society of Anesthesiologists patient classification (see p. 1372)
- Mediolateral and craniocaudal radiographs of the bone
- Electrocardiogram and thoracic radiography to evaluate for myocarditis or pneumothorax secondary to trauma
- Establish presence of deep pain perception and voluntary motor function in the limb to determine normal nerve function.

ADVANCED OR CONFIRMATORY TESTING

CT scan or MRI can be used to evaluate bone if pathologic fracture secondary to neoplasia is suspected.

TREATMENT

TREATMENT OVERVIEW

Treatment of humeral fractures commonly requires fracture stabilization to restore limb function and joint congruency (when involving the joint). If the fracture is displaced or comminuted, external coaptation is often unsuccessful, and referral to a surgeon would be warranted.

ACUTE GENERAL TREATMENT

- In young animals, minimally displaced fractures that do not involve a joint space may be treated with external coaptation such as a spica splint. The splint should remain on the leg until there is radiographic evidence of fracture healing.
- Most humeral fractures require surgical treatment with open reduction and internal/external fixations:
  - Physeal and metaphyseal fractures require stabilization with divergent pins.
  - Fractures of the greater tubercle require tension-band wiring.
  - Diaphyseal fractures require stabilization with a plate/screws, plate/rod, interlocking nail, or external fixation.
  - Supracondylar fractures require stabilization with cross-pinning, plate/screws, or plate/rod fixation.
  - Condylar fractures require stabilization with a lag screw and an antirotational Kirschner wire or small pin.

CHRONIC TREATMENT

- A carpal flexion bandage may be placed to prevent weight bearing for the first 2-3 weeks (see p. 1336).
- A spica bandage can also be used for limiting postoperative forelimb motion.
- Exercise restriction until radiographs confirm good fracture healing
- Elbow range-of-motion exercises multiple times daily maintain joint mobility.

POSSIBLE COMPLICATIONS

- Iatrogenic damage to the radial nerve with mid-diaphyseal fracture repair
- Degenerative joint disease with condylar fractures
- Infection
- Implant failure

RECOMMENDED MONITORING

- Suture removal and examination at 2 postoperative weeks
- Physical and radiographic examinations at 4-6 and 8-10 postoperative weeks to evaluate limb functions and bone healing (see p. 417)

PROGNOSIS AND OUTCOME

- Good to excellent with proper bone realignment, joint congruency, healing, and rehabilitation, along with minimal trauma occurring to soft-tissue structures (nerves, vessels, muscles)
- Guarded to poor with pathologic humeral fractures; healing is delayed or clinically nonexistent, pain often persists, and surgical repair is difficult or contraindicated (leading to amputation or euthanasia).

PEARLS & CONSIDERATIONS

COMMENTS

- Because cardiopulmonary injury may be present, patients should be stabilized before surgery/anesthesia.
- An osteotomy of the olecranon will improve visualization/reduction of a supracondylar or bicondylar fracture.
- Condylar fractures are difficult to identify on a single (lateral) radiographic projection.
- A disproportionately mild degree of trauma as a cause for humeral fracture should prompt the suspicion of a pathologic fracture and underlying bone disease.

SUGGESTED READING

Piermattei DL, Flo GL, DeCamp CL: Fractures of the humerus. In Brinker, Piermattei, and Flo&#65533;s handbook of small animal orthopedics and fracture repair, ed 4, Philadelphia, 2006, WB Saunders, pp 297–324.

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EDITOR: JOSEPH HARARI

Fractures of the Femur

BASIC INFORMATION

DEFINITION

Fractures of the femur may be classified as proximal (physis, femoral head or neck, trochanter), midshaft (diaphyseal), or distal (supracondylar, condylar).

SYNONYM

Capital (head) physeal fracture: “slipped” capital epiphysis or physis

EPIDEMIOLOGY

RISK FACTORS: Trauma to the caudal trunk or hind limbs

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Trauma to the caudal trunk/limb:
  - Motor vehicle accident
  - High-velocity impact
  - Falls
- Femoral capital physeal fractures in cats may occur without a history of trauma.

PHYSICAL EXAM FINDINGS

- Lameness
- Swelling, bruising, or shortening of limb
- Crepitation/pain at hip/stifle joint
- Loss of sensation to medial (femoral nerve) or lateral (sciatic nerve) digits due to regional soft-tissue swelling, bruising, and transient peripheral nerve dysfunction

ETIOLOGY AND PATHOPHYSIOLOGY

- Most common (45%) long-bone fracture
- Concurrent injuries to abdominal wall or organs, pelvis, and lumbar spine are common.
- Capital physeal fracture (immature animals) disrupts ascending vessels and compromises healing.
- Extensive hemorrhage with midshaft fractures contributes to shock.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on a history of trauma (most dogs, many cats) and typically severe to non–weight-bearing hindlimb lameness, proximal limb pain, soft-tissue swelling, and discoloration. Plain radiography is confirmatory.

DIFFERENTIAL DIAGNOSIS

- Coxofemoral luxation*
- Acetabular/pelvic fracture*
- Bone neoplasia and pathologic fracture*
- Spinal trauma: bilateral hindlimb paresis/paralysis, abnormal reflexes

INITIAL DATABASE

- Craniocaudal and lateral radiographs of affected hind limb and pelvis ± lumbar spine
- Abdominal and thoracic radiographs if whole-body trauma
- CBC/serum biochemistry panel dictated by systemic signs and patient stability
- Evaluation of medial/lateral sensations of digits
- Comprehensive neurologic exam to evaluate for spinal trauma

ADVANCED OR CONFIRMATORY TESTING

Biopsy if pathologic fracture suspected radiographically

TREATMENT

TREATMENT OVERVIEW

The goals of therapy are restoration of limb function and alignment, as well as reconstruction of damaged articular surface.

ACUTE GENERAL TREATMENT

- External coaptation (casts, splints, etc.) is usually ineffective and carries a high likelihood of inducing complications.
- Fractures involving the joint space require accurate joint reconstruction.
- Midshaft fractures are stabilized with bone plate/screws, external fixator, interlocking nail, intramedullary pins/cerclage, or plate/rod.
- Condylar fractures are repaired with lag screws, pins.
- Trochanteric fractures are repaired with pin and tension-band wiring or lag screws to counteract pull of gluteal muscles.
- Femoral neck fractures are repaired with multiple small pins, lag screw(s).
- Femoral head/neck ostectomy can be performed for neck and capital physeal fractures in cats and small dogs.

CHRONIC TREATMENT

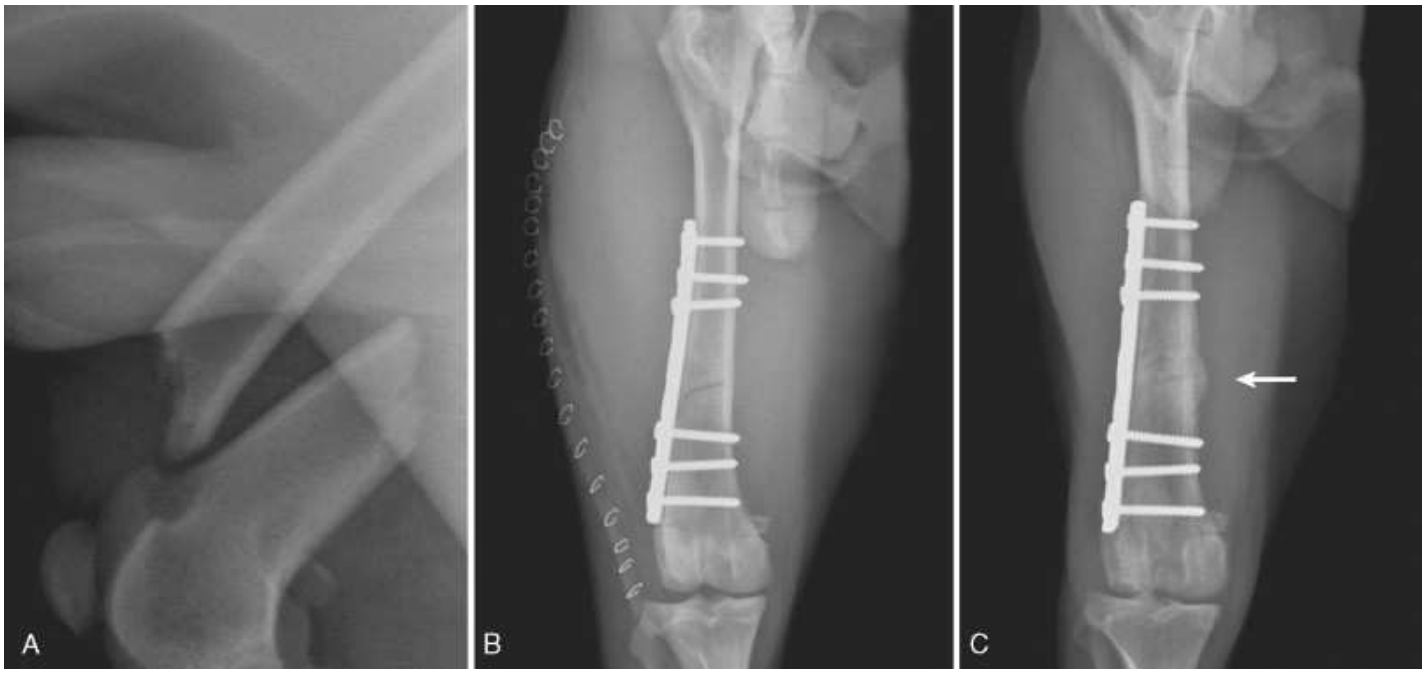
- Restricted activity until radiographs at 4-6 weeks to assess healing
- Radiograph early for suspected complications based on clinical signs of recurrent lameness, fever, limb swelling, peri-incisional draining tracts
- Femoral head/neck resection for failed proximal repairs

POSSIBLE COMPLICATIONS

- Malunion, nonunion (inadequate fixation)
- Degenerative joint disease (articular fractures)
- Sciatic nerve damage (retrograde intramedullary pin placement)
- Decreased hip motion with femoral head ostectomy
- Implant failure
- Infection
- Quadriceps contracture and inability to flex the stifle (young dogs with midshaft and distal femoral fractures)
- Limb shortening

RECOMMENDED MONITORING

- Lameness evaluation every 4 weeks for 2-3 months; expect gradual gait improvement.
- Evaluate patients with distal fractures 2 weeks after surgery to assess stifle mobility and avoidance of restrictive fibrosis.
- Radiographs every 4-6 weeks to evaluate fracture healing (1-3 months based on patient age) and implant stability; initiate physical rehabilitation and controlled activity based on normal imaging findings.



FRACTURES, FEMUR A, Lateral view of transverse, distal-third femoral fracture in an 18-month-old male Boxer weighing 45 lbs. **B,** Postoperative ventrodorsal radiograph of femoral fracture stabilized by a bone plate and screws applied to lateral aspect of bone. **C,** One-month follow-up radiograph

illustrating endosteal healing of fracture, along with a periosteal callus *(arrow)* on medial aspect of bone.

PROGNOSIS AND OUTCOME

- Based on severity of injury and presence or absence of complications (nerve damage, infection, etc.)
- Associated neuropraxia (temporary nerve damage): may need 2-12 weeks to assess for functional recovery
- Good to excellent for nonarticular lesions treated with appropriate surgical intervention
- Quadriceps contracture/tiedown requires physical therapy or surgical intervention.

PEARLS & CONSIDERATIONS

COMMENTS

- Additional orthopedic injuries of the same or other limbs are common.
- Initial proprioceptive deficits of the affected limb can be due to pain, shock, and fracture edema, and not a spinal injury.

SUGGESTED READING

Shires P: Fractures of the femur. In Birchard S, Sherding R, editors: Saunders manual of small animal practice, ed 3, St Louis, 2006, Saunders Elsevier, pp 1123–1131.

Simpson DJ, Lewis DD: Fractures of the femur. In Slatter D, editor: Textbook of small animal surgery, ed 3, Philadelphia, 2003, WB Saunders, pp 2059–2086.

AUTHOR: MARY E. SOMERVILLE

EDITOR: JOSEPH HARARI

Legend:- *Radiography will elucidate the lesion.

Fracture Disease

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Fracture disease includes muscle contracture, implant failure, inadequate bone union, and joint disease. These result in abnormal limb function.

SYNONYM

Fracture complications

EPIDEMIOLOGY

SPECIES, AGE, SEX: Muscle contracture is most common in young dogs with distal femoral or humeral fractures.

RISK FACTORS

- Limb trauma
- Poor surgical technique

ASSOCIATED CONDITIONS & DISORDERS: Trauma to other body systems

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Quadriceps contracture, joint ankylosis

FRACTURE DISEASE A 1-year-old, mixed-breed dog with quadriceps contracture after distal femoral fracture repair and no physical therapy to retain stifle joint range of motion. Note hyperextension of limb.

HISTORY, CHIEF COMPLAINT: Lack of normal limb function after fracture repair

PHYSICAL EXAM FINDINGS: Lameness, disuse atrophy of skeletal muscle, decreased range of motion of affected joint(s), draining tracts, nonhealing surgery site, fibrosis of major muscle groups.

ETIOLOGY AND PATHOPHYSIOLOGY

- Severe soft-tissue damage from injury/surgery and subsequent fibrosis
- Incongruent articular cartilage after joint fracture repair

- Inadequate postoperative rehabilitation to enhance limb function
- Nerve injury preventing use of limb
- Inappropriate use of implants during repair
- Excessive or unrestricted patient activity after surgery

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is made when a patient has poor return to function after sustaining a fracture. Radiographs and ancillary tests are useful for defining the extent of the disorder.

DIFFERENTIAL DIAGNOSIS

- Bone neoplasia
- Joint luxation
- Osteomyelitis
- Joint infection

INITIAL DATABASE

- Orthopedic and neurologic exams to evaluate limb function
- Orthogonal view radiography of affected bone(s)
- CBC, chemistry panel, urinanalysis, electrocardiogram based on patient American Society of Anesthesiologists classification (see p. 1372)

ADVANCED OR CONFIRMATORY TESTING

- Muscle biopsy (see p. 1305)
- Electromyography (see online chapter: Electromyography and Nerve Conduction Velocity)
- Nerve conduction studies (see online chapter: Electromyography and Nerve Conduction Velocity)

TREATMENT

TREATMENT OVERVIEW

Restoration of limb function(s)

ACUTE GENERAL TREATMENT

- Accurate joint reconstruction
- Adequate alignment and stable fixation of long-bone fracture(s)
- Gentle, aseptic surgical technique; avoidance of excessive soft-tissue dissection
- Initiation of physical therapy immediately after fracture repair
- Use of analgesics to alleviate patient discomfort and enhance movement

CHRONIC TREATMENT

- Replacement of failed implants and restabilization of fracture(s)
- Resection of scar tissue to regain joint range of motion
- Intensive postoperative rehabilitation (see p. 1329)

POSSIBLE COMPLICATIONS

Limb dysfunction: muscle atrophy, tissue fibrosis, degenerative joint disease

RECOMMENDED MONITORING

- Physical rehabilitation immediately after fracture repair to maintain joint(s) range of motion
- Serial radiography to evaluate bone healing

- Serial physical examinations to evaluate limb function

PROGNOSIS AND OUTCOME

- Poor if joint ankylosis or muscle contracture occurs
- Poor if irreversible nerve damage
- Joint fusion or limb amputation may be required in failed cases.

PEARLS & CONSIDERATIONS

COMMENTS

- Prevention is essential and easier than therapy.
- Avoid external splintage for humeral and femoral fractures.
- Consider case referral to an orthopedic specialist.
- In juvenile dogs, the coxofemoral joint will tend to luxate in a dorsal direction as the quadriceps contract.

PREVENTION

- Proper implant usage and fracture fixation allowing postoperative ambulation
- Anatomic joint surface reconstruction is a key goal.
- Avoid reliance on external coaptation to stabilize fractures.
- Use postoperative physical therapy to maintain limb function.

CLIENT EDUCATION

- Patients must be controlled after fracture fixation to prevent loss of implant stability.
- Physical therapy is necessary after surgery.
- Frequent recheck examinations are required to assess limb function and bone healing.

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Foreign Body, Respiratory Tract

BASIC INFORMATION

DEFINITION

Inhaled, penetrating, or migrating objects that cause obstruction or inflammation of the respiratory tract

SYNONYMS

Migrating foreign body, nasal foreign body, tracheal/bronchial foreign body

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs and cats can be affected. May be more prevalent in young or active animals.

GENETICS & BREED PREDISPOSITION

- Pyothorax secondary to aspiration of grass awn is most common in young or middle-aged medium to large hunting/sporting dogs.
- Small dogs are more prone to bone foreign body in the nasopharynx.

GEOGRAPHY AND SEASONALITY

May be more common during hunting season or in areas with oat/cereal fields or grass awns (“foxtails”)

ASSOCIATED CONDITIONS & DISORDERS

- Aspergillosis or bacterial rhinitis with chronic intranasal foreign body
- Focal tracheal stenosis with chronic intratracheal foreign body (granuloma)
- Lobar pneumonia with a foreign body in a bronchus
- Bronchoesophageal fistula with penetration of esophageal foreign body through bronchus
- Pyothorax with thoracic migration of foreign body into or through pleural space

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Rhinitis
- Tracheitis or tracheobronchial obstruction
- Pyothorax (empyema)

HISTORY, CHIEF COMPLAINT

- Nasal foreign body:
  - Nasal discharge
  - Acute onset of sneezing
  - Pawing at face or other signs of discomfort
- Nasopharyngeal foreign body:
  - Stridor
  - Sneezing
  - Halitosis possible with chronicity
- Tracheal/bronchial foreign body:
  - Acute onset of coughing, dyspnea
  - Chronic cough
  - Halitosis
  - Hemoptysis

- Retching/vomiting may occur
- Exercise intolerance or cyanosis if severe obstruction
- Temporary or recurring response to antibiotics in some chronic cases

- Intrathoracic foreign body:
  - Anorexia
  - Lethargy
  - Weight loss
  - Fever
  - Increased respiratory effort
  - Poor performance

PHYSICAL EXAM FINDINGS

- Nasal foreign body:
  - Decreased air movement through one nostril. Assessment:
    - By differentially occluding each nostril one at a time and either listening closely for air flow or watching for movement of an object held in the expected path of air flow (wisp of cotton ball, or of the pet's hair)
    - By holding a glass microscope slide in front of the nostrils and observing for fogging of the glass
  - Nasal discharge: unilateral bloody or blood-tinged, progressing to mucopurulent; may become bilateral after several months
  - Possibly ocular discharge
- Nasopharyngeal foreign body:
  - Stertor
  - Halitosis
  - Reverse sneezing
  - Acute onset of vomiting, retching, or gagging
- Tracheal/bronchial foreign body:
  - Dyspnea, which can be inspiratory and expiratory and worsens with degree of obstruction
  - Tachypnea
  - Cough
  - Increased respiratory noise: stridor; high frequency wheeze with partial obstruction
  - Cyanosis, collapse, or acute death with severe obstruction
- Intrathoracic foreign body (signs reflect pyothorax most often; see p. 956):
  - Cough
  - Fever
  - Increased inspiratory effort
  - Muffled heart sounds
  - Respiratory sounds muffled ventrally on thoracic auscultation
  - Pleural fluid line on percussion of the thoracic wall
  - Thorax may be noncompressible in cats with pyothorax.

ETIOLOGY AND PATHOPHYSIOLOGY

- Nasopharyngeal foreign body is usually bone in dogs.
- Inhalation most common path of entry for nasal, tracheal, bronchial, thoracic foreign bodies
  - Grass awns (seeds) and other plant material most common foreign objects
  - Plant material aspirated into lungs may migrate into pleural space (see Pyothorax, p. 956; Pneumothorax, p. 889)
- Sharp esophageal or gastric foreign bodies may migrate into lungs or pleural space.
- Local inflammatory reaction and contamination may result in secondary bacterial or fungal infection.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis of nasal, tracheal, and bronchial foreign bodies is suspected based on acute onset of clinical signs or chronic focal lung disease that can be responsive to antibiotics on a recurring basis. Confirmation can be made on radiographs (most often tracheal foreign bodies); however, endoscopy is often required. Migrating intrathoracic grass awns should be suspected in sporting/hunting breeds with a history of cough and fever that have focal pulmonary opacities, pleural effusion, and pleural thickening on radiographs or CT.

DIFFERENTIAL DIAGNOSIS

- Nasal foreign body:
  - Neoplasia
  - Fungal infection such as aspergillosis, cryptococcosis
  - Nasopharyngeal polyp
  - Lymphocytic-plasmacytic rhinitis
  - Nasal mites
  - Bacterial rhinitis
  - Oronasal fistula or tooth root abscess
  - Nasal trauma
  - Nasopharyngeal stenosis
- Nasopharyngeal foreign body:
  - Polyp
  - Granuloma
  - Neoplasia
  - Rhinitis
- Tracheal/bronchial foreign body:
  - Laryngeal paralysis
  - Tracheal collapse
  - Elongated soft palate
  - Trauma
  - Neoplasia
  - Infection
- Lung or intrapleural foreign body:
  - Bronchopneumonia
  - Pyothorax from trauma or systemic disease
  - Neoplasia

INITIAL DATABASE

- CBC
  - Neutrophilic leukocytosis, possibly with left shift and toxic neutrophils, with pyothorax, secondary bronchopneumonia, or severe secondary rhinitis
  - Eosinophilia possible with tracheobronchial grass awns
- Serum biochemistry profile and urinalysis often unremarkable with nasal, nasopharyngeal, or airway foreign bodies
  - With pyothorax from pleural foreign bodies, hypoalbuminemia, hypoglycemia, or proteinuria may be seen.
- Radiographs: findings other than radiopaque foreign body may include:
  - Nasal foreign body:
    - Increased intranasal soft-tissue opacity
    - Local bone destruction with chronic disease
  - Tracheal foreign body:
    - Increased airway soft-tissue/fluid opacity on cervical or thoracic films
    - Noncardiogenic pulmonary edema with severe obstruction
  - Bronchial foreign body:
    - Ill-defined peribronchial radiopacity
  - Lung or bronchial foreign body:
    - Lung consolidation with secondary bronchopneumonia
  - Intrapleural foreign body:
    - Focal pulmonary interstitial to alveolar opacities, most common in caudal or accessory lobes
    - Pleural effusion, pleural thickening
    - Collapsed lung lobes
    - Spontaneous pneumothorax may occur with penetrating or migrating thoracic foreign bodies.
- Cytologic evaluation/culture of nasal cavity to identify organisms associated with secondary rhinitis
- Neutrophilia on transtracheal wash cytologic study with tracheobronchial foreign body
- Pyothorax: inflammatory exudates (degenerate neutrophils ± bacteria) on cytologic study of pleural fluid obtained by thoracocentesis. Macrophages and plasma cells increase with chronicity.
  - Common organisms cultured from pyothorax: obligate anaerobes *(Fusobacterium), Nocardia asteroides*, *Actinomyces*in dogs; anaerobes, *Pasteurella multocida*in cats

ADVANCED OR CONFIRMATORY TESTING

- Nasopharyngeal foreign bodies may be visible in anesthetized patients by soft-palate retraction during oropharyngeal exam or retroflexed nasopharyngoscopy.
- Endoscopy is generally diagnostic for tracheal foreign bodies and some bronchial foreign bodies (may be obscured by mucopurulent exudates).

- Intranasal foreign bodies may be visible with anterior rigid scope or posterior flexible scope, although nasal discharge may obscure view.
    - Nasal flushing (see online chapter: Nasal Flush) removes discharge to improve visualization. Retrograde flushing may force nasal foreign bodies out through the nares.
- CT of nasal cavity: mucosal thickening, focal bone thickening and destruction; may not differentiate foreign body rhinitis from nasal aspergillosis.
- CT of animals with migrating grass awns: focal interstitial to alveolar pulmonary opacities, primarily in the right caudal lung lobe, and enlarged lymph nodes. Foreign body seen on CT in 33% of animals.
- Contrast rhinography or bronchography are rarely used but may outline radiolucent foreign body.

TREATMENT

TREATMENT OVERVIEW

Goals include oxygenation of the patient if needed, removal of the foreign body, and treatment of secondary infections. Animals in respiratory distress from obstruction may require immediate anesthesia and foreign-body retrieval.

ACUTE GENERAL TREATMENT

- Oxygen supplementation (see p. 1318).
- Sedation if extremely stressed (i.e., such that the anxiety is contributing to dyspnea):
    - Acepromazine, 0.1-0.5 mg total dose IM or IV if young and not systemically ill
    - Butorphanol, 0.2-0.4 mg/kg IV may be given additionally q 2-4 h as needed
- Rehydrate as needed.
- Thoracocentesis if respiratory compromise from pleural effusion or pneumothorax (see p. 1338)
- Immediate anesthesia and foreign body removal if trachea completely obstructed
    - Tracheostomy (see p. 1344) may be needed for short-term airway management.
- If possible, nonsurgical removal of nasal, laryngeal, tracheal, and some bronchial foreign bodies
    - Foreign bodies often removed endoscopically with forceps, basket retrievers
    - Nasal foreign bodies sometimes removed during retrograde or antegrade lavage/flush
    - Some tracheal foreign bodies removed with vacuum suction or passage of balloon (Fogarty) catheter beyond foreign body and then inflation and retraction of balloon. Tracheal foreign bodies in cats removed with forceps retrieval (24-in. custom-made grasping forceps) under fluoroscopic guidance.
- Rhinotomy (dorsal or ventral), tracheotomy, bronchotomy, or lung lobectomy for nonretrievable intraluminal foreign bodies
    - Lobectomy if lung lobe consolidation. Histopathologic evaluation and culture (aerobic and anaerobic) of excised tissue.
    - Anesthetic/oxygen delivery via contralateral bronchus intubation recommended for unilateral bronchotomy. Total IV anesthesia with endotracheal or endobronchial oxygen delivery if gas leakage expected.
- Lung lobectomy if bronchopneumonia secondary to foreign body or bronchoesophageal fistula
- Bilateral thoracostomy tubes or thoracotomy (median sternotomy for generalized disease) and thoracic lavage/drainage for pyothorax
    - Lavage through large-diameter chest tubes with sterile, lukewarm isotonic fluids (20 mL/kg) q 12 h for 5-7 days.
- Surgical exploration if intrathoracic mass, radiographic evidence of pulmonary or mediastinal lesions, pneumothorax, *Actinomyces*, or no improvement with medical therapy
- For pyothorax or bronchopneumonia, broad-spectrum antibiotics

CHRONIC TREATMENT

- Antibiotic therapy for secondary infections, based on culture/sensitivity
    - Ampicillin or amoxicillin plus clavulanic acid, 12.5-20 mg/kg PO q 12 h for obligate anaerobes, *Pasteurella*spp., *Actinomyces*spp.
    - Trimethoprim sulfa, 10-15 mg/kg PO q 12 h (possibly higher, but may increase risk of adverse effects); or amikacin for *Nocardia*spp.
    - For pyothorax, antibiotics are administered for 1-2 months.
- Bronchodilators (e.g., aminophylline, 10 mg/kg PO q 8 h) for 3-5 days after endoscopic removal of bronchial foreign bodies

POSSIBLE COMPLICATIONS

- Inability to oxygenate during endoscopy or surgery
- Increased severity of obstruction with flushing, foreign body manipulation, or endoscopic trauma (mucosal swelling)
- Pulmonary abscess or recurrent pyothorax if migrating foreign body remains or inappropriate antibiotic therapy used
- Chronic rhinitis possible if turbinates are removed during rhinotomy

RECOMMENDED MONITORING

- Tracheal/bronchial/lung/thoracic foreign bodies: repeat radiographs or endoscopy if clinical signs recur.
- Pyothorax or pneumonia: repeat radiographs 1 week after discontinuing antibiotics or if clinical signs recur.

PROGNOSIS AND OUTCOME

- Outcome excellent if patient survives foreign-body extraction and secondary infections are treated appropriately.
    - Bronchopulmonary abscess develops with foreign body migration if tracheobronchial grass awn present for more than 2 weeks.
- Complication and mortality rates higher with chronicity
- Tracheobronchial plant material can fragment, requiring multiple endoscopic episodes for complete removal.

PEARLS & CONSIDERATIONS

COMMENTS

- Some nasal foreign bodies can be removed with vigorous flushing (see online chapter: Nasal Flush).
- Right bronchial system more likely to be affected by inhaled bronchial foreign body because of direct tracheobronchial path
- Grass awns usually migrate to multiple sites, including pericardial sac, in dogs with pyothorax.
- If sulfur granules or branching filamentous gram-positive rods (suspicion of *Actinomyces*infection) are seen during cytologic examination of the pleural fluid, consider long-term treatment (4-6 weeks) with antibiotics.

TECHNICIAN TIPS

- During rhinoscopy for foreign body, fluids from lavaging or hemorrhage will pour out of the nares and nasopharynx; therefore, the endotracheal tube should be in place and inflated during the procedure.
- Teeth and pieces of dental calculus may become tracheal or bronchial foreign bodies if not removed from the mouth after dental cleaning.
- Intubation and endoscopy may inadvertently force tracheal foreign bodies toward the tracheal bifurcation or into the bronchi. Affected animals may require an emergency thoracotomy and intubation of the distal trachea or bronchus through the thoracotomy site; therefore, materials should be available for clipping, prepping, and thoracotomy.

CLIENT EDUCATION

- Acute onset of coughing in high-performance sporting dogs during hunting or harvest season may indicate tracheobronchial foreign body.
- Provide indestructible bones and toys that are appropriately sized for the dog.

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Foreign Body, Oral

BASIC INFORMATION

DEFINITION

Foreign object lodged or embedded in the oral cavity

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dog and cat, either sex. Potentially more of a problem in younger animals.

RISK FACTORS

- Habit of chewing on foreign objects:
  - Bones, sticks, string
- Longer-haired dogs playing or running in grassy/wooded areas
- Interacting with a porcupine

ASSOCIATED CONDITIONS & DISORDERS

- Retrobulbar abscess
- Submandibular/intermandibular abscess
- Necrosis of intraoral structures
- Linear foreign body gastrointestinal obstruction

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Dog playing or running in grassy or wooded area
- Dog seen interacting with porcupine
- Animal seen chewing on foreign object
- Signs of oral discomfort (pawing at mouth, face rubbing, reluctance to eat hard food)
- Facial swelling: exophthalmos, strabismus possible
- Nonspecific signs: depression, anorexia, vomiting

PHYSICAL EXAM FINDINGS

- Nonspecific findings:
  - Depression, pyrexia, dehydration
- Reluctance to open/discomfort on opening mouth
- Facial swelling:
  - Exophthalmos
  - Strabismus
  - Submandibular/intermandibular swelling
- Halitosis
- Oral discharge (hemorrhagic, purulent)
- Findings related to the foreign body:
  - Bone or stick lodged across hard palate, between premolars/molars, or encircling mandible (short segment of large diameter bone)
  - Burrs stuck in lingual, palatine, gingival mucosa
  - String foreign body around base of tongue
  - Porcupine quills in and around muzzle and oral cavity
- Penetrating oral injury, possibly associated with external facial swelling
- Findings associated with gastrointestinal linear foreign body:
  - Abdominal palpation: pain, plicated intestines

ETIOLOGY AND PATHOPHYSIOLOGY

- Foreign body penetration of the oral cavity may result in abscess formation in the surrounding tissues (most commonly retrobulbar or submandibular/intermandibular)
- Foreign body lodged between the maxillary premolars/molars can cause necrosis of the underlying palatine mucosa and palatine bone and development of oronasal fistula
- Burrs embedded in the oral mucosa—may incite granulomatous reaction
    - Focal: mass
    - Diffuse: across the whole surface of the tongue
- Linear foreign bodies (see p. 407) caught around the base of the tongue can become embedded into the tongue.
    - Can be difficult to identify
    - Can cause a significant inflammatory/granulomatous reaction

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on patient signalment, presenting history, and physical, including oral examination findings. Thorough oral examination may have to be performed under general anesthesia, owing to pain. Confirmation requires identification of an intraoral foreign body and/or fine-needle aspiration cytology of facial swelling/mass.

DIFFERENTIAL DIAGNOSIS

- Oral mass: neoplasia
- Facial swelling: neoplasia or salivary mucocele

INITIAL DATABASE

- CBC:
    - Neutrophilia associated with inflammation or infection
- Oral examination: general anesthesia usually necessary (see Acute General Treatment)
- Fine-needle aspiration of facial swelling:
    - Cytologic examination to confirm inflammation +/− infection
    - Microbiologic culture and sensitivity testing (aerobic and anaerobic)
- Ultrasound examination:
    - Exophthalmos
    - Facial swelling (abscess versus neoplasia)

ADVANCED OR CONFIRMATORY TESTING

- Histopathologic examination of biopsied oral mass
    - Foreign body granuloma versus neoplasia
- CT or MRI: extent of abscess/granulomas

TREATMENT

TREATMENT OVERVIEW

Removal of the foreign body may involve either direct extraction from the oral cavity or surgical exploration of an identified abscess. Associated inflammation, abscess formation and/or cellulitis are treated by surgical exploration, débridement and medical management. If a linear foreign body is found, appropriate surgical intervention of the gastrointestinal tract is indicated (see p. 407).

ACUTE GENERAL TREATMENT

Following induction of general anesthesia:

- Oral examination:
    - Routine (foreign material may be found incidentally)
    - Because could not be performed in awake patient (e.g., fractious behavior, physical obstruction)
- Radiographs:

    - Radiopaque foreign body
    - Soft-tissue swelling (abscess)
    - Destruction of underlying bone
- Removal of foreign body from oral cavity:
    - Porcupine quills: grasp at base (nearest to skin) with forceps and extract gently (see p. 1331).
    - Bone or stick: if tightly wedged, may be easier to remove by cutting (e.g., with Stryker saw) first
    - Release linear foreign body caught around base of tongue.
- Burrs embedded in oral mucosa:
    - Surgical débridement to remove plant material and chronic granulomatous lesions. Open wounds will rapidly be covered by proliferating mucosa.
- Surgical exploration, débridement, and lavage of abscess pocket(s):
    - Retrobulbar area explored through incision in oral mucosa just caudal to last upper molar tooth or through existing penetrating wound
- Provide postoperative drainage until abscess has resolved (submandibular/intermandibular).Antibiotic therapy for bacterial infection:
- Long-term therapy based on results of microbiologic culture and sensitivity tests
- Empirical therapy until results available:
    - Cefazolin, 22 mg/kg IV q 6 h, if animal receiving IV fluids and unable to take oral medications; *or*
    - Amoxicillin, 10-20 mg/kg PO q 12 h

CHRONIC TREATMENT

- Antibiotic therapy (see Acute General Treatment above) until resolution of infection
- Reconstructive surgery of damage caused to oral cavity by foreign body:
    - Oronasal fistula

NUTRITION/DIET

- If lesions or wounds that might hinder oral feeding are present in the oral cavity, it will be necessary to provide alternative route for nutrition and antibiotic administration.
    - Esophagostomy tube or PEG tube (see p. 1267 and p. 1270)
    - Reexamine oral cavity in 10-14 days. If healed, patient can return to oral feeding, and tube can be removed.

POSSIBLE COMPLICATIONS

- Failure to remove foreign body:
    - Persistent/recurrent abscess
    - Development of draining tract
- Development of late-onset tissue necrosis:
    - Osteomyelitis
    - Oronasal fistula

RECOMMENDED MONITORING

- Repeat visits to veterinarian as necessary
    - To ensure oral lesions or wounds heal
    - To ensure abscess has resolved (allowing drain removal)
    - To remove feeding tube once oral problems have healed
- Observe for recurrence of abscess and development of draining tract.

PROGNOSIS AND OUTCOME

- Usually good, provided all foreign material has been removed and abscess pockets are adequately drained
- Recurrent problems likely to occur or chronic draining tract may develop if:
    - Failure to remove all foreign material, especially porcupine quills
    - Late-onset tissue necrosis develops (oronasal fistula, osteomyelitis)

PEARLS & CONSIDERATIONS

COMMENTS

In situations where multiple foreign bodies are present in the oral cavity (porcupine quills, burrs), it is essential to ensure that a thorough examination is performed, extending throughout the entire pharynx, to ensure all foreign material is removed.

PREVENTION

Avoid situations that could lead to foreign bodies injuring or becoming lodged in the oral cavity.

TECHNICIAN TIPS

- In-hospital care may include:
  - Keeping drain/drainage site clean and free of discharge
  - Changing bandages as directed
  - Administration of antibiotics as directed
  - Ensuring adequate analgesia is provided
  - Ensuring that patient is receiving adequate nutritional support if NPO

CLIENT EDUCATION

- Do not let animals play with or chew on objects such as sticks that could cause penetrating oral injuries, or linear objects (fishing line, yarn, etc.) that could act as linear foreign bodies.
- Do not let dogs interact with porcupines.

SUGGESTED READING

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AUTHOR & EDITOR: RICHARD WALSHAW

Foreign Body, Linear Gastrointestinal

BASIC INFORMATION

DEFINITION

A common disorder involving ingestion of a linear object that lodges in the proximal alimentary system (commonly under the tongue or at the pylorus) and causes plication of intestines along the length of the object

SYNONYM

String foreign body

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Young animals are at risk for foreign object ingestion.
- Linear foreign body is a more common diagnosis in cats than dogs.
- Dogs with linear foreign bodies are generally older than cats.
- Cats frequently present with string or thread ingestion, while dogs ingest fabric such as clothing or carpet.

RISK FACTORS

Some animals are more prone to ingesting foreign objects than others (individual behavior) irrespective of age.

GEOGRAPHY AND SEASONALITY

December to January: ingestion of Christmas tree “icicles” (long, thin strips of foil-like plastic) or ribbons

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Owners may witness object ingestion.
- String may be visualized protruding from the anus.
- Clinical signs vary with duration of foreign body ingestion, as well as presence of a partial or complete obstruction.
- Vomiting, anorexia, ptyalism, depression, and weight loss (if chronic) are typical.

PHYSICAL EXAM FINDINGS

- Thorough examination at the base of the tongue should be performed to inspect for anchored foreign material.
    - In cats, elevation of the base of the tongue is best accomplished by opening the mouth via depressing the lower jaw using an index fingernail for pressure on the lower incisors. The thumb of the same hand is then used for externally pressing upward (dorsally) in the intermandibular space.
    - In dogs or cats, a complete examination may require sedation or general anesthesia.
- Painful and bunched intestines maybe detected with careful abdominal palpation.
- Dehydration, depression, or shock; severe with complete obstruction or peritonitis

ETIOLOGY AND PATHOPHYSIOLOGY

- Anchoring of ingested linear material around base of tongue, at the pylorus, or in the proximal intestinal tract
    - Without an anchor point, ingested linear foreign bodies may simply pass through the gastrointestinal (GI) tract without complication.
- Peristalsis results in plication of intestines along the length of the fixed material.
- Obstruction of intestinal tract results.
- Due to peristalsis, continued sawing action of the foreign material along mesenteric border may result in intestinal erosion and perforation and the development of peritonitis (see p. 865).
- Presence of an associated intussusception (see p. 622) is possible.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Any history of vomiting or anorexia in a dog or cat should prompt an inspection of the base of the tongue during physical examination; a circumferential erosive lesion containing the foreign body is pathognomonic. If no such finding is apparent, diagnostic imaging is indicated in all young animals presenting with vomiting, anorexia, abdominal pain, or a history of foreign-body ingestion. Plain abdominal radiography is often sufficient for a diagnosis, but occasionally the disorder is only confirmed during abdominal exploratory surgery.

DIFFERENTIAL DIAGNOSIS

- All other causes of intestinal obstruction such as neoplasia, intussusception, granuloma, stricture, adhesions, or volvulus
- Ileus

INITIAL DATABASE

- CBC: normal or shows evidence of inflammation/sepsis due to peritonitis
- Serum chemistry profile:
  - Hypokalemia associated with vomiting, anorexia
  - Hypoglycemia associated with peritonitis
  - Azotemia associated with dehydration
  - Hyponatremia may be more commonly seen in dogs with linear foreign bodies than in those with discrete foreign bodies.
- Urinalysis: unremarkable
- Abdominal radiographs:
  - Characteristic findings include plication of intestines with or without eccentric “comma-shaped” intraluminal gas bubbles.
  - Dogs may be more likely than cats to have characteristic radiographic findings, allowing the diagnosis of linear foreign body to be made radiographically.
- Abdominocentesis with fluid evaluation is indicated if peritonitis is suspected.

ADVANCED OR CONFIRMATORY TESTING

- Contrast radiography or abdominal ultrasound may be used if survey radiographic findings are inconclusive.
- Abdominal ultrasound:
  - May document a tortuous path of the proximal intestine as well as presence of an intraluminal linear object
  - May document associated disorders such as an intussusception or peritonitis
  - However, limited efficacy when gas or barium is present in the intestine
- Noniodinated contrast material is often recommended for upper GI radiographic contrast series, as up to 16% of cats and 41% of dogs may have perforation of the intestinal tract.
  - However, the advantage of iodine (will be resorbed from the peritoneal cavity if perforation exists, unlike barium) must be weighed against its reduced degree of contrast, foul taste (compliance), and the access to any spilled barium at the time of laparotomy, because surgical intervention is indicated if perforation is confirmed.

TREATMENT

TREATMENT OVERVIEW

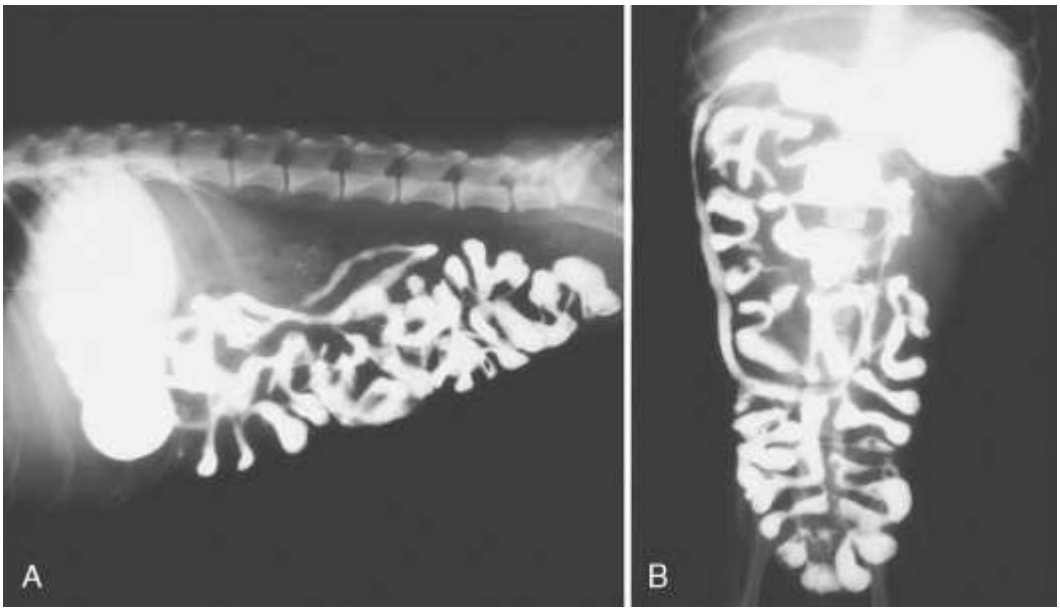
Rehydration and rapid surgical intervention are recommended. Specific goals are to:

- Correct dehydration and electrolyte imbalances.
- Remove obstructing foreign body:
  - Although conservative treatment in the cat has been reported, the high likelihood of perforation and the associated morbidity of peritonitis dictate that these cases be treated as surgical emergencies.
  - Conservative treatment is not de scribed in the dog, owing to the high risk of development of peritonitis.

ACUTE GENERAL TREATMENT

- Intravenous fluid therapy with electrolyte (potassium) supplementation according to need

- Prophylactic antibiotics:
  - Cefazolin, 22 mg/kg IV q 2 h during the perioperative period
- Surgical intervention includes thorough inspection of the entire intestinal tract for evidence of perforation.
- If the linear foreign body is fixed around the base of the tongue, it should be cut at this point.
- Foreign material is removed through a single or multiple enterotomies.
- Gastrostomy is performed to remove any foreign material trapped in the stomach, particularly at the pylorus.
- Single enterotomy removal using a red rubber catheter has been reported for use when no intestinal perforations are present.
  - This technique involves a single duodenal enterotomy with attachment of a red rubber catheter to the linear object. The enterotomy is closed, and the catheter with attached object is advanced distally until removed from rectum.
- If any necrosis, perforation, or intussusception of the intestines is present, a resection and anastomosis should be performed.
- Omentum or serosal patch may be placed to reinforce suture line.
- Change gloves and surgical instruments prior to abdominal lavage and closure.



FOREIGN BODY, LINEAR GASTROINTESTINAL Lateral **(A)** and ventrodorsal **(B)** radiographic projections of upper gastrointestinal (UGI) barium study. Patient had a gastrointestinal linear foreign body. Characteristic teardrop-shaped appearance of small-intestinal segments is apparent.

(Courtesy Dr. Richard Walshaw.)

CHRONIC TREATMENT

Postoperative considerations:

- Continue rehydration and daily electrolyte monitoring.
- NPO 6-12 hours after enterotomy, 12 hours after resection and anastomosis
- Administer GI protectants or antiemetics as needed.

NUTRITION/DIET

Feeding tube placement (typically esophageal) at the time of surgery should be considered in animals with marked weight loss, hypoalbuminemia, or in those patients with evidence of peritonitis.

POSSIBLE COMPLICATIONS

- Dehiscence; animals should be monitored in hospital for 48-72 hours postoperatively for signs of peritonitis. Risk factors include presence of preoperative peritonitis, serum albumin concentration <2.5 g/dL, and presence of a foreign body (versus neoplastic disease).
- Ileus
- Short bowel syndrome; unlikely if less than 70% of small intestine resected
- Stricture
- Recurrence

RECOMMENDED MONITORING

The following parameters should be monitored q 6-12 h until discharge from hospital:

- Body temperature
- Blood glucose
- Electrolytes
- Hematocrit and total solids
- Presence of abdominal pain

PROGNOSIS AND OUTCOME

- Delay in surgical intervention may increase risk of perforation and peritonitis.
- Presence of peritonitis or free abdominal gas on radiographs is associated with increased rate of mortality in the dog.
- Morbidity and mortality are 50% higher for dogs than cats.

PEARLS & CONSIDERATIONS

COMMENTS

- Do not put forceful traction on the linear object before or during surgery; this may cause iatrogenic laceration of the mesenteric border of the small intestine.
- Consider placing an intraoperative feeding tube (see p. 1267 , p. 1270 , and p. 1273) in these patients based on preoperative nutritional status, degree of patient debilitation, or anticipated postoperative anorexia.

SUGGESTED READING

Anderson S, et al: Single enterotomy removal of gastrointestinal linear foreign bodies. J Am Anim Hosp Assoc 28:487, 1992.

Boag AK, et al: Acid-base and electrolyte abnormalities in dogs with gastrointestinal foreign bodies. J Vet Intern Med 19(6):816– 821, 2005.

Macphail C: Gastrointestinal obstruction. Clin Tech Small Anim Pract 17(4):178–183, 2002.

AUTHOR: JANET KOVAK MCCLARAN

EDITOR: RICHARD WALSHAW

Foreign Body, Esophageal

Additional Images Available on Website

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Any solid object that lodges in the esophagus

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs and cats of any age, either sex

GENETICS & BREED PREDISPOSITION

Smaller dogs and cats seem to be affected more commonly.

RISK FACTORS

Feeding bones

ASSOCIATED CONDITIONS & DISORDERS

- Esophagitis is common.
- Esophageal perforation can cause septic mediastinitis, pyothorax, and/or pneumothorax.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Nonpenetrating foreign objects (main concerns: esophagitis, aspiration pneumonia)
- Penetrating foreign objects (main concerns: mediastinitis, pyothorax, esophagitis, aspiration pneumonia)

HISTORY, CHIEF COMPLAINT

- Acute onset of regurgitation is very suggestive.
  - Distinguish acute vomiting (active abdominal contractions leading to expulsion of food) from acute regurgitation (passive evacuation of food from the esophagus out of the mouth).
- Anorexia and ptyalism often occur (especially in cats).
- Some patients drink water but will not attempt to eat solid food.
- Dyspnea, nonspecific signs including lethargy and anorexia, and/or signs suggesting general discomfort may be seen if perforation occurs.
- Rarely, pressure of foreign object on trachea causes coughing or choking.

PHYSICAL EXAM FINDINGS

- Ptyalism occasionally noticed during exam
- Dysphagia or gagging may be seen during exam.
- Dyspnea/fever sometimes seen secondary to perforation and mediastinitis/pleuritis

ETIOLOGY AND PATHOPHYSIOLOGY

- Bones are the most common cause in dogs.
- Other causes include food boluses, fishhooks, rawhide treats, and dental chew toys.
- Hairballs are important in cats.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

An essential component of the history is asking whether the patient's behavior is one of frequent chewing or mouthing of objects (propensity to foreign-body ingestion). Thoracic radiographs are the screening test of choice; endoscopy is both confirmatory and therapeutic.

DIFFERENTIAL DIAGNOSIS

Regurgitation:

- Esophagitis
- Megaesophagus (acquired [idiopathic or secondary to systemic disease], or congenital)
- Esophageal mass
- Esophageal stricture
- Vascular ring anomaly

INITIAL DATABASE

- CBC and serum biochemistry panel: to look for evidence of inflammation and to prepare for anesthesia
- Plain thoracic radiographs:
  - Differentiate esophageal foreign body from megaesophagus (often generalized, as opposed to esophageal dilation associated with foreign body, which when present is seen cranial to the foreign body) and other thoracic masses (consider location relative to esophagus using at least two radiographic views).
  - Most foreign objects will be seen with good-quality films, but poultry bones and rawhide may be relatively radiolucent, requiring excellent technique for detection.
  - Evidence of pneumothorax, pneumomediastinum, and pleural effusion: any are suggestive of esophageal perforation.
  - Esophageal foreign objects can look like lung lesions radiographically.
  - Assess for complications: aspiration pneumonia and/or evidence of perforation (mediastinal widening, pleural effusion suggesting mediastinitis or pleuritis/pyothorax, respectively).
- Contrast esophageal radiographs:
  - Seldom needed and may obscure visualization during endoscopy
  - Risk of aspiration of contrast material

ADVANCED OR CONFIRMATORY TESTING

Esophagoscopy:

- Definitive differentiation of esophageal foreign body from esophagitis
- With good technique, the foreign object can virtually always be seen.

TREATMENT

TREATMENT OVERVIEW

Goals are to remove the foreign object and resolve any complications (e.g., esophagitis or perforation with resulting pleural/mediastinal sepsis).

ACUTE GENERAL TREATMENT

- Esophagoscopy to remove foreign object and determine degree of esophagitis (see p. 1279).
  - If foreign object cannot be removed, it can sometimes be pushed into the stomach where it is removed surgically or allowed to dissolve.
- Can use Foley catheter in some cases (i.e., place balloon behind foreign object, inflate balloon, then pull the catheter out so that the balloon draws the foreign object orad and out). Only for use with foreign objects that have no sharp edges.
- Surgery if endoscopy is unsuccessful at removing the foreign object
- Prokinetics (e.g., metoclopramide, 0.2-0.4 mg/kg IM or SQ PO q 8 h) and/or antacid (famotidine, 0.5-2 mg/kg IV, IM, SQ, or PO q 12-24 h; or omeprazole, 0.7-1 mg/kg PO q 12-24 h) to treat esophagitis (see p. 367). Do not give antacids if bone has been pushed into the stomach (gastric acid needed to dissolve the bone).
- Appropriate treatment of pulmonary disease/pleuritis if a perforation occurs

CHRONIC TREATMENT

Mechanical dilation of consequent stricture formation, if necessary (see p. 365)

NUTRITION/DIET

Place gastrostomy feeding tube (see p. 1270) if severe esophagitis is present.

POSSIBLE COMPLICATIONS

- Cicatrix leading to partial or complete esophageal obstruction
- Esophageal perforation leading to septic pleuritis/mediastinitis
- Excessive insufflation of air during endoscopy can cause tension pneumothorax.
- Severe bleeding is rare but possible when manipulating/removing foreign object.

PROGNOSIS AND OUTCOME

- Good if there is no perforation and esophagitis is not severe
- Good to guarded if severe, near-circumferential esophagitis is likely to cause stricture
- Guarded to poor if perforation has caused severe septic mediastinitis or pleuritis

PEARLS & CONSIDERATIONS

COMMENTS

- Rigid endoscopes are usually more effective than flexible ones in removing foreign objects.
- If a contrast esophagram is required, use a water-soluble iodide contrast agent; do not use barium.

TECHNICIAN TIP

Technicians involved in postoperative care of these patients should be familiar with use and maintenance of feeding tubes.

PREVENTION

- Avoid feeding bones.
- Be careful about allowing dogs to have/swallow rawhide chews.
- Use caution when dogs are in the area around baited fish hooks.
- Do not medicate cats with dry tablets or capsules; follow the medication with water or food.

SUGGESTED READING

Doran IP: Acute oropharyngeal and esophageal stick injury in forty-one dogs. Vet Surg 37:781, 2008.

Sale C, et al: Results of transthoracic esophageal retrieval of esophageal foreign body obstruction in dogs: 14 cases (2000-2004). J Am Anim Hosp Assoc 42:450, 2006.

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Footpad Disorders

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Pathologic condition involving the footpad skin. The most common causes are trauma, contact dermatitis, cornification defects, pigmentation disorders, autoimmune disease, secondary bacterial infection, and self-trauma.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs and cats. Although uncommon, footpad diseases are more frequently seen in cats in comparison to dogs, which develop more often interdigital lesions (see p. 891)
- Dogs less than 1 year of age: hereditary footpad hyperkeratosis, collagen disorder of the footpads of German shepherds, familial vasculopathies, acrodermatitis, junctional and dystrophic epidermolysis bullosa, and acral mutilation syndrome.
- Older dogs: superficial necrolytic dermatitis (SND; previously called *hepatocutaneous syndrome*) and epitheliotropic lymphoma

GENETICS & BREED PREDISPOSITION

- Vitiligo: Siamese cats and Belgian Groenendael dogs
- Footpad hyperkeratosis: Irish terriers and Dogues de Bordeaux
- Collagen disorders of the footpads: German shepherds
- Familial vasculopathy: German shepherds and Jack Russell terriers
- Acral mutilation syndrome: German shorthaired and English pointers, English springer spaniels, and French spaniels
- Dermatomyositis: Beauceron dogs (footpad lesions)
- Uveodermatologic syndrome: Akitas, Alaskan malamutes, and Siberian huskies
- Zinc-responsive dermatosis: Alaskan malamutes (genetic defect involving enteric zinc absorption) and Siberian huskies
- Systemic lupus erythematosus (SLE): collies, Shetland sheepdogs, and German shepherds

GEOGRAPHY AND SEASONALITY

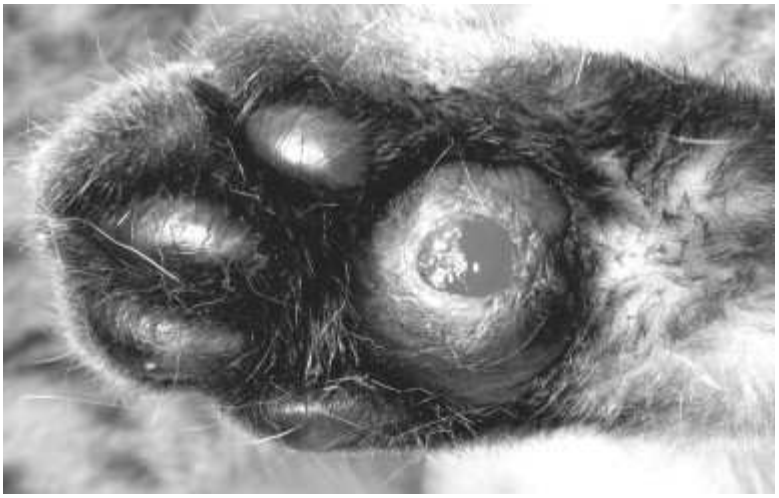
Leishmaniasis in endemic areas

RISK FACTORS

- Lacerations/trauma: outdoor activities, roaming
- Footpad calcinosis cutis: renal failure and hyperparathyroidism
- SND: hepatopathy or glucagonproducing pancreatic tumor

ASSOCIATED CONDITIONS & DISORDERS

- SLE: systemic signs, depending on the organs involved
- Feline paraneoplastic alopecia: pancreatic carcinoma or bile duct carcinoma
- Xanthomatosis: can be associated with diabetes mellitus in cats
- Feline plasma cell pododermatitis: possible concurrent feline immunodeficiency virus (FIV) infection or renal glomerulonephritis and amyloidosis
- Uveodermatologic syndrome: granulomatous uveitis
- Cutaneous horns: possible concurrent feline leukemia virus (FeLV) infection in cats



FOOTPAD DISORDERS Swollen, ulcerated footpad in a cat with plasma cell pododermatitis.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Skin lesions located on one or multiple footpads. Self-trauma and lameness may be observed. Foot involvement may also be part of a more generalized condition. With footpad lacerations, owner-observed bleeding often is the first sign.

PHYSICAL EXAM FINDINGS

- Number of feet affected: lesions on multiple feet (see Associated Conditions and Disorders above) versus on one foot only (neoplasia, trauma, infection)
- Depending on the disease, several changes can be present on the footpads:
  - Swelling and inflammation
  - Hyperkeratosis
  - Cracking and fissuring
  - Ulcers
  - Depigmentation or hyperpigmentation
  - Draining tracts
  - Change in footpad texture
  - Signs of pain on walking, or during handling of the paw(s)

ETIOLOGY AND PATHOPHYSIOLOGY

Footpad lesions can arise following various pathomechanisms, including:

- Direct trauma
- Contact with an irritant or corrosive substance, which can result in skin injury and inflammation
- Development of antibodies or activated lymphocytes against normal body constituents (autoimmune diseases), or against inciting antigens (drugs, bacteria, viruses), causing tissue damage
- Altered process of cornification (proliferation/differentiation/desquamation) resulting in hyperkeratosis
- Defective melanin production or a destruction of melanocytes, leading to pigment disorders. Moreover, a disorder at the basal epidermal cell level can result in hypopigmentation.
- Hereditary sensitive neuropathy in acral mutilation syndrome
- In addition to primary etiologies, self-trauma and secondary bacterial infection can result in footpad lesions.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Extent of testing varies widely and is adapted to each case. The diagnosis will be based on dermatologic examination as well as on complementary testing, which will vary depending on the list of possible differential diagnoses.

DIFFERENTIAL DIAGNOSIS

- Environmental: trauma, irritant contact dermatitis, calcinosis cutis caused by percutaneous penetration of calcium salts, and thallium toxicosis
- Hereditary: see Genetics & Breed Predisposition above.
- Allergic/immune-mediated:
    - Dogs: pemphigus foliaceus, SLE, vasculitis, toxic epidermal necrolysis, erythema multiforme, cryoglobulinemia and cryofibrinogenemia (cold agglutinin disease), bullous pemphigoid, epidermolysis bullosa aquisita, uveodermatologic syndrome, and drug reactions
    - Cats: eosinophilic granuloma complex, pemphigus foliaceus, SLE, erythema multiforme, toxic epidermal necrolysis, vasculitis, cryoglobulinemia and cryofibrinogenemia (cold agglutinin disease), drug reactions, and plasma cell pododermatitis
- Nutritional: zinc-responsive dermatosis
- Endocrine/metabolic:
    - Dogs: SND and footpad calcinosis cutis (often associated with chronic kidney disease and parathyroid hyperplasia)
    - Cats: paraneoplastic alopecia and xanthomatosis (idiopathic or associated with diabetes mellitus)
- Neoplastic: epitheliotropic cutaneous lymphoma, squamous cell carcinoma, fibrosarcoma, mast cell tumor, etc.
- Infectious: canine distemper, cowpox-virus infection in cats, subcutaneous or systemic mycotic infections, canine papillomatosis, and hookworm and *Pelodera*dermatitis
- Miscellaneous: noninflammatory hypomelanosis (vitiligo) or hypermelanosis (lentigo in orange cats), cutaneous horns, idiopathic footpad hyperkeratosis seen in older dogs, and idiopathic sterile granulomas and pyogranulomas

INITIAL DATABASE

- History and general examination are very important in the diagnostic process.
- Cytology of any exudates: bacteria, inflammatory cells, acantholytic keratinocytes (pemphigus), and fungal organisms
- CBC/biochemistry panel/urinalysis: results variable, depending on suspected cause
- Thoracic/abdominal imaging, if relevant, to confirm systemic disease (e.g., SND) or to stage tumors

ADVANCED OR CONFIRMATORY TESTING

- Skin biopsies for histopathology and possibly immunofluorescence or immunohistochemical stainings
- Endocrine tests and serology depending on suspected disease
- Coombs' test: cold agglutinin disease
- Antinuclear antibody test (ANA): positive in virtually all patients with SLE

TREATMENT

TREATMENT OVERVIEW

The goal of treatment is to reach permanent cure or control of the disease; however, sometimes palliative treatment is the only option (e.g., malignancy).

ACUTE TREATMENT

Depends on etiology of the lesion and possible secondary infection

- Foot soaks or bandages sometimes useful
    - Hyperkeratotic lesions: warm water foot soaks for 5-10 minutes, followed by application of a softening agent (e.g., petroleum jelly). The owners should be warned that this can be messy.
    - For more severe hyperkeratosis, daily foot soaks in 50% propylene glycol. Improvement is expected within a few days. Lifelong maintenance therapy (1-2 times weekly as needed) is often required.
    - Draining lesions can benefit from foot soaks in warm water with added Epsom salts (magnesium sulfate, 30 mL/L) for 10 minutes q 12-24 h, until draining stops.
- Surgery can be considered for some diseases: closure of uncontaminated sharp lacerations, excision of cutaneous horns and other tumors, surgical débridement of devitalized tissues.
- Medication varies depending on underlying cause.

PROGNOSIS AND OUTCOME

Will vary according to the disease; generally good with localized lesions, reversible causes, and dedicated owners, and guarded to poor with systemic illness that is progressive

PEARLS & CONSIDERATIONS

COMMENTS

- Successful therapy is based on identifying the underlying cause.
- Skin biopsies are often needed for the diagnosis of footpad disorders.

PREVENTION

Advise against breeding of animals with hereditary diseases.

SUGGESTED READING

White SD: An approach to pododermatitis. In Foster AP, Foil CS, editors: BSAVA manual of small animal dermatology, ed 2, Gloucester, 2003, British Small Animal Veterinary Association, p 112.

AUTHOR: NADIA PAGÉ

EDITOR: MANON PARADIS

Food Allergy, Gastrointestinal

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Food allergy and food intolerance are repeatable adverse reactions to specific dietary components that respond to exclusion of the causative agent. Food allergy is immune-mediated, whereas food intolerance is not.

SYNONYMS

Dietary/food hypersensitivity, adverse reaction to food

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs and cats
- Reported age 4 months to 14 years; up to 33% of cases in dogs <1 year old

GENETICS & BREED PREDISPOSITION

- Dogs: cocker spaniel, springer spaniel, Labrador retriever, collie, miniature schnauzer, shar-pei, West Highland white terrier, Wheaten terrier, boxer, dachshund, dalmatian, Lhasa apso, German shepherd, and golden retriever at increased risk
- Irish setter, soft-coated Wheaten terrier: familial gluten-sensitive enteropathy
- Cats: Siamese and Siamese-cross

RISK FACTORS

- Increased intestinal permeability (e.g., viral enteritis, inflammatory bowel disease [IBD])
- Immunoglobulin (Ig) A deficiency
- Allergic disease (atopy)

GEOGRAPHY AND SEASONALITY

Usually nonseasonal, as the provocative agent is typically part of the normal diet

ASSOCIATED CONDITIONS & DISORDERS

- Gastrointestinal (GI): antibiotic-responsive enteritis (small-intestinal bacterial overgrowth), IBD, exocrine pancreatic insufficiency, pancreatitis, chronic gastritis, gastroesophageal reflux, lymphangiectasia
- Skin disease: dermatologic food allergy, (see p. 400), atopic dermatitis (see p. 106)

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Vomiting, weight loss, intermittent signs of abdominal pain, soft feces, diarrhea, excessive flatulence, increased frequency of defecation, irritable demeanor, and/or concurrent cutaneous signs
- The allergen(s) typically have been ingested for months to years before signs develop. If an allergen is ingested intermittently, the owner may note an association between ingestion and occurrence of signs.

PHYSICAL EXAM FINDINGS

- Systemic: thin body condition, decreased appetite, weight loss, lethargy, urticaria/angioedema/anaphylaxis
- GI-specific: as above (History), diarrhea
- Skin: pruritus (face, neck, ears, ventral trunk, and feet), otitis externa, urticaria, or angioedema. In cats, self-inflicted alopecia or miliary dermatitis may be observed.
- Allergic conjunctivitis possible

ETIOLOGY AND PATHOPHYSIOLOGY

- Food allergens + altered GI mucosal barrier or poor oral tolerance
- Gliadin in gluten portion of wheat, barley, or rye serves as potent antigen (see online chapter: Gluten-Sensitive Enteropathy)
- Abnormal immunologic response (often IgE mediated)
- Immediate and/or delayed hypersensitivity reaction
- Altered GI structure and function (any level of GI tract from stomach to large intestine)

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Dietary hypersensitivity is diagnosed based on negative results of routine diagnostic tests, GI biopsy results indicating inflammation (if biopsy performed), and positive response to an elimination food trial. An accurate diagnosis depends on ensuring that: (1) an elimination diet is truly novel (complete dietary history elicited by veterinarian and provided by owner, and all ingredients ever ingested are eliminated during the trial), (2) client compliance is optimal, and (3) confounding factors (e.g., treatment with antibiotics or corticosteroids) do not occur concurrently.

DIFFERENTIAL DIAGNOSIS

- Any chronic GI disorder (e.g., lymphangiectasia, IBD, lymphoma, enteritis [bacterial, viral, fungal])
- Dietary indiscretion
- Pancreatic disease (pancreatitis, exocrine pancreatic insufficiency [EPI])
- Liver disease
- Hyperthyroidism (cats)
- Metabolic/endocrine (diabetes mellitus, hypoadrenocorticism, acid/base or electrolyte disturbances)

INITIAL DATABASE

- Dietary history:
    - Thoroughly evaluate the current diet, including regular food, treats, snacks, human food, scraps, flavored medications, and anything else ingested; read all ingredient labels
    - CBC: often unremarkable; mild anemia of chronic disease, increased eosinophils or basophils possible
    - Serum biochemistry profile: nonspecific changes
    - Urinalysis: nonspecific; dogs with chronic inflammatory diseases may have concurrent proteinuria (protein-losing nephropathy)
    - Fecal flotation and smear: rule out parasitism
    - Feline immunodeficiency virus/feline leukemia virus testing in cats
    - Serum T4 thyroid profile: for hyperthyroidism in cats

ADVANCED OR CONFIRMATORY TESTING

- Elimination food trial: diagnostic test of choice; both diagnostic and therapeutic
- Intradermal skin or serum allergen testing (patients with concurrent cutaneous signs); however, both skin and serum tests for specific food allergens are unreliable and do not correlate with results of elimination food trials.
- Abdominal radiography and ultrasonography to rule out other causes of GI disease (e.g., evidence of ob-struction, masses, infiltration, non-GI abdominal lesions); findings usually unremarkable.
- GI endoscopy with biopsies to rule out other structural GI diseases. With food allergy, as with IBD, nonspecific increases in lymphocytes, plasma cells, or eosinophils in the lamina propria are found; confirmation requires favorable response to dietary modification.
- Serum trypsin-like immunoreactivity (to rule out EPI)
- Serum bile acids: hepatopathies; severe GI disease may falsely lower serum bile acid concentrations.

TREATMENT

TREATMENT OVERVIEW

- Control clinical signs; usually achievable solely by eliminating the provocative dietary component(s).
    - Feed a limited number of protein sources (with high digestibility), such as novel protein sources or protein hydrolysate–containing diet.

- Avoidance of wheat, barley, or rye ingredients (gluten-induced enteropathy)
- Long-term control: feed a satisfactory diet not containing the provocative component(s); most owners prefer a commercial diet. Must be sustainable for months to years. Identify treats without the allergen.

NUTRITION/DIET

- Elimination food trial lasting 4 to 8 weeks:
  - Provide a single specific food, ideally with a novel protein (e.g., venison, duck, or other meat not found in foods previously eaten by the pet) and carbohydrate source. Commercial or homemade limited-antigen or hydrolyzed protein diets may be used. Many commercial limited-antigen diets are available; selection is based on patient's current diet and avoidance of known provocative ingredients.
  - *No* other food (or supplements, treats, chewable medications, or other consumables) may be consumed during the trial. Because the problem is immune mediated, even a single violation can reactivate hypersensitivity.
  - Client compliance is essential. Both deliberate (e.g., treats, human foods and snacks, etc.) and inadvertent (e.g., chewable heartworm tablets) violations of the trial must be avoided.
- GI signs typically start to abate within days, and substantial improvement usually occurs within 4 weeks:
  - Although partial improvement is expected within 4 weeks, up to 8 weeks may be needed before significant abatement of clinical signs occurs.
  - Absence of clinical improvement after 8 weeks of strict diet adherence makes food allergy extremely unlikely.
- Skin lesions may take 8 weeks or longer to resolve, although significant improvement is seen within 8 weeks in the vast majority of cases.
- Concurrent treatment with corticosteroids (prednisone, 1-2 mg/kg PO q 24 h, tapering to lowest effective dose and stopping if signs resolve; prednisolone is preferred for cats) is often necessary but will invalidate conclusions if implemented during the trial.
  - If a positive response to the diet is seen, a food challenge is performed to confirm the diagnosis and unambiguously identify the provocative antigen. Additional ingredients are added individually until the signs recur. Clients often are reluctant to do this, but if the patient becomes allergic to the current hypoallergenic diet, there is no way to identify which specific ingredient was allergenic to permit rational choice of an alternative diet.
  - Challenge with the regular food(s) usually results in recrudescence of clinical signs within hours to a few days.
  - Any diet without allergens identified via provocative challenge may be fed, even regular commercial diets.
  - Absence of signs within 14 days of continuous provocative challenge makes any improvement during the trial unlikely to have resulted from diet therapy.

POSSIBLE COMPLICATIONS

- Inappetence, weight loss
- Nutritional-related problems if imbalanced homemade food used
- Intestinal neoplasia (lymphoma) as consequence of chronic GI inflammation

RECOMMENDED MONITORING

If clinical improvement and resolution of clinical signs occur with the trial diet, diagnosis of food sensitivity is confirmed by recurrence of the same clinical signs (provocative challenge) after reintroduction of the original diet (including all treats, snacks, flavored medications, etc.).

PROGNOSIS AND OUTCOME

Good prognosis if offending foods or ingredients are identified and eliminated from the diet

PEARLS & CONSIDERATIONS

COMMENTS

- Food hypersensitivity should be a differential diagnosis in almost all animals presenting with chronic GI signs.
- Although it can be difficult to convince owners to complete a strict food trial for 4-8 weeks, they should be encouraged to do so, as food sensitivity is a “good” disease (i.e., entirely curable by simply changing the diet).
- Using a food diary during the elimination trial helps the owner monitor clinical response and compliance.

TECHNICIAN TIPS

Gradual transition to a new food is critical for a pet with health problems and may be the single most important thing animal caretakers can do to help a pet accept a new food. Mixing more of the new food with less of the old food over a period of at least seven days can make acceptance optimal as a transition into the elimination trial. An alternative method for transitioning, especially for cats, is to offer the new food side by side with the old food in identical dishes, instead of mixing them both in the same dish.

CLIENT EDUCATION

- Human food sources, snacks, treats, and food for other animals (e.g., dog having access to cat food) can be an allergen.
- Provide a handout listing all items the animal may not ingest during the food trial to be read by all household members.
- Contact the owner during the first week of the food trial to check that the elimination diet has been started, provide support, and address any problems that may have arisen (e.g., patient will not eat the food).

SUGGESTED READING

Jackson HA: Hypoallergenic diets: principles in therapy. In Bonagura JD, Twedt DC, editors: Kirk's current veterinary therapy XIV, St Louis, 2009, Saunders, pp 395–397.

Roudebush P, Guilford WG, Jackson HA: Adverse reactions to food. In Hand MS, Thatcher CD, Remillard RL, Roudebush P, Novotny BJ, editors: Small animal clinical nutrition, ed 5, Topeka, KS, 2010, Mark Morris Institute, pp 609–635.

AUTHOR: PHILIP ROUDEBUSH

EDITORS: DEBRA L. ZORAN, KATHRYN E. MICHEL

Food Allergy, Dermatologic

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

A well-recognized, abnormal response to an ingested food or food additive that produces clinical signs affecting the skin, most commonly pruritus

SYNONYMS

The preferred term is *dermatologic adverse food reaction* (DAFR). The terms *food allergy* or *food hypersensitivity* are often incorrectly used synonymously with adverse food reaction. These terms more accurately refer specifically to the subcategory of adverse food reactions that have an immunologic basis. The term *food intolerance*, also encompassed within DAFR, is reserved for the subcategory of adverse food reactions without an immunologic basis and includes metabolic food reactions, food poisoning, food idiosyncrasies, and pharmacologic reactions to food.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs: from 4 months to 14 years:
  - Up to one-third of cases occur in dogs <1 year old.
- Cats: from 6 months to 12 years:
  - 50% develop signs by 2 years

GENETICS & BREED PREDISPOSITION

- Dogs: no strong breed predilection
- Cats: the Siamese cat may be at increased risk.

RISK FACTORS

Risk factors include certain foods or food ingredients, poorly digestible proteins, any disease that increases intestinal mucosal permeability, selective IgA deficiency, age (<1 year), and concurrent allergic disease.

GEOGRAPHY AND SEASONALITY

Nonseasonal

ASSOCIATED CONDITIONS & DISORDERS

- 20%-30% of cases may have concurrent atopic dermatitis or flea allergy dermatitis
- 10%-15% of cases may have concurrent gastrointestinal (GI) signs such as vomiting and/or diarrhea
- Secondary skin infections with bacteria and yeast are common.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- The chief complaint is of nonseasonal pruritus, recurrent pyoderma, or otitis externa.
- There may be a history of a poor response to glucocorticoid therapy.
- Adverse food reactions with an immunologic component (food allergy, food hypersensitivity) usually develop after prolonged exposure to a food allergen, whereas food intolerance may occur after a single exposure, as immune mechanisms are not involved.

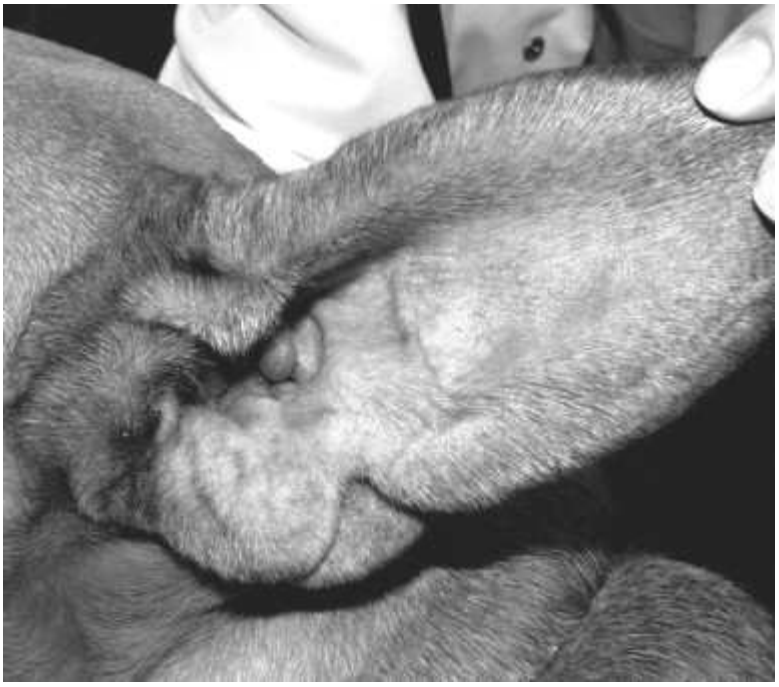
PHYSICAL EXAM FINDINGS

- No specific pattern of skin lesions exists

- Dogs:
  - Lesion distribution: feet, face, axillae, perineal region, inguinal region, rump, and ears.
  - 25% may show only otitis externa
  - Lesions may consist of papules, pustules, wheals, angioedema, erythema, ulcers, excoriations, lichenification, alopecia, scales, crust, acute moist pyotraumatic dermatitis.
- Cats:
  - Lesion distribution: usually centered around the head and neck but may be generalized
  - Manifestations may consist of generalized pruritus without lesions; miliary dermatitis; pruritus with self-trauma centered around the head, neck, and ears; self-induced alopecia; scaling dermatoses; lesions of the eosinophilic granuloma complex; angioedema; urticaria; conjunctivitis.

ETIOLOGY AND PATHOPHYSIOLOGY

- A variety of etiologies are proposed to cause DAFR.
- The majority are attributed to food allergies; however, immunologic tests are rarely performed to confirm this suspicion.
- Common food allergens in dogs include beef, dairy products, wheat, eggs, chicken, lamb, and soy. Common food allergens in cats include beef, dairy products, and fish.
- Food allergies are thought to be the result of primarily a type I hypersensitivity reaction, although type III and IV reactions have also been proposed.
- Several host defenses exist to prevent absorption of intact allergens from the GI tract, including effective digestion, intestinal peristalsis, an intact intestinal mucus layer, tight junctions between mucosal cells, and mucosal IgA. The small amounts of food proteins that do cross the intestinal mucosa activate T-suppressor cells and stimulate an immune response in the gut-associated lymphoid tissue that leads to tolerance. A defect in any of these defense mechanisms may lead to sensitization of the immune system and development of a food allergy.
- Idiosyncratic adverse reactions to food and food additives, such as erythema multiforme, are suspected to occur in animals (unproven).
- Some foods contain products that may directly produce a pharmacologic effect. Scombroid fish such as tuna, mackerel, skipjack, and bonito contain vasoactive amines such as histamine and have been reported to cause adverse reactions in cats and dogs. Cadaverine, another vasoactive amine, may exacerbate adverse food reactions by inhibiting histamine metabolism.



FOOD ALLERGY, DERMATOLOGIC Otitis externa in a dog with food allergy. Extensive erythema of the concave surface of the pinna was present.

FOOD ALLERGY, DERMATOLOGIC Facial erythema and excoriation in a Himalayan cat with food allergy.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The clinical presentation is similar to several other common dermatoses, and the diagnosis can only be confirmed through the completion of a strict elimination diet trial. Concurrent bacterial and yeast infections are common and should be identified and treated. Many differential diagnoses can be identified (and should be sought) prior to determining the need for a diet trial. Note that environmental allergy/atopic dermatitis is a diagnosis of exclusion and cannot be ruled out by testing.

DIFFERENTIAL DIAGNOSIS

- Ectoparasites (*Sarcoptes*, *Demodex*[uncommonly], *Cheyletiella*, *Notoedres*, *Otodectes*, fleas, lice)
- Bacterial folliculitis (*Staphylococcus pseudintermedius*[*S. intermedius* was reclassified in 2007])
- *Malassezia* dermatitis
- Other hypersensitivity disorders (environmental allergens, flea bite, other ectoparasites, intestinal parasite, contact, drug)
- Dermatophytosis (ringworm)
- Cornification disorders
- Behavioral disorders (feline psychogenic alopecia, flank sucking, tail-biting, self-nursing)
- Neoplasia (mast cell tumor, epitheliotropic lymphoma)

INITIAL DATABASE

- Cytologic evaluation: Secondary microbial infections with bacteria and yeast are common. Acetate tape, direct impression smears, and superficial skin scrapings are appropriate methods for obtaining cytologic samples. Ears and interdigital and intertriginous regions are commonly affected. The contribution of a confirmed secondary microbial infection to clinical signs is determined by assessing the patient's response to appropriate antimicrobial therapy.
- Skin scrapings: deep focal skin scrapes should be used for detecting *Demodex canis*, whereas broad superficial scrapes may be more beneficial in detecting *Sarcoptes*, *Cheyletiella*, and *Demodex gatoi*(cats). Note: *Sar-coptes*, *Cheyletiella*, and *D. gatoi*mites may not be detected on all skin scrapings; they require a trial course of appropriate therapy to be fully ruled out when the index of suspicion for infection is high.
- Examination for fleas/flea comb: presence of fleas, flea dirt, or tapeworms raises the index of suspicion for flea allergy dermatitis as a cause of clinical signs, but this entity should be fully ruled out by treatment with an appropriate adulticidal flea control product in patients presenting with pruritic skin disease.
- Elimination diet: only useful test for confirming the diagnosis of DAFR. Current serologic tests correlate poorly with the true offending allergen. The ideal diet should be nutritionally adequate and use a single highly digestible protein source or protein

hydrolysate, avoiding additives and vasoactive amines. The exact protein source is not important, but it should be one to which the animal has not been previously exposed. This diet should be fed exclusively for 8-12 weeks, ensuring that treats, flavored heartworm preventives, table scraps, and any other sources of food are also eliminated from the diet. A significant decrease in pruritus is typically seen within 4-6 weeks, but may take up to 12 weeks. Properly prepared home-cooked diets are an alternative to commercial products, although it may be challenging to ensure they are nutritionally balanced (this requirement may be waived for the duration of the diet trial so long as the patient is full grown, otherwise healthy, and appears to be maintaining body condition).

ADVANCED OR CONFIRMATORY TESTING

Dietary challenge: necessary step to confirm the diagnosis. The original diet is fed back to the animal for 10-14 days. In most cases of true DAFR, there is an exacerbation in pruritus within 3-7 days, but it may take up to 14 days. Once the pruritus is under control again, individual ingredients may be fed for 14 days each to determine which ingredients caused the adverse reaction. In most cases, only 1 or 2 substances are the cause of the adverse reaction.

TREATMENT

TREATMENT OVERVIEW

Treatment consists of the identification and permanent removal of the offending food from the patient's diet. Secondary infections require identification and treatment to achieve full resolution of clinical signs.

ACUTE GENERAL TREATMENT

- Manage any secondary microbial infections with appropriate antimicrobial therapy. A 3-4 week course of cephalexin, 22-30 mg/kg PO q 12 h, is appropriate for most superficial bacterial infections. Topical or oral azole antifungals can be used for *Malassezia*dermatitis.
- Systemic or topical antipruritic therapy, such as oral antihistamines or topical oatmeal-based shampoos, may be necessary initially to control self-trauma. Corticosteroid use should be avoided where possible, as it may mask other conditions and make it more difficult to assess response to the elimination diet trial. In cases of marked pruritus, corticosteroids may be necessary initially (e.g., prednisolone, 0.5-1 mg/kg PO q 24 h × 1-2 weeks maximum, to avoid masking effect of elimination diet).

NUTRITION/DIET

The patient may be maintained on a balanced home-cooked or commercial elimination (hypoallergenic) diet which avoids the offending food, or provocative testing with individual ingredients may be used for determining which dietary components can be tolerated.

PROGNOSIS AND OUTCOME

The prognosis is excellent with avoidance of offending foods.

PEARLS & CONSIDERATIONS

COMMENTS

- The first step when dealing with any suspect DAFR is to make sure other causes of pruritus have been ruled out.
- In some cases, a single elimination trial may be insufficient, and a second elimination trial using an alternative commercial novel protein or hydrolyzed protein source, or a novel-protein home-cooked diet, may be required to see improvement.
- Considering that canine atopic dermatitis is much more prevalent than food allergy, it is important to inform the owner that approximately 70%-80% of dogs will not show appreciable reduction in pruritus during the food trial. Doing so may help avoid owner frustration and ensure better compliance.

TECHNICIAN TIPS

- It is helpful to label the patient's file in a readily identifiable manner so that inappropriate treats or diets are not fed inadvertently if the patient is in hospital.
- Technicians can have an important role in informing/educating clients on the feeding changes and need of strict food intake

during the elimination diet trial in order to ascertain that food allergy is indeed confirmed or ruled out at the end of the trial period. Many owners do not understand that “just one treat” may invalidate the entire process, and hearing this reinforced by the technician can be extremely valuable.

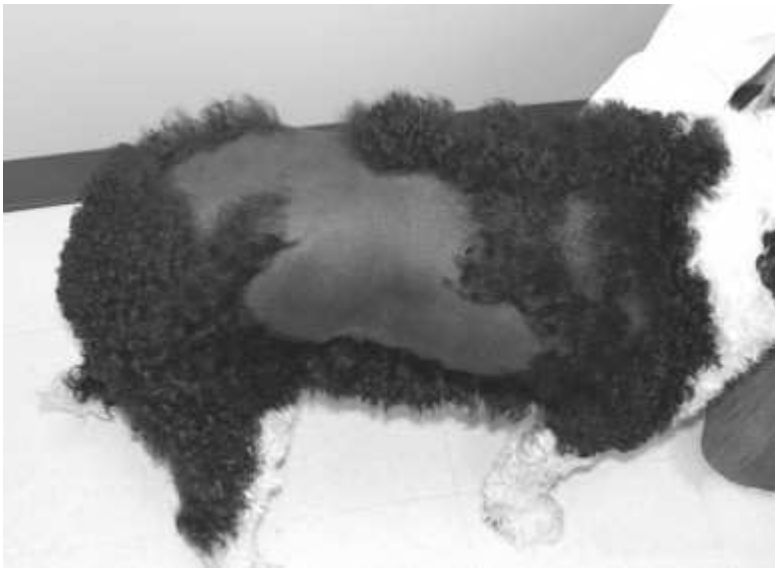
SUGGESTED READING

Jackson HA: Diagnostic techniques in dermatology: the investigation and diagnosis of adverse food reactions in dogs and cats. Clin Tech Small Anim Pract 16:4, 2001.

AUTHOR: ANDREW LOWE

EDITOR: MANON PARADIS

Follicular Dysplasia, Canine



Follicular Dysplasia, Canine Follicular dysplasia in a Portuguese water dog.

BASIC INFORMATION

DEFINITION

Follicular dysplasias are noninflammatory disorders of the haircoat that result in hair loss and altered coat quality. An underlying genetic predisposition for abnormal follicular development has been noted in specific breeds.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- These disorders affect dogs of either sex and any reproductive status.
- Color dilution alopecia (CDA) and black hair follicular dysplasia (BHFD) are disorders of early onset (usually <1 year of age).
- Non–color-linked follicular dysplasias usually start during adulthood.

GENETICS & BREED PREDISPOSITION

- CDA: seen in several breeds with dilute coat colors such as in blue Doberman pinscher, dachshund, Great Dane, Yorkshire terrier, and Chihuahua
- BHFD: recognized in several bi- or tri-colored breeds (e.g., saluki, basset hound) as well as mixed breeds but can also be seen in solid-colored (black) breeds

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Canine recurrent flank alopecia (see p. 966)
- Alopecia X (see p. 58)
- CDA
- BHFD
- Follicular dysplasia of specific breeds (Irish water spaniel, Portuguese water dog, red and black Doberman, Chesapeake Bay retriever, Pont Audemer spaniel dog, etc.)

HISTORY, CHIEF COMPLAINT

Dogs born with a normal haircoat are presented for evaluation of a gradual thinning of the haircoat.

PHYSICAL EXAM FINDINGS

- CDA: progressive alopecia involving exclusively hair follicles in the areas with diluted coat color, usually starting around 6 months of age (light blue) but as late as 2-3 years of age (steel blue Doberman). The rate of hair loss is variable, but most light-colored dogs are almost completely alopecic by 2-3 years of age. These dogs are prone to follicular plugging and secondary recurrent bacterial folliculitis that can aggravate the hair loss and may cause pruritus.
- BHFD: progressive alopecia and excessive scaling, exclusively involving the black-haired areas, seen as early as 4 weeks of age.

ETIOLOGY AND PATHOPHYSIOLOGY

- Follicular dysplasia can be divided histologically into categories in which the hair cycle is abnormal (canine recurrent flank alopecia, alopecia X) and those in which there are abnormalities in the process of melanization of the pilosebaceous units (CDA, BHFD).
- All known forms of follicular dysplasia appear to be genetically determined.
- In CDA, an inherited autosomal recessive disorder of melanosome transportation has been demonstrated.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is based on history, clinical findings, and ruling out other differentials. A diagnosis of follicular dysplasia is suspected based on breed predilection and in some cases an early onset of color-linked alopecia (CDA, BHFD).

DIFFERENTIAL DIAGNOSIS

- Endocrinopathies (hypothyroidism, hyperadrenocorticism, hyperestrogenism)
- Infectious process (pyoderma, demodicosis, dermatophytosis) in some clinical presentations

INITIAL DATABASE

- Trichogram: large melanin clumps along the hair shaft, causing distortion and fracture of the hair in CDA and BHFD

ADVANCED OR CONFIRMATORY TESTING

Skin biopsy and dermatohistopathologic evaluation: dilated and cystic hair follicles with melanin clumping in follicular basal cells, hair bulbs, hair shafts, follicular lumen in CDA and BHFD.

TREATMENT

TREATMENT OVERVIEW

The main goals are to attempt hair regrowth and control secondary bacterial folliculitis, seen commonly in CDA.

GENERAL TREATMENT

Anecdotal evidence exists for the efficacy of melatonin at 3-6 mg/dog PO q 8-12 h for 1-2 months to stimulate hair growth reported in CDA.

PROGNOSIS AND OUTCOME

- These entities are incurable, genetically based dermatoses.
- Affected dogs are healthy otherwise, with the exception of secondary pyoderma in CDA.

PEARLS & CONSIDERATIONS

COMMENTS

- The early onset, color link (CDA, BHFD), and/or breed predisposition make the diagnosis straightforward in many cases.
- The main impact of these disorders is cosmetic rather than medical, unless secondary infection or sunburn occurs.

SUGGESTED READING

Cerundolo R, Paradis M, Mecklenburg: Breed specific hair-cycle abnormalities. In Mecklenburg L, Linek M, Tobin DJ, editors: Hair loss disorders in domestic animals, Ames, Iowa, 2009, Wiley-Blackwell, pp 169–175.

Paradis M, Cerundolo R: An approach to symmetrical alopecia in the dog. In Foster A, Foil C, editors: BSAVA manual of small animal dermatology, ed 2, Gloucester, UK, 2003, British Small Animal Veterinary Association, pp 83–93.

AUTHOR & EDITOR: MANON PARADIS

Flea Bite Allergy

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Development of hypersensitivity reaction(s) and subsequent skin lesions accompanied by variable pruritus in response to exposure to flea salivary antigens. Very common in flea-endemic regions. Must be differentiated from flea infestation alone, where fleas are present on the animal or in the environment, but the animal does not develop clinical signs of skin disease.

SYNONYMS

Flea allergy dermatitis (FAD), flea bite hypersensitivity

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs: develops at any age but is most common in 3- to 5-year-olds and uncommon if <6 months old
- Cats: no age predilection reported

GENETICS & BREED PREDISPOSITION

- Dogs: breed predilections not well established
- Cats: no breed predilections reported

RISK FACTORS

- Genetic predisposition to develop allergic dermatitis
- Dogs: intermittent flea exposure
- Cats: persistent flea exposure
- Atopic patients are at greater risk for flea bite allergy.

GEOGRAPHY AND SEASONALITY

- Diagnosed worldwide wherever fleas reside
- Seasonal in climates with cold winters
- Continuous in warm, humid climates
- Nonseasonal when indoor infestation is present

ASSOCIATED CONDITIONS & DISORDERS

- Infestation with *Dipylidium caninum*
- Gastric trichobezoars (hairballs) associated with excessive grooming
- Secondary bacterial pyoderma

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Canine flea bite allergy:
  - Pruritic papular dermatitis
  - Acute moist dermatitis (“hot spot”)
  - Fibropruritic nodules in chronic cases
- Feline flea bite allergy:
  - Pruritic papulocrustous dermatitis (“miliary dermatitis”)
  - Symmetric self-induced alopecia
  - Eosinophilic granuloma complex

HISTORY, CHIEF COMPLAINT

- Dogs: acute onset of moderate-severe pruritus. Hair loss and malodor in longer-standing cases. Clients may report live fleas on their pet or experience flea bites themselves.
- Cats: hair loss, pruritus, excessive grooming, vomiting hairballs, or small crusted papules noted under the haircoat. Lip ulcers, raised plaques, or granulomas may be noted. Fleas are less commonly observed than in dogs.

PHYSICAL EXAM FINDINGS

Dogs:

- Papulocrustous lesions, varying degrees of alopecia, erythema, and excoriations. Most commonly affected regions: dorsal lumbosacral region, tailhead, and caudomedial thighs. Ventral abdomen, especially near the umbilical area, flanks, and neck may also be affected.
- Well-demarcated, moist, erythematous, exudative skin lesions with alopecia
- Lichenification, lattice pattern hyper-pigmentation, scaling
- Poor body condition, weight loss, worn incisor teeth
- ± Fleas, flea excreta (“flea dirt”)

Cats:

- Self-inflicted symmetrical hair loss on the ventral abdomen, lateral flanks, and caudomedial thighs
- Erythematous crusted papules around the neck and on the lumbosacral region (miliary dermatitis)
- Lesions consistent with eosinophilic granuloma complex (indolent ulcer, eosinophilic plaque, eosinophilic granuloma)
- Excoriations, crusts
- Weight loss, poor body condition, peripheral lymphadenopathy
- ± Fleas, flea excreta (“flea dirt”)

ETIOLOGY AND PATHOPHYSIOLOGY

- Repeated exposure to flea salivary antigens induces development of various hypersensitivity reactions (see p. 1399):
  - Type I (immediate/anaphylactic) hypersensitivity (dogs, cats)
  - Cutaneous basophil hypersensitivity (dogs)
  - Type IV (delayed/cell-mediated) hypersensitivity (dogs, cats)
  - Late-phase IgE-mediated reactions (dogs)
- Hypersensitivity reactions, when recurrent or persistent, may become more intense and be triggered with progressively less antigen (flea saliva).

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

The diagnosis of flea bite allergy is based almost entirely on history and physical exam findings. Even in the absence of live fleas or flea excreta, physical signs as described warrant empirical antiflea treatment before or while pursuing advanced diagnostic testing for other causes of pruritus.

DIFFERENTIAL DIAGNOSIS

- Dogs, cats:
  - Other hypersensitivities (atopic dermatitis, foods, intestinal parasites, drugs)
  - Ectoparasitic dermatoses
  - Bacterial folliculitis
- Dogs:
  - *Malassezia* dermatitis
- Cats:
  - Dermatophytosis
  - Anal sac disease (excessive grooming of ventral abdomen, lateral flanks and caudomedial thighs)

INITIAL DATABASE

- History
- Physical examination findings

- ± Observation of fleas, excreta

ADVANCED OR CONFIRMATORY TESTING

- Intradermal testing with 1 : 1000 w/v aqueous solution of whole flea antigen
- ELISA serologic allergen screening for flea saliva antigens
- Response to flea eradication—considered by many to be most definitive

TREATMENT

TREATMENT OVERVIEW

In flea infestation, the goals of treatment are focused on eradication of the flea population from the animal and its environment (i.e., integrated flea management). In flea bite allergy, the goals of treatment also include providing rapid relief of the clinical signs and discomfort.

ACUTE GENERAL TREATMENT

- Corticosteroids:
  - Dogs: prednisone/prednisolone, 1 mg/kg PO daily for 5-7 days, then taper; may also use 0.0584% hydrocortisone acetonate spray topically once daily as monotherapy or in addition to oral predniso(lo)ne
  - Cats: prednisolone, 2.2 mg/kg PO daily for 5-7 days, then taper. If daily oral drug administration is not possible, may substitute methylprednisolone injectable, 5 mg/kg or 20 mg per cat IM or SQ; however, multiple risks with use (diabetes mellitus, iatrogenic hyperadrenocorticism, iatrogenic congestive heart failure, etc.)
- Topical flea adulticide: several options
  - Permethrin sprays/spot applications (Active-3)
  - Imidacloprid (Advantage)
  - Fipronil (Frontline)
  - Selamectin (Revolution)
  - Dinotefuran, permethrin, pyriproxyfen (Vectra) for dogs, without permethrin for cats
  - Metaflumizone, amitraz (ProMeris) for dogs, without amitraz for cats
- Oral flea adulticide
  - Nitenpyram (Capstar)
  - Spinosad (Comfortis) for dogs
- Specific therapy of any secondary infections

CHRONIC TREATMENT

Integrated flea management: essential for eradication of the problem

- Ongoing use of topical flea adulticide
- Insect growth regulators: methoprene, pyriproxyfen, others. Note: some products are formulated for spraying the patient; others are for treating the environment.
- Insect development inhibitors: lufenuron (Program) oral, monthly
- Environmental control
  - Identify “point sources” of infestation.
  - Cleaning or frequent vacuuming
  - Organic debris removal outdoors
  - Use of an approved insect growth regulator premise spray
- Immunotherapy is experimental at this time.

POSSIBLE COMPLICATIONS

- Neurotoxicosis with the use of pyrethrins, permethrins in cats
- Diabetes mellitus, iatrogenic hyperadrenocorticism (glucocorticoids, especially sustained-release injections)

RECOMMENDED MONITORING

Routine flea combing

PROGNOSIS AND OUTCOME

Good with long-term management

PEARLS & CONSIDERATIONS

COMMENTS

- Clients may not recognize excessive grooming as a manifestation of pruritus.
- Trichograms (microscopic examination of hair plucks) confirm self-induced alopecia: broken ends of hair shafts.
- Excessive grooming decreases live flea population.

PREVENTION

- Avoidance of flea bites prevents disease recurrence in flea-allergic patients.
- Continued integrated flea control is mandatory.

CLIENT EDUCATION

- Progressive disease unless fleas are eradicated
- Preventable, not curable, disease
- Treatment of all in-contact pets is mandatory.

TECHNICIAN TIPS

- Clients are frequently in denial, and compliance with a treatment plan may be poor.
- Challenge the clients to follow through with the treatment plan and “disprove” the diagnosis.

SUGGESTED READING

Bevier DE: Flea allergy dermatitis. In Campbell KL, editor: Small animal dermatology secrets, Philadelphia, 2004, Hanley & Belfus, pp 208–213.

AUTHOR: STEPHANIE R. BRUNER

EDITOR: MANON PARADIS

Flatulence and Borborygmi

BASIC INFORMATION

DEFINITION

- Flatulence is the excessive formation of gas in the stomach or intestine, which is expelled via the anus.
- Borborygmus is the rumbling noise caused by the propulsion of gas through the intestine.

EPIDEMIOLOGY

SPECIES, AGE, SEX: More prevalent in dogs than cats

GENETICS & BREED PREDISPOSITION

- Borborygmus more prevalent in brachycephalic breeds and working/sporting dogs because of increased aerophagia
- Cats with flatulence will generally have underlying gastrointestinal (GI) tract disease: inflammatory bowel disease, food sensitivity

RISK FACTORS

- Diets high in nonabsorbable oligosaccharides, carbohydrates, fiber or poorly digestible protein
- GI tract disease
- Low activity or exercise level

ASSOCIATED CONDITIONS & DISORDERS: GI tract disease in dogs and especially cats

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Owner may describe flatulence, belching, borborygmus or abdominal distension.
- May be associated with other signs of GI disease: vomiting, diarrhea, weight loss

PHYSICAL EXAM FINDINGS

- Generally unremarkable
- Palpation of gas in the intestines is not in itself an abnormal finding.
- Mild abdominal discomfort may be caused from intestinal distension. If excessive, fermentation may be associated with severe distension of the GI tract and signs of colic and shock.

ETIOLOGY AND PATHOPHYSIOLOGY

- Gas occurs naturally in the GI tract and is caused by:
  - Aerophagia (the major cause: 17 mL of air accompanies 10 mL of swallowed water in humans).
  - Interaction of gastric acid and alkaline food
  - Diffusion from the bloodstream
  - Bacterial metabolism and fermentation, especially in the colon
- Gas is removed from the GI tract by passage through the esophagus (belching) or anus (flatus), diffusion into the blood, or utilization by bacteria. Intestinal transit time for gas is 15-35 minutes.
- Aerophagia and fermentation of dietary carbohydrates are major contributors to natural intestinal gas volume, of which 99% is odorless. The foul odor is caused by sulfur-containing gases that originate from bacterial metabolism of endogenous substances (mucin, bile acids) and dietary sources (onions, nuts, spices, cruciferous vegetables). Additional sources are ammonia, amines, indoles and phenols, originating mainly from dietary protein.
- Causes of excessive GI gas:
  - Excessive aerophagia: brachycephalic breeds, vigorous exercise, competitive eating habits
  - Excessive bacterial fermentation: dietary substances—nonabsorbable oligosaccharides such as soy beans, legumes, rapidly fermentable fibers [pectin]
  - Gastrointestinal disease: maldigestion and malabsorption—large amounts of malassimilated substances are available

for fermentation, especially with lactose-containing foods, as lactase is lost with adulthood. Adult dogs are lactose intolerant.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A common disorder which is of no clinical significance unless associated with other GI tract signs

DIFFERENTIAL DIAGNOSIS

Abdominal distension (organomegaly, ascites)

INITIAL DATABASE

Laboratory testing is required only if additional GI signs are also present.

TREATMENT

TREATMENT OVERVIEW

Management is generally aimed at long-term modification of the dietary and exercise regimen of the dog. Aim: decrease the amount of gas passed, reduce the odor, encourage passage of gas outdoors while exercising, and finally, prescription of carminatives.

ACUTE GENERAL TREATMENT

If very severe gas accumulation occurs secondary to excessive intake of a fermentable substance, emergency decompression, pain control, and shock therapy may be indicated.

CHRONIC TREATMENT

- The condition is controlled using long-term management strategies affecting diet, feeding habits, and exercise.
- Treat any underlying GI tract disease.
- Surgically correct upper airway stenoses in brachycephalic dogs.
- Use of carminatives (preparations decreasing flatulence) should only be considered after surgical, dietary, and behavioral interventions are unsuccessful.
- Ingestion of activated charcoal has not been proven successful in humans.
- Bismuth subsalicylate has antibacterial and antiendotoxic properties. The efficacy is dose dependent, which needs to be frequent. High doses are contraindicated in cats.
- Zinc acetate, 1% of diet, reduces the malodor of flatus.
- Simethicone, an antifoaming agent has no effect.
- A combination of activated charcoal, zinc acetate, and *Yucca schidigera* showed a significant decrease in flatus.

NUTRITION/DIET

- Decrease intake of substances causing odiferous gas production.
    - Decrease and change dietary protein levels and sources.
    - Eliminate supplements and treats.
    - Avoid cruciferous vegetables.
    - Avoid canned foods containing carrageenan (an algal-based thickening agent).
- Decrease the volume of intestinal gas production.
- Diet must be highly digestible, thus limiting substances supporting bacterial fermentation.
- Avoid foods containing legumes, dairy products, and fruit.
- Use rice as the main carbohydrate source, although this does have a high glycemic index.

BEHAVIOR/EXERCISE

- Control aerophagia.
    - Feed at least twice a day.
    - Discourage rapid, competitive feeding.

- Increase exercise/activity.
    - Exercise dogs within 30 minutes of meals to encourage defecation and elimination of gas.
    - Active outdoor dogs have been shown to exhibit less flatulence while with the owners.

DRUG INTERACTIONS

Activated charcoal can alter the absorption of concurrently administered medication.

RECOMMENDED MONITORING

- Progression of clinical signs may warrant an evaluation for GI disease.
- Intermittent relapses usually indicate dietary indiscretion.

PROGNOSIS AND OUTCOME

Prognosis for control is good in most cases.

PEARLS & CONSIDERATIONS

COMMENTS

“After trying empirical therapy for pets with chronic flatulence, sound advice for the client is to always stand upwind of the patient and keep windows open.” (Roudebush, Lorenz)

SUGGESTED READING

Giffard C, et al: Administration of charcoal, *Yucca schidigera*, and zinc acetate to reduce malodorous flatulence in dogs. J Am Vet Med Assoc 218(6):892, 2001.

AUTHOR: LIESEL VAN DER MERWE

EDITOR: ETIENNE CÔTÉ

Flail Chest

BASIC INFORMATION

DEFINITION

Two or more adjacent rib fractures at two or more sites on each rib. The fractures result in chest wall segment instability and therefore in asynchronous chest wall movement during respiration.

SYNONYMS

Flail segment, multiple rib fractures

EPIDEMIOLOGY

SPECIES, AGE, SEX: Young male animals that roam are at increased risk for trauma.

RISK FACTORS: Unmonitored activity

ASSOCIATED CONDITIONS & DISORDERS

- Pulmonary contusions
- Diaphragmatic hernia
- Pneumothorax
- Hemothorax

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Trauma
  - Hit by car
  - Bite wound
- Increased respiratory rate and effort
- External thoracic skin wounds

PHYSICAL EXAM FINDINGS

- Increased respiratory rate and effort
- Paradoxical movement of the flail segment during respiration: pathognomonic
  - Flail segment moves inward during inspiration and outward during expiration.
- Concurrent injuries are common:
  - Skin lacerations
  - Other fractures

ETIOLOGY AND PATHOPHYSIOLOGY

- Trauma results in two or more fractures per rib on two or more adjacent ribs.
- Hypoxemia due to abnormal pulmonary airflow (traditional model). Air from the lung in proximity to the flail chest segment flows to the opposite lung during inspiration and then back to the lung in proximity to the flail chest during expiration. This abnormal airflow provides no effective contribution to ventilation and is essentially an increase in dead space.
- Recent evidence indicates that hypoxemia and respiratory distress arise primarily from pulmonary contusions associated with pneumothorax and not from abnormal airflow.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Flail chest is first suspected in any patient with thoracic trauma. Confirmation is on physical exam: observation of the paradoxical movement of the flail segment is diagnostic.

DIFFERENTIAL DIAGNOSIS

- Pathologic rib fractures due to neoplasia or osteomyelitis (very rare)
- Increased work of breathing leading to rib fractures (chronic bronchitis/asthma; also uncommon)

INITIAL DATABASE

- Thoracic radiographs:
  - Lateral and dorsoventral (much less stressful to the patient than ventrodorsal) views required, as fractures may be apparent on only one view
  - If respiratory distress is severe, horizontal beam technique may be preferable (less restraint of patient, recumbency not necessary); alternatively radiographs may be delayed until the patient is more stable.
- CBC, serum chemistry panel, urinalysis: generally unremarkable unless abdominal organs affected or preexisting illness

ADVANCED OR CONFIRMATORY TESTING

Arterial blood gas analysis:

- May help confirm a clinical suspicion of hypoxemia
- Serial analysis may be useful to monitor trends.
- Hypoxemia (Pao2 < 80 mm Hg) is common, warranting oxygen supplementation (see p. 1318).
- In severe cases, hypoventilation may develop (Pco2 > 50 mm Hg).

TREATMENT

TREATMENT OVERVIEW

Therapeutic goals are to:

- Normalize oxygenation and control pain.
- Provide surgical stabilization if required (rare).

ACUTE GENERAL TREATMENT

- Pain control is essential; hypoventilation otherwise contributes to decreased blood oxygenation.
- Local nerve blocks, systemic opioids (e.g., hydromorphone, 0.05-0.1 mg/kg IV q 4-6 h, or buprenorphine 0.005-0.02 mg/kg IV, SQ, or IM) and nonsteroidal antiinflammatory drugs (e.g., carprofen, 2-3 mg/kg PO or SQ q 12 h) may be used.
- Oxygen supplementation often necessary (nasal oxygen, oxygen mask, oxygen cage; see p. 1318)
- Pneumothorax management (see p. 889):
  - Intensity of treatment determined mainly by degree of patient distress
  - Treatment options, in increasing order of intensity, include: monitoring only, oxygen supplementation, thoracocentesis (see p. 1338), chest tube placement (see p. 1230), and thoracotomy (if large segments of rib are perforating the lung).
- Mechanical ventilation (see p. 1362) may be necessary with patients unresponsive to oxygen supplementation:
  - Response to oxygen supplementation is best assessed clinically by evaluating patient respiratory rate and effort.
  - However, pulse oximetry reading < 88%-90% or an arterial blood gas oxygen level (Pao^2) < 60 mm Hg with supplemental oxygen is an indication for mechanical ventilation.
- Surgery is rarely required:
  - Flail chest segments resulting from bite wounds may be stabilized when the bite wounds are repaired.
- Chest wraps are unlikely to be of benefit and may be detrimental.

POSSIBLE COMPLICATIONS

- Hypoventilation associated with pain
- Pneumothorax associated with rib segments piercing lung parenchyma

RECOMMENDED MONITORING

- Electrocardiogram if cardiac arrhythmias occur
- Monitor respiratory rate and effort closely; use this information to guide decisions regarding oxygen supplementation, thoracocentesis, or chest tube placement.
- Signs of pain may include restlessness, tachycardia, anorexia, and excessive vocalization.

PROGNOSIS AND OUTCOME

Good with adequate supportive care and if no other concurrent traumatic injuries

PEARLS & CONSIDERATIONS

COMMENTS

Hypoxemia surrounding flail chest more commonly reflects the underlying pulmonary contusion rather than chest wall instability.

PREVENTION

- Keep animals indoors and confined to a leash.
- Neutering may prevent roaming behavior.

CLIENT EDUCATION

Don't let animals roam; monitor dog-dog interactions.

SUGGESTED READING

Olsen D, et al: Clinical management of flail chest in dogs and cats: a retrospective study of 24-cases (1989-1999). J Am Anim Hosp Assoc 38:315–320, 2002.

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EDITOR: ELIZABETH ROZANSKI

Fibrosarcoma

BASIC INFORMATION

DEFINITION

A common primary, malignant neoplasm of fibrous tissue. Fibrosarcoma is most common in the skin, subcutaneous tissue, and the oral cavity but can occur anywhere, including the spleen.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Fibrosarcomas are more common in middle-aged to older dogs and cats. Injection-site sarcomas have many similarities and are discussed separately (see p. 610).

GENETICS & BREED PREDISPOSITION: Genetic factors are not well defined in dogs or cats.

RISK FACTORS: Prior irradiation and metal implants have been implicated as a cause for fibrosarcomas. There are cases of a fibrosarcoma in cats developing at sites of microchips and surgical sponges.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- The most common form of fibrosarcoma in dogs is a solitary mass, typically found on the head, limbs, or oral cavity.
- Sarcomas that are histologically low grade but biologically high grade (malignant behavior) are an uncommon variant of fibrosarcoma found in the maxilla and mandible in large-breed dogs.

HISTORY, CHIEF COMPLAINT: Most animals present for a progressive mass noticed by the owner or clinical signs related to the location of the tumor (e.g., oral and splenic tumors).

PHYSICAL EXAM FINDINGS

- Fibrosarcoma often appears as a firm, palpable mass in the subcutaneous or deep tissues; occasionally hairless or ulcerated. Oral fibrosarcomas often appear as smooth, round masses. On the hard palate, fibrosarcomas are frequently a flat and ulcerated.
- Regional lymphadenomegaly may be present secondary to inflammation or (rarely) lymph node metastasis.
- Dogs with a splenic fibrosarcoma may present with abdominal mass, pain, or enlargement.

ETIOLOGY AND PATHOPHYSIOLOGY

- Fibrosarcomas are spontaneously occurring tumors in most cases in dogs.
- Specific dysfunction caused by fibro-sarcomas depends on the location of the primary tumor.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Definitive diagnosis can only be confirmed via histopathology although additional tests such as diagnostic imaging are often helpful in defining the extent of the tumor, especially for oral fibrosarcomas.

DIFFERENTIAL DIAGNOSIS

- Other soft-tissue sarcomas
- Other skin and subcutaneous tumors:
  - Mast cell tumors, etc.
- Other oral tumors (epulis, melanoma, squamous cell carcinoma)
- Benign or nonneoplastic masses:
  - Benign tumor (e.g., lipoma)

- Abscess

INITIAL DATABASE

- Fine-needle aspiration and cytologic evaluation may help identify the tumor type before other diagnostics.
- Three-view thoracic radiographs to rule out pulmonary metastases
- Radiographs of the affected area may reveal involvement of underlying bone.
- Abdominal ultrasound to identify splenic tumors and rule out metastasis
- Fine needle aspiration and cytologic examination of the regional/draining lymph node to assess for metastasis.

ADVANCED OR CONFIRMATORY TESTING

- Biopsy of mass:
  - The definitive diagnosis of fibrosarcoma is based on histopathologic evaluation of tumor tissue.
  - Special immunohistochemical stains may be necessary to differentiate fibrosarcoma from other soft-tissue sarcomas, especially poorly differentiated tumors.
- CT or MRI may be necessary to delineate the local extent of the tumor and to plan for surgery or radiation therapy.
- Histopathologic grade of the tumor is necessary for determining the prognosis and treatment of most soft-tissue sarcomas (see p. 1034).

TREATMENT

TREATMENT OVERVIEW

Definitive treatment is based on complete eradication of the primary tumor whenever possible. Since metastasis of this type of tumor is uncommon, additional treatment such as chemotherapy is rarely used but could be considered for high-grade tumors or tumors that have already metastasized. Palliative treatment options, such as palliative radiation, may help control pain or discomfort in patients with advanced tumors or in patients where definitive treatment cannot be tolerated.

ACUTE AND CHRONIC TREATMENT

- Aggressive surgical resection, radiation therapy, and/or chemotherapy may be used for treatment of fibrosarcoma (see for specific details).
- Chemotherapy may be indicated for tumors of the spleen or high-grade tumors (see p. 1034).

POSSIBLE COMPLICATIONS

Complications of treatment for fibrosarcomas depend on the types of treatments and the location of the primary tumor (see p. 1034).

RECOMMENDED MONITORING

After appropriate local treatment, follow-up examination should be done on a routine basis to monitor for recurrence and metastasis. High-grade tumors may require more frequent monitoring for metastases during and after chemotherapy administration.

- Dogs that are likely to develop metastasis (splenic tumors, high-grade tumors) should be monitored closely (every 2-3 months) with physical exam, lymph node palpation, and thoracic radiographs.
- Dogs with low- or intermediate-grade tumors that have adequate local treatment should have physical examinations every 2-3 months or more frequently depending on risk of side effects from treatment. Thoracic radiographs could be done less frequently (6 months and 1 year after therapy).

PROGNOSIS AND OUTCOME

- A combination of radiation therapy and surgery has resulted in long-term tumor control in 86% of dogs with fibrosarcoma in peripheral sites and 54% of fibrosarcomas from all sites including the oral cavity.
- Radiation alone has resulted in 1-year tumor control rates of 33% and therefore is not typically recommended for fibrosarcomas. However, this statistic may underestimate efficacy, as it is derived from studies that used suboptimal radiation dose schedules.
- In certain situations where surgery is not indicated (e.g., nonresectable tumors or metastatic disease), radiation may be used to provide some degree of tumor control.
- Prognosis is excellent for low- to intermediate-grade fibrosarcomas with appropriate local treatment. This includes either

surgical resection with clean histopathologic margins or incomplete resection combined with radiation therapy.
- Information is limited regarding prognosis for high-grade fibrosarcomas, but it is considered to be guarded based on the increased likelihood for metastases.
- Dogs with splenic fibrosarcomas are more likely to develop metastases and therefore have a poor prognosis.

PEARLS & CONSIDERATIONS 

COMMENTS

Many animals with fibrosarcoma are successfully treated with wide surgical excision of the tumor. Animals with tumors that are difficult to treat in this manner (oral sarcomas, grade 3 sarcomas, nonresectable tumors, etc.) should be referred for consultation with a specialist (surgeon, oncologist, or radiation oncologist) to develop a multimodality treatment approach.

CLIENT EDUCATION

Pet owners can be educated to monitor their pets for the occurrence of tissue masses such as fibrosarcomas. Early detection and treatment may allow for less aggressive treatments with fewer side effects.

SUGGESTED READING

Liptak JM, Forrest LJ: Soft tissue sarcomas. In Withrow SJ, Vail DM, editors: Small animal clinical oncology, Philadelphia, 2007, WB Saunders, pp 425–454.

AUTHOR: JOHN FARRELLY

EDITOR: KENNETH M. RASSNICK

Fibrocartilaginous Embolism

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Fibrocartilaginous embolism (FCE) is a syndrome of acute spinal cord, and rarely brainstem, infarction and subsequent necrosis secondary to embolization of arterial and/or venous vasculature within the central nervous system. Although it is unconfirmed at this time, it is suspected that the embolus originates from the nucleus pulposus of the intervertebral disk.

SYNONYMS

Fibrocartilaginous embolic encephalomyelopathy, fibrocartilaginous embolic myelopathy, ischemic myelopathy

EPIDEMIOLOGY

SPECIES, AGE, SEX: FCE has been described in dogs, cats, horses, pigs, sheep, turkeys, cattle, and humans. Male dogs may be at higher risk than females, and middle-aged dogs (3-6 years) are most commonly affected.

GENETICS & BREED PREDISPOSITION: FCE most commonly affects nonchondrodystrophoid, large to giant breeds of dogs. Breeds at risk include Labrador retrievers, German shepherds, golden retrievers, Great Danes, and Doberman pinschers. Miniature schnauzers and Shetland sheepdogs can also be affected. FCE has not been reported in chondrodystrophoid breeds with intervertebral disk disease, though it has been reported in chondrodystrophic breeds.

RISK FACTORS: There may be a history of mild trauma and/or vigorous exercise before the onset of clinical signs of FCE.

ASSOCIATED CONDITIONS & DISORDERS: Concurrent Hansen type II intervertebral disk disease (fibroid degeneration of the nucleus pulposus) may be present in the affected animal.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Dogs with FCE will present with neurologic deficits that reflect the severity of the infarction and ischemia, as well as the location of the lesion within the central nervous system. The onset of FCE is peracute to acute, and clinical signs generally stabilize within 24 hours, after which the disease is often nonprogressive. This disease is nonpainful, although the affected dog may yelp or cry out at the onset of signs.

PHYSICAL EXAM FINDINGS

- The patient's neurologic deficits depend on the level of spinal cord affected, and clinical findings are consistent with a focal myelopathy.
- If the brachial plexus or lumbosacral intumescence is involved, lower motor neuron signs will predominate; if the C1-C5 or T3-L3 segments are involved, upper motor neuron signs will prevail.
- Nociception and proprioception may also be affected.
- Brainstem involvement can occur, in which case cranial nerve deficits, change in the level of consciousness, and/or cardiorespiratory difficulty may be seen.
- Spinal hyperesthesia is not a consistent finding.
- FCE is often lateralizing and should be suspected in a patient with the peracute to acute onset of nonpainful, nonprogressive, lateralizing/asymmetric focal myelopathy.

ETIOLOGY AND PATHOPHYSIOLOGY

- FCE is thought to affect large, non-chondrodystrophoid dogs because their nucleus pulposus remains soft and gelatinous longer relative to chondrodystrophoid dogs and can extrude along tears or fissures in the annulus fibrosus. Histopathologically, the nature of the embolus is similar to that of the nucleus pulposus of the intervertebral disk. Several theories have been proposed to explain the presence of disk material in the vasculature:
  - Chronic inflammation (e.g., type II intervertebral disk disease) may induce neovascularization of the intervertebral disk. With increased intradiskal pressure, the nucleus pulposus could extrude into this arterial system and into the radicular artery.
  - Embryonic vasculature of the annulus fibrosus may persist, and the nucleus pulposus could herniate into this arterial system with an increase in intradiskal pressure.

- The fibrocartilaginous material could extrude directly into an artery (radicular, vertebral, or ventral spinal). However, these arteries have thick, muscular walls, and one would expect to see evidence of hemorrhage if such damage occurred (hemorrhage has not been documented consistently on postmortem examination of dogs with FCE).
- The disk material could herniate into the vertebral venous sinuses and enter the arterial system in a retrograde manner, induced by a Valsalva maneuver (trauma, exercise, coughing, straining) in which increased intraabdominal pressure would induce retrograde blood flow, despite the presence of valves in the radicular veins.

- Another theory postulates that the source of the fibrocartilage is endothelial metaplasia.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Clinically, this is generally a diagnosis of exclusion that is reached based on history, clinical presentation, and the exclusion of other disorders. Characteristic MRI findings for fibrocartilaginous embolism also support the diagnosis.

DIFFERENTIAL DIAGNOSIS

- Other causes of embolism:
  - Sepsis
  - Leukemia
  - Polycythemia
  - *Dirofilaria immitis* microfilaria
  - Hyperviscosity or hyperlipidemia
  - Fat embolism
- Nonpainful myelopathies
  - Intramedullary neoplasia
  - Focal myelitis
  - Intramedullary hemorrhage
- Painful myelopathies
  - Intervertebral disk disease
  - Spinal trauma
  - Extradural or intradural, extramedullary neoplasia
  - Diskospondylitis
  - Vertebral osteomyelitis

INITIAL DATABASE

- CBC, serum biochemistry profile, and urinalysis: results usually within normal limits
- Survey radiographs will usually be within normal limits.

ADVANCED OR CONFIRMATORY TESTING

- Cerebrospinal fluid (CSF) analysis may be within normal limits, or it may reveal mild, nonspecific changes, including pleocytosis and increased protein content, inflammatory changes which may be associated with secondary spinal cord necrosis (myelomalacia). CSF analysis is not sufficiently sensitive or specific for the diagnosis of FCE, but it can be useful to rule out other causes of focal myelopathy.
- Myelography may be within normal limits, or it may reveal focal intramedullary swelling. This can be useful to rule out causes of myelopathy that produce spinal cord compression (e.g., IVDD).
- MRI is the imaging modality of choice in FCE. Initially, evidence of intramedullary spinal cord ischemia and swelling may be seen (hyperintense signal on T2-weighted images, and hypo-or isointense signal on T1-weighted images. Later, the findings may be consistent with ischemia, with increased intensity noted at the infarcted level on T2-weighted images. Recent studies have shown that the addition of the gradient echo sequence in multiple planes may increase the MRI sensitivity of detecting intraparenchymal spinal cord changes.

TREATMENT

TREATMENT OVERVIEW

Treatment consists of supportive care and physical rehabilitation, as there is no definitive treatment for FCE.

ACUTE GENERAL TREATMENT

- Because FCE is not a compressive lesion, surgical decompression is not indicated. In addition, because the fibrocartilaginous material occludes microscopic blood vessels, surgical removal of the embolus should not be attempted.
- The embolus is composed of fibrocartilaginous material and not blood; thus attempts at medical dissolution with fibrinolytic therapy are unsuccessful.
- Good nursing care is crucial. For patients with urinary incontinence, it is important to prevent an atonic urinary bladder; bladder expression or catheterization is necessary. In addition, patients with urinary and/or fecal incontinence must be kept clean and dry. The recumbent patient needs to be placed on appropriate bedding and rotated frequently or placed in a sling to prevent the formation of pressure sores. Nutritional and intravenous fluid support may be indicated in a patient who cannot maintain adequate nutrition per os.
- Free-radical scavenger drugs may prevent secondary ischemic complications, including edema and hemorrhage. Although controversial, corticosteroids may be given only if the patient presents within 6 hours of the initial insult (see Intervertebral Disk Disease, p. 617, for protocols).

CHRONIC TREATMENT

The patient will likely benefit from physical rehabilitation (see p. 1329), though a recent study reported that such treatment was not significantly associated with clinical outcome. It can be instituted immediately, and modalities include passive range of motion exercises, massage, hydrotherapy, and electrical stimulation.

POSSIBLE COMPLICATIONS

Complications, including the development of decubital ulcers and pneumonia, can arise secondary to the patient's recumbency.

RECOMMENDED MONITORING

Observation of respiratory effort and onset of cough, pulse oximetry, and lung auscultation are recommended to monitor for the development of pneumonia.

PROGNOSIS AND OUTCOME

- The presence of unilateral spinal cord damage yields a better prognosis than a transverse myelopathy.
- Lower motor neuron deficits suggest destruction of the ventral gray matter of the cervicothoracic or lumbosacral intumescence and yield a guarded to poor prognosis; upper motor neuron deficits indicate a better prognosis.
- The absence of deep pain perception lends a poor prognosis.
- The length and cross-sectional area of a lesion on MRI is correlated with functional outcome.
- Animals that display a functional recovery within the first 1-2 weeks after insult have a better prognosis. After this time period, it is less likely for further improvements to appear.
- In the acute setting, the patient should be evaluated frequently with neurologic examinations to detect signs of ascending or descending myelomalacia. If evidence of myelomalacia is present (i.e., clearly progressive deterioration of spinal cord function over a period of hours), the prognosis is grave.
- The patient with nonprogressive lateralizing signs, intact deep pain perception, and no evidence of spinal cord swelling on diagnostic imaging has a relatively good prognosis compared with the patient with symmetric lower motor neuron deficits, absent deep pain perception, and CSF changes.

PEARLS & CONSIDERATIONS

COMMENTS

One should be highly suspicious of FCE in the patient with a peracute to acute onset of nonpainful, nonprogressive, lateralizing focal myelopathy.

CLIENT EDUCATION

Clients must be advised of the intensive nursing and supportive care required of animals with FCE. The client should also have a commitment to rehabilitation and physical therapy, which can be time consuming and costly.

SUGGESTED READING

De Risio L, Adams V, Dennis R, et al: Association of clinical and magnetic resonance imaging findings with outcome in dogs suspected to have ischemic myelopathy: 50 cases (2000-2006). J Am Vet Med Assoc 233:1, 2008.

Tefend MB, Dewey CW: Nursing care for patients with neurologic disease. In Dewey CW, editor: A practical guide to canine and feline neurology, ed 2, Ames, IA, 2008, Blackwell Publishing, pp 566–579.

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Fever of Unknown Origin

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

- Fever is defined as a higher than normal body temperature >102.5°F [>39.1°C]) due to altered thermoregulatory mechanisms in the hypothalamus.
- Fever of unknown origin (FUO) is a fever that is documented repeatedly, lasts for 3 weeks or longer, and for which a cause is not identified initially (human medical definition).
- The normal range of body temperatures in calm, normal individuals in a cool environment is 100.2°F-102.5°F (37.8°C-39.1°C) in the dog and 100.5°F-102.5°F (38.0°C-39.1°C) in the cat.

SYNONYM

Pyrexia

Note: Fever is a subset of hyperthermia, not a synonym. Nonfebrile hyperthermia (e.g., physical exertion, heat stroke, muscle fasciculations) does not involve alterations in the hypothalamic thermoregulatory mechanisms and is not treated with antipyretic drugs.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Any age, breed, or sex
- Young dogs may be more likely to have infectious causes.
- Older dogs may be more likely to have neoplastic causes.

GENETICS & BREED PREDISPOSITION

- Shar-pei: idiopathic, possible cytokine abnormality
- Weimaraner: neutrophil function deficiency
- Irish setter: leukocyte adhesion deficiency

RISK FACTORS

- Immunosuppression
- Exposure to infectious agents or vectors
- Travel to endemic areas of disease

CONTAGION & ZOONOSIS: Risk varies, dependent on causative agent.

GEOGRAPHY AND SEASONALITY: Some regions are endemic for particular infectious diseases. See individual specific topics.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Will vary with organ systems involved and causative agent but usually associated with nonspecific clinical signs such as lethargy, depression, and anorexia

PHYSICAL EXAM FINDINGS

- A complete physical exam in all patients with FUO must include rectal exam (dog), fundic exam (dog, cat), oral exam (dog, cat), meticulous examination of the skin (dog, cat), orthopedic, and neurologic exam (dog, cat)
- Fever:
  - Individual (haircoat, anxiety) and environmental (ambient temperature) influences may raise the body temperature of normal, healthy dogs and cats and must be considered when interpreting a patient's temperature.
- Depression
- Lethargy
- Tachycardia

- Hyperpnea
- Dehydration
- Lymphadenopathy with infectious or neoplastic disease
- Neck or back pain or central signs with meningitis, meningoencephalitis, diskospondylitis
- Joint pain or swelling with monoarthritis or polyarthritis
- Heart murmur may indicate bacterial endocarditis
- Chorioretinitis or hemorrhage suggestive of infectious cause
- Localized swelling and/or pain with wounds or abscesses

ETIOLOGY AND PATHOPHYSIOLOGY

Etiology:

- Infectious:
  - Localized or systemic bacterial infections (dog, cat): diskospondylitis, osteomyelitis, bacterial endocarditis, septic arthritis, prostatitis, pyelonephritis, septic meningitis, cholangiohepatitis, abscesses, pyothorax, peritonitis, pneumonia, pyometra, catheter site infections
  - Specific bacterial infections: leptospirosis (dog), borreliosis (dog), brucellosis (dog), mycobacterial infections (dog, cat), bartonellosis (dog, cat), hemotropic *Mycoplasma (Haemobartonella)* (dog, cat), tularemia (dog, cat), salmonellosis (dog, cat)
  - Viral: canine influenza (dog), canine distemper virus (dog), parvovirus/panleukopenia (dog/ cat), feline leukemia (FeLV) (cat), feline immunodeficiency virus (FIV) (cat), feline infectious peritonitis (cat), systemic calicivirus (cat)
  - Rickettsial: ehrlichiosis/anaplasmosis (dog, cat), Rocky Mountain spotted fever *(Rickettsia rickettsii)* (dog)
  - Fungal (dog, cat): histoplasmosis, blastomycosis, coccidioidomycosis cryptococcosis, systemic aspergillosis
  - Protozoal: babesiosis (dog), leishmaniasis (dog), trypanosomiasis (dog), hepatozoonosis (dog), toxoplasmosis (dog, cat), cytauxzoonosis (cat)
- Immune mediated: immune-mediated polyarthritis (dog, cat), systemic lupus erythematosus (SLE) (dog, cat), rheumatoid arthritis (dog), vasculitis (dog, cat), meningitis (dog), pemphigus (dog, cat), immune-mediated hemolytic anemia (IMHA) (dog, cat), immune-mediated thrombocytopenia (ITP; dog, cat), transfusion reaction (dog, cat)
- Neoplastic (dog, cat): histiocytic sarcoma, lymphoma, leukemia, multiple myeloma, necrotic solid tumors
- Other (dog, cat):
  - Pancreatitis
- Drug induced (tetracyclines, penicillins, sulfas), toxins, metabolic bone disorders, hyperthyroidism, tissue necrosis

Pathophysiology:

- The hypothalamus is responsible for thermoregulation. Fever occurs when the hypothalamic setpoint is reset to higher than normal.
- Inflammation and bacterial endotoxins increase the hypothalamic set point by causing the release of endogenous pyrogens such as interleukin (IL)-1, IL-6, and tumor necrosis factor a.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis of FUO is justified when an elevated body temperature has been documented on several occasions (typically over a period of several days) in the absence of confounding factors, which are common: anxiety in the hospital setting and warm ambient temperatures. Confirmation justifies testing to differentiate infectious from noninfectious causes.

DIFFERENTIAL DIAGNOSIS

Rule out nonpyrogenic causes of an elevated body temperature (heat stroke, overexertion, muscle fasciculations, etc.)

INITIAL DATABASE

- CBC, chemistry profile, urinalysis: results will vary with organ system involvement.
- Urine bacterial culture and sensitivity should be performed in all cases of FUO even if urine sediment is inactive. Helpful with detection of pyelonephritis or prostatitis.
- FeLV antigen and FIV antibody tests in all cats

ADVANCED OR CONFIRMATORY TESTING

Further laboratory testing depends on history, physical exam findings, and minimum database results.

- Laboratory tests:
  - Serial blood cultures: to detect bacteremia associated with diskospondylitis, endocarditis, or other foci of infection. A negative culture does not rule out bacteremia (intermittent bacterial showering).
  - Specific serologic tests: antibody titers or antigen tests are obtained for evidence of infectious disease. If infectious disease is suspected and initial titers are negative, repeat in 2-4 weeks.
  - PCR testing for specific infectious agents
  - Fungal cultures and/or serologic titers
  - Fungal antigen tests: blastomycosis (urine, blood), cryptococcosis (blood)
  - Cytology and cultures of cerebrospinal fluid (CSF) or synovial fluid
  - Immune tests: antinuclear antibody test if suspected SLE; Coombs' test if suspicion of IMHA or immune-mediated thrombocytopenia (ITP); serum protein electrophoresis
- Imaging:
  - Thoracic radiographs: to evaluate for evidence of neoplasia, effusions, or pulmonary infiltrates
  - Abdominal radiographs: evaluate for abdominal masses, effusions, free gas.
  - Spinal and long bone radiographs: examine for evidence of diskospondylitis, osteomyelitis, periosteal proliferation.
  - Abdominal ultrasound: rule out pyelonephritis, prostatitis, or pyometra; identify ± aspirate any enlarged abdominal organs or masses (unless highly vascular or bleeding disorder).
  - Echocardiogram: identify vegetative valvular lesions associated with bacterial endocarditis.
  - CT/MRI often indicated before CSF tap to rule out an intracranial mass and decrease risk of herniation
- Diagnostic procedures:
  - Arthrocentesis: polyarthritis
  - Cytologic study of enlarged lymph nodes or affected organs: neoplasia or identification of infectious agents
  - Bone marrow aspirates and/or biopsy: if CBC changes are reflective of bone marrow involvement or neoplasia is suspected
  - CSF tap if neurologic signs (± fundic exam) suggest meningoencephalitis or meningitis
  - Muscle biopsy: hepatozoonosis
  - Abdominocentesis: peritonitis and pancreatitis
  - Transtracheal wash or bronchoalveolar lavage if respiratory involvement

TREATMENT

TREATMENT OVERVIEW

- The goal in all cases of FUO is to obtain a specific diagnosis and treat accordingly.
- A therapeutic trial should be initiated only when a specific diagnosis cannot be ascertained.

ACUTE GENERAL TREATMENT

- Intravenous crystalloid fluid therapy at 1.5-2 times maintenance for fevers where temperature >103.5°F (>39.7°C)
- Mechanical cooling methods such as cool water baths or fans when patient's temperature >106°F (>41.1°C)
- Antipyretic agents (e.g., nonsteroidal antiinflammatories [NSAIDs], to be given only when animal is fully hydrated) may be considered if temperature exceeds 106°F (41.1°C) and does not respond to fluids and cooling.
  - Antipyretic drugs should be reserved only for patients with fevers >105°F (40.6°C) and have failed to respond to fluids and mechanical cooling, as such drugs can mask the effects of other therapies and can be associated with adverse effects such as gastrointestinal ulceration and hepatic and/or renal toxicity.
- Patients with persistent fevers <105°F (40.6°C) should be treated with supportive care, including IV fluids.

CHRONIC TREATMENT

- Antibiotic trials:
  - Broad-spectrum antibiotic therapy may be initiated after all culture specimens have been collected.
  - Therapy should be based on the agents most likely present, their known antibiotic sensitivity, and the organ or system affected.
  - Commonly used empirical antibiotics include amoxicillin-clavulanate, 10-20 mg/kg PO q 8-12 h; or cephalexin, 22 mg/kg PO q 8 h or 30 mg/kg PO q 12 h; or if tickborne diseases are suspected, doxycycline, 10 mg/kg PO q 24 h or 5 mg/kg PO q 12 h. The actual recommendation depends on the previously listed factors.
- Glucocorticoid trials (duration: 24-72 h):
  - Used when immune-mediated disease is suspected
  - Should be used only when infectious disease has been ruled out
  - A dramatic response (fever reduction) should be seen within 24-48 hours.

- Examples: prednisolone, 1 mg/kg PO q 12 h, or dexamethasone, 0.2 mg/kg IV q 24 h; doses for longer-term use are adjusted based on the specific underlying cause.

DRUG INTERACTIONS

The use of NSAIDs in combination with glucocorticoids should be avoided.

POSSIBLE COMPLICATIONS

- Drug therapy trials without a definitive diagnosis may interfere with future diagnosis and exacerbate an undiagnosed condition that may be life threatening.
- Glucocorticoids may lead to immunosuppression or may mask clinical signs due to their antiinflammatory effects.

RECOMMENDED MONITORING

Monitor temperature at least every 12 hours. Response to trial therapy may be nonspecific or coincidental, so monitoring should continue for a sufficient time to confirm that resolution of the fever can be attributed to selected therapy.

PROGNOSIS AND OUTCOME

Dependent on specific cause

PEARLS & CONSIDERATIONS

COMMENTS

- Infectious disease, immune-mediated conditions, and neoplasia account for more than 75% of FUO cases.
- With aggressive diagnostic testing, usually only 10% of FUO cases are considered idiopathic.
- Immune-mediated polyarthritis will frequently *not* be associated with detectable joint swelling; therefore arthrocentesis is indicated in all FUO cases where no underlying cause has been identified.

PREVENTION

- Ectoparasite prevention may reduce risk of vector-borne disease transmission.
- Indoor pets are less likely to be exposed to vector-borne diseases.
- Vaccination against specific disease agents for high-risk pets
- Yearly retroviral testing and vaccination in high-risk cats
- Routine screening of geriatric pets to facilitate early diagnosis and treatment of cancer

CLIENT EDUCATION

- Animals may serve as sentinels for infections or transmit some infections to humans (zoonoses).
- Exposure to vectors may increase risk of disease transmission.

SUGGESTED READING

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Feline Lower Urinary Tract Signs, Idiopathic

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Lower urinary tract signs (LUTS) include stranguria, hematuria, dysuria (difficult or painful urination), pollakiuria (frequent passage of small amounts of urine), and periuria (urination in inappropriate locations). These signs can occur with lower urinary tract disease (LUTD) of any cause. Idiopathic feline LUTD refers to LUTS in the absence of a known cause and is a diagnosis of exclusion (see differential diagnosis) and the most common cause of LUTS in cats.

SYNONYMS

Feline lower urinary tract disease (FLUTD), feline idiopathic cystitis (FIC), feline urologic syndrome (FUS)

EPIDEMIOLOGY

SPECIES, AGE, SEX: Can affect cats of either sex at any age. Male cats develop lower urinary tract obstruction more than female cats (narrow penile urethra).

GENETICS & BREED PREDISPOSITION: Siamese cats at reduced risk of LUTS, whereas Persians and long-haired cats may be at increased risk. Epigenetic familial factors (e.g., quality of maternal care) may play a role.

RISK FACTORS: Stress (e.g., changes in feeding, litter boxes, human and animal family members, and owner schedule), neutering, indoor housing, increased weight, decreased activity, multicat households.

GEOGRAPHY AND SEASONALITY: None

ASSOCIATED CONDITIONS & DISORDERS: Cats with LUTS also may be at increased risk for separation anxiety disorder and other behavioral abnormalities (fear, nervousness, aggression), dilated cardiomyopathy, and obesity. Urethral obstruction may occur in male cats with LUTS.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Common history is abrupt onset of LUTS (e.g., hematuria, periuria) in an otherwise healthy young adult cat (2-6 years old).
- Often, affected cats are housed entirely indoors and are neutered.
- Male cats with obstructive LUTD have unproductive stranguria, may vocalize, vomit, and become progressively depressed/obtunded.

PHYSICAL EXAM FINDINGS

- Affected cats are often anxious and may be aggressive or shy.
- Unless urethral obstruction is present, the bladder is typically small and difficult to palpate.
- Male cats with urethral obstruction will have a large, painful, turgid, inexpressible bladder.

ETIOLOGY AND PATHOPHYSIOLOGY

- The etiology is not known, although a subset of patients appears to have a congenital disorder of the stress-response system that results in persistent sensitization of the system and reduced adrenocortical function. This sensitivity may be unmasked by cat-perceived threats in the environment, such as unpredictable owner schedules, conflict with other animals, and impoverished environments.
- The enhanced sympathetic drive may reduce epithelial tight-junction integrity, resulting in increased exposure of afferent neurons to environmental stimuli. When this occurs in the bladder of a cat with an activated stress-response system, LUTS may result.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

- Signalment, history, and physical examination often are sufficient to make the clinical diagnosis. Urinalysis with sediment examination can help rule out differential diagnoses such as urinary tract infection. Additional diagnostics are warranted in cats with atypical presentations, persistent or frequent episodes of LUTS, or urethral obstruction.

DIFFERENTIAL DIAGNOSIS

- Urolithiasis
- Behavioral disorder (e.g., territorial marking)
- Anatomic urinary tract defect (notably vesicourachal diverticula)
- Urinary tract infection
- Bladder neoplasia (uncommon; transitional cell carcinoma most often identified tumor type)

INITIAL DATABASE

- Urinalysis with sediment examination will often reveal hematuria, hypersthenuria (USG > 1.035), proteinuria +/− crystalluria.
- Urine culture and susceptibility: infection is rare in the United States, seemingly more common in European studies.
- For cats with a typical initial presentations, no additional diagnostic tests may be required.

ADVANCED OR CONFIRMATORY TESTING

- For cats with complicated initial presentations or recurrent episodes, diagnostic testing is aimed at ruling out the most common alternative diagnosis. With idiopathic LUTS, no abnormalities are expected.
    - Radiography of the entire lower urinary tract (including the distal urethra)
    - CBC, biochemical analysis and FIV/FeLV testing
- Other lower urinary tract imaging (e.g., ultrasonography, double contrast cystography) or cystoscopy are rarely indicated.

TREATMENT

TREATMENT OVERVIEW

Treatment focuses on stress reduction through owner education and environmental enrichment (EE). Lower urinary tract obstruction is a life-threatening condition requiring prompt attention to manage the associated metabolic derangements and reestablish urine flow.

ACUTE GENERAL TREATMENT

If the cat is obstructed, relieve the obstruction (see p. 1355), reestablish urine flow, and correct fluid, electrolyte, and acid-base imbalances.

Drugs Commonly Used for Cats With LUTS

Drug	Dose	Potential Side Effects
Acute Analgesic		
Butorphanol (Torbugesic)	0.2-0.4 mg/kg IV, IM, SQ q 8 h (IV: use lower end of dose range)	Sedation
Buprenorphine (Buprenex)	0.01-0.02 mg/kg IM, IV, or SQ q 8-12 h; 0.015 mg/kg PO or sublingual q 8-12 h (anecdotal)	
Fentanyl (Duragesic) patch	25 mcg/h	Respiratory depression, bradycardia
Bladder/Urethral Contractility		
Acepromazine (PromAce)	0.05 mg/kg SQ q 8 h	Sedation, hypotension
Prazosin (Minipress)	0.5 mg per cat PO q 12 h	
Phenoxybenzamine (Dibenzyline)	2.5 mg per cat PO q 12 h	Hypotension
Bethanechol (Urecholine)	2.5-5 mg per cat PO q 12 h	Salivation, vomiting, diarrhea
Chronic Analgesic/Anxiolytic		
Clomipramine (Anafranil)	0.5 mg/kg PO q 24 h	Sedation, anticholinergic effects
Amitriptyline (Elavil)	5-12.5 mg per cat PO q 12-24 h	Sedation, weight gain, urine retention; urolith formation

Drug	Dose	Potential Side Effects

- Establish IV access and provide appropriate analgesia.
- Submit samples for serum biochemical profile, CBC, and urinalysis. It is not necessary to evaluate the results before treating obstructed cats that present with urethral obstruction and severe systemic signs, with the exception of the potassium concentration.
- Resuscitate moribund cats with intravenous (IV) fluids, and correct serious electrolyte and acid-base disturbances before anesthesia for placement of a urinary catheter.
    - Obtain an electrocardiogram (ECG) of all systemically ill cats with urethral obstruction, as rescue from the cardiotoxic effects of severe hyper-kalemia may be necessary even before laboratory values for serum potassium (K^+) return if arrhythmias are present:
        - Slow IV administration of 2-10 mL of 10% calcium gluconate to effect will protect the myocardium from the deleterious effects of hyperkalemia, without lowering serum potassium concentration (monitor ECG for slowing of heart rate of 10% or more, warranting termination of calcium administration). Usually 0.2-0.5 mL/kg over 15 minutes is adequate (i.e., 1-2.5 mL/5 kg cat); can be repeated in 5 minutes if no improvement.
        - Administration of sodium bicarbonate (1-2 mEq/kg IV) or insulin (0.2-0.4 U regular insulin IV, while supplementing IV fluids to 2.5% dextrose and closely monitoring blood glucose concentration, owing to risk of hypoglycemia) may be used to drive potassium intracellularly and lower serum potassium concentrations prior to reestablishment of urine flow.
        - Consider decompressing the bladder by cystocentesis before attempting to pass a urinary (urethral) catheter. Insert a 22- or 23-gauge butterfly needle into the bladder wall midway between the apex and urethral outflow and directed caudoventrally. If a longer needle is necessary, it can be attached to an extension set and urine removed using a syringe. Palpate the bladder during drainage to empty it as completely as possible. Rare complications include extravasation of urine into the peritoneal cavity and damage to the bladder wall. This procedure may be sufficient to restore normal urine flow but remains controversial because of potential complications.
    - Pass a urinary catheter only if necessary. General anesthesia is needed to allow proper manipulation of the penis to pass the catheter. If the combination of IV ketamine and diazepam does not provide adequate relaxation, isoflurane gas in oxygen, or propofol infusion may provide both adequate sedation and urethral relaxation.
    - If a plug or urethrolith is retrieved, it should be submitted for quantitative analysis.
        - An indwelling urinary catheter (e.g., 3.5-Fr red rubber feeding tube–type) is placed in cats with pronounced azotemia or poor urinary stream after catheter placement. An indwelling urinary catheter also is used for cats with very large bladders at presentation, as they are more likely to develop detrusor atony.
- Manage cats medically unless future recurrent obstructions occur.
    - For most, analgesics (see table) and appropriate fluid therapy are indicated. Some α-blocking drugs (e.g., phenoxybenzamine) have not been shown to be effective. They act on the proximal feline urethra, whereas most obstructions in cats involve the distal urethra.
    - Monitor urine output frequently in severely ill cats. Those that recover from severe postrenal uremia generally undergo a substantial post-obstructive diuresis >2 mL/kg/h shortly after relief of obstruction and rehydration). During this period, it is essential to give sufficient IV fluids to replace the volume lost as urine. The diuresis declines to normal during 2-5 days.
- The role of glucocorticoids (e.g., prednisone), and nonsteroidal antiinflammatory drugs (e.g., aspirin, meloxicam) remains poorly defined, and none of these drugs has been shown to be an effective treatment for acute LUTS.

CHRONIC TREATMENT

- Step 1: Environmental enrichment (EE)/multimodal environmental modification (MEMO).
    - Provide at least one food bowl, one water bowl, and one litter box per cat, plus one. Locate these resources in quiet places where the cat is not startled during use.
    - Provide opportunities for the cat to hide safely and explore its environment. Placing “perches” at windows so the cat can look outside and structures the cat can climb on seem to be important parts of EE.
    - Provide a regularly scheduled time for petting, play, and/or trick-teaching, working toward at least 10 minutes a day.
    - Identify and resolve intercat conflict to the extent possible.
    - If ineffective, proceed to step 2.
- Step 2: step 1 plus consider use of pheromones (Feliway). If ineffective, proceed to step 3.
- Step 3: steps 1 and 2 plus consider use of a tricyclic agent such as clomipramine or amitriptyline at the lowest effective dose possible (see table). These drugs should be used only after steps 1 and 2 have been implemented and the cat is so severely affected he/she continues to have recurrences. Conclusive results regarding the efficacy of behavior-modifying drugs are lacking.
- A perineal urethrostomy may be needed in severe recurrent obstructive cases.
    - This surgery increases the risks of bacterial urinary tract infections, however, and postoperative strictures are a potential complication.
    - Clients should be made aware that this surgery does not correct the underlying problem, and recurrent episodes of

urolithiasis and LUTS still can occur.

NUTRITION/DIET

- Dietary therapy may be indicated if uroliths or crystals are identified and will depend on the type of urolith.
- Glycosaminoglycan (GAG) supplementation has been suggested, but its efficacy remains unproven in cats.

BEHAVIOR/EXERCISE

- See recommendations for environmental enrichment under Chronic Treatment.

POSSIBLE COMPLICATIONS

- When introducing EE, offer changes to the cat (e.g., new food in a separate bowl rather than in place of the familiar diet) to avoid precipitating a threat response. Make changes the client wants to make, if possible, to secure support and adherence to the EE effort. Make changes sequentially.
- When tricyclic drugs are used, they should be tapered slowly over at least 2 weeks to avoid adverse reactions.

RECOMMENDED MONITORING

Liver and kidney function should be assessed before use of tricyclic drugs and at least annually in young animals if therapy is extended.

PROGNOSIS AND OUTCOME

Most cases of idiopathic, nonobstructive, feline LUTS are self-limiting, usually resolving in 5-10 days. However, recurrent episodes of clinical signs, including urinary tract obstruction, occur with variable frequency. Overall prognosis depends on the cat, client, and environment:

- Cat:
  - Genetic predisposition
  - Duration of the problem
  - Frequency of occurrences
  - Number of areas and different types of surfaces soiled
- Client:
  - Ability to identify modifiable causes
  - Strength of bond to affected cat
  - Willingness to pay for treatment
  - Amount of time to devote to solution
  - Willingness to accept and use medications
- Environment:
  - Number of cats in the household
  - Number of affected cats
  - Practicality of allowing limited outdoor access
  - Ability to rearrange the environment

PEARLS & CONSIDERATIONS

COMMENTS

EE often is sufficient to suppress clinical signs and should be offered to all owners of cats exclusively housed indoors.

PREVENTION

EE recommendations should be provided to all owners of indoor cats, not just those with a clinical problem.

CLIENT EDUCATION

Client-oriented information is available at www.indoorcat.org.

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Feline Leukemia Virus Infection

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Virus infection of cats that can result in immunosuppression, myelosuppression, and neoplasia

SYNONYM

FeLV

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Mainly domestic cats (rare examples in wild felids) are infected
- Young cats (<1 year old) are more likely to become persistently viremic. Male cats are slightly more commonly infected than female cats.

RISK FACTORS

- Free-roaming cats are more likely to be exposed to FeLV.

CONTAGION & ZOONOSIS

- FeLV is most commonly transmitted through saliva during grooming and playing and sharing food and water bowls. FeLV can also be transmitted through blood or transplacentally.
- Environmental contamination is of lesser concern, because the virus is highly sensitive to desiccation, disinfectants, and heat, although in experimental conditions, FeLV can be transmitted through feces.
- FeLV is not zoonotic.

GEOGRAPHY AND SEASONALITY: FeLV is found worldwide. However, there is a worldwide decrease in the prevalence (currently 2.3%-3.3% in the United States), possibly as a result of test and removal programs and vaccination.

ASSOCIATED CONDITIONS & DISORDERS: FeLV causes immunosuppression, which in turn is associated with op portunistic infectious diseases. It can also cause neoplasia.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: FeLV occurs in three major subgroups, A, B, and C. Subgroup A is present in all infected cats. Subgroup B and C are deletions and recombinations of the subtype A genome with host DNA. Subtype B is common in cats with neoplasia. Subgroup C is rare and can cause nonregenerative anemia.

HISTORY, CHIEF COMPLAINT

- FeLV infection can occur without overt clinical signs, as there is a long subclinical phase, and in these cats, infection is commonly discovered during routine screening.
- Persistent viremia may cause signs due to immunosuppression and secondary infections (e.g., weight loss, diarrhea, nasal or ocular discharge) or from non-specific signs attributable to anemia or tumors, such as weakness, lethargy, or inappetence.

PHYSICAL EXAM FINDINGS

- Signs are often nonspecific, including poor body condition, depression, weakness, or lymphadenopathy. Signs may be attributable to immunosuppression with secondary infection, myelosuppression (mainly nonregenerative anemia), or neoplasia (mainly lymphoma).
- Clinical signs of hematologic abnormalities may include pale mucous membranes due to anemia, sepsis secondary to neutropenia, or hemorrhage due to thrombocytopenia.
- The most common sign attributable to FeLV-associated lymphoma is dyspnea due to a mediastinal mass and pleural effusion.

Other signs include diarrhea (with intestinal lymphoma), vomiting (due to renal failure in cats with renal lymphoma), or icterus (hepatic lymphoma). The occurrence of other tumors may lead to various clinical abnormalities, including FeLV-associated osteochondromas (multiple cartilaginous exostoses) that may produce orthopedic abnormalities (palpable bony enlargements) or neurologic deficits, depending on site of involvement.

- FeLV may cause abortion and infertility.
- Newborn kittens may have “fading kitten syndrome” and die within the first 2 weeks of life.

ETIOLOGY AND PATHOPHYSIOLOGY

- FeLV is an oncornavirus (RNA virus) of the family *Retroviridae*.
- Infection occurs most commonly through exposure to saliva through the oral or nasal cavity. The virus replicates in the oropharyngeal lymphoid tissues.
- Cats can mount a full immune response and eliminate the infection, or mount an ineffective immune response resulting in viremia.
- Once the patient is viremic, the virus replicates within disseminated lymphoid tissues and later within the bone marrow. An effective immune response at this stage can result in elimination of the virus but more commonly results in the development of latent infection.
- With an ineffective immune response during viremia, the cat may become persistently viremic and is likely to develop FeLV-associated diseases (hematologic abnormality, malignancy, chronic infection, or other clinical signs).
- Latent infection may be reactivated, and cats may again become viremic after stress or immunosuppression.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is usually made by detecting FeLV antigen in ELISA or other immunochromatography tests (using a similar technique). Negative results are highly reliable (in an area with low prevalence), but positive results should be considered carefully because false-positive results occur. Thus, a positive test should always be confirmed.

DIFFERENTIAL DIAGNOSIS

Other immunosuppressive conditions, such as FIV infection

INITIAL DATABASE

- CBC, serum chemistry panel, urinalysis
  - Initial database that is routinely performed to rule out other illnesses or infections; changes are not specific to FeLV infection, and results are often normal in FeLV-infected cats.
  - CBC in cats with myelosuppression may show mild to marked abnormalities, including nonregenerative anemia, neutropenia, thrombocytopenia, or pancytopenia.
  - Serum biochemistry profile and urinalysis are usually normal, or changes may be nonspecific.
- Chest radiographs
  - Mediastinal mass and pleural effusion (mediastinal lymphoma)
- Screening tests of choice are fast in-house ELISA or other immunochromatography tests (using a similar technique) which detect free FeLV antigen in blood. In addition, IFAs are used that detect intracellular FeLV antigen in neutrophils and platelets in blood smears.
  - ELISA is more sensitive and detects viremia earlier than IFA, it is the diagnostic test of choice for general screening.
  - Positive results for both ELISA and IFA indicate that a cat has been infected for more than 3 weeks. Persistent viremia is likely in these cats.
  - Positive ELISA and negative IFA usually indicates early infection (<3 weeks). Therefore, cats with positive ELISA and negative IFA results should be retested with both tests 6 weeks later.
  - Latently infected cats are negative for both ELISA and IFA testing.
  - Vaccination (against FeLV) does not lead to positive ELISA, IFA, or PCR.
  - Saliva- or tear-based tests are not recommended (poor sensitivity due to intermittent shedding).

ADVANCED OR CONFIRMATORY TESTING

PCR testing is available for use in cats with a clinical suspicion of FeLV infection despite negative ELISA and IFA results, or discordant ELISA and IFA test results. PCR may also be used for detecting virus in latently infected cats (in blood, bone marrow, or tumor tissue).

TREATMENT

TREATMENT OVERVIEW

The most important advice is to keep FeLV-infected cats indoors only, away from the risk of secondary infections. In cats with no clinical signs, no other treatment is required. Secondary infections require prompt and thorough treatment. When overt clinical signs are present, antiviral treatment, e.g., with feline interferon-omega, is potentially beneficial.

ACUTE TREATMENT

May include intensive antibiotic therapy for secondary infections or blood transfusion in life-threatening anemia.

CHRONIC TREATMENT

- Management of FeLV-associated secondary infections
  - Any secondary infections should be treated intensively and with a prolonged course (e.g., antibiotics).
- Treatment of FeLV-associated lymphoma
  - Chemotherapy is used, but prognosis is worse than with non-FeLV-associated tumors
- Treatment of FeLV-associated myelosuppression
  - Severe nonregenerative anemia may be managed with blood transfusions.
  - Neutropenia may transiently respond to human granulocyte colony-stimulating factor (G-CSF 5 µg/kg q 12 h SQ). Antibody development eventually limits its use.
- Antiviral chemotherapy and immunomodulatory drugs
  - Antivirals such as AZT (zidovudine) are most effective when given within 96 hours of exposure to the virus, which is seldom clinically relevant.
  - Recombinant feline interferon-omega (Japan, Europe) showed some efficacy in reducing mortality.
  - The immunomodulator *Staphylococcus* protein A (SPA) may increase owners' perception of the cat's quality of life.

BEHAVIOR/EXERCISE

FeLV-infected cats should stay strictly indoors, both to prevent spread to other cats and reduce risk of exposure to secondary infections.

DRUG INTERACTIONS

All immunosuppressive and myelosuppressive drugs should be avoided.

POSSIBLE COMPLICATIONS

Treatment with AZT can result in reversible nonregenerative anemia.

RECOMMENDED MONITORING

Assess regularly for evidence of secondary infectious diseases, neoplasia, and progression of illness (e.g., recheck visits, with exam and CBC, every 6 months).

PROGNOSIS AND OUTCOME

- Historic findings of 3 years lifespan are likely outdated. Nowadays normal longevity is possible, though FeLV-associated syndromes require treatment.
- The prognosis for cats that develop lymphoma, leukemia, or myelosuppression is guarded to poor. Cats with lymphoma may experience a remission and an improved quality of life with chemotherapy for a median of 6 months. Cats with leukemia, severe anemia, and myelodysplasia respond poorly to therapy.

PEARLS & CONSIDERATIONS

COMMENTS

- The FeLV status of all cats should be known. Thus, every cat should be tested independent of age. Viremia can be detected

from birth onward.

- A diagnosis of FeLV is not a reason for euthanasia. Infected cats can live several years with a good quality of life. However, the diagnosis has certain implications.
    - The cats should only be kept indoors.
    - More intense and regular veterinary care is required in such a cat.
    - Vaccination programs to prevent common serious infectious diseases (using killed vaccine, since immune function may be compromised) should be maintained; revaccination on a more frequent basis should be considered given these cats' immunoincompetence.

PREVENTION

- Vaccination against FeLV is efficacious in cats at risk for exposure to the virus, but level of protection is not sufficient in the case of very high infectious pressure (e.g., if a naive cat lives together with a FeLV-shedding cat).
- The FeLV vaccine is associated with development of injection site–associated sarcomas (see p. 610) in cats. Thus, only cats at risk should be vaccinated (e.g., not cats that live indoors with no other cats). Cats should be vaccinated against FeLV distally in the left hind limb, to allow easy removal of injection-site sarcomas if they occur.

TECHNICIAN TIPS

- Technicians should be aware that the FeLV status of every cat should be known.
- As FeLV lives only minutes outside the host and is susceptible to all disinfectants including common soap, simple precautions and routine cleaning procedures will prevent transmission while in the hospital. FeLV-infected patients should not be placed in an “infectious disease ward” with cats with contagious diseases (e.g., upper respiratory infections).

CLIENT EDUCATION

Every cat should be tested for FeLV.

SUGGESTED READING

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Feline Infectious Peritonitis

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

A serious, often fatal disease that mainly occurs in young cats from multicat households and often is characterized by body cavity effusions or neurologic signs. Importantly, feline infectious peritonitis (FIP) is caused by a common feline coronavirus (FCoV) that, in affected cats, has spontaneously mutated from a benign, minimally pathogenic type to an aggressive, lethal type.

SYNONYMS

Feline coronaviral polyserositis (wet/effusive form), FIP, granulomatous feline infectious peritonitis (dry/noneffusive form), feline coronaviral vasculitis

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Young cats during postweaning periods are most susceptible; peak age 6 months to 2 years
- Males > females

GENETICS & BREED PREDISPOSITION: Purebred cats are most susceptible, especially Asian breeds (e.g., Birman, Himalayan).

RISK FACTORS

- Stress: vaccinations, elective surgery, placement in a new home
- Multicat households: catteries, pure breeds, shelters

CONTAGION & ZOONOSIS

- FCoVs are mainly transmitted by fecal-oral route or through saliva (e.g., mutual grooming).
- Can also be transmitted transplacentally
- FCoV infection is widespread or even ubiquitous in multicat environments.
- No two cats with FIP are infected with exactly the same virus. This fact suggests that horizontal transmission (cat to cat) is minimally important to the development of FIP. Rather, it is the ability of the virus to mutate inside the cat and the cat's immune response that determine whether a coronavirus infection remains innocuous or develops into FIP.
- No known zoonotic potential

ASSOCIATED CONDITIONS & DISORDERS: Feline enteric coronavirus causes mild, self-limiting diarrhea.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- FCoV has a spectrum of pathogenicity, and its direct effects range from none (carrier individuals with no clinical signs) to life threatening (FIP).
- Two clinical forms of FIP: dry form (noneffusive) and wet form (effusive). Clinical signs are substantially different, but treatment options and outcome are equally poor.
- Two serotypes of feline coronavirus: type I and type II. Of no clinical importance, as each serotype can cause a range of clinical illnesses varying from benign infections with no clinical signs to fulminant FIP.

HISTORY, CHIEF COMPLAINT

- Nonspecific signs are most commonly reported by owners, including lethargy, inappetence, and weight loss.
- Cats with FIP may have a history of failure to grow, often having received multiple antibiotic therapies with no success.
- In cats with ascites due to effusive FIP, owners uncommonly notice the abdominal distension.
- Diarrhea is noted only occasionally in FIP; gastrointestinal signs suggesting intestinal obstruction are sometimes noted when the FIP lesion is confined to the intestine (colonic/intestinal FIP).

PHYSICAL EXAM FINDINGS

- Effusive form: abdominal distension with palpable fluid wave; dyspnea, muffled heart sounds, and muffled lung sounds due to pleural effusion; +/− palpable abdominal masses
- Noneffusive form: signs of central nervous system dysfunction, including ataxia, personality changes, nystagmus, seizures
  - Ocular abnormalities, including change in iris color due to iritis/uveitis, hyphema, aqueous flare, keratic precipitates, vitreous clouding, and vascular cuffing, manifesting as gray lines parallel to retinal vessels
  - Icterus
  - Palpable abdominal mass(es), usually due to organomegaly (e.g., enlarged mesenteric lymph nodes, nodules in other organs, intestinal thickening)
  - Raised intradermal pustules (nonpruritic cutaneous lesions)

ETIOLOGY AND PATHOPHYSIOLOGY

- FCoV related to transmissible gastroenteritis virus in pigs, canine, and human coronaviruses
- Largest known RNA genome; therefore, highly susceptible to mutation
- FIP virus is a mutation of the ubiquitous and otherwise benign FCoV.
  - Factors that allow or trigger mutation are not known; possibly breed susceptibility.
- Once mutated, the virus replicates within macrophages and regional lymph nodes.
- Virus pathogenicity and the cat's immune response then determine outcome:
  - Elimination
  - Complement-mediated pyogranulomatous vasculitis, causing effusive “wet” FIP
  - Partial cell-mediated response, causing the formation of “classic granulomas” and “dry” noneffusive FIP
  - Antibody-antigen complex formation and deposition in vascular endothelium, causing vasculitis

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The most reliable diagnostic test for FIP is biopsy of affected tissue (e.g., intestine), with or without immunohistochemical staining. Noninvasive clinical tests all have limitations, and an initial diagnosis of FIP generally relies on a combination of information:

- Compatible signalment and history
- Nonspecific (e.g., fever) and more specific (e.g., nonseptic exudative body cavity effusion, neurologic abnormalities, or characteristic ocular changes) physical exam findings
- Suggestive results on laboratory tests (e.g., with effusion: positive PCR result, presence of antibody titer, or immuno-fluorescent staining of antigen in macrophages)

DIFFERENTIAL DIAGNOSIS

- Neoplasia (lymphoma)
- Lymphocytic/nonsuppurative cholangitis
- Pyothorax/chylothorax
- Congestive heart failure
- Toxoplasmosis, FIV, FeLV, and systemic mycosis: ocular changes
- Lymphoma, multiple myeloma, chronic infection: hyperglobulinemia

INITIAL DATABASE

- CBC: lymphopenia, nonregenerative anemia, neutrophilic leukocytosis, higher number of Heinz bodies in RBCs (colonic FIP)
- Serum biochemistry profile
  - Hyperglobulinemia (and secondary low albumin/globulin ratio) are hallmarks of both effusive and noneffusive FIP.
  - Elevated liver enzymes: common
  - Elevated bilirubin: common, especially with noneffusive FIP
- Thoracic and abdominal radiographs: pleural effusion and ascites (effusive FIP)
- Abdominal ultrasound: abdominal mass, lymphadenopathy, ascites
- Ocular and neurologic examination
- Fluid analysis (ascites, pleural/pericardial effusion)
  - Clear, viscous (may contain clumped/precipitated protein), straw colored
  - Exudate: protein > 3.5 mg/dL and often much higher
  - Nonseptic: total cell count low (e.g., 2000/mcL); lymphocytes, nondegenerate neutrophils, macrophages predominate.
  - High globulin concentration (>32%) strongly suggests FIP. Effusion albumin/globulin ratio < 0.9 is 74% sensitive and

86% specific for FIP.

- Feline coronavirus serologic evaluation
  - Positive titer only represents exposure to FCoV, not specifically FIP.
  - Therefore, titer result must be interpreted jointly with remaining clinical and laboratory information.
  - Most cats with positive titers for feline coronavirus never develop FIP.
  - Titers > 1:16,000 are suggestive of FIP in cats showing signs of clinical disease.
  - Rarely, cats with FIP can have negative titers, especially in the terminal stages of disease.

ADVANCED OR CONFIRMATORY TESTING

- Serum protein electrophoresis in hyperglobulinemic patients:
  - To differentiate from neoplastic causes, which typically produce a monoclonal gammopathy
  - Polyclonal gammopathy with FIP (effusive and noneffusive forms), elevated globulins (usually a^2 and γ globulins)
- Cerebrospinal fluid (CSF) analysis:
  - High protein content>20 mg/dL, often markedly higher) and cell count >5 cells/µL, often much higher; mononuclear pleocytosis with some neutrophils)
  - Caution: patient may be at increased risk of cerebellar/medullary herniation after CSF tap
- a^1 Acid glycoprotein (AGP):
  - Acute phase protein that is often elevated in different infectious diseases of cats
  - AGP measurement on plasma or effusion >1500 µg/dL consistent with FIP
- CT:
  - Hydrocephalus detected grossly/histologically in 75% of cats in one study of CNS FIP
  - May be suggestive of FIPif documented on CT
- PCR:
  - Must involve reverse transcription, because test amplifies DNA, but coronavirus is an RNAvirus.
  - Blood test: interpret results with caution; cannot differentiate between enteric coronavirus and FIP.
  - Effusion test: sensitive and specific, as are conventional means (fluid analysis, serology)
  - Note: Handle all PCR samples carefully, keep frozen, and analyze as soon as possible after collection.
- FIP mRNA PCR Multi Test:
  - Test detects mRNA of M gene for feline coronavirus (only expressed during replication).
  - Relies on fact that FCoV can enter the bloodstream but cannot replicate outside the intestinal epithelium
  - FIP virus, however, replicates in mononuclear cells. This test detects replicating virus particles in the blood in cats with FIP. Cats with enteric coronavirus have replicating virus in the stool but not in the blood.
  - Use EDTA whole blood. Assay performed at Auburn University Molecular Diagnostics Lab (www.vetmed.auburn.edu).
  - Use in combination with clinical suspicion and other diagnostic tests.
- Definitive diagnosis only by histopathologic examination of suspected affected tissues: pyogranulomatous inflammation with vasculitis and perivascular cuffing. Immunohistochemical staining of tissues can confirm FIP.

TREATMENT

TREATMENT OVERVIEW

FIP is an incurable disease, so the goal is to provide comfort and supportive/palliative care.

ACUTE GENERAL TREATMENT

- See Thoracocentesis, p. 1338 .
- Oxygen therapy (see p. 1318)
- Fluid therapy

CHRONIC TREATMENT

Various drugs have been used. None has been shown effective, and the possibility of adverse effects often contraindicates use.

- Antiviral drugs: ribavirin (severely toxic in cats)
- Immunomodulating drugs:
  - α-Interferon (human): 30 U PO q 24 h on alternating weeks; few to no adverse effects
  - Recombinant feline interferon (may be combined with corticosteroids for better efficacy)
  - Acemannan
- Immune suppression: prednisolone (2-4 mg/kg PO q 24 h, tapering over 10-14 days) ± cyclophosphamide (2-4 mg/kg PO q 24 h for 4 days a week)
- Thalidomide: 50-100 mg PO given at night. Must get owners consent to use, teratogenic.

- Supportive therapy as indicated by clinical condition:
  - Environmental management: reduction of stress, including providing place to nest/hide, reducing conflicting cat-cat interactions
  - Intravenous fluids
  - Broad-spectrum antibiotics for secondary bacterial infections (uncommon)
  - Vitamins (A, C, B complex, B1, E)

NUTRITION/DIET

Nutritional support, including warming of food, offering multiple types of dry and moist food, and hand feeding if ill cats are unwilling to eat, can be an important cornerstone of supportive care.

PROGNOSIS AND OUTCOME

Poor irrespective of treatment:

- Cats with the effusive form generally die within 2 months of onset of clinical signs.
- Cats with the noneffusive form tend to have a more chronic disease course that is also generally fatal.

PEARLS & CONSIDERATIONS

COMMENTS

A "feline infectious peritonitis titer" does not exist. A positive FCoV titer indicates only exposure to a feline coronavirus, which may be pathogenic (e.g., FIP) or benign.

TECHNICIAN TIP

A patient with overt FIP does not need to be handled with supplemental precautions regarding contagion, because the risk of transmission of FIP is essentially zero.

PREVENTION

- Intranasal FIP vaccination:
  - Replicates only in respiratory epithelium; does not cause systemic infection
  - Protects 50%-75% of cats from exposure to virulent FIP virus
  - Not recommended for routine use in low-risk cats
- Optimize husbandry practices:
  - A minority of cats are seronegative to FCoV. In catteries, these cats should be kept apart from other cats, as they can be used for breeding and raising litters with a low risk of any coronavirus.
  - In catteries, remove kittens from positive queens and other adult cats in the cattery at 5-6 weeks old to reduce risk of acquisition of coronavirus.
  - When possible, only seronegative cats should be added to the cattery. Otherwise, seropositive cats may be kept with other seropositive cats.

CLIENT EDUCATION

- Select new cats from reputable breeder with low numbers of cats.
- See Cornell Feline Health Center brochure on FIP: http://www.vet.cornell.edu/fhc/brochures/fip.html

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Feline Immunodeficiency Virus Infection

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Virus infection of cats that may result in chronic immunosuppression after a long clinically latent stage

SYNONYM

Feline acquired immunodeficiency syndrome (AIDS)

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Feline immunodeficiency virus (FIV) and related viruses can infect all Felidae.
- Male cats are at least twice as likely to be infected as female cats, and adult cats are more commonly infected than kittens.
- Adult male sexually intact free-roaming cats ("fighting cats") are at higher risk for infection.

CONTAGION & ZOONOSIS

- FIV is transmissible through cell-containing saliva and blood inoculated parenterally, most commonly through bite wounds and mating. Experimental evidence has shown that FIV may be transmitted in utero or in milk (not common under natural circumstances).
- FIV is not zoonotic.

GEOGRAPHY AND SEASONALITY

- FIV is common worldwide, with a higher prevalence in regions with larger numbers of free-roaming cats (e.g., Italy, Japan). In the United States, the prevalence is 2.5%-6% (client-owned cats) and 3.5%-23% (stray cats).

ASSOCIATED CONDITIONS & DISORDERS

Immunosuppression caused by FIV infection can result in opportunistic infections. Cats with FIV may be more susceptible to stomatitis, upper respiratory infections, feline leukemia virus (FeLV) infection, feline infectious peritonitis (FIP), fungal infections, and toxoplasmosis.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- FIV infection most often occurs without overt clinical signs, and the infection is most commonly discovered incidentally during routine screening or when evaluating a cat for other illness.
- When clinical manifestations occur, history and complaints are usually associated with secondary infections that develop due to immunosuppression, with signs due to neoplasia (increased risk of lymphoma), or with FIV-associated neurologic dysfunction.

PHYSICAL EXAM FINDINGS

- The acute phase of infection is usually unnoticed but may cause fever, lethargy, or lymphadenopathy.
- In the ensuing clinically latent ("asymptomatic") phase, cats show no clinical signs.
- Conversion to the terminal phase of infection cannot be predicted. Clinical signs of the terminal phase are related to secondary infections, tumors, and FIV infection of the CNS, leading to behavioral changes, seizures, and paresis.

ETIOLOGY AND PATHOPHYSIOLOGY

- FIV is a lentivirus (RNA virus) of the family *Retroviridae*.
- It is most commonly spread through bite wounds and blood contamination. Vertical transmission from queen to offspring has

been reported in experimental infection but is unlikely in the field.
- At least five subtypes (or clades) worldwide, based on sequence differences in a hypervariable region of the *env* gene: clades subtypes A, B, C, D, and E. Routine diagnostic testing does not differentiate them.
- FIV infection has three clinical phases:
    - Acute phase
        - Viral replication begins in the salivary glands, peripheral lymphoid tissues, and thymus, then spreads to infect mononuclear cells throughout nonlymphoid tissues. Lasts days to a few weeks; usually unnoticed.
    - Clinically latent ("asymptomatic") phase
        - Most common phase during which cats with FIV infection are usually presented in veterinary practice
        - Host immune response contains, but does not eliminate, the virus.
        - No clinical signs are present.
        - Cats are transmitting the infection (through bites, blood).
        - Generally lasts for months to several years
    - Terminal phase
        - Organism replication eventually overwhelms host's immune response.
        - Overt signs of immune deficiency, manifesting with refractory opportunistic infections (enteric, respiratory, cutaneous, or other), neoplasia, or neurologic disorders

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Two diagnostic contexts exist: routine screening of healthy pets, and suspicion of FIV underlying signs of infection, neoplasia, or neurologic dysfunction. In either context, diagnosis is usually made by detecting FIV-specific antibodies in ELISA or similar tests. Negative results are highly reliable (in an area with low prevalence), but positive results should be considered carefully, because vaccination causes antibody development that leads to a positive result, and false-positive results are possible. Thus, a positive test should always be confirmed.

DIFFERENTIAL DIAGNOSIS

- Other immunosuppressive conditions, such as FeLV infection
- Primary neurologic disease or systemic causes of encephalopathy

INITIAL DATABASE

- CBC, serum chemistry panel, urinalysis
    - Rarely suggestive of FIV infection; rules out other illnesses
    - CBC, serum biochemistry profile, urinalysis results often normal in the latent stage
        - FIV may sometimes cause lymphopenia (because FIV replicates mainly in lymphocytes and macrophages) or hyperglobulinemia (because of an immune-mediated response).
- The screening tests of choice are fast in-house ELISA or other immunochromatography tests (using a similar technique) which detect anti-FIV antibodies in blood.
    - The presence of anti-FIV antibody is considered consistent with infection, because a cat, once infected, will never clear infection.
    - There are two exceptions in which a cat not infected still may have antibodies:
        - FIV vaccination (no commercially available antibody test can distinguish between vaccine-induced and infection-induced antibodies.)
        - Presences of maternal antibodies (if the queen was infected or vaccinated) that can be detected up to age 6 months
    - There are also two conditions in which an infected cat may have no detectable antibodies:
        - Acute infection: up to 8 weeks required to produce antibody
        - Terminally ill cats, owing to loss of detectible antibodies secondary to severe immunodeficiency (very rare)
    - False-positive result more likely than false-negative in countries with lower prevalence of FIV (e.g., United States)
    - Positive results always should be retested (preferentially using a different test system, e.g., Western blot) before communication of the result to the owner.

ADVANCED OR CONFIRMATORY TESTING

- Western blot (detects antibodies)
    - Confirmatory antibody test of choice (in cats not vaccinated against FIV)
    - Has a higher sensitivity and specificity than ELISA and related tests, but ELISA is used more commonly for initial testing because it is technically easier

- PCR test (detects viral DNA)
    - Especially if a cat is vaccinated against FIV or has an unknown vaccination history, PCR is currently the only test that accurately confirms infection.
    - However, up to 50% false-negative results occur, and the test requires meticulous lab conditions to avoid false-positive results

TREATMENT

TREATMENT OVERVIEW

Lifestyle management is a cornerstone of treatment and prevention. The FIV-infected cat should stay indoors only, away from the risk of secondary infections. In cats with no clinical signs, no other treatment is required. If cats have secondary infections, these should be treated comprehensively. In FIV-infected cats with stomatitis or neurologic signs, azidothymidine (AZT) can be considered.

ACUTE AND CHRONIC TREATMENT

- Any secondary infections should be treated immediately and with a prolonged course as appropriate (e.g., antibiotics).
- Antiviral treatment with AZT has been associated with an improvement in clinical signs, immune signs, and quality of life, especially in cats with stomatitis and neurologic signs. Doses of 5 mg/kg PO q 12 h have been given without side effects.

BEHAVIOR/EXERCISE

The most important life-prolonging advice is to keep FIV-infected cats strictly indoors: doing so prevents contagion with FIV to other cats and reduces exposure of the immunosuppressed cat to infection.

DRUG INTERACTIONS

- Griseofulvin should not be used for treating dermatophyte infections in FIV-positive cats (risk of severe neutropenia).
- All immunosuppressive drugs should be avoided.

POSSIBLE COMPLICATIONS

- AZT can cause a reversible regenerative anemia.

RECOMMENDED MONITORING

FIV-infected cats should be monitored regularly for evidence of secondary infectious diseases, neoplasia, and progression of illness. Recheck visits are recommended q 6 mos.

PROGNOSIS AND OUTCOME

FIV-positive cats may have an excellent quality of life for many years. FIV infection is not a reason for euthanasia.

PEARLS & CONSIDERATIONS

COMMENTS

- The FIV status of all cats should be known. Thus, every cat should be tested independent of age. If a young cat (<6 months old) is FIV antibody-positive, it should be retested when >6 months. In vaccinated cats, antibody tests are useless, and other tests (e.g., PCR) have to be used.
- A diagnosis of FIV infection is not a reason for euthanasia. Infected cats can live many years with an excellent quality of life. However, the diagnosis has certain implications.
    - The cats should only be kept indoors.
    - More intense veterinary care is generally required in such a cat.
    - Vaccination for other infectious diseases is recommended (as it may lead to progression of FIV infection) only for those cats at high risk of developing an infectious disease (e.g., open multicat households). When vaccinating an FIV-positive cat against other infectious diseases, only inactivated vaccines should be used.

PREVENTION

- FIV vaccination is controversial. The incidence of FIV is low in household pets, and infection may be prevented (without vaccination) by inhibiting FIV-negative cats from interacting with unfamiliar and unowned cats.
- FIV vaccination interferes with routine testing methods. FIV vaccination will result in antibody production that cross-reacts with routine testing (e.g., ELISA) for at least 1 year after vaccination. Additionally, kittens born to vaccinated queens will have positive test results due to passive transfer of antibodies.
- For high-risk cats with a known FIV-negative status, FIV vaccination may be considered.

TECHNICIAN TIPS

- Clients should be aware that the FIV status of every cat should be known.
- As FIV lives only minutes outside the host and is susceptible to all disinfectants including common soap, simple precautions and routine cleaning procedures will prevent transmission while in the hospital. FIV infection does not justify being housed in an “infectious disease ward” in which cats with contagious diseases (e.g., upper respiratory infections) are kept.

CLIENT EDUCATION

- Every cat should be tested for FIV.
- The importance of neutering cats should be emphasized.

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Fear Due to Veterinary Visits/Treatments

BASIC INFORMATION

DEFINITION

Extremely common, truly iatrogenic condition in which the animal learns to avoid the veterinarian, the practice, and/or all veterinary experiences because these engender fear and behavioral distress.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- All species are affected, more so those not wholly domesticated (e.g., cats).
- Dogs, which may have coevolved with humans, are least affected before 2 years of age but may worsen with exposure. Females > males.
- At least 60% of all veterinary patients may be affected.

GENETICS & BREED PREDISPOSITION: Onset/worsening: possibly worse in breeds with apparent familial behavioral concerns associated with social anxieties (e.g., Bernese mountain dogs: generalized anxiety disorder), fear (e.g., German shepherd dogs), phobias (e.g., German shepherd dogs, Australian shepherds, Border collies for noise phobia) and/or panic (many herding and coursing breeds)

RISK FACTORS

- +/− Social maturity (occurring during age 12-18 [up to 36] months in dogs, 24-48 months in cats)
- Dogs/cats who appear developmentally delayed and/or overly fearful within their first few months of life may be more susceptible to this form of learned fear.

CONTAGION & ZOONOSIS: This condition is the result of learning about environments viewed as threatening or uncertain from behavioral cues given by other animals and people. Affected animals often bite veterinary professionals.

ASSOCIATED CONDITIONS & DISORDERS

- Generalized anxiety disorder
- Noise phobia
- Fear (generalized or specific)
- Fear aggression

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Clients recognize that their pets “do not like to go to the vet.” Physical and behavioral signs of stress, distress, and anxiety are generally recognized by most people present but ignored because they are considered “normal” for veterinary patients.

PHYSICAL EXAM FINDINGS: Physical exam findings are those associated with the physical and behavioral signs of stress, distress, and anxiety. These may include but are not restricted to:

- Social withdrawal with or without complete freezing (no interaction with anyone)
- Physical freezing and rigidity
- Salivation and/or clear nasal discharge
- Panting
- Shaking/trembling
- Increased shedding of hair/exfoliation of dry skin
- Avoidance of stimulus or stimulus modality that triggers response (e.g., metal table, smell of alcohol, all flooring that is not nonslip)
- Vocalization including whining, barking, growling, hissing, whimpering
- Mydriasis
- Escape behaviors
- Grabbing with mouth or paws

- Yawning/licking lips
- Scratching
- Chewing through restraints (e.g., leads)
- Hiding
- Crouching
- Tucking tail
- Tachypnea
- Tachycardia
- Hyperthermia
- Increased or decreased sensitivity to pain
- Increased or decreased reactivity to touch or approach
- Hyperemic mucous membranes
- Dehydration
- Exacerbation of any cardiac, respiratory, or skeletal condition that may be comorbid

ETIOLOGY AND PATHOPHYSIOLOGY

- The etiology is exposure to stimuli and environments animals feel are worrisome, threatening, or uncertain and from which they cannot escape in time or space, despite signaling their need to do so. Regardless of whether the humans feel the environment is not threatening, what matters is the animal's perception and response.
- The pathophysiology is as for any condition involving behavioral stress, distress, and/or anxiety and appears to be rooted in neurochemical encoding of information in the amygdala.
- Rodent studies show that fear is most easily erased in very young animals whose brains are still developing. After this period (which is undefined for cats and dogs), perineuronal nets protect memories of fear from modification. This is why it is so important not to learn to fear.

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

The diagnosis is made based on visual observation of signs of stress, distress, and/or anxiety in association with veterinary premises or activities. Since this problem is highly prevalent, such signs are at risk of being downplayed or ignored, and the diagnosis missed.

DIFFERENTIAL DIAGNOSIS

All signs of this iatrogenic condition are shared by other behavioral conditions and by many physical conditions including various neuropathies and toxicoses. The key to assigning a cause to the signs is to ask whether the signs are manifest only under physical and behavioral environmental conditions involving veterinary care.

INITIAL DATABASE

- No diagnostic testing is required to make the diagnosis.
- Many laboratory databases can be skewed by the condition. Examples include but are not restricted to:
  - Altered lymphocyte/neutrophil ratios and leukocytosis, often with a left shift (stress leukogram)
  - Increased cortisol
  - Hyperglycemia (especially cats)
  - Increased creatine phosphokinase
  - Increased hematocrit due to splenic pooling and/or margination associated with mild dehydration

TREATMENT 

TREATMENT OVERVIEW

- Treatment should be focused on ameliorating any signs of stress, distress, or anxiety as they appear, and at preventing them from worsening by learning in the future. This means specific triggers must be identified and addressed for the patient population as a whole and for each animal as an individual.
- A list of potential triggers of stress, distress, or anxiety should be compiled at each visit and long-term and short-term plans made for how to address the triggers (e.g., replace slippery tile flooring with nonslip flooring; vaccinate outside while dog is watching other dogs).

ACUTE AND CHRONIC TREATMENT

- Cease exposure to or engagement in whatever environments or behaviors are provoking the animal (e.g., if animals are resistant to getting on the table, let them sit on the floor; if they slip on the table, give them a nonslip mat).
- If the animal continues to manifest distress, consider panicolytic medication to abort the distress while the animal is with the veterinarian. The first drug of choice is alprazolam (dogs, 0.01-0.1 mg/kg [likely most effective range: 0.02-0.04 mg/kg] PO q 4-6 h PRN; cats, 0.0125-0.025 mg/kg PO q 12-24 h PRN; some published sources mistakenly recommend a tenfold higher dose). May also be used as a preventive: 0.5-1 dose given 2 hours before the expected provocative event and repeated 30 minutes beforehand. Alternatively, clonidine (dogs: 0.01 mg/kg PO q 12-24 h increased stepwise up to 0.05 mg/kg PO q 12-24 h (maximum dose 0.9 mg/day) or gabapentin (dogs: 10-20 mg/kg PO q 8-12 h) may be useful.
- Have all staff work to reward the dog for calm and comfortable behaviors.
- Integrate Certified Pet Dog Trainers (CPDTs) with extensive experience in behavior modification into the practice (www.ccpdt.org).
- Treatment of phobias (see p. 875) and separation anxiety (see p. 1012) as needed.

BEHAVIOR/EXERCISE

- Prophylactic veterinary visits should be fun. Interventional veterinary visits should be nonthreatening, calming, reassuring, and as stress free as possible.
- Animals learn fear as they age, so early appointments should involve treats, play, massage, and lots of fun activities before anything threatening (e.g., a vaccination) should be attempted. Therefore, puppy and kitten visits should be longer, and the animals should be allowed to interact with the staff and explore the hospital.
- On-site puppy/kitten and young dogs manners classes are an excellent vehicle for these exposures.
- Environments should be friendly to animals. This means that practices should attempt to do the following:
    - Modulate the noise environment by using acoustic tiles, plexiglass cage doors/walls when possible. Consider Muttmuffs (www.muttmuffs.com) for hospitalized/anesthetized animals.
    - Modulate the visual environment by the use of movable barriers and flexible and non-harsh lighting conditions. Consider calming caps (www.premier.com), Doggles (www.doggles.com), or eye shades as needed, especially when recovering from anesthesia.
    - Modulate the olfactory environment by allowing animals to have T-shirts or gloves worn by their humans with them in cages and during manipulations or anesthetic inductions. Rinse common areas with plain water. Spraying hands with pheromonal analog products (e.g., Feliway) has been anecdotally reported to decrease locomotor behavior/increase calm behaviors in cats.
    - Provide hiding and perching boxes/containers for caged cats.
    - Change tactile environments through nonskid flooring, yoga mats, and covering tables and scales with nonslip surfaces.
    - Use treats to reward good behaviors, and teach animals to participate in the exam process by offering body parts.

POSSIBLE COMPLICATIONS

Left untreated, these animals are more at risk for relinquishment, euthanasia, or absence of any preventative veterinary care.

RECOMMENDED MONITORING

Screen each animal at every visit for behavioral concerns manifest at home or during examinations/interventions.

PEARLS & CONSIDERATIONS

COMMENTS

- Iatrogenic fear conditioned by veterinary visits and care may trigger otherwise latent pathologic behavioral conditions.
- Because manifestations of fear are commonly cited as reasons for relinquishment, euthanasia, or avoidance of veterinary visits, the single most important welfare concern for pet animals may be how they react to veterinary care and visits.
- Everyone can recognize the signs associated with this condition. Only if we begin to find it unacceptable to scare animals will we stop doing it.

PREVENTION

- This condition is completely preventable.
- Cats should be exposed to humane interactions with people between 2-9 weeks of age, and dogs should be exposed to nonterrifying interactions with people and other animals and to new environmental experiences between 3 weeks and 16 weeks of age. Any profoundly fearful or distressed reactions during this period should trigger a behavioral consult and inform

the quality and quantity of future interactions/exposure.

TECHNICIAN TIPS

- This is one condition where technicians, particularly those with an interest in behavior modification, can make a huge change for the better in an animal's life. Technicians should be comfortable with how to examine cats in carriers using towels, how to use head collars and no-pull harnesses, how to trim toenails and draw blood without restraints, how to teach dogs and cats to offer body parts for examination, and how to modify the environment according to the pet's needs.
- Many practices have one or a few technicians who are very adept at deciphering and acting favorably and appropriately on cues of stress (the “pet whisperers”), and much can be learned by example from these individuals.

CLIENT EDUCATION

- Clients should be taught that this condition need never develop and that it need not be normal for pets to fear veterinary visits or care. Working with a good CPDT, they can teach their pets to willingly participate in the physical exam.

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Fanconi Syndrome

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Uncommon constellation of renal tubular resorptive defects (including amino acids, phosphates, glucose, bicarbonate, calcium, and potassium) with renal tubular acidosis and antidiuretic hormone (ADH)-resistant polyuria

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Primarily affects dogs; has been seen in cats
- No sex predilection
- Onset of phosphaturia and renal sodium loss around 3 years of age, with glucosuria and aminoaciduria at 4 years of age in inherited forms

GENETICS & BREED PREDISPOSITION

- Inherited form in basenji; mode of inheritance unknown; affects 10%-30% of basenji dogs in United States
- Documented disease in other breeds (not necessarily inherited): border terriers, Norwegian elkhounds, single reports in a Yorkshire terrier, Labrador retriever, cocker spaniel, dachshund, whippet, Shetland sheepdog, and mixed breed
- Bedlington terrier, West Highland white terrier, Skye terrier, Dobermanpinscher, Labrador retriever, and dalmatian dogs are predisposed to copper storage diseases; West Highland white terriers and other breeds with copper storage disease have been noted to have a reversible Fanconi syndrome.

RISK FACTORS

- Copper storage hepatopathy has been associated with transient Fanconi syndrome, similar to Wilson's disease in humans.
- Newly recognized form of acquired Fanconi syndrome is suspected but not proven to be caused by ingestion of contaminated jerky treats (pathophysiology unknown).

ASSOCIATED DISEASES & CONDITIONS: Metabolic acidosis, electrolyte disorders, urinary tract infection; bone abnormalities are uncommon in adult dogs (rickets common in children with Fanconi syndrome).

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Not all dogs have all components of tubular resorptive defects, and the degree of each defect varies from dog to dog.

HISTORY, CHIEF COMPLAINT

- Polyuria
- Polydipsia
- Weight loss
- Poor haircoat
- None (routine screening/incidental finding)
- Severe GI signs (vomiting, diarrhea, anorexia) if associated with jerky treat ingestion

PHYSICAL EXAM FINDINGS

- Dehydration
- Muscle weakness
- Exam may be unremarkable

ETIOLOGY AND PATHOPHYSIOLOGY

Can be acquired or inherited. Acquired disease can be due to heavy metal intoxication (lead, copper, mercury, organomercurials),

maleic acid, Lysol, drugs (outdated tetracycline, gentamicin, cephalosporins, cisplatin, salicylate), contaminated jerky treats (presumptive), copper storage hepatopathy, nephrotic syndrome, amyloidosis, neoplasia (multiple myeloma), hyperglobulinemia, hyperparathyroidism, vitamin D deficiency, hypokalemia, or interstitial nephritis associated with antibodies to the glomerular basement membrane or transplantation.

- Defects are primarily proximal tubular resorptive defects.
  - Filtered glucose is normally completely reabsorbed in the proximal tubule, so long as tubular concentration (similar to plasma concentration) does not exceed the transport maximum (about 180 mg/dL). A defect in the transport mechanism can lead to renal glucosuria despite normoglycemia.
  - Aminoaciduria may be generalized or involve only certain groups of amino acids, because different carrier molecules are involved in transport of acidic, basic, and neutral amino acids. Some dogs have cystinuria with minor defects in resorption of methionine, glycine, and dibasic amino acids.
  - Phosphate is reabsorbed primarily in the proximal tubule, with very little reabsorbed in the distal tubule. Excessive phosphaturia due to tubular defects may lead to hypophosphatemia.
  - Hyperchloremic metabolic acidosis may develop secondary to severe bicarbonaturia.
  - Hypokalemia may result from excess renal potassium loss associated with bicarbonaturia.
- In addition to proximal tubular defects, dogs with Fanconi syndrome are resistant to ADH, creating a form of nephrogenic diabetes insipidus. This results in urinary concentrating defects. Before the onset of renal failure, urine specific gravity is frequently less than 1.008.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The presence of glucosuria and ketonuria in the absence of hyperglycemia is a hallmark of Fanconi syndrome, but other tubular defects will be present in addition.

DIFFERENTIAL DIAGNOSIS

- Diabetes mellitus
- Central diabetes insipidus
- Any cause of nephrogenic diabetes insipidus
- Renal failure
- Primary renal glucosuria (glucosuria only without aminoaciduria, etc.)

INITIAL DATABASE

- Urinalysis: isosthenuria or minimally concentrated urine, glucosuria and proteinuria common, +/− ketonuria
- Urine culture: glucosuria leads to increased risk of UTI.
- CBC: anemia occurs late in disease secondary to kidney failure.
- Serum biochemistry panel: normoglycemia; hyperchloremic metabolic acidosis, and azotemia occur late in disease process.
- Venous blood gas (preferred to total CO2 from serum biochemistry panel because of artifactual changes associated with storage and handling): metabolic acidosis

ADVANCED OR CONFIRMATORY TESTING

- In a basenji with glucosuria and normoglycemia, no further confirmation necessary
- For other breeds:
  - Amino acids
    - Cyanide nitroprusside-based array for cystinuria
    - Urine amino acid excretion: either 24-hour excretion or fractional excretion compared to creatinine excretion; normally 98%-100% resorption (available from http://research.vet.upenn.edu/penngen)
  - Fractional excretion of electrolytes: (Ux/Sx)× (Scr/Ucr) × 100, where Ux is urine concentration of electrolyte, Sxis serum concentration of electrolyte, Scr is serum creatinine, and Ucris urine creatinine
    - Expect elevated fractional excretion values (normal values in parentheses): Na^+ (0.31 ± 0.2), Cl^- (0.31 ± 0.25), K^+ (9.3 ± 5.9), Phos (21 ± 9), Ca^{++} (0.15 ± 0.13)
  - Parathyroid hormone level if suspicion of hypoparathyroidism (hypocalcemia)
  - Heavy metal testing if indicated

TREATMENT

TREATMENT OVERVIEW

One treatment protocol (www.basenji.org/fanconi.pdf) replaces nutrients excreted in urine to maintain plasma concentrations. This protocol has not been compared to other (potentially simpler) protocols to determine whether it improves survival or quality of life, but it is used by many owners of basenji dogs with Fanconi syndrome.

ACUTE GENERAL TREATMENT

- If acute uremic crisis, hospitalize for intravenous fluid therapy and other management appropriate for decompensated chronic renal failure (see p. 207)
- Electrolyte and acid base disorders treated as appropriate
- If severe GI signs associated with jerky treats, hospitalization for IV fluid therapy and potentially feeding tube placement may be appropriate.

CHRONIC TREATMENT

- Acidosis: sodium bicarbonate titrated to keep venous pH normal. Doses may exceed 11 mEq/kg per day (650 mg = 10 grain = 7.8 mEq). Starting dose can be based on pH and Pco^2 using a chart in the basenji club website protocol, or if immediate blood gas monitoring not available, 30 grains q 12 h.
- Hypokalemia: supplement 5-15 mEq per day, depending on severity of hypokalemia. Potassium gluconate has 8 mEq K^+ per tsp. Potassium citrate provides 5 mEq K^+ per 540 mg tablet; the citrate is metabolized to 5 mEq bicarbonate, which may help control acidosis.
- Chelation therapy if copper storage hepatopathy

NUTRITION/DIET

- Vitamin and mineral replacement: 1-2 canine multivitamins per day (e.g., Pet-Tab Plus), 1-2 Pet-Cal (calcium, phosphorus, and vitamin d supplement) per day, and 1 human multivitamin with trace minerals (i.e., Centrum) per week in dogs with polyuria and polydipsia. Do not give Pet-Cal if dog is in renal failure.
- Amino acid replacement: 1 AminoFuel tablet per week

POSSIBLE COMPLICATIONS

- Neurologic signs (seizures, ataxia, dementia, or central blindness) of unknown cause are seen in up to 20% of dogs.
- Manipulation of electrolyte and acid-base balance can lead to overcorrection of deficiencies.

RECOMMENDED MONITORING

- Recheck chemistry panel and venous blood gas 8-10 weeks after starting therapy, then in 6 months. Recheck annually if animal remains stable and requires no dose adjustments.
- Recheck potassium 1 week after any dose adjustment.
- Culture urine at least every 6 months.

PROGNOSIS AND OUTCOME

Lifespan is not substantially reduced from normal (median survival time 5.25 years from diagnosis). Renal failure is the most common cause of death (40%).

PEARLS & CONSIDERATIONS

COMMENTS

Overall, this is a rarely encountered disease.

PREVENTION

Inherited disease in basenji dogs. Dogs with this disease should not be bred, although late onset of disease (3-8 years) complicates reproductive planning.

SUGGESTED READING

The Basenji Club of America: www.basenji.org/fanconi.pdf. Yearley JH, et al: Survival time, lifespan, and quality of life in dogs with idiopathic Fanconi syndrome. J Am Vet Med Assoc 225:377–383, 2004.

AUTHOR: CATHY LANGSTON

EDITOR: LEAH A. COHN

Facial Paralysis, Idiopathic

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

An acute neuropathy of unknown etiology affecting one or both facial nerves

EPIDEMIOLOGY

SPECIES, AGE, SEX: Mature (>5 years) dogs and cats may be affected.

GENETICS & BREED PREDISPOSITION: Cocker spaniels, golden retrievers, beagles, and domestic long-haired cats are overrepresented.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Rapid onset of drooling from one side of the mouth
- Inability to blink:
  - This deficit may be somewhat inapparent to owners, since dogs and cats with facial paralysis retain the ability to periodically retract the globe, which may give the appearance of a blink, owing to passive motion of the third eyelid.
- Dogs usually have an apparent ear droop and occasionally will have deviation of the nose away from the affected side. Food may collect in the affected commissure of the lips, and there may be associated halitosis.
- Occasionally clinical signs are bilateral, but they may begin on one side and take several days or weeks to affect the contralateral side.

PHYSICAL EXAM FINDINGS

- The menace response and palpebral reflex on the affected side are absent.
- Facial drooping, ptyalism, and ptosis may be evident.
- When a noxious stimulus is applied to the upper lip, the muscles of facial expression will fail to contract (trigeminofacial reflex); sensation of the face remains unaffected.
- In chronic cases, there may be permanent lip contracture.
- Corneal ulceration may be evident as a result of damage to the parasympathetic fibers responsible for tear production and/or exposure keratitis from the inability to blink.

ETIOLOGY AND PATHOPHYSIOLOGY

- The pathogenesis in domestic animals is unknown, but in humans, a similar condition (Bell's palsy) is associated with herpes simplex virus infection.
- Histopathologic studies reveal active degeneration of large- and small-caliber myelinated fibers. Inflammation is absent.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis of idiopathic facial paralysis requires a complete neurologic exam and eliminating structural or metabolic causes of facial nerve dysfunction.

DIFFERENTIAL DIAGNOSIS

- Idiopathic facial paralysis must be differentiated from other conditions involving the peripheral aspect of the facial nerve (e.g., otitis media interna, hypothyroidism, ear polyps, and polyneuropathies).
- When they cause facial paralysis, disorders of the central nervous system such as neoplasia, encephalitis, congenital malformations, and trauma are usually accompanied by additional neurologic deficits.

INITIAL DATABASE

- Complete neurologic and otoscopic examination (see p. 1311 and p. 1316, respectively)
- Serum chemistry panel and CBC: un remarkable with idiopathic facial paralysis
- Thyroid panel
- Schirmer tear test

ADVANCED OR CONFIRMATORY TESTING

Advanced imaging (e.g., CT, MRI) may be indicated for evaluation of the tympanic bullae and brainstem. Enhancement patterns in the intratemporal segment of the facial nerve as seen on MRI may be used for predicting recovery times.

TREATMENT

TREATMENT OVERVIEW

The main goal is prevention of corneal ulceration. No specific therapy is indicated for the remaining manifestations of facial paralysis.

ACUTE GENERAL TREATMENT

- Treatment is primarily supportive. Sterile lubricant ophthalmic ointment should be applied to the affected eye(s) at least q 6-8 h to prevent exposure keratitis and corneal ulceration.
- The use of corticosteroids is controversial and unlikely to be of benefit, given the paucity of inflammation. However, in people with Bell's palsy, such drugs may be efficacious in hastening recovery.

CHRONIC TREATMENT

Some animals require lifelong eye lubrication. Others will eventually begin to reflexively use the third eyelid to moisten the cornea and will no longer need topical medication.

PROGNOSIS AND OUTCOME

Prognosis for complete recovery is guarded. Some animals will regain variable levels of function to the facial nerve, but many have some degree of residual deficit.

PEARLS & CONSIDERATIONS

COMMENTS

Facial paralysis was reported to be idiopathic in 75% of dogs and 25% of cats in one study. Therefore it is imperative that practitioners do a complete neurologic evaluation to rule out other common causes of facial nerve dysfunction (see Differential Diagnosis above).

SUGGESTED READING

Dewey CW: Encephalopathies: Disorders of the brain. In Dewey CW editor: A practical guide to canine and feline neurology, ed 2, Ames, IA, 2008, Wiley-Blackwell Publishing, pp 160–162.

Varejao AS, et al: Magnetic resonance imaging of the intratemporal facial nerve in idio-pathic facial paralysis in the dog. Vet Radiol Ultrasound 47:328, 2006.

AUTHOR: GEORGINA BARONE

EDITOR: CURTIS W. DEWEY

Facial Muscle Wasting

BASIC INFORMATION

DEFINITION

Atrophy of the muscles of mastication, mainly the temporal and masseter muscles

SYNONYM

Masticatory muscle atrophy

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs (most commonly) and cats (rarely), any age, any sex; with muscular dystrophy (MD), only males affected; with hereditary Labrador retriever myopathy (HLRM), males and females affected.

GENETICS & BREED PREDISPOSITION

- German shepherd, retrievers, Doberman pinscher, spaniels: masticatory myositis (MM)
- Shetland sheepdogs, rough- and smooth-coated collies: dermatomyositis
- German shepherds, other large breeds: idiopathic polymyositis (IP)
- Large-breed dogs: glucocorticoid-induced muscle atrophy
- Young male golden retriever: muscular dystrophy
- Labrador retriever: HLRM
- Bassett hounds: temporomandibular joint (TMJ) dysplasia

ASSOCIATED CONDITIONS & DISORDERS

- Submandibular and prescapular lymphadenopathy (see p. 662)
- Generalized muscle atrophy

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Detailed history to include inquiries regarding previous bouts of painful mastication or chronic corticosteroid use
- History may reflect abnormalities isolated to facial musculature or reflective of generalized myopathy.
    - Facial:
        - Prominence of external occipital protuberance noticed by owner
        - Difficulty or inability to prehend food (less common)
        - Reflects either weakness (decreased jaw tone) or masticatory muscle fibrosis (increased jaw tone or trismus [inability to open the mouth])
        - Prior episode(s) of painful mastication and crying while chewing: MM
    - Generalized:
        - Concomitant mild to severe weakness, exacerbated by exercise; generalized muscle atrophy: IP
        - Bunny hopping gait, progressing to a more stilted gait with a plantigrade stance: MD

PHYSICAL EXAM FINDINGS

- Full physical examination, paying particular attention to the head, the condition of other muscle groups, and the skin
- Bilateral atrophy of the temporal and masseter muscles; skull-like appearance of the head
    - Dogs with MM can show salivation, dysphagia, and difficulty in opening their mouths, progressing to trismus.
    - Dogs with dermatomyositis can show generalized muscle atrophy, decreased jaw tone, facial nerve paralysis, stiff gait, dysphagia, regurgitation, and skin lesions.
- Enophthalmos, with third eyelid protrusion and small palpebral fissure due to dramatic loss of retrobulbar muscular support
- Unilateral temporal muscle atrophy: ipsilateral denervation of the mandibular branch of the trigeminal nerve

ETIOLOGY AND PATHOPHYSIOLOGY

- Developmental
  - MD
  - HLRM
  - Dermatomyositis
- Idiopathic
  - Trigeminal neuropathy
- Infectious
  - Toxoplasmosis (rare)
  - Neosporosis (rare)
- Immune-mediated
  - Systemic lupus erythematosus
  - Idiopathic polymyositis
  - MMM
- Iatrogenic
  - Glucocorticoid administration
- Metabolic
  - Hyperadrenocorticism
  - Cardiac cachexia
- Neoplastic
  - Cachexia and protein energy malnutrition resulting in muscle atrophy are features of many chronic neoplastic and inflammatory conditions.
- Disuse atrophy
  - TMJ dysplasia
  - Traumatic luxation of the TMJ (cats)
  - TMJ ankylosis (cats)

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The specific diagnosis is often made histopathologically, with the exception of serologic titers for infectious causes or for the detection of antibodies against type 2M muscle fibers.

DIFFERENTIAL DIAGNOSIS

As for Etiology, above

INITIAL DATABASE

- CBC usually normal by the time the muscles are atrophied
- Serum biochemistry profile
  - Elevated muscle enzyme levels (creatine kinase and aspartate aminotransferase): IP, MM, DM, MD, HLRM
  - Hyperglobulinemia: IP

ADVANCED OR CONFIRMATORY TESTING

- Muscle biopsies and histopathology (see p. 1305):
  - Immunohistochemistry shows lack of dystrophin (MD).
  - Paucity of type 2 myofibers (HLRM)
  - Antibodies against type 2 myofibers on frozen sections of muscle (MM)
  - Myofiber necrosis with mononuclear cell infiltrates, atrophy, and fibrosis (dermatomyositis)
  - Multifocal necrosis and phagocytosis of type 1 and type 2 myofibers (IP)
- Circulating serum antibodies against type 2 myofiber muscle fibers: MM
- Serology for *Toxoplasma* and *Neospora:* protozoal myositis
- Electromyography is more useful in determining neurologic rather than muscular etiology of the atrophy.

TREATMENT

TREATMENT OVERVIEW

Immunosuppressive drugs are the mainstay of treatment and have to be instituted early to halt the process of muscle inflammation

and atrophy. Antibiotics should be used for protozoal myositis.

CHRONIC TREATMENT

- Glucocorticoid therapy
  - Masticatory myositis (see p. 704)
  - Idiopathic polymyositis (prednisone, 1-2 mg/kg q 12 h for 14 days, then tapering over at least 4 weeks to 12 months or longer)
  - Dermatomyositis (variable response)
- Upright feeding of dogs with concomitant megaesophagus
- Clindamycin (12-25 mg/kg PO q 12 h): protozoal myositis

POSSIBLE COMPLICATIONS

Corticosteroid side effects

RECOMMENDED MONITORING

Monitor for corticosteroid side effects, and taper the dose depending on muscle condition and function.

PROGNOSIS AND OUTCOME 

Variable, depending on the underlying etiology. Process is reversible provided the muscles have not yet undergone extensive fibrosis.

PEARLS & CONSIDERATIONS 

COMMENTS

- Facial muscle atrophy is a common feature of many emaciating conditions in which there is also accompanying generalized loss of lean body mass.
- Generalized muscle atrophy is often first noticed in the facial muscles, especially in long-haired breeds.
- Of all the differentials discussed in this section, only trigeminal nerve abnormalities, MM, and anomalies of the TMJs are strictly confined to facial muscle atrophy.

CLIENT EDUCATION

Encourage clients to present patients early in the disease process

SUGGESTED READING

Taylor SM: Disorders of muscle. In Nelson RW, Couto CG, editors: Small animal internal medicine, St Louis, 2003, Mosby, pp 1062–1070.

AUTHOR: JOHAN P. SCHOEMAN

EDITOR: ETIENNE CÔTÉ

Gunshot Wounds

Additional Images Available on Website

BASIC INFORMATION

DEFINITION

A type of projectile injury involving handguns, air-powered weapons, shotguns, or rifles

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs and cats of any age
- Male dogs may be overrepresented

RISK FACTORS

- Unsupervised roaming, notably intact male dogs
- Night and early morning hours
- Stray dogs in rural areas (e.g., deliberately shot if considered a nuisance or potential threat to livestock)
- During hunting season, dogs may be mistakenly shot as game or maliciously for sport.
- Guard dogs, police dogs, and hunting dogs are at risk of being shot during work.

GEOGRAPHY AND SEASONALITY

- Higher-crime urban neighborhoods
- In rural areas, shotgun and rifle injuries are more common.
- Air-powered weapons: more likely discharged in residential or rural areas

CLINICAL PRESENTATION

Subtypes:

- Pellet guns and BB guns (air-powered projectiles)
- Handguns
- Rifles
- Shotguns

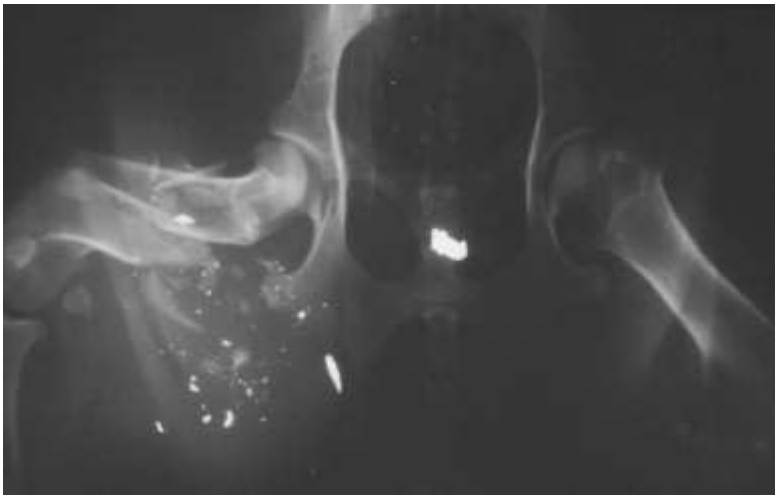
HISTORY, CHIEF COMPLAINT

- Pets may present with respiratory distress, internal hemorrhage, neurologic injury, or musculoskeletal injuries (fracture).
- Wound may escape notice, especially if event was not witnessed
- Dogs and cats with extensive blood loss will present in shock, with pale mucous membranes and tachycardia.
- Patient may present in pain; in minor cases, the patient may show little evidence of overt discomfort.

PHYSICAL EXAM FINDINGS

- Open wounds:
  - Circular, oval, or angular cutaneous entry wounds with solitary projectiles, often smaller than the projectile
  - Cutaneous burns/lesions if firearm was at close range
  - There may be no exit wound if the projectile is retained: low-velocity projectiles are more likely to be retained than high velocity projectiles.
  - Exit wounds are frequently larger and irregular in shape; shards of bone form secondary projectiles, increasing exit wound size.
  - At close range, shotgun injuries can cause extensive destruction of the skin and underlying tissues.
  - Low-velocity BBs and pellets (air-powered) create small entry wounds. Because of their low mass and comparatively low velocity, many of these projectiles will be retained (no exit wound).
- Internal injuries:
  - Clinical signs are commensurate with tissues impacted and the severity of trauma (orthopedic, spinal, ocular,

gastrointestinal, pulmonary involvement).
- Elastic tissues (lung, muscle) are capable of stretching, thereby partially dissipating the kinetic energy of the projectile. Inelastic organs, such as the liver (low collagen content), may show massive tissue destruction from the high-velocity rifle round compared to a low-velocity bullet.
- Abdominal gunshot wounds have a high probability for peritonitis (gastrointestinal tract penetration).



GUNSHOT WOUNDS Hunting rifle round, shattering the patient's femur. Note the bone and projectile fragments, creating secondary projectiles within the wound, enhancing soft tissue trauma.

ETIOLOGY AND PATHOPHYSIOLOGY

- The destructive potential of a projectile can be assessed in part by the formula:

$$\frac{\text{Mass} \times \text{Velocity}^2}{2}$$

- Bullets may have an outer metallic jacket to control the shape or expansion of the bullet as it impacts a target.
  - Hollow points are designed to mushroom on impact.
  - Frangible bullets are designed to break apart on impact.
  - Military-style full metal jacket bullets are designed to minimize deformation.
- Projectiles are capable of lodging and then migrating through the respiratory tract, urogenital tract, gastrointestinal tract, cardiovascular system, and fascial planes.
- Shotgun pellets expand in a conical pattern; they are very destructive in the first 20 yards or less.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

- Bullets, BBs, and pellets may be found as an incidental finding on radiographs. This may cause confusion when evaluating an acutely sick or injured patient. It is important to remember that acute gunshot wounds will have an entry wound.
- Gunshot wounds are most commonly mistaken for bite wounds and vehicular trauma.
- Because most animals are shot while wandering, radiographs are an important tool in looking for evidence of a retained projectile.

DIFFERENTIAL DIAGNOSIS

Other penetrating objects can create a skin opening that may mimic a bullet wound, including sticks, pointed metallic objects, and the like.

INITIAL DATABASE

- CBC, serum chemistry profile, and urinalysis as indicated by likely organs injured
- Radiographs (two-view minimum) for the body region shot, based on bullet retention or entry/exit wound locations. In a gunshot wound with no evidence of exit, additional views may be needed to locate a retained projectile.

ADVANCED TESTING OR CONFIRMATORY TESTING

- Abdominocentesis (see p. 1194), fluid analysis, cytology, and gram stains may be used to confirm the possible presence of peritonitis.
- Thoracocentesis can be both life saving and diagnostic for patients with pneumothorax or hemothorax; aerobic and anaerobic cultures if infection is suspected.

TREATMENT

TREATMENT OVERVIEW

- A team effort by doctors and technical support is necessary to efficiently stabilize critically injured patients.
- Control visible blood loss.
- Maintain an established airway, and assure patient is breathing satisfactorily.
- Placement of one or more intravenous lines for fluid support.
- Address life-threatening injuries and overlapping medical crises.
- Initiate pain therapy to reduce patient discomfort and stress.
- Initiate wound care and a plan for long-term management of the injuries.

ACUTE GENERAL TREATMENT

- Control external hemorrhage by external compression, tourniquets, ligatures, vascular clips. Attendants should wear gloves to prevent bacterial contamination and protect individuals from bloodborne disease.
- Intravenous fluid support (crystalloids, colloids, hypertonic saline, whole blood products)
- Establish and maintain respiratory system: intubation, emergency tracheotomy, thoracic tube insertion (hemo-thorax, pneumothorax, etc.) if indicated.
- Initiate pain medications that will not mask or compromise the patient's status. Consider a pure opioid agonist such as morphine, 0.1-1 mg/kg IV or IM q 2-6 h, for good analgesic activity and the ability for reversal as needed. Partial agonists (buprenorphine) and agonist/antagonists (butorphanol) acceptable for minor gunshot wounds.
- A muzzle or Elizabethan collar may be used to protect health care providers from being bitten by the anxious or painful patient.
- The external gunshot wound can be clipped, cleansed, and pressure lavaged (35-mL syringe and an 18-G needle); the wound may require enlargement to prevent entrapment of lavage fluids. A protective dressing may then be applied to the individual wounds.
- Broad-spectrum intravenous antibiotics (e.g., cefazolin, 22 mg/kg IV q 6 h) can be initiated in the seriously injured patient.
- Not all critical patients can be fully stabilized prior to surgery. For example, following initial attempts to support the hypovolemic patient, surgical intervention may be needed to control massive hemorrhage.
- Wound exploration is best performed under general anesthesia for detailed wound examination, débridement, and definitive wound repair.
- All acute abdominal gunshot wounds should be explored because of the high risk of peritonitis secondary to bowel penetration/perforation. All organs must be inspected closely for concomitant trauma.

CHRONIC TREATMENT

- Prolonged open wound management (serial débridement, multiple dressing applications, etc.) may be needed for contaminated or necrotic injuries.
- Peritonitis may require prolonged wound drainage (open abdomen, vacuum drain systems, sump drains), abdominal lavage, and possible reexploration (see p. 1250).
- Problematic soft-tissue wounds, including extensive skin loss, may require reconstructive surgery.
- With extensive orthopedic trauma (reparable), vacuum drains and lidocaine infusion catheters can be used for controlling dead space and reduce tissue pain. Lidocaine also may be temporarily infused using the tubing in a vacuum drain system (Jackson-Pratt drains).

POSSIBLE COMPLICATIONS

- The eyes are especially vulnerable to projectile wounds. Blindness and loss of the eye may result from extensive trauma.
- Paresis or paralysis may result from spinal cord trauma.
- Infection is a primary concern in gunshot wounds highlighted by extensive tissue destruction.
- Patients generally are at low risk for lead poisoning, except for lead in joints (should be removed).
- Delayed or nonhealing wounds

RECOMMENDED MONITORING

Vital signs in critical injuries

PROGNOSIS AND OUTCOME

- Determined by extent of injury and subsequent treatment
- Prompt stabilization of the patient and definitive medical/surgical intervention can improve the rate of survival and positive long-term outcome of the patient.
- Gunshot wounds to the brain, spinal cord, and abdomen normally carry a worse prognosis.

PEARLS & CONSIDERATIONS

COMMENTS

- Due to potential legal ramifications of gunshot wounds, records must be detailed and accurate; all conversations should be detailed, complete, and noted in the medical record. Photographs of the injuries (entry, exit, tissue trauma inflicted) are useful evidence in court, along with supporting radiographs.
- A board-certified veterinary pathologist is best utilized to conduct detailed postmortem examination of deceased animals.
- It is critically important to transfer bullets and bullet fragments only to a qualified law enforcement officer, handling bullets gently (no metal forceps; wrap in tissue paper, and place in labeled, sealed container) should they be used as evidence in court.

SUGGESTED READINGS

Pavletic MM: Atlas of small animal wound management and reconstructive surgery, Ames, Iowa, 2010, Wiley-Blackwell.

AUTHOR: MICHAEL PAVLETIC

EDITOR: RICHARD WALSHAW

Grapes and Raisins Toxicosis

Additional Images Available on Website

BASIC INFORMATION

DEFINITION

Acute renal failure (ARF) following ingestion of grapes *(Vitis* spp.) or raisins

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Documented in dogs only
- Anecdotally reported in cats, ferrets
- No known age or sex predisposition; all breeds susceptible
- Ingestion of grapes or raisins does not consistently cause acute renal failure in all dogs.

RISK FACTORS

Animals with preexisting kidney disease may be at increased risk of developing ARF.

GEOGRAPHY AND SEASONALITY

Intoxication can occur any time of the year.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Ingestion suspected or directly observed
- Evidence of grapes/raisins in vomitus or stool
- Most common signs are manifestations of acute renal failure: vomiting, lethargy, anorexia, diarrhea, decreased urine output, signs of abdominal pain, ataxia, and weakness
- Vomiting, lethargy, anorexia within 24 hours; vomiting is usually seen within 12 hours after ingestion.

PHYSICAL EXAM FINDINGS

- Dehydration
- Signs of abdominal pain in some dogs
- Lethargy

ETIOLOGY AND PATHOPHYSIOLOGY

- Etiology unknown
- Renal tubular necrosis is a consistent histopathologic finding.
- Tubular basement membrane often remains intact, providing possibility for recovery. Evidence of tubular regeneration may be present in some dogs.
- Mineralization of kidneys, gastric mucosa, myocardium, lungs, and blood vessels

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis of grape or raisin toxicosis is suspected based on possibility or certainty of exposure, presence of grapes/raisins in the vomitus/stool, and if several hours have passed, possibly the onset of vomiting, anorexia, lethargy, diarrhea, decreased urine output, ataxia or weakness, or a combination of these. Azotemia and other serum chemistry changes consistent with ARF are seen in 1-3 days, but supportive treatment is warranted as soon as possible.

DIFFERENTIAL DIAGNOSIS

Rule out other causes of ARF:

- Ethylene glycol toxicosis
- Leptospirosis
- Bacterial pyelonephritis
- Lily toxicosis in cats
- Iatrogenic/medication nephrotoxicosis (e.g., aminoglycoside antibiotics)
- Renal thromboembolism (usually accompanied by thromboembolism of other aortic branches)

INITIAL DATABASE

- Serum chemistry profile, CBC, calcium × phosphorus product (Ca × P):
  - Azotemia, hyperphosphatemia, elevated Ca × P (>60 when both are measured in mg/dL) almost always present if enough time has passed and ingestion was substantial; hypercalcemia frequent
  - Serum creatinine, phosphorus, and Ca × P can be elevated in less than 24 hours.
  - Blood urea nitrogen and calcium may be slower to rise (1-3 days).
- Urinalysis before giving fluids:
  - Urine specific gravity <1.030
  - Glucosuria, proteinuria
  - Cylindruria (casts)
- Abdominal radiographs; abnormalities uncommon:
  - Increased renal size
  - Metastatic mineralization

ADVANCED OR CONFIRMATORY TESTING

- Ultrasonography to assess kidneys and pancreas
- Renal biopsy may help determine prognosis

TREATMENT

TREATMENT OVERVIEW

If any reasonable possibility exists of a patient having eaten a significant quantity of grapes (e.g., >10-12 grapes in an 8-kg dog) or raisins (>0.1 oz/kg [>3 g/kg]), treatment is justified to reduce the risk of permanent renal lesions. Treatment aims to decrease absorption (induction of vomiting and administration of activated charcoal) in early/mild ingestions when no clinical signs are apparent. When clinical signs are present, treatment consists of fluid diuresis, nutritional support, vomiting, seizure control, and management of acute renal failure (see p. 31) as needed.

ACUTE GENERAL TREATMENT

- Decontamination of patient:
  - Emesis: useful 6-12 hours after exposure (see p. 1364)
  - Activated charcoal (1-2 g/kg PO): useful up to 12-24 hours after exposure
- Fluid diuresis:
  - Intravenous fluid diuresis for 48 hours in patients not yet showing clinical signs may prevent ARF.
  - Treat signs of ARF as needed (see p. 31). Currently no unique treatment identified. If concurrent hypercalcemia, consider using 0.9% normal saline.
- Manage vomiting:
  - Metoclopramide: 0.2-0.4 mg/kg q 6 h PO, SQ or IM or 1-2 mg/kg/d constant rate infusion (CRI); *or*
  - Maropitant: 1 mg/kg SQ (or 2 mg/kg PO) q 24 h up to 5 consecutive days
- Treat anuria/oliguria:
  - Correct dehydration first.
  - Mannitol: 0.25-0.5 g/kg IV over 3-5 minutes or CRI of 2-5 mL/min of 5%-10% mannitol in lactated Ringer's solution
  - Furosemide: 2-4 mg/kg IV up to 6 mg/kg if needed (if subnormal urine production persists) q 8 h; or combine 1 mg/kg/h furosemide (CRI or IV boluses) with dopamine CRI
  - Dopamine: 2-5 mcg/kg/min IV CRI. Efficacy in ARF questioned, and may cause nausea
  - Hemodialysis or peritoneal dialysis may be useful in some cases.

CHRONIC TREATMENT

Ongoing supportive care based on initial severity, response to treatments, individual's intrinsic ability to compensate, and extent of permanent renal injury

POSSIBLE COMPLICATIONS

- Uremia-related neurologic signs (seizures, ataxia)
- Metastatic mineralization (renal, cardiac, vascular, pulmonary)
- Pancreatitis

RECOMMENDED MONITORING

- Baseline blood urea nitrogen, creatinine, calcium, phosphorus, Ca × P, potassium, total protein, hematocrit, daily at first then as needed
- Urine output
- Signs of overhydration (respiratory character/effort, body weight)
- Acidosis

PROGNOSIS AND OUTCOME

- Of 43 dogs with grape/raisin toxicosis, 53% recovered with treatment, 12% died, and 35% were euthanized.
- Oliguria/anuria, ataxia, and weakness indicate poor prognosis.
- Higher serum [calcium] and Ca × P indicate poor prognosis.

PEARLS & CONSIDERATIONS

COMMENTS

- Raisins at 0.1 oz/kg (3 g/kg) and grapes (10 to 12 grapes in an 8-kg dog) have led to ARF.
- Not all dogs that ingest raisins or grapes develop ARF.
- Raisins are 4.5 times more concentrated than grapes on an ounce-per-ounce basis.
- Treatment may be required for days to weeks.

PREVENTION

Keep raisins and grapes out of dogs' reach.

TECHNICIAN TIPS

- Decontamination with induction of vomiting can be effective up to 6-12 hours after exposure, and administration of charcoal up to 24 hours after exposure.
- Oliguria is defined as <0.25 mL/kg/h urine production, and treatment should aim to ensure that urine production remains greater than this level.

CLIENT EDUCATION

- Do not feed grapes or raisins to dogs.
- Treatment may be extensive and expensive and may be associated with a guarded prognosis.

SUGGESTED READING

Eubig PA, et al: Acute renal failure in dogs after the ingestion of grapes or raisins: A retrospective evaluation of 43 dogs (1992-2002). J Vet Intern Med 19:663–674, 2005.

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Granulomatous Meningoencephalomyelitis (GME)

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

A common, idiopathic, inflammatory, noninfectious meningoencephalomyelitis of dogs, the definitive diagnosis of which is dependent on characteristic histopathologic features

EPIDEMIOLOGY

SPECIES, AGE, SEX

Any age and either sex can be affected by granulomatous meningoencephalomyelitis (GME). This is a canine disease, being virtually nonexistent in cats. The median age is 5 years, and there appears to be a female predominance.

GENETICS AND BREED PREDISPOSITION

The genetics of GME are unknown. Small-breed dogs (e.g., poodles, terriers) are predisposed, although larger breeds are occasionally affected.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Three forms of GME have been described:

- Multifocal (disseminated)
- Focal
- Ocular (uncommon)

HISTORY, CHIEF COMPLAINT

- The history and chief complaint are reflective of the form of GME and the particular region or regions of the central nervous system involved.
- Central vestibular dysfunction is a common presentation for dogs with GME.
- Other common complaints include seizures, abnormal mental status, neck pain, and nonambulatory status.
- Dogs with multifocal and ocular forms of GME tend to have acute onset of clinical signs.
- Multifocal GME is usually rapidly progressive.

PHYSICAL EXAM FINDINGS

- Patients with GME are occasionally febrile on presentation.
- There are usually no other abnormalities on general physical examination.
- Neurologic abnormalities (see p. 1311) depend on the form of GME affecting the patient. Clinical evidence of fore-brain, brainstem, cerebellar, and cervical spinal cord dysfunction are prominent, either alone or in combination.

ETIOLOGY AND PATHOPHYSIOLOGY

The etiology of GME is unknown. However, there is strong evidence that this is an autoimmune disorder, most likely a T-cell mediated, delayed-type (type IV) hypersensitivity reaction.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A working clinical diagnosis of GME is dependent on compatible history, neurologic exam findings, diagnostic imaging, and

cerebrospinal fluid [CSF] analysis.

DIFFERENTIAL DIAGNOSIS

- Necrotizing encephalitis
- Infectious meningoencephalitis
- Neoplasia
- Caudal occipital malformation syndrome
- Intracranial intra-arachnoid cyst (quadrigeminal cyst)

INITIAL DATABASE

- CT, MRI: most cases exhibit contrast-enhancing lesions with white matter predominance.
- Characteristic CSF findings are a sterile, mixed-cell (primarily mononuclear) pleocytosis with elevated protein levels.

ADVANCED OR CONFIRMATORY TESTING

Definitive diagnosis of GME is dependent on histopathologic examination of brain and/or spinal cord parenchymal lesions, which are uncommonly obtained in the clinical setting.

TREATMENT

TREATMENT OVERVIEW

Treatment goals are:

- Suppression of the inflammatory process
- Recovery of functional neurologic status
- Pain management
- Seizure control, if seizures are part of the clinical picture

ACUTE GENERAL TREATMENT

- The standard treatment for GME has traditionally been immunosuppressive doses of glucocorticoids (e.g., prednisolone, 1-2 mg/kg PO q 12 h).
- Current treatment protocols include cyclosporine (3-5 mg/kg PO q 12 h), procarbazine (25 mg/m^2 PO q 24 h), and cytosine arabinoside (50 mg/m^2 SQ q 12 h for 2 days, then repeated initially q 3 wk), in addition to prednisone therapy. These drugs are reported to be used as single agents in combination with prednisone. The author typically administers these drugs concurrently.
- If the patient is seizuring, intravenous diazepam or levetiracetam can be administered while starting a maintenance anticonvulsant drug (see p. 1009).

CHRONIC TREATMENT

- One or more of the previously mentioned drugs is/are continued indefinitely. Coincident with clinical improvement, one or more drugs can be slowly weaned to lowest possible levels.
- A maintenance anticonvulsant without sedative tendencies and without the side effects of polyuria and polydipsia is recommended for seizure control (e.g., zonisamide, levetiracetam).
- Radiation therapy has been shown to be beneficial in cases of focal GME.

POSSIBLE COMPLICATIONS

- Typical glucocorticoid side effects are to be expected.
- Procarbazine may cause hemorrhagic gastroenteritis.
- Procarbazine and cytosine arabinoside may cause bone marrow suppression. The author has witnessed bone marrow suppression with the former but not the latter drug.
- Potential adverse effects of cyclosporine (infrequently observed) include vomiting, diarrhea, systemic hypertension, weight loss, anorexia, gingival hyperplasia, and excessive shedding.

RECOMMENDED MONITORING

CBCs should be evaluated for dogs receiving immunosuppressive/chemo-therapeutic agents (e.g., cytosine arabinoside, procarbazine) every week for the initial month of therapy, then monthly thereafter.

PROGNOSIS AND OUTCOME

- The prognosis for GME has improved dramatically coincident with the addition of new treatment protocols (i.e., cyclosporine, procarbazine, cytosine arabinoside).
- With the use of prednisone alone, the overall median survival is 14 days.
- With the use of prednisone alone, the median survival for focal GME is 114 days and for multifocal GME, 8 days.
- With procarbazine use, the overall median survival is 14 months.
- With the use of cytosine arabinoside, the overall median survival is approximately 18 months.
- Cyclosporine therapy is associated with an overall median survival of approximately 2.5 years.
- Dogs with focal GME treated with radiation therapy have a median survival of more than 400 days.

PEARLS & CONSIDERATIONS

COMMENTS

- The author routinely uses multiple drug therapy to achieve clinical remission in GME cases, often using cyclosporine, procarbazine, and cytosine arabinoside in addition to prednisone. In most cases, an obvious response to therapy is observed within 1 week. After 1-2 months of combination therapy, one drug is weaned at a time, usually starting with prednisone.
- Procarbazine is often weaned to every other day after several months to avoid adverse drug effects.
- In many GME cases, prednisone can be weaned to a very low dose (minimizing adverse effects) but not entirely discontinued.
- It is the author's clinical experience that most GME dogs improve dramatically or achieve clinical remission with multi drug therapy and often survive for more than 2 years.

SUGGESTED READING

Adamo PF, et al: Cyclosporine use in multi-drug therapy for meningoencephalomyelitis of unknown etiology in dogs. J Small Anim Pract 48:486, 2007.

Coates JR, et al: Procarbazine as adjunctive therapy for treatment of dogs with presumptive antemortem diagnosis of granulo-matous meningoencephalomyelitis: 21 cases (1998-2004). J Vet Intern Med 21:100, 2007.

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Zarfoss M, et al: Combined cytosine arabino-side and prednisone therapy for meningo-encephalitis of unknown aetiology in 10 dogs. J Small Anim Pract 47:588, 2006.

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Granulomatous Enteritis/Colitis

BASIC INFORMATION

DEFINITION

Uncommon cause for persistent (>3 weeks) signs of small-intestinal/colonic inflammation associated with mucosal infiltration of macrophages. Affected animals have large-bowel diarrhea and will also show systemic signs of fever, anorexia, and weight loss.

SYNONYMS

"Boxer colitis" when referring to the inflammatory bowel disease (IBD) variant, histiocytic ulcerative colitis (HUC). Histiocytic ulcerative colitis is characterized by mucosal infiltrates of PAS-positive histiocytes.

EPIDEMIOLOGY

SPECIES, AGE, SEX

HUC appears to be more prevalent in young male dogs. Granulomatous colitis of any cause is much less common in cats than in dogs. Granulomatous enteritis associated with primary gastrointestinal histoplasmosis may be seen in both the dog (common) and cat (rare).

GENETICS & BREED PREDISPOSITION

Boxers are predisposed to HUC. Large-breed dogs are more commonly affected with systemic fungal infections.

GEOGRAPHY AND SEASONALITY

Midwestern and southern United States for gastrointestinal (GI) histoplasmosis

ASSOCIATED CONDITIONS & DISORDERS

HUC is often recognized as an IBD variant that is much less common than lymphocytic plasmacytic colitis. Note than HUC may not be IBD but rather a unique and specific form of infectious (e.g., enteroinvasive *E. coli*) colitis.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Histiocytic ulcerative colitis: IBD variant characterized by mucosal infiltration with PAS-positive histiocytes
- Infectious causes for granulomatous colitis: includes both systemic fungal infections caused by *Histoplasma capsulatum* and *Pythium insidiosum*, and algal infection caused by *Prototheca* spp. Gastrointestinal histoplasmosis is the most common form of infectious enteropathy.

HISTORY, CHIEF COMPLAINT

- Persistent large-bowel diarrhea: tenesmus (straining to defecate), increased frequency of defecation, mucoid feces, and fresh (red) blood
- Cachexia, anorexia, and weight loss are frequently observed with granulomatous colitis, which is in sharp contrast to other causes of colonic inflammation.

PHYSICAL EXAM FINDINGS

Fever, cachexia, weight loss, and peripheral/mesenteric lymphadenopathy are observed with infectious causes. Dogs with HUC may not have mesenteric lymphadenopathy. Ocular signs (uveitis) and/or neurologic abnormalities (e.g., paresis, head tilt, ataxia) are often reported with *Prototheca* spp. infection.

ETIOLOGY AND PATHOPHYSIOLOGY

- HUC: a severe but uncommon IBD variant
- Infiltrative mucosal disease caused by fungal or algal agents, resulting in granulomatous colonic inflammation. Dissemination to other organ systems is common with systemic mycotic and algal infections.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis may be suspected based on history of signs of chronic GI disturbance, prompting endoscopic or full-thickness intestinal biopsies (definitive confirmation).

DIFFERENTIAL DIAGNOSIS

- Specific causes: see Etiology and Pathophysiology above
- Other differential diagnoses: severe colonic IBD, neoplasia

INITIAL DATABASE

- CBC, serum biochemistry, urinalysis, and fecal tests are indicated to evaluate involvement of diverse organ systems.
- Exfoliative cytology (e.g., rectal scrape; see p. 1334) is a useful tool for confirming the presence of *Histoplasma* organisms contained within colonic macrophages. An easy and inexpensive screen which should be performed in endemic regions.
- Urinary excretion of histoplasmosis antigen is a highly sensitive and specific assay. This is a simple noninvasive diagnostic test for gastrointestinal histoplasmosis.
- Abdominal imaging (survey radiographs, contrast radiography, and/or ultrasonography) will identify diffuse colonic wall thickening, loss of wall layering, and/or mesenteric lymphadenopathy indicative of infiltrative mural disease.

ADVANCED OR CONFIRMATORY TESTING

- PCR or ELISA techniques on serum or tissues will confirm *Pythium* spp. infection.
- Oculocentesis may detect *Prototheca* spp. organisms in animals with ocular lesions.
- Urinary excretion of histoplasmosis antigen
- Mucosal biopsy obtained endoscopically or surgically will demonstrate the presence of PAS-positive histiocytes or granulomatous inflammation with infectious organisms.
- Fluorescence in situ hybridization (FISH) performed on tissue sections confirms the presence of adherent/invasive *E. coli* organisms in boxer dogs.

TREATMENT

TREATMENT OVERVIEW

- Treatment requires a specific definitive diagnosis determined by mucosal biopsy.
- Surgical excision of diseased tissues (if possible) is required for pythiosis.

NUTRITION/DIET

- Dogs with protein-losing enteropathy due to gastrointestinal histoplasmosis are generally protein-caloric malnourished and may benefit from low-fat rations. Assess cobalamin status in these patients and correct if present.
- Dietary management includes supplementation with sources of soluble fiber, which bind colonic irritants, normalize dysmotility, and promote colonic epithelial repair and renewal.

CHRONIC TREATMENT

- Treat HUC with enrofloxacin (5 mg/kg PO q 24 h for 14-21 days) alone or in combination with metronidazole or amoxicillin. Some dogs may respond to single drug therapy, but others may require combination therapy. Extend treatment 14 days past resolution of signs, owing to severity of most *E. coli* infections.
- Nutrition: low-fat, fiber-enriched, and highly digestible commercial ration. In some instances, a restricted-antigen (e.g., elimination) diet may also be helpful, since dogs may develop dietary sensitivity.
- Supplementation with increased n-3: n-6 fatty acids to reduce mucosal inflammation
- If the animal will not eat a commercial fiber-containing diet, addition of fiber (small to moderate amounts of soluble fiber [Metamucil sprinkled on the food at a dosage of 1-2 teaspoons/10 kg body weight per feeding]) to the regular diet.

- Infection with *Histoplasma* spp. requires antifungal therapy (see p. 538).
- Aggressive surgical resection will be required for animals infected with *Pythium* spp.
- There is no effective therapy for protothecosis.

POSSIBLE COMPLICATIONS

- Cure is often not possible in animals with pythiosis or protothecosis. These animals will likely die regardless of therapy.
- Animals having GI histoplasmosis and treated with amphotericin B are at risk for drug-induced renal disease.
- Boxers with HUC may require repeated intermittent or long-term therapy for remission of signs. If dogs fail to respond to enrofloxacin therapy, consider antibiotic resistance to this drug a strong possibility for treatment failure. A second-choice drug to consider would be ciprofloxacin; however, clinical trials attesting to efficacy with this medication in therapy of HUC have not been published.

RECOMMENDED MONITORING

- Rechecks are required at 2-to 4-week intervals initially in animals with HUC. Gradual drug reduction may occur as clinical signs lessen.
- Monitor renal function in animals treated with amphotericin B.

PROGNOSIS AND OUTCOME

- HUC carries a good prognosis short term, although long-term studies addressing the maintenance of a positive outcome (e.g., full remission) are lacking.
- GI histoplasmosis carries a guarded prognosis; however, most animals respond favorably to antifungal therapy (itraconazole) in spite of disease burden.
- Granulomatous colitis caused by *Pythium* spp. and *Prototheca* spp. carries a poor prognosis.

PEARLS & CONSIDERATIONS

COMMENTS

- Major causes for granulomatous colitis include infectious and infiltrative disorders.
- A thorough diagnostic evaluation is warranted to rule out the varied causes for colonic inflammation.
- Colonoscopy with targeted mucosal biopsy is imperative for diagnosis.

TECHNICIAN TIPS

- Many patients with GI histoplasmosis will require fastidious nursing care to remain hydrated and maintain adequate nutritional status.
- Clients should be apprised that antifungal therapy may be expensive and require long-term (6-9 months) treatment.

CLIENT EDUCATION

- Dietary modification to a diet suitable for colonic disease may be required for the life of the pet.
- Educate clients about treatment costs and duration of therapy in dogs with GI histoplasmosis.

SUGGESTED READING

Simpson WS, et al: Adherent and invasive *Escherichia coli* is associated with granulo-matous colitis in boxer dogs. Infect Immun 74:4778, 2008.

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Glyphosate Herbicide Toxicosis

BASIC INFORMATION

DEFINITION

Glyphosate is a phosphanoglycine herbicide. It is currently the most commonly used broad-spectrum, systemic, nonselective postemergence herbicide. Toxicosis occurs when pets accidentally walk through the sprayed area and groom themselves, or lick a sprayed plant, or puncture the glyphosate container. Clinical signs of toxicosis are seen usually within 4 hours of exposure and are limited to mild signs of gastrointestinal upset such as hypersalivation, vomiting, or diarrhea.

SYNONYMS

N-(phosphonomethyl) glycine. Some common brand names are Accord, Bio-active, Bronco, Kleen-up, Landmaster, Rodeo, Roundup, RoundupPro, Round-upUltra, Roundup plus, Network, Spark, Vision.

EPIDEMIOLOGY

SPECIES, AGE, SEX

There are no known increases in risks based on species, age, or sex. Dogs are more commonly exposed owing to indiscriminate eating habits, compared to cats.

RISK FACTORS

Toxicosis more frequent during spring or summer months when herbicides are more frequently available and used.

GEOGRAPHY AND SEASONALITY

Exposure is more common in warm growing months when lawns are commonly treated with herbicides.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Observed licking or ingestion of a glyphosate-treated plant
- Evidence that the pet chewed a container of the product
- Recent use of a glyphosate product in the animal's environment and possible exposure
- Spontaneous hypersalivation, vomiting, and diarrhea may be present and noted by the owner. After exposure, vomiting may occur within the first 4 hours and diarrhea within 24 hours.

PHYSICAL EXAM FINDINGS

Drooling or licking motions may be evident, but otherwise the physical exam findings should be unremarkable.

ETIOLOGY AND PATHOPHYSIOLOGY

Glyphosate herbicides are primarily available as water-soluble liquids (ready-to-use spray) or concentrated solutions.

- Glyphosate herbicidal mechanism. Absorbed through the leaves or roots of the plant and transported throughout the plant. Interferes with phenylalanine, tyrosine, and tryptophan synthesis (inhibits a plant-only biochemical pathway, the shikimic acid pathway).
- Surfactant blends are used in varying concentrations as carriers in some formulations.
    - Surfactants account for the majority of signs of toxicosis.
- Different formulations may also contain other herbicides such as diquat or triclopyr.

DIAGNOSIS

OVERVIEW STATEMENT

Since clinical signs are nonspecific, an exact diagnosis of intoxication relies on observation or suspicion of exposure. A tentative diagnosis is sufficient to initiate treatment.

DIFFERENTIAL DIAGNOSIS

Any other etiology that can cause nausea, vomiting, and diarrhea (dietary indiscretion, garbage toxicosis, inflammatory bowel disease, intestinal neoplasia, intestinal obstruction, viral or bacterial gastroenteritis, pancreatitis)

INITIAL DATABASE

Since toxicosis is usually mild and self-limiting, no significant laboratory abnormalities are expected.

- In most cases, laboratory work (CBC, serum biochemistry profile) is not indicated.
- If severe signs, monitor hydration status and electrolytes.

ADVANCED OR CONFIRMATORY TESTING

Advanced confirmatory testing not needed or required. Glyphosates can be analyzed by HPLC or gas chromatography/mass spectrometry. However, no method is readily available for clinical use.

TREATMENT 

TREATMENT OVERVIEW

If no clinical signs are present after oral exposure, treatment centers on dilution (milk or water). Rarely, severe signs are present, warranting antiemetics and supportive care (rarely needed). Dermal exposures require topical decontamination.

ACUTE GENERAL TREATMENT

- Dermal exposure: bathe with a dilute solution of a mild dishwashing liquid and monitor for gastrointestinal (GI) signs at home.
- Oral exposure without clinical signs:
  - Dilution: give milk or water (45 mL PO syringe fed or via orogastric tube for 10-15 kg/dog) and monitor for GI signs at home for 4 hours.
- If clinical signs (vomiting, other) are present:
  - Nothing by mouth × 2-4 hours if mild vomiting
  - Antiemetics (rarely needed) only if severe vomiting:
    - Maropitant, 1 mg/kg SQ (or 2 mg/kg PO) SID up to 5 days, *or*
    - Metoclopramide, dog/cat: 0.1-0.4 mg/kg q 6 hours PO, SQ, or IM *or*
    - Dolasetron, dog/cat: 0.6-1 mg/kg PO q 12 h
  - Intravenous fluids (rarely needed) if severe signs are present

NUTRITION/DIET

Bland diet may be indicated if diarrhea develops.

PROGNOSIS AND OUTCOME 

Excellent; most cases can be treated at home by the owner and do not require veterinary care.

PEARLS & CONSIDERATIONS 

COMMENTS

- Glyphosates have very low oral toxicity in mammals. Oral LD50 in most animals is >5000 mg/kg. NOEL (no observable effect level) for 1 year in dogs is 500/mg/kg/day.
- Clinical signs of toxicosis (hypersalivation, vomiting, and diarrhea) are more related to the surfactant in the formulation than the active-ingredient glyphosate.

- Certain surfactants in the formulation are more toxic to fish and invertebrates; therefore, some formulations are not for aquatic applications.
- Structurally, glyphosate is classified as an organophosphate herbicide. However, this agent does not inhibit cholinesterase like organophosphate pesticides (see p. 792). Therefore, no cholinergic signs of toxicosis are seen in animals.

PREVENTION

Keep pets out of the sprayed area until it has completely dried.

CLIENT EDUCATION

Use products per label directions. Keep animals away from treated area until the product is dried on the plants. Store pesticides out of reach of pets.

SUGGESTED READING

Farmer D: Inhibitors of aromatic acid biosynthesis. In Kreiger RI, editor: Handbook of pesticide toxicology agents, ed 2, San Diego, 2001, Academic Press, p 1667.

Internet source: Integrated Risk Information System, US Environmental Protection Agency, retrieved March 30, 2009 from http://www.epa.gov/iris/subst/0057.htm http://www.epa.gov/EPA-PEST/1998/ October/Day-08/p26906.htm.

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Gluten-Sensitive Enteropathy

BASIC INFORMATION

DEFINITION

A chronic small-intestinal disease triggered in susceptible animals by the ingestion of gluten, a protein found in wheat

SYNONYMS

Celiac disease (humans), gliadin enteropathy, gluten enteropathy, GSE, wheat-sensitive enteropathy

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Uncommon disorder in dogs
- Can potentially occur in cats but poorly documented
- Disease is first seen in young dogs (4-7 months old) after weaning.
- No gender predisposition described

GENETICS & BREED PREDISPOSITION

Irish setter, Samoyed, soft-coated Wheaten terrier (SCWT), but potentially any breed. In SCWT, gluten-sensitive enteropathy may be part of a spectrum of small-intestinal disease, as resolution of clinical signs does not occur with dietary restriction.

RISK FACTORS

- Exposure to gluten-containing cereal grains after weaning
- Inflammatory small-bowel disease may lead to secondary gluten sensitivity.

ASSOCIATED CONDITIONS & DISORDERS

Humans with gluten-sensitive enteropathy may also suffer from gluten-sensitive skin disease (dermatitis herpetiformis) and are predisposed to alimentary lymphoma.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Chronic intermittent gastrointestinal signs (diarrhea is most common)
- Ill thrift but lack of overt gastrointestinal signs sometimes seen

HISTORY, CHIEF COMPLAINT

- Chronic intermittent or persistent small-bowel diarrhea, with weight loss or failure to thrive.

PHYSICAL EXAM FINDINGS

- Thin and/or stunted dog
- Poor body and coat condition

ETIOLOGY AND PATHOPHYSIOLOGY

- Gliadins are antigenic proteins that make up part of gluten, the main protein of wheat.
- Other proteins of flour from various grains have different degrees of crossreactivity: secalins (rye), hordeins (barley), and avenins (oats) are also implicated in gluten-sensitive enteropathy, whereas oryzenins (rice) and zeins (corn) do not exacerbate this disorder.
- These peptides cause intestinal damage, probably by an immune-mediated mechanism.

- An underlying defect in the intestinal mucosal barrier of Irish setters is reported and may predispose to this disease. This predisposition may be related to MHC gene expression.
- Serum antibody reactivity to gluten and serum immune complexes was not demonstrated in affected setters but has been seen in intestinal inflammation.
- The age of exposure to and dose of gluten may modulate expression of the disease.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Chronic gastrointestinal signs in dogs of susceptible breeds that fail to thrive are typical. Confirmation comes from resolution of clinical signs after withdrawal of gluten from the diet, followed by recurrence of signs with reintroduction of gluten.

DIFFERENTIAL DIAGNOSIS

- Other dietary sensitivities/hypersensitivities
- Idiopathic inflammatory bowel disease (IBD)
- Antibiotic-responsive diarrhea (small-intestinal bacterial overgrowth)
- Exocrine pancreatic insufficiency (EPI)
- Intestinal parasitism (e.g., giardiasis)
- Atypical hypoadrenocorticism
- Chronic intussusception
- Any cause of malabsorption (e.g., lymphangiectasia)

INITIAL DATABASE

- CBC, serum biochemistry profile, urinalysis: usually unremarkable
- Fecal parasite examination
- Normal trypsin-like immunoreactivity: rule out EPI
- Abdominal radiographs and ultrasound are typically unremarkable.

ADVANCED OR CONFIRMATORY TESTING

- Serum folate and cobalamin levels are variable; often normal, but decreased serum folate is the most common abnormality (see p. 220).
- Intestinal biopsy shows nonspecific changes of villous atrophy and intraepithelial lymphocyte infiltration, but similar changes are seen in other dietary sensitivities and idiopathic IBD.
- Serologic tests cannot reliably diagnose this condition, although reductions in fecal IgE excretion during a gluten-free diet trial have been reported in SCWT.
- Conclusive diagnosis: proof of gluten sensitivity depends on demonstration of resolution of signs and histologic changes on a gluten-free diet (typically 2-4 weeks) and relapse when challenged with gluten.

TREATMENT

TREATMENT OVERVIEW

All clinical signs should resolve when the patient is treated with a gluten-free diet. The therapeutic goal is complete resolution of clinical signs through elimination of gluten-containing grains (wheat, rye, barley, oats, buckwheat) from diet, treats, supplements, and chewable/flavored medications.

ACUTE GENERAL TREATMENT

Feed a diet lacking wheat and other gluten-containing related cereals.

CHRONIC TREATMENT

Evaluate for other causes of small-bowel diarrhea if response to dietary modification is suboptimal.

NUTRITION/DIET

Feed a diet lacking wheat gluten and related cereals (cornerstone of diagnosis and treatment).

BEHAVIOR/EXERCISE

No specific recommendations required

POSSIBLE COMPLICATIONS

Potential for nutritional deficiencies with homemade diets (see p. 868)

RECOMMENDED MONITORING

Centered on response to treatment (resolution of clinical signs) and physical exam (body weight, quality of coat, etc.)

PROGNOSIS AND OUTCOME

Good to excellent in dogs that respond to strict gluten-free diet

PEARLS & CONSIDERATIONS

COMMENTS

- This is predominantly a disease of young Irish setter dogs/puppies.
- Consider the development of gluten-sensitive enteropathy as a potential complication to underlying inflammatory small-bowel disease (IBD, protein-losing enteropathy).
- Gluten sensitivity has not been recorded in cats and is probably quite rare in dogs.
- Be aware that owner noncompliance may be a cause of treatment failure.

PREVENTION

- Selective breeding, as condition is probably familial
- Feeding a gluten-free diet will prevent disease.

CLIENT EDUCATION

- Awareness of gluten content of various foodstuffs
- Awareness of cross-reactivity to rye, barley, and possibly oats
- Monitor for recurrence of clinical signs
- Lifetime careful attention to diet may be required, although some affected dogs may develop tolerance over time.

SUGGESTED READING

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Glomerulonephritis

BASIC INFORMATION

DEFINITION

Glomerulonephritis is a common disorder characterized by proteinuria due to immune complex deposition in the glomeruli and resultant inflammation. The condition is often idiopathic, but it can result from inflammatory, infectious, or neoplastic disease processes.

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs affected more often than cats, with no gender predilection. While animals of any age may be affected, most are middle-aged or older at diagnosis.

GENETICS & BREED PREDISPOSITION

Membranoproliferative glomerulonephritis

- Bernese mountain dogs
- Labrador retrievers and golden retrievers with positive *Borrelia* titers

RISK FACTORS

- Chronic bacterial infections (e.g., pyoderma, endocarditis, pyelonephritis, borreliosis, mycoplasmal polyarthritis)
- Fungal infection (e.g., coccidioidomycosis)
- Parasitic (e.g., heartworm disease)
- Rickettsial disease (e.g., ehrlichiosis)
- Protozoal infection (e.g., babesiosis, hepatozoonosis, leishmaniasis)
- Viral disease (e.g., feline immunodeficiency virus, feline leukemia virus, canine adenovirus)
- Neoplasia (e.g., mastocytosis, leukemia, lymphoma, systemic histiocytosis)
- Immune-mediated disease (e.g., polyarthritis, pemphigus, systemic lupus erythematosus)
- Chronic inflammatory disease (e.g., inflammatory bowel disease, pancreatitis, cholangiohepatitis, granulomatous meningoencephalitis, thyroiditis)
- Corticosteroid excess
- Trimethoprim-sulfa therapy
- Congenital C3 deficiency
- Genetic predisposition

See p. 1391.

CONTAGION & ZOONOSIS

Some causes of secondary glomerulonephritis are zoonotic (e.g., leptospirosis, leishmaniasis).

GEOGRAPHY AND SEASONALITY

Several causes of secondary glomerulonephritis have specific geographic distributions (e.g., borreliosis in the northeastern and north central United States).

ASSOCIATED CONDITIONS & DISORDERS

- Protein-losing nephropathy
- Nephrotic syndrome
- Chronic kidney disease
- Hypertension
- Hyperlipidemia

- Thromboembolic disease, including pulmonary thromboembolism
- Sideroblastic anemia

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Morphologic classification: histopathologic (clinical correlates to therapy and prognosis not as well developed as in human nephrology)

- Membranoproliferative glomerulonephritis: most common
  - Type I: mesangiocapillary glomerulonephritis associated with infectious disease; most common type
  - Type II: dense deposit disease
- Proliferative glomerulonephritis: relatively rare

HISTORY, CHIEF COMPLAINT

Clinical signs may be absent. When signs are present, they may be due to uremia (see p. 207), nephrotic syndrome (see p. 762), or to the underlying disease responsible for glomerulonephritis:

- Vomiting (uremia or underlying disease)
- Lethargy (uremia or underlying disease)
- Anorexia (uremia or underlying disease)
- Weight loss (uremia, proteinuria, or underlying disease)
- Peripheral edema (hypoalbuminemia)
- Pendulous abdomen/ascites (hypoalbuminemia)
- Polyuria/polydipsia (chronic kidney disease)
- Halitosis (uremia)
- Dyspnea/panting (pulmonary thromboembolism events, ascites)
- Blindness (systemic hypertension)
- Signs associated with underlying infectious, inflammatory, or neoplastic disease

PHYSICAL EXAM FINDINGS

Clinical findings may be absent or may include:

- Poor body condition
- Dehydration
- Poor haircoat
- Signs associated with hypoalbuminemia:
  - Peripheral edema
  - Ascites (pure transudate)
  - Pleural effusion (rare)
- Signs associated with uremia:
  - Oral ulceration
  - Halitosis (uremia)
- Pallor (either due to anemia [chronic disease, renal failure] or poor perfusion [severe illness])
- Lipid corneal deposits
- Retinal hemorrhage/detachment (systemic hypertension)
- Kidneys may be normal sized or small.
- Other findings related to underlying disease

ETIOLOGY AND PATHOPHYSIOLOGY

- Immune complexes form or are trapped in the glomeruli. While it is often a primary process (idiopathic), there are many infectious, inflammatory, endocrine, or neoplastic conditions that can provide the antigen to which antibody is produced, resulting in secondary immune complex formation.
- Glomerular immune complexes initiate an inflammatory cascade. Inflammation directly damages the glomerulus, neutralizes glomerular endothelial electrical charge, and results in vasoconstriction and decreased glomerular filtration. The glomerulus responds to these insults with cellular proliferation.
- Albumin and similarly sized proteins are lost in the urine and may result in hypoalbuminemia and the nephrotic syndrome (see p. 762). Eventually, tubular function is lost as well, resulting in azotemia and uremia.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on the identification of proteinuria, an elevated urine protein/creatinine ratio, and characteristic blood and imaging findings. Confirmation requires renal biopsy.

DIFFERENTIAL DIAGNOSIS

Proteinuria:

- Preglomerular (e.g., Bence Jones proteinuria, exercise, hemolysis, fever, seizure)
- Glomerular
  - Glomerulonephritis
  - Amyloidosis
  - Glomerulosclerosis, including chronic kidney disease
  - Familial renal disease
- Postglomerular (e.g., urinary tract infection, neoplasia, urolithiasis)

INITIAL DATABASE

- Retinal exam: tortuous retinal vessels, retinal hemorrhages (acute or chronic), or retinal detachments are possible (a result of systemic hypertension).
- Blood pressure: systemic hypertension (repeatable systolic readings > 180 mm Hg in calm environment) is commonly noted.
- CBC: often unremarkable; nonregenerative anemia (due to chronic kidney disease), leukocytosis (if inflammatory disease is present)
- Serum biochemical profile:
  - Hypoalbuminemia with normal globulin level
  - Hypercholesterolemia
  - Hypocalcemia (relative, owing to hypoalbuminemia)
  - Azotemia, hyperphosphatemia, hyperamylasemia, metabolic acidosis (in advanced disease)
- Urinalysis: proteinuria, variable urine concentration, sometimes hematuria
  - Proteinuria must be interpreted in light of urine concentration and urine sediment examination.
  - Dipstick measure of proteinuria should be confirmed by sulfosalicylic acid test (SSA) method or quantitative measures (e.g., urine protein: creatinine ratio).
  - Significant proteinuria may often precede loss of urine concentration or azotemia.
- Urine culture: indicated in all cases
- Thoracic radiographs: unremarkable. Evidence of underlying disease (neoplasia, chronic infectious or inflammatory disease) or pulmonary thromboembolism occasionally identified.
- Abdominal radiographs: often unremarkable. Kidneys may be small. May identify evidence of underlying disease (neoplasia, chronic infectious or inflammatory disease) or be unremarkable.
- Abdominal ultrasound: hyperechoic, small kidneys, decreased corticomedullary distinction, evidence of underlying disease (neoplasia, chronic infectious or inflammatory disease), or unremarkable.

ADVANCED OR CONFIRMATORY TESTING

- Urine protein/creatinine ratio:
  - Concurrent culture and sensitivity must be negative to rule out bacterial infection as cause of elevated ratio.
  - Normal for dogs, <0.5; cats, <0.4. Most animals with glomerulonephritis or amyloidosis have ratios >2.
- Microalbuminuria testing:
  - Assay for the presence of microalbuminuria does not provide additional benefit in animals with elevated protein/creatinine ratio. These assays detect very small quantities of urine albumin that would be missed on routine dipstick and are thus redundant when proteinuria has been identified.
- Renal biopsy is the only definitive means of diagnosis of glomerulonephritis, allowing morphologic classification of disease, and identifying type and location of immunoglobulin. Cortical tissue examined by light microscopy, immunofluorescence, and electron microscopy.
- Determining serum antithrombin concentrations may help quantify risk of thromboembolic disease (<80% suggests increased risk).
- A variety of other tests may be indicated in a search for an underlying cause of glomerulonephritis. The choice of tests depends on history and physical exam, results of initial evaluation (CBC, serum biochemistry, imaging studies), geographic region, and environmental exposures. Common examples include:
  - Serologic tests for heartworm, borreliosis, feline leukemia virus, feline immunodeficiency virus, *E. canis*,

coccidioidomycosis
- Antinuclear antibody test
- Arthrocentesis, echocardiography, bone marrow aspirates, thoracic radiographs
- Adrenocorticotropic hormone stimulation or low-dose dexamethasone suppression tests
- Species-specific pancreatic lipase, trypsin-like immunoreactivity

TREATMENT

TREATMENT OVERVIEW

Treatment mainly consists of medications to decrease the degree of proteinuria. When appropriate, medications for the management of hypertension and thromboembolic disease are indicated. If the patient is in renal failure, supportive management is advised.

ACUTE AND CHRONIC TREATMENT

- Address underlying disease conditions directly.
- If respirations are compromised by large-volume pleural effusion or severe ascites, thoracocentesis and/or abdominocentesis is indicated. Diuretic drug are largely ineffective for rapid mobilization of body-cavity fluid (see pp. 1338, p. 1192).
- Oxygen support may be required for animals with pulmonary thromboembolism.
- Proteinuria may be diminished through the use of angiotensin-converting enzyme (ACE) inhibitors; for dogs, enalapril, 0.5 mg/kg PO q 12-24 h; or benazepril, 0.25 mg/kg PO q 24 h.
- If hypertension persists despite ACE inhibitors, calcium channel blockers are indicated (amlodipine, 0.05-0.5 mg/kg PO q 24 h for dogs; 0.625 mg/cat PO q 12-24 h).
- Anticoagulant therapy to reduce the risk of thromboembolic disease. Unfractionated heparin is not effective because of loss of antithrombin.
  - Aspirin, 0.5 mg/kg q 12 h PO in the dog
  - Coumadin initial dose is 0.1-0.2 mg/kg PO q 24 h.
    - With coumadin, the prothrombin time should be monitored and dose adjusted until 1.5 to 2.5 times normal.
    - Protein-bound drug; therefore very difficult to titrate the dose effectively in patients with hypoalbuminemia, and not generally recommended unless benefit outweighs risk (e.g., prior embolic event while on aspirin)
- Uremic animals may require fluid therapy (see p. 207). Hypoalbuminemia may result in edema, in which case colloidal support may be necessary.
  - Hetastarch, 10-20 mL/kg/day IV
  - Dextrans; use with caution because of reported link to renal failure.
  - Large volumes of species-specific plasma or human albumin; expensive and short-lived effect
- Glucocorticoids and cyclosporine are ineffective in the treatment of idiopathic glomerulonephritis and may increase thromboembolic potential (glucocorticoids) or worsen renal protein loss (cyclosporine). Therefore they should be used only when documented autoimmune disease is present (e.g., systemic lupus erythematosus).
- Clinical signs of uremia and electrolyte and acid-base disorders are addressed as for overt chronic kidney disease (see pp. 205 and p. 207).

NUTRITION/DIET

- Moderate dietary restriction of protein (2-3 g/kg/d for dog; 4 g/kg/d for cat), phosphorus, and sodium are recommended. A variety of commercial or homemade diets can be used (e.g., Hill's k/d, Iams Veterinary Formula Renal Purina NF). To avoid food aversions, diet changes are best made when animal is not uremic.
- Omega-3 fatty acid supplementation may be renoprotective, decrease inflammation and proteinuria, and decrease cholesterol. Many commercial renal diets are so supplemented.

DRUG INTERACTIONS

- ACE inhibitors may cause hypotension when combined with diuretics or other vasodilators.
- ACE inhibitors may reduce proteinuria and ameliorate hypertension but may worsen azotemia, requiring that blood urea nitrogen (BUN) and creatinine be monitored during therapy.
- Nonsteroidal antiinflammatory agents may reduce efficacy of ACE inhibitors.

POSSIBLE COMPLICATIONS

- Third-space retention of fluids
- Worsening renal azotemia as a result of ACE inhibitor use (uncommon)
- Hypotension secondary to ACE inhibitor and calcium channel blocker
- Worsening of renal azotemia with dextran use

- Thromboembolic disease as a result of antithrombin and protein C level abnormalities
- Bleeding tendency from aspirin, warfarin use
- Gastrointestinal ulceration as a result of azotemia or aspirin therapy

RECOMMENDED MONITORING

Stable animals are monitored every 3-4 months. Rechecks should be more frequent if changes are made in therapy or when indicated by changing clinical signs.

- Physical examination
- Urine protein/creatinine ratio
- Serum BUN/creatinine/phosphorus
- Serum albumin
- Blood pressure
- Urinalysis/culture

PROGNOSIS AND OUTCOME

- Prognosis is best when an underlying disease can be identified and eliminated.
- When elimination of an underlying disease is not possible, survival is variable, but disease is usually progressive over months to 1-2 years.
- In dogs, prognosis for glomerulonephritis in general is better than for renal amyloidosis.
- Prognosis is worse when azotemia/uremia is/are present at diagnosis.
- Prognosis is worse for cats than dogs.
- Prognosis is poor for dogs where glomerulonephritis is associated with borreliosis.

PEARLS & CONSIDERATIONS

COMMENTS

- Investigation of potential underlying diseases can become expensive. Clinical judgment should guide the choice of ancillary tests for each animal.
- Once protein-losing nephropathy is identified, renal biopsy is useful primarily as a prognostic tool. Although biopsy is required to distinguish the type of glomerular disease, therapy is often similar for each type.

PREVENTION

- Ectoparasite prophylaxis
- Heartworm prophylaxis

CLIENT EDUCATION

- Diligent rechecks are very important for adjusting medications and identifying complications early.
- Finding an underlying disease process may mean a better prognosis for the pet.

SUGGESTED READING

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Glaucoma

Additional Images Available on Website

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

- The glaucomas are a group of diseases characterized by visual impairment and blindness from damage to the retina and optic nerve caused by increased intraocular pressure (IOP).
- Glaucoma may be the result of primary eye disease (i.e., abnormalities of the drainage/iridocorneal angle; *primary glaucoma),* secondary to other eye diseases *(secondary glaucoma),* or less commonly, the result of anomalies of the anterior segment of the eye *(congenital glaucoma).*
- In dogs in North America, the prevalence of primary glaucoma is 0.9%, while it is 0.8% for secondary glaucomas.

SYNONYMS

Ocular hypertension. Buphthalmos: megaloglobus (enlargement of the globe secondary to elevated IOP)

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs and cats: variable age of onset depending on underlying cause
- Primary glaucoma:
  - Typically middle-aged to older dogs (3-12 years; average 8 years); rare in cats
  - In some breeds of dogs, primary glaucoma occurs more frequently in females.
- Secondary glaucoma due to:
  - Lens luxation: usually affects young to middle-aged dogs (3-7 years); older cats
  - Intraocular neoplasia: usually older animals (>7 years)
- Congenital glaucoma:
  - Young animals; elevation in IOP develops soon after birth.

GENETICS & BREED PREDISPOSITION

- Primary glaucoma:
  - Top breeds of dogs affected between 1994 and 2002 include American cocker spaniel, basset hound, chow chow, shar-pei, Boston terrier, wire fox terrier, Norwegian elkhound, Siberian husky, Cairn terrier, and miniature poodle.
  - Primary open-angle glaucoma is inherited in the beagle as an autosomal recessive trait.
  - Primary closed-angle glaucoma in the Welsh springer spaniel and Great Dane appears inherited as an autosomal dominant trait with variable expression.
  - Cats: Siamese breed may have inherited primary glaucoma.
- Secondary glaucoma:
  - Lens luxation: terrier breeds
  - Pigmentary uveitis: golden retrievers

RISK FACTORS

- Primary glaucoma:
  - Abnormalities of the iridocorneal angle (often termed *pectinate ligament dysplasia)* may narrow the opening to the sclerociliary cleft and increase the probability of glaucoma (dogs).
- Secondary glaucoma:
  - Anterior uveitis due to:
    - Cataract formation (common in dogs)
    - Systemic bacterial and mycotic diseases (dogs and cats)
    - Feline leukemia and feline immunodeficiency viruses (cats)
  - Lens luxation (see p. 644)
  - Intraocular neoplasia (see p. 620)
  - Hyphema (see p. 571).
  - Uveal cysts (see p. 1149).

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Glaucoma may be classified based on:

- Cause: primary, secondary, or congenital
- Duration: acute (vision potential) versus chronic (typically blind, buphthalmic eye)

HISTORY, CHIEF COMPLAINT

Transient or constant red or cloudy eye with any or all of the following:

- Variable ocular pain (usually present when IOP >40 mm Hg) manifesting as unwillingness to be handled around the face or head, or blepharospasm.
- Bumping into objects or other manifestations of visual impairment or blindness
- Increased green reflection from eye (i.e., tapetal reflection from dilated pupil)
- Enlargement of the globe (buphthalmos)

PHYSICAL EXAM FINDINGS

Unilateral or bilateral ocular changes; initially unilateral with primary glaucoma:

- Corneal edema (typically diffuse)
- Episcleral hyperemia (tortuous episcleral vessels)
- Dilated pupil and sluggish to absent pupillary light reflexes
- Possible lens subluxation/luxation
- Variable optic nerve and retinal degeneration (see p. 983)
- Corneal stria (breaks in Descemet's membrane appearing as white lines within cornea; rare)

ETIOLOGY AND PATHOPHYSIOLOGY

- Impediment to aqueous humor outflow, causing elevated IOP
- Elevated IOP can damage the retina (retinal ganglion cells) and optic nerve head by reducing retinal, choroidal, and optic nerve head blood flow and axoplasmic flow in the optic nerve head.
- Onset and severity of these glaucomatous changes appear influenced by the duration and extent of the IOP elevation.
- About 50% of first eyes of dogs presented with the primary glaucomas are blind at initial ophthalmic examination.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A diagnosis of glaucoma should be considered for any case that presents for evaluation of (a) red eye(s), particularly if the ocular hyperemia is accompanied by mydriasis and corneal edema and especially if it occurs in a predisposed breed. Elevated IOP on tonometric evaluation is confirmatory.

DIFFERENTIAL DIAGNOSIS

Glaucoma must be differentiated from other causes of red eye (see p. 967)

INITIAL DATABASE

Complete ophthalmic examination (see p. 1313) including:

- Tonometry (the measurement of IOP): the most important diagnostic test
  - Schiøtz indentation tonometry (requires conversion of value from instrument to mm Hg using human calibration chart accompanying instrument or dog/cat calibration chart)
  - Applanation tonometry (e.g., TonoPen)
  - Rebound tonometry (e.g., TonoVet)
  - Normal IOP values range from 15-25 mm Hg; >30 mm Hg = glaucoma (dogs and cats).

ADVANCED OR CONFIRMATORY TESTING

- Referral to veterinary ophthalmologist for:
  - Additional or multiple tonometric measurements
  - Gonioscopy (direct observation of the iridocorneal angle)
  - Ophthalmoscopy of the ocular fundus (posterior segment of the eye including retina and optic nerve)
- Ocular ultrasound if ocular media are opaque and prevent evaluation of deeper ocular structures; helps rule out concurrent ocular abnormalities (i.e., lens luxation; lens capsule rupture; retinal detachment; intraocular masses)

TREATMENT 

TREATMENT OVERVIEW

In acute cases, it is critical that the IOP be lowered as soon as possible to maintain or restore vision (topical and oral medications). If tonometry is unavailable, glaucoma suspects should be referred to a veterinary ophthalmologist (as an emergency) for IOP measurement. Early surgical intervention may permit better and longer control of IOP; the clinician is urged to consider early referral, especially when vision in one eye has already been lost. Long-term treatment of glaucoma can be a frustrating endeavor, since the disease tends to progress despite medical therapy, particularly with primary glaucoma. Diligent monitoring, regular reassessment of therapeutic success, and client education are critical. Therapeutic goals are to lower IOP of affected eye to maintain vision for as long as possible, eliminate ocular pain, and treat contralateral eye prophylactically with IOP-lowering drugs to delay onset of glaucoma from ~*6* months (untreated) to 30 months (with prophylactic treatment) (primary glaucoma).

ACUTE GENERAL TREATMENT

Medical:

- Regardless of the type of glaucoma, the following may be administered initially and then long term if indicated:
  - Topical β-adrenergic antagonists or blockers (0.5% timolol or 0.5% betaxolol, usually q 8 h) *and*
  - Topical or systemic carbonic anhydrase inhibitors (CAI; topical: 2% dorzolamide or 1% brinzolamide q 8 h; oral: methazolamide, 5 mg/kg q 12 h)
- Mannitol (1-2 g/kg IV over 20 minutes) to rapidly lower IOP (first effects in 1-2 hours; maximum effect in 4-6 hours; duration ~8-10 hours) when there is a chance for return of vision (e.g., acute primary glaucoma)
- Topical (1% q 6 h) and/or systemic (1-2 mg/kg PO q 24 h) prednisolone is indicated when anterior uveitis is also present, unless an infectious cause for the uveitis is documented or strongly suspected (see p. 1151)

CHRONIC TREATMENT

Medical:

- Topical prostaglandins (PGF analogs, 0.005% latanoprost, 0.03% bimatoprost, or 0.004% travoprost q 12-24 h): used for primary glaucoma in dogs; not effective in the feline glaucomas)
- ± Topical and/or systemic prednisolone (when anterior uveitis also present; taper to lowest effective dose)
- In all of the breed-related *primary glaucomas,* the disease continues to progress (even though IOP may be controlled), and often combinations of several topical and systemic IOP-lowering drugs or surgery (see below) are eventually necessary.

Surgical:

- Anterior chamber shunts and laser cyclophotocoagulation are procedures offered by most veterinary ophthalmologists to prolong vision and prevent ocular pain. Laser cyclophotocoagulation may be performed with either a transscleral approach or with the assistance of a microendoscope.
- Removal of the lens (referable procedure; glaucoma secondary to lens luxation, see p. 644). This should be performed as soon as possible in cases of anterior lens displacement.
- End-stage blind and buphthalmic glaucomatous globes may be treated by:
  - Enucleation
  - Evisceration and intrascleral prosthesis
  - Intravitreal gentamicin injection (dogs)
  - Enucleation or evisceration and implant surgeries should be followed with histopathologic examination of the removed tissue to help determine cause of glaucoma (i.e., primary versus secondary) and prognosis for fellow eye.

DRUG INTERACTIONS

- Topical β-adrenergic blockers may lower heart rate and blood pressure and may cause bronchoconstriction in small-breed

dogs and in cats.
- Systemic CAIs in dogs and cats may cause metabolic acidosis and electrolyte imbalances as evidenced by depression (perhaps related to hypokalemia), and in dogs, vomiting and diarrhea that require drug cessation. Topical CAI preparations are not associated with these side effects.
- Topical prostaglandins often cause conjunctival hyperemia within minutes after instillation that gradually declines over an hour or so, and miosis that persists with the IOP reduction.
- Mannitol, an osmotic diuretic, should be avoided in patients with heart disease (risk of fluid overload/iatrogenic pulmonary edema) or oliguric/anuric renal failure (rarely concurrent with acute glaucoma).

POSSIBLE COMPLICATIONS

With poor or inadequate control of IOP, any or all of the following may occur:

- Buphthalmos (see Ocular Size Abnormalities,) causing increased corneal exposure ± recurrent corneal ulceration/corneal vascularization/corneal pigmentation
- Lens luxation/subluxation
- Optic nerve and retinal degeneration
- Ocular, head pain
- Blindness

RECOMMENDED MONITORING

- Regular reexaminations with tonometry (e.g., monthly once IOP control initially achieved) are necessary to control IOP (should be maintained at <20 mm Hg) and maintain vision for as long as possible.
- As the glaucoma progresses, increased frequency and/or additional topical and systemic drugs to lower IOP are usually necessary.

PROGNOSIS AND OUTCOME

- Prognosis is usually poor for the first eye presented with the primary glaucomas in dogs, because the disease is often advanced and refractory to medical therapy.
- Prognosis for the fellow eye is better, and prophylactic therapy with a β-adrenergic blocker or prostaglandin can significantly delay the onset of glaucoma for up to about 30 months.

PEARLS & CONSIDERATIONS

COMMENTS

- Patients with dilated pupils, corneal edema, and conjunctival hyperemia require tonometry to estimate IOP.
- Clinical management of the glaucomas is often difficult; therefore referral of these cases to a veterinary ophthalmologist is advised.
- Medical therapy of the glaucomas is expensive and is often required long term.
- Buphthalmos indicates chronic glaucoma, whereas acute glaucoma, with its potentially better prognosis for vision, presents episcleral injection and almost never buphthalmos.
- Even in a permanently blind, persistently glaucomatous eye, treatment (e.g., evisceration and implant, or enucleation) is generally indicated to remove the source of chronic intense pain.
- Digital pressure (pressing on the eyes through closed eyelids) cannot be used for accurately assessing IOP.

PREVENTION

The benefits of periodic tonometry in breeds and/or eyes at risk are unknown but should be considered. Anterior uveitis that is unrecognized or inadequately treated and controlled will predispose an eye to the development of secondary glaucoma. Cataractous eyes should be examined regularly for evidence of lens-induced uveitis, and treatment should be initiated when signs appear so as to prevent or delay the development of glaucoma.

TECHNICIAN TIPS

- Veterinary nurses and technicians should encourage clients to bring their pets in for evaluation promptly to rule out glaucoma if they complain of a “bloodshot” eye or acute visual disturbance.
- Restraint for animals undergoing tonometry is important. Care should be taken not to place any pressure on the jugular veins

or eyelids, as excessive pressure in these areas may result in falsely elevated IOP estimates. Excessive struggling should be avoided as well, as this may alter IOP readings.

CLIENT EDUCATION

- Glaucoma is a chronic disease that requires regular and diligent therapy. Missed medication will result in inadequate control of IOP, loss of sight, and pain.
- The primary glaucomas in the dog are concentrated in about 20 breeds.
- Dogs with cataracts that are not surgical candidates require periodic eye examinations and tonometry indefinitely because they are at increased risk of developing glaucoma.

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Giardiasis

Additional Images Available on Website

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Giardia duodenalis is a flagellate protozoan parasite that can be found in the intestinal tract of humans and most domestic animals. Clinical disease usually appears as acute small-bowel diarrhea but can vary, with some animals, showing chronic small-bowel or acute or chronic large-bowel diarrhea.

SYNONYM

Giardia duodenalis; Giardia lamblia; Giardia intestinalis

EPIDEMIOLOGY

SPECIES, AGE, SEX

Can affect humans and most domestic animals. Infection is most common in younger animals.

RISK FACTORS

Immunodeficient adults, young animals, and animals confined in large crowded groups are at increased risk.

CONTAGION & ZOONOSIS

Various genotypes differing in host range occur. Species-specific genotypes are the most commonly encountered in dogs and cats. Of the genotypes found in dogs (A, B, C, D) and cats (A, F), several (A, B) also infect humans, and therefore the potential for zoonotic exposure to people from pets exists.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

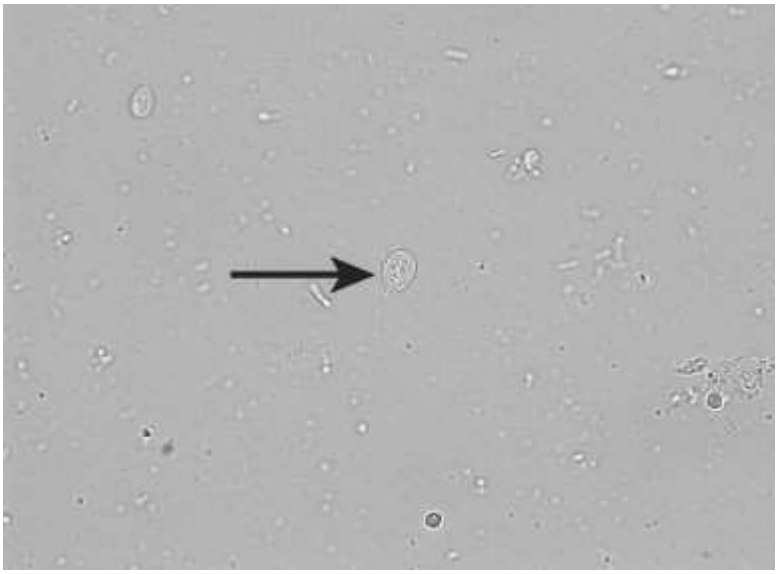
- Infections are usually subclinical.
- If diarrhea results, it can be acute and short lived, intermittent, or chronic.
- Steatorrhea or weight loss may be observed.
- Excessive fecal mucus is often observed in clinically affected cats.
- Emesis, fever, and anorexia may occur but are not typical.

PHYSICAL EXAM FINDINGS

No specific abnormalities

ETIOLOGY AND PATHOPHYSIOLOGY

- The *Giardia* life cycle is direct (no intermediate host). Cysts are ingested and exist in the duodenum, each cyst producing two motile trophozoites that replicate within the lumen of the small intestine. Before being shed in feces, the trophozoite encysts. On excretion, the cysts are immediately infective to another host. Cysts can survive for days to weeks in a cool, moist environment.
- Autoinfection from fecal material adhered to the haircoat or cysts in drinking water/environment is possible. Reinfection is probable in catteries and kennels, owing to environmental contamination.
- Trophozoites cause sloughing of intestinal epithelial cells and blunting of intestinal villi, resulting in a reduction in absorptive surface area, causing malabsorption.
- Abnormalities in cellular and humoral immune system function likely predispose individuals to clinical infection.



GIARDIASIS A *Giardia duodenalis* trophozoite *(arrow)* detected on a direct saline smear of feces from a dog, viewed under the high-dry objective. Trophozoites are teardrop shaped with 2 nuclei, 2 comma-shaped median bodies, and 8 flagella. They are 12-17 × 7-10 microns in size, slightly larger than a red blood cell by comparison (not seen here). Motile trophozoites have a typical "falling-leaf" movement and are easily kept in the microscopic field of view.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other intestinal parasitoses
- Idiopathic inflammatory bowel disease
- Maldigestion secondary to pancreatic exocrine insufficiency
- Neoplastic intestinal disease (i.e., lymphoma)
- Infectious intestinal disease (viral, bacterial, fungal)
- Food intolerance or dietary indiscretion (acute cases)

INITIAL DATABASE

- Direct fecal smear in saline: observation of viable, motile trophozoites
  - Trophozoites may predominate in diarrheic feces but due to their fragile nature are usually only detected in fresh samples (feces examined within 20 minutes of defecation).
  - Positive result is definitive; negative result does not rule out infection.
- Zinc sulfate centrifugal fecal flotation (ZSCF): detection of cysts. Due to intermittent fecal cyst shedding, sensitivity is increased by examining 2-3 fecal samples obtained over 3-5 days. If samples are shipped for testing, they should be maintained at 4°C. Lack of centrifugation and/or use of sugar or one of the other salts as flotation media will greatly decrease the detection sensitivity for *Giardia* cysts.

ADVANCED OR CONFIRMATORY TESTING

- ELISA kits to identify fecal *Giardia* antigens. Fresh, frozen, or formalin-preserved feces suitable. Sensitivity of one ELISA is similar to that of 2 or 3 fecal samples tested using ZSCF.
- Direct immunofluorescent testing for *Giardia* cysts in feces. Samples should be preserved in 10% formalin before being shipped to the laboratory.

TREATMENT

TREATMENT OVERVIEW

Treatment goals are to eliminate clinical signs of *Giardia* infection, including diarrhea and weight loss, and eliminate shedding of infective cysts.

ACUTE GENERAL TREATMENT

- Fenbendazole, 50 mg/kg PO q 24 h for 3-5 days (dogs and cats) *or*
- Febantel-pyrantel-praziquantel, 37.8 mg/kg febantel PO q 24 h for 3 days (dogs) *or*
- Febantel-pyrantel-praziquantel, 56 mg/kg febantel PO q 24 h for 5 days (cats) *or*
- Metronidazole, 15-25 mg/kg PO q 12-24 h for 5-7 days (dogs and cats). Use as second choice; less effective than fenbendazole.
- *Giardia* vaccination has not been shown to be an effective treatment.

CHRONIC TREATMENT

- Allowing the environment to dry, cleaning contaminated surfaces with disinfectants containing quaternary ammonium, bathing animals, and treating animals again before returning to the clean environment are important in preventing reinfection.

POSSIBLE COMPLICATIONS

- Albendazole (alternative to fenbendazole): myelosuppression, hepatotoxicity (especially in cats) and suspected teratogen. Not recommended.

PROGNOSIS AND OUTCOME

Prognosis is usually good; clinical signs resolve in most individuals, but recurrent clinical signs due to persistent infection may occur in some animals.

PEARLS & CONSIDERATIONS

COMMENTS

- Empirical fenbendazole treatment is recommended in dogs with diarrhea, to address both *Giardia* and occult whipworm infection as possible underlying causes.
- The *Giardia* vaccine may be effective in reducing fecal shedding of cysts in dogs but is ineffective in prevention of infection. In a study of cats, the vaccine was ineffective for both.
- *Giardia-ELISA* kits have limited usefulness for posttreatment diagnostic surveillance because of prolonged persistent antigen shedding even in animals where clinical signs have resolved and no cysts can be detected on ZSCF.

SUGGESTED READING

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Thompson RCA, Palmer CS, O' Handley R: The public health and clinical significance of *Giardia* and *Cryptosporidium* in domestic animals. Vet J 177:18–25, 2008.

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Gastrointestinal Obstruction: Foreign Body or Mass Lesion

Additional Images Available on Website

BASIC INFORMATION

DEFINITION

Common disorder caused by a foreign object or mass that partially or completely occludes the intestinal lumen

SYNONYMS

Intraluminal obstruction, intestinal blockage

EPIDEMIOLOGY

RISK FACTORS

- Younger animals are at greater risk for dietary indiscretion and therefore foreign body ingestion.
- Some animals are more prone to ingesting foreign objects than others (individual behavior) irrespective of age.
- Older animals are at greater risk for development of neoplasia.

ASSOCIATED CONDITIONS & DISORDERS

Animals with diseases that cause pica may be more at risk for foreign-object ingestion.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Vomiting, anorexia, and depression are common primary complaints.
- Severity of clinical signs varies depending on duration and location of obstruction.
- Proximal and complete obstructions are generally associated with more severe clinical signs of illness.
- Distal or partial obstructions may be associated with vague and chronic signs such as intermittent vomiting, anorexia, weight loss, or diarrhea. When associated with gastrointestinal (GI) obstruction, diarrhea is usually scant and not profuse.

PHYSICAL EXAM FINDINGS

- Abdominal splinting or signs of pain on palpation may be noted.
- Mass or foreign object may be identified with careful palpation.
- Dehydration, depression, or shock; severe in proximal and complete obstructions

ETIOLOGY AND PATHOPHYSIOLOGY

- Mechanical obstruction of the intestinal lumen causes fluid and gas accumulation proximal to the foreign object or mass.
- Duodenal and proximal jejunal obstruction is often associated with acute and severe signs.
- Persistent vomiting and loss of gastric secretions associated with proximal obstructions may lead to electrolyte imbalances (hypochloremic metabolic alkalosis).
- Lymphatic and capillary stasis cause intestinal wall edema.
- Impaired intestinal mucosal barrier allows bacterial translocation, potentially resulting in endotoxemia and sepsis.
- High intraluminal pressure causes intestinal wall ischemia that may progress to necrosis and peritonitis.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on history and physical examination, is supported by imaging (radiographic and/or ultrasonographic) findings, and is confirmed surgically. Diagnostic imaging should be considered in any young animal that presents with vomiting, anorexia, a painful abdomen, or has a history of foreign-body ingestion.

DIFFERENTIAL DIAGNOSIS

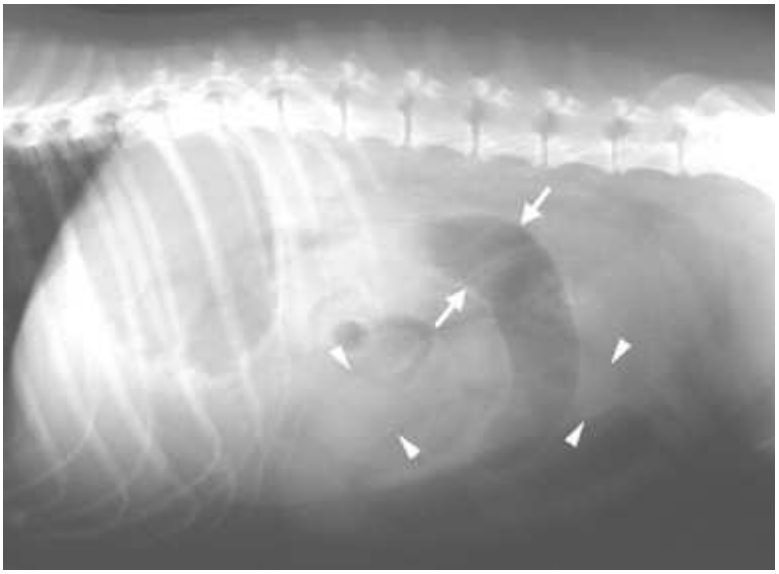
- Foreign body
- Mass
- Intussusception
- Linear foreign body
- Trichobezoar
- Intestinal volvulus or torsion
- Stricture or adhesions
- Functional obstruction (i.e., ileus)
- Infectious disease of the GI tract (e.g., parvoviral or coronaviral enteritis)
- Intoxication

INITIAL DATABASE

- CBC, serum biochemistry profile, and urinalysis
  - Evidence of dehydration (e.g., blood urea nitrogen, creatinine elevations with urine specific gravity > 1.030; hemoconcentration/elevated packed cell volume)
  - Electrolyte imbalances
    - Hypochloremia occurs in 51% of cases and is the most common abnormality.
    - Hypokalemia: 25%
    - Hyponatremia: 20% (occurs more commonly with linear rather than discrete foreign bodies)
  - Metabolic alkalosis with proximal obstruction; metabolic acidosis with hypoperfusion, sepsis secondary to peritonitis, or other systemic effects
- Abdominal radiographs: often the most informative test. Urgent consultation with a radiologist may be very helpful.
  - Radiopaque foreign objects may be visualized.
  - Fluid-or gas-distended intestinal loops
  - Pathologic dilation of intestinal loops: bowel lumen should not exceed the diameter of twice the width of a rib or be greater than 1.6 times the height of the fifth lumbar vertebra.
  - Radiographs that demonstrate a foreign body must be recent (minutes or hours before induction of general anesthesia, or better still, retaken just after induction) if surgery is planned. A gastric or duodenal foreign body can be displaced into the esophagus during anesthetic induction, while an intestinal foreign body may have been defecated since the original radiographs were taken.

ADVANCED OR CONFIRMATORY TESTING

- Contrast radiographs
  - Barium sulfate suspension for upper GI study unless perforation suspected (see p. 1351)
    - If perforation suspected, consider using nonionic iodinated contrast medium or other diagnostic techniques (centesis, lavage).
  - Barium enema (see p. 1204)
    - For assessing an obstructive pattern in the distal intestine
    - For differentiating small bowel from large bowel if it is not clear whether a gas-filled viscus is a pathologically distended segment of small intestine or the normal colon
- Abdominocentesis (see p. 1194) and fluid analysis if perforation/peritonitis suspected
- Abdominal ultrasound
  - Site of obstruction may be visualized.
  - Identification of small amounts of free abdominal fluid
  - Localization of free fluid for accurate centesis
- Diagnostic peritoneal lavage (see p.1250)
  - If peritonitis is suspected but centesis is unrewarding
  - Limited efficacy
- Thoracic radiographs in older animals with suspected neoplasia



GASTROINTESTINAL OBSTRUCTION: FOREIGN BODY OR NEOPLASIA Radiographic appearance of the abdomen of a dog with small-intestinal obstruction, lateral view. A small-intestinal segment is markedly distended with gas *(arrows)*, and another is markedly distended with fluid/soft tissue *(arrowheads)*.

(Courtesy Dr. Richard Walshaw.)

TREATMENT

TREATMENT OVERVIEW

Rehydration and rapid surgical intervention are recommended in any patient with intestinal obstruction. Correct dehydration and electrolyte abnormalities with intravenous fluid administration. Exploratory laparotomy is indicated to relieve the obstruction.

ACUTE GENERAL TREATMENT

- Exploratory laparotomy for foreign-body retrieval or mass resection
- An enterotomy may suffice for acute foreign body removal; if intestinal viability is questionable, resection and anastomosis are warranted.
- Wide margin (4-8 cm) resection and anastomosis should be performed if neoplastic disease is suspected based on the gross appearance of the lesion. In this case, also perform lymph node and liver biopsies.
- Omentum or serosal patch may be placed to reinforce suture line.
- Change gloves and surgical instruments before abdominal lavage and closure to minimize contamination.
- Administer prophylactic antibiotics.
    - Cefazolin, 22 mg/kg IV q 2 h during the perioperative period
- Obtain gastric, small-intestinal, and liver biopsies, even if all appear grossly normal. Biopsy any abnormal-looking organ. Future course of illness may evolve in such a way as to make these specimens essential for diagnosis.

CHRONIC TREATMENT

Postoperative considerations:

- Continue rehydration and daily electrolyte monitoring. Treat accordingly (especially hypokalemia arising from dilution [IV fluids] and anorexia).
- Nothing by mouth (NPO) 6-12 hours post enterotomy, 12 hours post resection and anastomosis
- Administer GI protectants as needed.
    - Famotidine, 0.5-1 mg/kg IV, IM, SQ, or PO q 12-24 h; *or*
    - Ranitidine, 0.5-2 mg/kg slow IV, IM, SQ, or PO q 8-12 h
        - Ranitidine also has promotility properties similar to those of metoclopramide.
- Administer antiemetics as needed.
    - Contraindicated before resolution of obstruction
    - Metoclopramide, 0.2-0.4 mg/kg PO, SQ, or IM q 6 h; *or*
    - Cisapride, 0.1-0.5 mg/kg PO q 8 h

POSSIBLE COMPLICATIONS

- Dehiscence: animals should be monitored in hospital for 48-72 hours in the postoperative period for signs of peritonitis. Risk factors include presence of preoperative peritonitis, serum albumin concentration <2.5 g/dL, and presence of a foreign body (versus neoplastic disease).
- Ileus
- Short bowel syndrome: unlikely if less than 70% of small intestine resected
- Stricture
- Recurrence

RECOMMENDED MONITORING

- The following parameters should be monitored daily until discharge from hospital: body temperature, blood glucose, electrolytes, abdominal pain.
- The patient should be eating and not vomiting. If anorexia or vomiting persists after surgery, consider performing abdominocentesis and CBC to valuate for possible development of peritonitis.

NUTRITION/DIET

Feeding tube placement (see pp. 1267, p. 1269, p. 1270, and p. 1273) at the time of surgery should be considered in animals with marked weight loss, hypoalbuminemia, or in those patients with evidence of peritonitis (esophageal in the latter case). If anorexia persists post operatively, syringe feeding, feeding tubes or total parenteral nutrition may be considered.

PROGNOSIS AND OUTCOME

- A good prognosis may be expected for acute disease, while those animals with preoperative debilitation or shock should be given a more guarded prognosis.
- Prognosis for neoplastic disease depends on histopathologic grade, evidence of metastasis, and completeness of surgical excision. Lymphosarcoma and adenocarcinoma are the most frequently encountered intestinal tumors.

PEARLS & CONSIDERATIONS

COMMENTS

Consider placing an intraoperative feeding tube (esophagostomy, gastrostomy, or gastrojejunostomy tube) in these patients based on preoperative nutritional status, degree of patient debilitation, or anticipated postoperative anorexia.

TECHNICIAN TIPS

Intestinal obstruction patients may be in a critical state and require intensive care. Technicians treating and caring for these patients should be familiar with and competent in:

- Fluid therapy
- Intensive patient monitoring including blood pressure, CBC and serum biochemistry profile, blood gases, urine output
- Nutritional support (see above)
- Analgesia

SUGGESTED READING

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Fossum TW, Hedlund CS: Gastric and intestinal surgery. Vet Clin North Am Small Anim Pract 33:1117, 2003

Ralphs CS, et al: Risk factors for leakage following intestinal anastomosis in dogs and cats: 115 cases (1991-2000). J Am Vet Med Assoc 223:73, 2003.

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Gastrointestinal Endocrine Disease

BASIC INFORMATION

DEFINITION

Gastrointestinal (GI) endocrine disease occurs as a result of a tumor of one or more hormone-secreting cells in the GI tract. Insulinoma (p. 613) and gastrinoma (p. 442) are discussed in detail elsewhere.

SYNONYMS

- General: amine precursor uptake and decarboxylation (APUD) tumors; APUDoma
- Specific: gastrinoma (Zollinger-Ellison syndrome, delta cell tumor), glucagonoma (alpha cell tumor), VIPoma (Verner-Morrison syndrome), carcinoid tumors (Thorson-Bioerck syndrome, argentaffinoma syndrome)

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Gastrinoma: rare; middle-aged to old dogs and cats
- Glucagonoma: rare; middle-aged to old dogs; not reported in cats
- Carcinoid syndrome: rare; middle-aged to old dogs and cats

ASSOCIATED CONDITIONS & DISORDERS

Superficial necrolytic dermatitis and diabetes mellitus: glucagonoma

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Gastrinoma: gastrin
- Glucagonoma: glucagon
- Carcinoid syndrome: serotonin (primary substance)
- Somatostatinomas*: somatostatin
- Pancreatic polypeptideoma*: pancreatic polypeptide
- VIPoma*: vasoactive intestinal polypeptide

Legend:- *Documented in human but not veterinary medicine

HISTORY, CHIEF COMPLAINT

- Gastrinoma: vomiting, weight loss, anorexia, diarrhea, gastric hemorrhage
- Glucagonoma: ulcerative dermatitis, diarrhea, lethargy, weight loss, inappetence, possible polyuria and polydipsia
- Carcinoid tumors: often no overt clinical signs; possible abdominal pain, diarrhea, vomiting, weight loss, anorexia, or other signs of gastrointestinal obstruction or metastasis; carcinoid syndrome not reported in dogs or cats

PHYSICAL EXAM FINDINGS

- Gastrinoma: weight loss, lethargy, abdominal pain, pale mucous membranes, melena, and/or collapse and shock as a result of GI ulceration
- Glucagonoma: ulcerative dermatitis, lethargy
- Carcinoid tumor: no specific findings; possible anorexia, weight loss, acute abdomen due to obstruction

ETIOLOGY AND PATHOPHYSIOLOGY

- Specialized endocrine cells that secrete peptides are found throughout the GI tract.
- Neoplasia of these cells results in excess secretion of the hormone(s).

- Clinical signs occur as a result of the specific hormone oversecretion.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Nonspecific clinical signs in the history often lead to the passage of a protracted period of time prior to establishment of the diagnosis. A combination of clinical signs that become more obvious with clinical progression and ruling out of disorders that are more likely leads to diagnosis.

DIFFERENTIAL DIAGNOSIS

See Vomiting, ; Weight Loss, ; Diarrhea (Acute), 303; Acute Abdomen, 28; Ulcerative and Erosive Skin Disorders, ; Superficial Necrolytic Dermatitis, 1061

INITIAL DATABASE

- The diagnosis is made based on appropriate clinical signs and immunohistochemical staining of the tumor.
- A CBC, serum biochemical profile, and urinalysis should be evaluated to help rule out other diagnoses.
    - Mild hyperglycemia, increased liver enzymes, hypoalbuminemia, and possible glucosuria may be seen with glucagonoma.
    - A regenerative or iron-deficiency anemia, possible leukocytosis, hypoproteinemia, and increased liver enzymes may be seen with gastrinoma.
    - Results are usually normal with carcinoid syndrome.
- Radiographs and ultrasound results are usually normal but may help identify the primary tumor or metastatic lesions.

ADVANCED OR CONFIRMATORY TESTING

- Confirmation requires exploratory laparotomy and histopathology (immunohistochemical staining) of the tumor.
- Glucagonoma: increased plasma glucagon concentrations (in the absence of other diseases causing hyperglucagonemia), histopathologic evaluation of skin lesions, and hypoaminoacidemia are supportive. Results of liver function tests are normal (versus abnormal function with superficial necrolytic dermatitis).
- Gastrinoma: increased fasting serum gastrin concentration (in the absence of other diseases causing hypergastrinemia) and gastric hyperacidity; GI ulceration and/or increased prominence of gastric rugal folds seen with endoscopy, contrast radiography, or ultrasound; and excessive response to a gastrin secretagogue (secretin or calcium) are supportive.
- Carcinoid syndrome: increased serotonin metabolites (5-hydroxyindoleacetic acid) in urine are supportive.
- Indium-labeled somatostatin analogs (octreotide) are used in scintigraphy for detecting tumors expressing somatostatin receptors. CT scan and MRI can also be useful.

TREATMENT

TREATMENT OVERVIEW

Goals of treatment consist of:

- Removal of tumor
- Management of associated clinical signs

ACUTE GENERAL TREATMENT

- Fluid and electrolyte abnormalities should be corrected if present.
- Gastrinoma: treat hyperacidity and GI ulceration (see 440).
- Surgical removal of the primary tumor and any visible metastasis if possible. With gastrinoma, ulcer excision may also be needed.
- If the pancreas is manipulated during surgery, treat postoperatively for pancreatitis.

CHRONIC TREATMENT

- Because of the high incidence of metastasis at the time of diagnosis, surgery is not often curative, and subsequent medical management is needed.

- Gastrinoma: treat hyperacidity and GI ulcerations (see above); somatostatin analog treatment (octreotide, 5-20 mcg SQ q 8 h) can be tried.
- Glucagonoma: amino acid supplementation (eggs, prescription diets, possible IV amino acid infusion) has been suggested but is unproven; manage skin lesions (see pp. 1061 and p. 1122); octreotide (6 mcg SQ q 8 h) can be tried.
- Carcinoid syndrome: octreotide and cyproheptadine have been used. Methysergide maleate (antiserotonin agent) is not used because of serious side effect of retroperitoneal fibrosis.
- Effective chemotherapy for these tumors has not been reported in the dog and cat. Streptozotocin, doxorubicin, and 5-fluorouracil have been used in humans, with limited success.

POSSIBLE COMPLICATIONS

The most common postoperative complication is pancreatitis in dogs.

RECOMMENDED MONITORING

Monitor recurrence of clinical signs.

PROGNOSIS AND OUTCOME

- Glucagonoma: poor if concurrent advanced liver disease (mean 5 months) or metastasis
- Gastrinoma: poor long-term prognosis because metastasis is present in 70% of cases at time of diagnosis (mean 8 months)
- Carcinoid syndrome: many are clinically silent and found postmortem. Prognosis is guarded if metastatic disease is present.

PEARLS & CONSIDERATIONS

COMMENTS

These are complex tumors and very difficult to diagnose; referral to a specialist center is advised.

SUGGESTED READING

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Johnson SE: Pancreatic APUDomas. Semin Vet Med Surg Small Anim Pract 4:202–211, 1989.

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Gastroenteritis: Acute, Nonspecific

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Sudden onset of vomiting and/or diarrhea; may be accompanied by anorexia and evidence of abdominal discomfort. Generally self-limiting, although supportive care may be necessary in severe cases.

SYNONYMS

Acute gastritis, dietary indiscretion, acute enteritis

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs are more ofteffected owing to less discriminatorigestive behaviors.

RISK FACTORS: Poor supervision, access to garbage or other inappropriattems

ASSOCIATED CONDITIONS & DISORDERS: In severe cases: dehydration, hypokalemia, metabolic acidosis

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Acute onset of vomiting and/or diarrhea.
- Vomitus may contain food or foreign material.
- Diarrhea may be accompanied by mucus, urgency, tenesmus.
- Anorexia, lethargy, and mild abdominal discomfort may be noted in some cases.
- Owner may report recent dietary indiscretion.

PHYSICAL EXAM FINDINGS

- Normal vital parameters (temperature, heart rate, respiratory rate, pulse quality, blood pressure) in most cases
- Possible dehydration in more severe cases
- Mild nonlocalized abdominal discomfort may be noted.
- Mucoid stool may be noted on rectal examination.

ETIOLOGY AND PATHOPHYSIOLOGY

- Etiology is often not determined.
- Vomiting is likely due to direct gastric irritation or dysmotility.
- Diarrhea is likely due to irritation, dysmotility, or dysregulation of normal microbial populations within small and/or large intestine.
- Diagnosis usually based on history, absence of an identifiable cause, and prompt response to supportive therapy
- Often associated with dietary indiscretion (e.g., ingestion of garbage, nontoxic plants, spoiled food)

DIAGNOSIS

DIAGNOSTIC OVERVIEW

This is a diagnosis of exclusion; pursue other differentials only if the patient's condition does not support this diagnosis or if the clinical signs persist for more than 48 hours.

DIFFERENTIAL DIAGNOSIS

- Infection: parasitic, bacterial, viral, protozoal
- Gastrointestinal (GI) obstruction

- Systemic diseases: acute hepatic injury, renal failure, pancreatitis, hypoadrenocorticism
- Drugs or toxin ingestion
- All causes of acute vomiting or diarrhea

INITIAL DATABASE

- Extensive diagnostics usually not necessary if clinical examination and hydration status are within normal limits
- CBC: stress leukogram is expected in canine patients; polycythemia may be noted if the patient is dehydrated.
- Serum biochemistry profile: hypokalemia commonly noted; metabolic acidosis; mild increase in BUN and creatinine may be evident if patient is substantially dehydrated.
- Urinalysis: no abnormalities expected; specific gravity may be increased depending on patient's hydration status.
- Fecal evaluation (centrifuged flotation and saline preparation): no pathogens noted
- Radiographs: generally unremarkable; ileus may be apparent.
- +/− Pancreatic lipase immunoreactivity (if high-risk breed, other risk factors): within normal range
- +/− Fecal ELISA for parvovirus (if neonate, questionable vaccination status): negative

TREATMENT

TREATMENT OVERVIEW

- Provide supportive therapy until normal GI tract function resumes.
- Select appropriate therapies based on physical examination and clinical evaluation.

ACUTE GENERAL TREATMENT

- Small quantities of water or an oral electrolyte solution may be offered if vomiting is infrequent.
- Subcutaneous crystalloids may be used for small animals with mild dehydration deficits.
- Intravenous fluids are required if patient is moderately dehydrated or has any evidence of hypovolemia.
- Antiemetics should be administered if vomiting is unremitting, provided GI obstruction has been ruled out.
    - Maropitant (1 mg/kg SQ q 24 h) is an effective first choice (only licensed for dogs; patient must be >16 weeks old).
    - Metoclopramide (0.2-0.4 mg/kg SQ q 6-8 h) must be given frequently to manage vomiting or provided as a constant rate infusion.
- Gastric acid–reducing drugs may reduce the risk of esophagitis; are always appropriate if hematemesis is noted.
    - Famotidine (0.5 mg/kg PO, IV, or SQ q 12-24 h) has a longer duration of effect than other drugs in this class.
- Protectants/adsorbents provide little clinical benefit and may be aspirated in vomiting animals. Products containing salicylate should be avoided in cats.
- Anticholinergics (e.g., aminopentamide) are not recommended; GI motility can be substantially compromised. Other side effects include dry mouth and tachycardia.
- Antibiotics are generally not indicated and may contribute to intestinal microbial disturbances and prolongation of diarrhea.

NUTRITION/DIET

- Food should be provided as soon as the patient is interested in eating. Easily digestible diets may be beneficial (e.g., boiled white rice with cottage cheese, boiled chicken, commercially available highly digestible enteric diets) because gastric emptying times are shorter, and fecal volume is minimized.
- Probiotics +/− prebiotics should be considered in patients with diarrhea, as disruption of the normal intestinal flora is both a likely cause and consequence of acute nonspecific gastroenteritis.

DRUG INTERACTIONS

- Maropitant is protein bound and may affect metabolism of other highly protein-bound drugs such as nonsteroidal antiinflammatories and anticonvulsants.
- Metoclopramide may increase absorption of drugs absorbed primarily in the small intestine; the adverse CNS effects of metoclopramide may be enhanced by concurrent use of sedatives (such as phenothiazines), tranquilizers, and narcotics.

RECOMMENDED MONITORING

- Hydration status
- Temperature, pulse, respiratory rate
- Volume of fluid losses

PROGNOSIS AND OUTCOME

Prognosis is excellent; this disorder usually resolves within 48 hours of onset.

PEARLS & CONSIDERATIONS

COMMENTS

- Animals with marked dehydration, hypovolemia, depression, or abdominal pain require a prompt and detailed diagnostic evaluation.
- Melena or substantial hematemesis are not consistent with a diagnosis of acute nonspecific gastroenteritis. Patients with these signs may require more investigation and aggressive management.

CLIENT EDUCATION

- This disorder should resolve within 48 hours. Further veterinary care should be sought if vomiting or diarrhea are persistent.
- Neonates, geriatric animals, and those with preexisting disorders are more prone to dehydration and may need more aggressive fluid support.

SUGGESTED READING

Neiger R: Diseases of the stomach. In Steiner JM editor: Small animal gastroenterology. Hannover, 2008, Schlutersche, pp 155–161.

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EDITOR: DEBRA L. ZORAN

Gastrinoma

BASIC INFORMATION

DEFINITION

Uncommon malignant amine precursor uptake and decarboxylation (APUD) cell tumors that secrete excessive amount of gastrin, resulting in gastric acid hypersecretion

SYNONYM

Zollinger-Ellison syndrome

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs: average age 8.2 years (range 3.5-12 years). Cats: average age 10-12 years
- Female dogs and cats may be at a slightly higher risk than males.

GENETICS & BREED PREDISPOSITION: No breed predisposition is known.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Associated with gastrointestinal ulceration:
  - Chronic vomiting (most common)
  - Anorexia or ravenous appetite
  - Weight loss
  - Depression
  - Lethargy
  - Diarrhea
  - Polydipsia
  - Obstipation
  - Hematemesis
  - Melena
  - Pale mucous membranes
  - Abdominal pain
- Associated with perforating ulcer and peritonitis:
  - Collapse
  - Acute abdomen (pain)
  - Shock

PHYSICAL EXAM FINDINGS

- Nonspecific findings: lethargy, depression, poor body condition
- Pale mucous membranes
- Melena on rectal exam or apparent on rectal thermometer
- Palpable abdominal mass reported in one cat
- May be unremarkable

ETIOLOGY AND PATHOPHYSIOLOGY

APUD-cell tumors secrete excessive gastrin, resulting in hypersecretion of gastric acid by the stomach wall parietal cells. Gastric mucosal hypertrophy, gastrointestinal ulceration, esophagitis, and malassimilation secondary to enzyme inactivation and bile salt precipitation follow.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on the presence of vomiting, anorexia, weight loss, and diarrhea or a combination of these, typically in a middle-aged to older dog/cat. Confirmation requires the presence of hypergastrinemia in fasted patients, in conjunction with histopathologic and immunohistochemical evaluation of excised pancreatic or duodenal neoplasms.

DIFFERENTIAL DIAGNOSIS

- Refractory gastritis/gastric ulcer disease
- Inflammatory bowel disease
- Gastrointestinal tract neoplasia
- Chronic pancreatitis
- Common bile duct obstruction

INITIAL DATABASE

- CBC: regenerative anemia due to gastrointestinal bleeding; neutrophilia associated with gastrointestinal ulceration.
- Serum chemistry panel and electrolytes: hypoalbuminemia and hypoproteinemia due to protein loss through gastroduodenal ulcerations. Chronic vomiting may result in hypokalemia, hyponatremia, and hypochloremia. Metabolic alkalosis, with or without aciduria, is consistent with a gastric outflow obstruction, which may be present in some cases. Metastasis to the liver may result in bilirubinemia and elevated liver enzymes.
- Abdominal radiographs: loss of abdominal detail if gastrointestinal perforation has occurred; otherwise, they are generally unremarkable. Contrast radiographs may reveal deep ulcers, prominent gastric rugae, or gastric outflow obstruction in some cases.
- Three-view thoracic radiographs: usually are within normal limits. Metastatic lesions usually occur late in the course of the disease.
- Abdominal ultrasound: thickened gastric wall or pylorus; evidence of metastatic disease to the liver or lymph nodes; diffuse increased echogenicity of the liver with severe gallbladder dilation and marked dilation of the cystic duct, common bile duct, and extrahepatic ducts.

ADVANCED OR CONFIRMATORY TESTING

- Endoscopy: esophagitis, gastric or duodenal ulceration, hypertrophy of gastric mucosa are evident on visual inspection. Histopathologic evaluation: rugae often appear normal, suggesting submucosal or muscular hypertrophy; duodenal villous blunting and ulceration is supportive of chronic hyperacidity but not diagnostic of gastrinoma.
- Basal gastric acid secretion: increased in more than 80% of human gastrinoma patients. Of the four reported dogs tested, all values were low.
- Basal serum gastrin concentration: best survey test in humans (increased in 98% of human gastrinoma patients). Correlates with dog and cat disease but can also be elevated in nonfasting sample, renal failure, gastric outflow obstruction, hypochlorhydria, pyloric stenosis, gastric dilatation and volvulus, atrophic gastritis, chronic gastritis, small intestine resection, hepatic disease, drug administration (H2 blockers, proton pump inhibitors, or glucocorticoids), immunoproliferative enteropathy of basenji dogs, and possibly *Helicobacter* spp. infection.
- Secretin stimulation test (2-4 U/kg IV, samples at 0.2, 5, 10, and 20 minutes postinjection): preferred provocative test for the diagnosis of gastrinoma in humans (gastrin levels greater than 200 pm/mL diagnostic in humans). Data regarding the procedure and its interpretation are limited in dogs and cats.
- Calcium stimulation test: data regarding the procedure and its interpretation are limited in dogs and cats (may be risky).
- ^{111}Iridium-octreotide or pentetreotide: somatostatin analogs bind to receptors expressed on gastrinomas and have facilitated localizing metastatic lesions in one dog.
- Histopathologic evaluation with immunohistochemistries or radioimmunoassay of extracts from the gastrinoma allow for a definitive diagnosis.
- Electron microscopy may also be used for detecting pancreatic Langerhans D cell intracytoplasmic secretory granules that are found in gastrinomas.

TREATMENT

TREATMENT OVERVIEW

Treatment mainly includes medical therapy to control clinical signs associated with gastric acid hypersecretion. Surgical reduction of

gastrinoma and metastatic lesions is palliative.

ACUTE GENERAL TREATMENT

- Intravenous fluids and electrolyte therapy to correct abnormalities associated with vomiting
- Control gastric hyperacidity:
  - H2 receptor antagonists (cimetidine, 10 mg/kg IV, IM, SQ, or PO q 8 h; ranitidine, 0.5-2 mg/kg IM, SQ, PO [minimal efficacy in the dog; IV may cause vomiting] q 8-12 h; famotidine, 0.2-1 mg/kg IV, IM, SQ, or PO q 12-24 h; or nizatidine, 2.5-5 mg/kg PO q 24 h)
  - H^+/K^+-ATPase (proton pump) inhibitors (omeprazole, 0.7-1 mg/kg PO q 12-24 h)
  - Somatostatin analog (octreotide, 10-40 mg [per dog] q 8-12 h)
- Promote healing:
  - Sucralfate, 0.25-1 g per dog PO q 6-12 h
  - Misoprostol, 1-5 mcg/kg PO q 8 h
- Surgical and medical management for gastrointestinal ulceration/perforation

CHRONIC TREATMENT

- Acute treatment management, along with antiemetics
- Surgical debulking of the primary and metastatic lesions decreases clinical signs associated with gastrinomas.
- Chemotherapy, receptor-mediated radiotherapy, and long-acting somatostatin analogs (+/− alpha-interferon) yield mixed responses.

POSSIBLE COMPLICATIONS

Gastrointestinal ulceration/perforation if hyperacidity is not controlled; common bile duct obstruction if due to a duodenal gastrinoma

RECOMMENDED MONITORING

According to clinical signs

PROGNOSIS AND OUTCOME

- Poor due to high rate of metastasis
- Animals that are managed medically and surgically live 1 week to 18 months (mean, 4.8 months).

PEARLS & CONSIDERATIONS

COMMENTS

A palpable abdominal mass or one that is visualized either at ultrasound or at surgery is uncommon with gastrinoma.

CLIENT EDUCATION

- Monitor for recurrence of clinical signs.
- Rapid deterioration is possible if gastrointestinal perforation occurs.

SUGGESTED READING

Hughes SM: Canine gastrinoma: a case study and literature review of therapeutic options. N Z Vet J 54(5):242, 2006.

AUTHOR: M. RAQUEL BROWN

EDITOR: DEBRA L. ZORAN

Gastric Ulcer

BASIC INFORMATION

DEFINITION

Disruption of the gastric mucosa as a result of coagulative necrosis that breeches the muscularis layer and exposes the submucosa or deeper layers of the stomach wall

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs and cats; no age, sex, or breed predisposition

RISK FACTORS

- Iatrogenic: administration of cyclooxygenase (COX) inhibitors, other nonsteroidal antiinflammatory drugs (NSAIDs), or corticosteroids
- Hypergastrinemia due to any number of causes
- Severe hypovolemia or ischemia (shock) leads to reduced gastrointestinal (GI) blood flow and increased risk of gastritis/ulcer.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Vomiting, hematemesis, melena are common complaints.
- Inappetence or anorexia and hyper-salivation are variably seen.
- Acute encephalopathic signs (e.g., stupor, seizures, or drooling in cats) may be observed in patients with concurrent severe liver disease.

PHYSICAL EXAM FINDINGS

- Generally nonspecific
- Abdominal pain, either on palpation or manifested as a “praying” position, is possible.
- Pale mucous membranes and circulatory shock possible with severe bleeding or gastric perforation

ETIOLOGY AND PATHOPHYSIOLOGY

- Primary gastroduodenal diseases (e.g., toxins or foreign bodies, chronic gastritis, *Helicobacter* spp. infection, inflammatory bowel disease, neoplasia [mastocytosis, lymphoma, adenocarcinoma, or gastrinoma], pyloric outflow obstruction)
- Gastric hyperacidity disorders (e.g., gastrinomas, hypergastrinemia due to drugs)
- Drug-induced ulcers (e.g., COX inhibitors, other NSAIDs, corticosteroids)
- Other metabolic, endocrine, or systemic causes (e.g., pancreatitis, disseminated intravascular coagulation, hypoadrenocorticism, chronic kidney disease, liver failure, hypovolemic/septic shock, neurologic diseases, especially intervertebral disk disease or stress)
- The causes of ulceration are similar to those of gastritis and erosion, but for unknown reasons the reparative mechanisms of the mucosa are overwhelmed, resulting in deep indolent lesions.
- The process of ulcer healing starts as the necrotic mucosa sloughs and granulation tissue fills the ulcer. Mucus and bicarbonate are actively secreted by the neighboring mucosa to protect the ulcer. Granulation tissue eventually organizes, a connective-tissue bed develops, and epithelial tissues finally slide across the surface to reepithelialize it. Glandular structures are the last to repopulate the denuded area.
- Reduced gastric acid secretion facilitates this process, both by decreasing tissue damage from acid and by decreasing further damage from pepsin, which is less active at higher pH.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Gastric ulceration typically should be suspected in patients with any signs of GI disturbance that persist or worsen beyond the

degree expected for the primary diagnosis. A history of receiving ulcerogenic medications is suggestive but not essential. In many mild cases, clinical confirmation is only presumptive (response to antiulcer medications); a definitive clinical diagnosis requires endoscopy or laparotomy, particularly if severe/associated with gastric perforation and peritonitis.

DIFFERENTIAL DIAGNOSIS

- Acute vomiting:
  - Dietary indiscretion
  - Parasites
  - *Helicobacter* gastritis
  - Foreign bodies
  - Pancreatitis
  - Other acute metabolic conditions (renal failure, hypercalcemia, etc.)
- Hematemesis:
  - Coagulopathies or lack of platelets (number or function)
  - Ingested blood (nasopharyngeal, oral, esophageal, or pulmonary bleeding)
  - Hemorrhagic gastroenteritis (all causes of severe gastrointestinal erosion)
- Melena:
  - All causes of hematemesis ○ Intestinal neoplasia
  - Intestinal parasites (hookworm)
  - Intestinal ischemia
  - Inflammatory bowel disease or other infiltrative enteropathies
- Abdominal pain:
  - Hepatitis
  - Splenomegaly/splenic rupture/torsion
  - Intestinal obstruction
  - Acute renal failure
  - Intussusception/mesenteric torsion
  - Peritonitis
  - Pancreatitis

INITIAL DATABASE

- Rectal examination should be performed to assess presence of melena.
- CBC, serum biochemistry profile, urinalysis: important to identify underlying cause of gastric ulceration, and are especially needed if hematemesis or melena is present.
  - CBC may show anemia (variably regenerative if acute, depending on the time between onset of bleeding and time of testing; nonregenerative in the presence of underlying chronic disease; and microcytic, hypochromic, and regenerative [dogs] if associated with iron deficiency from chronic blood loss), neutrophilia (± left shift if associated with perforation), hypoproteinemia, or mild thrombocytopenia (rarely less than 75,000/µL).
  - Serum biochemistry profile may show an elevated blood urea nitrogen (BUN)/creatinine ratio or identify conditions associated with ulcers (renal failure, etc.). Not all cases will demonstrate an elevated BUN, however.
  - Urinalysis: essential for differentiating BUN elevation due to kidney disease (urine specific gravity 1.008-1.020) from BUN elevation due to prerenal causes (urine specific gravity > 1.035)
- Fecal occult blood test has limited utility.
  - *O*-tolidine-based tests are significantly more specific (0/108 false-positive results in healthy dogs) than guaiac-based tests (64/108 false-positive results in same dogs).
- Imaging studies:
  - Plain radiographs cannot confirm gastric ulceration. However, if perforation has occurred, loss of detail (suggesting peritonitis or free abdominal fluid) or free peritoneal gas may be present.
  - Contrast radiographs may identify a mucosal filling defect.
  - Ultrasonography may show local gastric wall thickening, loss of normal layering, the presence of a wall defect or "crater," fluid accumulation in the stomach, and diminished gastric motility. In animals with perforation due to the ulcer, there may be evidence of free fluid in the abdomen.

ADVANCED OR CONFIRMATORY TESTING

- Serum gastrin levels may help diagnose gastrinoma (see p. 442), but the animal must not have been on histamine-2 receptor blockers or proton pump inhibitors before testing.
- If a gastrointestinal perforation is suspected, abdominocentesis (see p. 1194) is indicated. If free fluid can be obtained during the ultrasound examination, that is often sufficient. However, a diagnostic peritoneal lavage may be needed to obtain samples if the perforation is relatively recent and the fluid accumulation is minimal.
- Gastroscopy: preferred for confirmation of gastric ulcer and tissue sampling; however, if a perforation is suspected, endoscopic examination is contraindicated, as it will increase abdominal contamination.

- A solitary ulcer in an otherwise normal stomach should raise the suspicion of gastric neoplasia, especially if the edges and surrounding mucosa are thickened.
- NSAID-induced ulcers can be solitary, but the surrounding mucosa is usually not normal, owing to generalized mucosal disease (gastritis and other erosions are common).
- Multiple diffuse small ulcers can be seen with NSAIDs, uremia, liver disease, mastocytosis, gastrinoma, and possibly *Helicobacter* gastritis.
- Biopsies should be obtained from the ulcer periphery to avoid perforation. Repeated biopsies from the same site may improve the likelihood of identifying neoplasia. However, in some cases, endoscopic biopsies will be inadequate for diagnosis (neoplastic tissue is deeper than superficial mucosal tissues sampled with endoscopic biopsies), and laparotomy is required for full-thickness biopsies.

TREATMENT

TREATMENT OVERVIEW

- Remove primary cause
- Promote healing
- Stabilization of patient with circulatory collapse from massive bleed or perforation

ACUTE GENERAL TREATMENT

- Supportive care:
  - Intravenous fluids, antibiotics, antiemetics, and opioid analgesics may be required for the patient with severe vomiting that has resulted in dehydration and electrolyte disturbances.
  - Blood transfusion for the patient with severe anemia as a result of massive bleeding
- Surgery:
  - Surgical resection is indicated when the ulcer appears deeply penetrating (volcano crater appearance), is bleeding continuously, has perforated, or is very large and fails to heal.
  - Surgical exploration may identify the etiology (neoplasia) and allow resection of the mass/ulcer.
- Medical:
  - H2 blockers. Options include:
    - Famotidine: 0.5-1 mg/kg PO, IV, or SQ q 12-24 h
    - Ranitidine: 1-4 mg/kg PO, IV, or SQ q 8-12 h
    - Cimetidine: 5-10 mg/kg PO, IV, or SQ q 6-8 h
  - Proton pump inhibitor: reduces gastric acid by >90% (not for use in cats). Options include:
    - Omeprazole: 0.7 mg/kg PO q 24 h (alternately 20 mg/dog)
    - Esomeprazole (Nexium): 1 mg/kg PO q 24 h
    - Lansoprazole (Prevacid): 1 mg/kg IV q 24 h
  - Prostaglandin E2-inhibitor: drug of choice for prevention/treatment of NSAID-induced ulcers; not for use in cats or pregnant females:
    - Misoprostol: 3-5 mcg/kg PO q 8 h
  - Sucralfate: mucosal protectant. As oral suspension, or dissolved in 6-10 mL tap water if tablet; is most effective if administered in an acidic environment (give 1-2 hours before acid-blocking drugs):
    - Dogs: 0.5-1 g PO q 8 h
    - Cats: 0.25 g PO q 8 h
  - Antiemetics: use as needed to control emesis:
    - Metoclopramide: 0.2-0.4 mg/kg PO or SQ q 8 h
    - Dolasetron: 0.3 mg/kg IV q 12-24 h

CHRONIC TREATMENT

Misoprostol is indicated for preventing ulcers in dogs that need to be on NSAIDs (e.g., arthritis) but are prone to developing ulcers.

DRUG INTERACTIONS

- Cimetidine and ranitidine inhibit a subset of the cytochrome P450 enzyme systems and may delay metabolism of some drugs.
- The dose of ranitidine must be altered (reduced) in dogs with kidney disease.

POSSIBLE COMPLICATIONS

The most important complications of gastric ulceration are blood-loss anemia (can be severe, requiring transfusions) and perforation, resulting in septic peritonitis and shock.

RECOMMENDED MONITORING

In dogs or cats with acute hematemesis, the packed cell volume/total protein must be monitored to determine if a blood transfusion or surgical intervention is needed.

PROGNOSIS AND OUTCOME

The prognosis for most gastric ulcers is good unless the underlying etiology is not identified or cannot be corrected.

PEARLS & CONSIDERATIONS

COMMENTS

- Careful endoscopic evaluation of the lesser curvature of the stomach is critical for identification of gastric adenocarcinoma.
- Patients with GI bleeding often have BUN elevations with normal creatinine, concentrated urine, and normal renal function.
- The combination of an H2 blocker with sucralfate is frequently used in the belief that healing is improved with the combination. A study in people comparing ranitidine to ranitidine-sucralfate showed no benefit from using the combination.
- Proton pump inhibitors (e.g., omeprazole) are the only effective means of completely reducing acid secretion. H2 blockers are much less potent, and of the group, only famotidine has been shown in dogs to adequately decrease gastric acid levels.

PREVENTION

Careful administration of NSAIDs, or use of NSAIDs with COX-2 selective properties, to minimize the risk of ulceration

CLIENT EDUCATION

- Advise clients of the dangers of consistent NSAID use, and provide them with signs to watch for that may indicate gastritis or ulcer formation.
- Advise clients about the potential dangers of over-the-counter NSAIDs in dogs and cats, as some of the most potent ulcerogenic drugs in dogs are ibuprofen, regular aspirin, and naproxen.
- Advise clients about the risk of potentially life-threatening complications from any over-the-counter NSAID given to cats.

SUGGESTED READING

Cariou M, Lipscomb VJ, Brockman DJ, et al: Spontaneous gastroduodenal perforations in dogs: a retrospective study of 15 cases. Vet Rec 165(15):436–441, 2009.

Cariou MP, Halfacree ZJ, Lee KC, et al: Successful surgical management of spontaneous gastric perforations in three cats. J Feline Med Surg 12(1):36–41, 2010.

AUTHOR: KENNETH R. HARKIN

EDITOR: DEBRA L. ZORAN

Gastric Parasites

BASIC INFORMATION

DEFINITION

Nematode parasites of the stomach affecting dogs and cats

EPIDEMIOLOGY

SPECIES, AGE, SEX: *Physaloptera* spp. infect dogs and cats. *Ollulanus tricuspis* is found exclusively in the cat. There is no age or sex predisposition.

RISK FACTORS

- Dogs and cats that habitually ingest the intermediate host (crickets, beetles, cockroaches) or transport hosts (e.g., rodents and snakes) for *Physaloptera* spp. are at greater risk of infection.
- Multicat households are a risk factor for *Ollulanus* spp. infection.

CONTAGION & ZOONOSIS: These are not zoonotic diseases. *Ollulanus* spp. is spread from cat to cat in the vomitus.

GEOGRAPHY AND SEASONALITY: Worldwide

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Chronic vomiting is the chief complaint for both parasitic infections. A good appetite is usually retained, and weight loss is usually insignificant, particularly for *Physaloptera* spp. infections. Cats with *Ollulanus* spp. infection may have chronic weight loss. The duration of signs may be from a few days to many months.

PHYSICAL EXAM FINDINGS: Typically there are no significant abnormal findings on physical examination. Emaciation may be present.

ETIOLOGY AND PATHOPHYSIOLOGY

- *Physaloptera* spp., most commonly *P. rara*. They range in length from 1 to 6 cm, although most are 1 to 2 cm.
  - Subclinical infections are believed to occur in many animals, but chronic vomiting due to gastritis or penetration of parasite into the gastric wall is the typical pathophysiologic presentation.
  - Intermediate hosts: beetles and crickets
- *O. tricuspis*. Size range is 0.7-1 mm long.
  - Presence *of Ollulanus* may induce gastric irritation and inflammation or in severe cases, a chronic fibrosing gastritis; however, infections with the parasite can also be inapparent.
  - Life cycle is direct: infection from eating vomitus containing larvae.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Affected individuals are identified by a chief complaint of vomiting that resolves with anthelmintic treatment (presumptive diagnosis based on response to treatment); alternatively, confirmation may come from demonstration of the parasites (endoscopic or microscopic).

DIFFERENTIAL DIAGNOSIS

- Dietary indiscretion
- Food intolerance or hypersensitivity/allergy
- Gastric foreign body
- *Helicobacter* gastritis
- Drugs or toxins (nonsteroidal antiinflammatory drugs, antibiotics, plants, lead)

- Idiopathic gastritis (lymphoplasmacytic, eosinophilic)
- Pyloric antral hypertrophy
- Pythiosis

INITIAL DATABASE

- CBC, serum biochemistry profile, and urinalysis are usually normal, although a rare dog or cat may have peripheral eosinophilia.
- Fecal flotation is usually negative. On rare occasions, the translucent eggs of *Physaloptera* spp. may be identified.
- Abdominal radiographs are normal.
- Abdominal ultrasound is normal.
- Microscopic examination of the vomitus may yield the presence of *Ollulanus* spp.

ADVANCED OR CONFIRMATORY TESTING

- In many cases of unconfirmed *Physaloptera*- or *Ollulanus*-associated gastritis, empirical anthelminthic treatment is highly effective, and advanced testing may be unnecessary.
- Gastroscopy is the only method to reliably identify the presence of *Physaloptera* spp. in the stomach.
- *Ollulanus* spp. can be identified from microscopic examination of vomitus, squash preps, or touch preps of gastric mucosal biopsies (endoscopy or surgery), or on histologic evaluation of the biopsies (less reliable).

TREATMENT

TREATMENT OVERVIEW

Removal of the parasite rapidly resolves vomiting.

ACUTE GENERAL TREATMENT

- Mechanical removal of *Physaloptera* spp. resolves clinical signs.
- Anthelminthics for *Physaloptera* spp.:
  - Pyrantel: 5 mg/kg PO (dog), 20 mg/kg PO (cat). Using a higher dose in dogs (10-15 mg/kg) and repeating in 2-3 weeks may yield a higher response rate.
  - Fenbendazole: 50 mg/kg/d PO for 3 days is reportedly effective (dog, cat). This author uses 75 mg/kg/d PO for 5 days in dogs.
  - Ivermectin: may be effective at 0.2 mg/kg PO (dog, cat). Not for use in ivermectin-sensitive breeds.
- Anthelminthics for *O. tricuspis*:
  - Fenbendazole: 50 mg/kg/d PO for 3 days
  - Pyrantel: 20 mg/kg PO, repeat in 2-3 weeks

POSSIBLE COMPLICATIONS

Fenbendazole is not labeled for use in cats and may be associated with idiosyncratic hepatotoxicosis with high doses or prolonged use.

PROGNOSIS AND OUTCOME

The prognosis for complete resolution of chronic vomiting is excellent. Reinfection with *Physaloptera* spp. is likely in most cases, as repeated ingestion of intermediate and transport hosts occurs. Treatment of all cats in a household for *O. tricuspis* should eliminate the parasite.

PEARLS & CONSIDERATIONS

COMMENTS

- At gastroscopy, the presence of small erosions or pinpoint hemorrhages on the gastric mucosa should prompt a careful inspection for *Physaloptera* spp.
- The elusive nature of the parasites, minimal severity of clinical signs, and expense of endoscopy all warrant a therapeutic trial

with an anthelminthic before advanced diagnostic testing. Gastric parasites may still be found after a failed therapeutic trial.

PREVENTION

- Block access to intermediate hosts or transport hosts.
- Administration of a monthly heartworm preventive that contains pyrantel may be beneficial in management of dogs with continued access to intermediate or transport hosts.

SUGGESTED READING

Guilford WG, Strombeck DR: Chronic gastric diseases: parasitic gastritis. In Guilford WG, et al, editors: Strombeck's small animal gas-troenterology, ed 3, Philadelphia, 1996, WB Saunders, pp 285–286.

Theisen SK, et al: *Physaloptera* infection in 18 dogs with intermittent vomiting. J Am Anim Hosp Assoc 34:74–78, 1998.

AUTHOR: KENNETH R. HARKIN

EDITOR: DEBRA L. ZORAN

Gastric Neoplasia

BASIC INFORMATION

DEFINITION

Benign or malignant tumors of epithelial, lymphoid, or mesenchymal origin. These tumors affect gastric function, are often painful, and may cause secondary systemic effects such as electrolyte disturbances, anemia, and weight loss.

SYNONYMS

Gastric adenocarcinoma, gastric adenoma, gastric polyps (benign), gastric carcinoma, gastric extramedullary plasmacytoma, gastric lymphoma (see p. 678), gastrointestinal stromal tumor (GIST), leiomyoma, leiomyosarcoma, scirrhous carcinoma of the stomach.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- In dogs, gastric tumors account for<1% of all malignancies:
  - Median age for adenocarcinoma is 10 years.
  - Median age for leiomyomas and GIST is 11 years.
- In cats, gastric tumors are most commonly lymphoma, which occurs in cats > 7 years old.

GENETICS & BREED PREDISPOSITION

- Gastric adenocarcinomas: rough collies, Staffordshire terriers, Belgian shepherds, and chow chows (may be familial)
- Leiomyoma and GIST: German shepherds

RISK FACTORS

Gastric adenocarcinomas:

- Chronic nitrosamine exposure experimentally
- Association of gastric carcinoma and lymphoma with chronic inflammation from *Helicobacter pylori* infection in people; unproven in companion animals

CONTAGION & ZOONOSIS

- *Helicobacter* spp. organisms may be frequently found in normal dogs and cats, but significance is undetermined.
- Zoonotic potential exists for *H. pylori,* but the prevalence of infection in animals is low.

ASSOCIATED CONDITIONS & DISORDERS: Gastric lymphoma in cats is generally not associated with retroviral infection (feline leukemia virus, feline immunodeficiency virus).

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Chronic vomiting
- Hematemesis/melena
- Anorexia, weight loss
- Depression and lethargy, pain or restlessness

PHYSICAL EXAM FINDINGS

May include some or all of the following:

- Physical exam may be normal
- Poor body condition score (e.g., body condition score 1/9-2/9)

- Pale mucous membranes, signs of anemia
- Abdominal mass
- Abdominal pain

ETIOLOGY AND PATHOPHYSIOLOGY

- Chronic vomiting may result in weight loss, electrolyte imbalance.
- Anemia secondary to chronic gastrointestinal (GI) bleeding may be hypochromic, microcytic due to iron depletion.
- Panhypoproteinemia due to GI blood loss
- Hypoglycemia may occur secondary to insulin-like growth factor II release from smooth muscle tumors.
- GISTs are associated with activating mutation of the c-kit receptor tyrosine kinase oncogene.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is typically reached when nonspecific signs of gastrointestinal disturbance fail to respond to conservative management and/or are accompanied by systemic disturbances (e.g., weight loss). Radiographs and ultrasound may help to localize the lesion; confirmation requires a biopsy.

DIFFERENTIAL DIAGNOSIS

Any gastrointestinal or systemic cause of chronic vomiting may mimic gastric neoplasia:

- Gastric foreign body
- Gastric ulceration
- Granulomatous gastritis
- Chronic pancreatitis
- Systemic disease associated with chronic vomiting (renal, hepatic, diabetic ketoacidosis)

INITIAL DATABASE

CBC, serum chemistry panel with electrolytes, urinalysis: frequently normal or changes are nonspecific and secondary to GI electrolyte or blood losses (nonregenerative anemia, increased blood urea nitrogen, normal creatinine, normal urine specific gravity).

- Three-view thoracic staging radiographs (metastasis)
- Abdominal ultrasound evaluation: to assess gastric wall changes often not seen on routine radiographs and to rule out other causes of vomiting (pancreatitis, liver disease, etc.)
- Positive contrast gastrogram: assessment for outflow obstruction; does not differentiate neoplasia from other infiltrative diseases such as pythiosis
- Ultrasound-guided fine-needle aspiration cytology: if a gastric wall abnormality or lymphadenopathy is present. Lymphoma exfoliates most readily; GIST or gastric muscle tumors do not.
- Endoscopic biopsy: histopathologic diagnosis is essential for treatment and prognosis. Endoscopy rapidly and effectively provides mucosal tissue specimens, but if the tumor is in the gastric muscular or serosal layers, results may be inadequate, requiring surgical biopsy.
- Surgical biopsy: exploratory surgery provides opportunity for both diagnosis and treatment (surgical removal of the affected region).

ADVANCED OR CONFIRMATORY TESTING

Diagnosis is confirmed by biopsy with histopathology:

- Immunohistochemical stains for c-kit in GIST
- Cytokeratin, vimentin immunohistochemistry for undifferentiated tumors
- Immunophenotyping for lymphoma

TREATMENT

TREATMENT OVERVIEW

Benign gastric lesions may be cured surgically, as can early-diagnosed low-grade malignancy. Other surgical goals might be to relieve gastric obstruction or remove tumors that are painful or bleeding for palliation. Chemotherapy is potentially helpful in prolonging survival, although malignant gastric tumors are typically incurable.

ACUTE GENERAL TREATMENT

- Antiemetics (maropitant, 1 mg/kg PO, SQ; or dolasetron, 0.3 mg/kg q 12-24 h IV, SQ; or metoclopramide, 0.2-0.4 mg/kg q 8 h, PO, or IV if no obstruction present), gastroprotectants (famotidine, 0.5 mg/kg IV, PO q 12 h).
- Rehydration with intravenous fluids
- Antibiotics for *Helicobacter* infection if indicated
- Blood transfusion and hematinic therapy as indicated for nonregenerative iron-deficiency anemia
- Analgesic management as indicated by clinical signs
- Diet modification to easily digested, high-energy content food
- Parenteral alimentation as indicated (if the patient has not eaten for > 3 days or will not be able or willing to eat after surgery)

CHRONIC TREATMENT

- Gastric tumor resection often results in motility disorders.
  - May require motility modifiers (metoclopramide, 0.2-0.4 mg/kg IV, PO q 8 h; or cisapride, 0.25 mg/kg q 24 h PO)
- Chronic antiemetic therapy may be required.
- Chemotherapy with doxorubicin, platinum agents, or antimetabolites may prove helpful.
- Systemic chemotherapy for gastric lymphoma provides remission and prolonged survival (see p. 678).

POSSIBLE COMPLICATIONS

- Surgical wound dehiscence with secondary peritonitis, pneumoperitoneum
- Chemotherapy-induced leukopenia might predispose to infection.
- Chemotherapy-induced thrombocytopenia might increase gastric hemorrhage.
- Chemotherapy might result in gastric perforation of transmural lesions.

RECOMMENDED MONITORING

- Postoperative follow-up with chest radiographs and abdominal ultrasound for signs of recurrence or metastasis on a 1-to 2-month basis for 1 year
- Monitor CBC for recovery from nonregenerative anemia.
- Monitor for signs of dissemination of alimentary lymphoma.

PROGNOSIS AND OUTCOME

- Favorable for benign lesions (adenomas, leiomyomas), although complete resection of mesenchymal tumors is unlikely
- Poor for adenocarcinoma, carcinoma, GIST, especially when metastatic:
  - These dogs generally do not live beyond 6 months even with therapy.
- Guarded to fair for focal mass presentation of lymphoma
- Guarded for diffuse or multicentric alimentary lymphoma, as these lesions typically regress slowly and may have an indolent course but are ultimately incurable

PEARLS & CONSIDERATIONS

COMMENTS

- Gastric carcinoma is associated with early lymphatic spread. Lymph nodes detected on ultrasound can be used for diagnosis and prognosis.
- Gastric carcinomas may overexpress cyclooxygenase-2; nonsteroidal antiinflammatory drugs (piroxicam, 0.3 mg/kg PO q 24 h) may be palliative.
- Scirrhous carcinoma is rapidly fatal.

SUGGESTED READING

Frost D, Lasota J, Miettinen M: Gastrointestinal stromal tumors and leiomyomas in the dog: a histopathologic, immunohistochemical

and molecular genetic study of 50 cases. Vet Pathol 40:42, 2003.

AUTHOR: BARBARA E. KITCHELL

EDITOR: DEBRA L. ZORAN

Gastric Dilatation/Volvulus

BASIC INFORMATION

DEFINITION

Rotation of the stomach on its mesenteric axis associated with gastric distention, well recognized in large-and giant-breed dogs

SYNONYMS

Bloat, gastric torsion, GDV

EPIDEMIOLOGY

SPECIES, AGE, SEX: Older dogs (>7 years) are at greatest risk; rarely reported in cats.

GENETICS & BREED PREDISPOSITION

- Large-and giant-breed dogs
- Purebred dogs at greater risk than mixed breeds
- Having a first-degree relative with gastric dilatation/volvulus (GDV) is associated with an increased risk.
- The most commonly affected breeds are the Great Dane, weimaraner, Saint Bernard, Gordon setter, Irish setter, Doberman pinscher, Old English sheepdog, and standard poodle. Bassett hound is at greatest risk among smaller breeds.

RISK FACTORS

Increased risk may be associated with:

- Narrow and deep thoracic cavity
- Long hepatogastric ligament
- Stress
- Fearful temperament
- Being underweight
- Nutritional risk factors including once-daily feeding, rapid ingestion of food, exercise after eating, consumption of large volumes of food or water, eating from a raised feeding bowl, and feeding dry dog food with oil or fat listed as one of the first four ingredients

GEOGRAPHY AND SEASONALITY: Possible increased incidence in the months of November, December, and January (United States)

ASSOCIATED CONDITIONS & DISORDERS

- Inflammatory bowel disease
- Previous splenectomy for splenic torsion or mass

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Abdominal distension
- Abdominal pain
- Ptyalism
- Retching or vomiting (may be nonproductive)
- Acute collapse

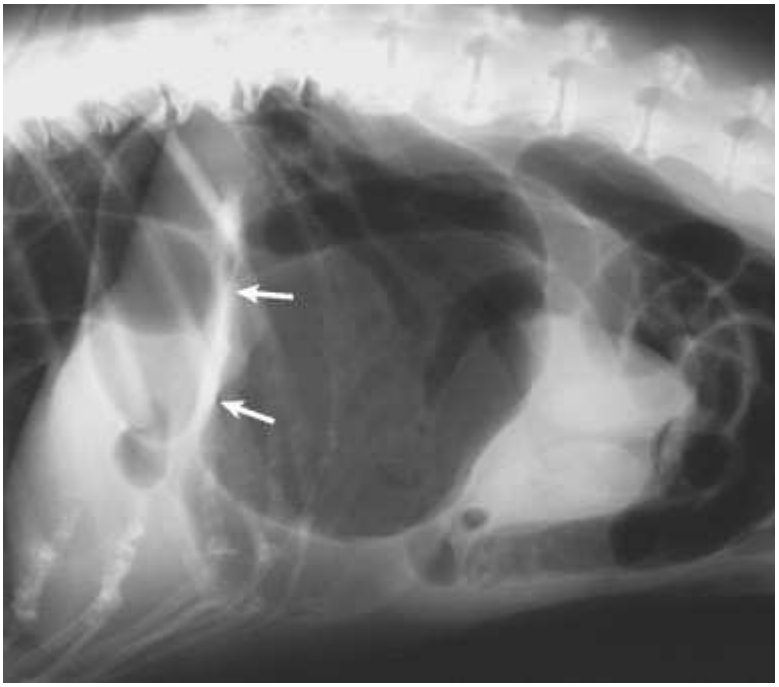
PHYSICAL EXAM FINDINGS

- Abdominal distension and tympany:
  - Simultaneous auscultation and percussion of the abdomen may reveal a tympanic sound, indicating the presence of a

taut, gas-filled viscus (stomach).
- Splenomegaly
- Clinical signs of hypovolemic shock: weak pulses, tachycardia, pale mucous membranes, prolonged capillary refill time, dyspnea

ETIOLOGY AND PATHOPHYSIOLOGY

- In most cases, the pylorus moves ventrally and from right to left; the rotation may be 90○-360○.
- Gastric dilation occurs secondary to failure of eructation and pyloric outflow obstruction. This occurs before or after gastric rotation.
- The distended stomach results in caudal vena cava and portal vein compression, causing decreased venous return to the heart.
- Decreased venous return results in decreased cardiac output, decreased arterial blood pressure, and myocardial ischemia.
- Myocardial ischemia causes cardiac arrhythmias.
- In the case of volvulus, increased intraluminal gastric pressure, portal hypertension, and avulsion of the short gastric vessels compromise blood flow to the gastric wall. Gastric necrosis and perforation can result.
- Portal vein compression/hypertension causes sequestration of splanchnic blood and decreased ability to clear gram-negative endotoxins.
- Endotoxemia further potentiates hypotension and decreased cardiac output.
- Pressure on the diaphragm, decreased lung perfusion, and decreased lung compliance cause respiratory dysfunction and exacerbate tissue hypoxia.



GASTRIC DILATATION/VOLVULUS Lateral abdominal radiograph of a dog with gastric dilatation/volvulus. Characteristic septation *(arrows)* of the gastric shadow is seen; displaced, gas-filled antrum is cranial to the arrows (to the left on this image), whereas gas-filled fundus is caudal (arrows are within it). A gas-filled esophagus and evidence of ileus in the form of distended, gas-filled small intestine are also present.

(Courtesy Dr. Richard Walshaw.)

DIAGNOSIS

DIAGNOSTIC OVERVIEW

GDV should be suspected in large-or giant-breed dogs presenting with an acute history of a distended or painful abdomen, often with preceding or concurrent attempts at vomiting. Physical examination usually reveals a tympanic abdomen and often signs of shock. The diagnosis is confirmed with radiography, but treatment for shock is initiated beforehand based on clinical suspicion alone.

DIFFERENTIAL DIAGNOSIS

- Gastric bloat associated with overeating
- Mesenteric volvulus
- Splenic torsion
- Diaphragmatic hernia with stomach herniation

INITIAL DATABASE

- Abdominal radiographs:
  - Right lateral view is preferred.
  - Shows gas-filled pylorus cranial and dorsal to the fundus ("popeye sign," "C sign," or "double bubble")
  - Free abdominal air suggests gastric perforation.
- Quick assessment tests:
  - Packed cell volume/total solids (PCV/TS): often increased due to hypovolemia
  - Serum electrolyte and glucose concentrations: hypokalemia and hypoglycemia may be seen.
  - Acid-base analysis: metabolic acidosis due to lactic acidosis frequently seen
- Coagulation panel and platelet count: thrombocytopenia, increased prothrombin time/activated partial thromboplastin time/fibrinogen concentration and/or fibrin degradation product concentration associated with disseminated intravascular coagulation
- Electrocardiogram (ECG): ventricular arrhythmias are common

ADVANCED OR CONFIRMATORY TESTING

- Diagnosis confirmed at surgery
- Measurement of lactic acid concentration prior to surgery may assist in determining prognosis
  - Lactic acid (lactate) concentration >6.0 mmol/L associated with gastric necrosis and increased mortality

TREATMENT

TREATMENT OVERVIEW

The initial therapeutic goal is to manage hypovolemia with intravenous (IV) fluids and to decompress the stomach to reestablish systemic and gastric mural perfusion. Definitive treatment involves surgery to correct the position of the stomach, remove devitalized tissue, and perform a gastropexy to prevent recurrence.

ACUTE GENERAL TREATMENT

- Place large-bore IV catheters in both cephalic veins and infuse isotonic crystalloids at a rate of 90 mL/kg/h. Colloids can be administered in combination with crystalloids at 5-20 mL/kg over 15-30 minutes. For severe shock, hypertonic saline can be administered at 4 mL/kg over 5 minutes followed by crystalloids.
- Prophylactic antibiotic therapy
- Decompress the stomach by orogastric intubation (see p. 1281).
- If orogastric intubation is not possible and patient has visible abdominal distension with a radiographically confirmed GDV, perform percutaneous trocarization of the stomach:
  - Aseptically clip and prepare an area at least 4 × 4 in. (10 × 10 cm) on the left lateral or dorsolateral abdomen, just caudal to the last rib and over the region of most obvious distension.
  - Identify a point that is within the prepared area and ventral to the hypaxial muscles and caudal to the last rib.
  - Using a large-bore needle or needlestyleted catheter (e.g., 16 or 14 G) directed ventrally and slightly cranially, penetrate all layers of the body wall and stomach. When successful, the procedure should produce a hissing sound associated with a release of fetid-smelling gas through the needle.
- Immediate surgery to return stomach to a normal position:
  - Placing traction on the pylorus and elevating it while putting downward pressure on the fundus will aid derotation in a counterclockwise direction (most but not all cases will have rotated clockwise).
  - Evaluate stomach and spleen for irreversible vascular compromise and necrosis.
  - Perform partial or complete splenectomy if splenic necrosis, infarction, or torsion. Perform resection or invagination of necrotic areas of stomach.
  - Perform gastropexy of pyloric antrum to the right body wall.
- Medical treatment alone (repeated intubation, trocarization) has been uniformly disappointing.

CHRONIC TREATMENT

- Postoperative potassium supplementation if hypokalemic:
  - Do not exceed 0.5 mEq/kg/h IV.

- If ventricular arrhythmias are noted on the ECG:
  - Is hypokalemia present? If so, institute potassium replacement immediately.
    - Ventricular arrhythmias are caused by hypokalemia.
    - Ventricular arrhythmias are refractory to treatment with lidocaine, procainamide, and other antiarrhythmics when hypokalemia is present.
  - Is there anemia, hypoxemia, or acidosis? Many ventricular arrhythmias will resolve spontaneously if these systemic disturbances are corrected.
  - Is the rate rapid (>160 bpm), or is the pulse weak, despite addressing the systemic disturbances already mentioned? If so, consider treatment with lidocaine (see p. 1165).
- Treat peritonitis (see p. 865) if gastric perforation has occurred (fluids, antibiotics, abdominal lavage ± drainage).
- Treat gastric ulceration with H2 receptor antagonists:
  - Famotidine, 0.5-1 mg/kg IV, IM, SQ, or PO q 12-24 h; *or*
  - Ranitidine, 0.5-2 mg/kg IV, IM, SQ, or PO q 8-12 h
    - Ranitidine also has promotility properties similar to those of metoclopramide.
- Use drugs that increase gastric motility (i.e., metoclopramide, 0.2-0.4 mg/kg PO, SQ, or IM q 6 h, or 1-2 mg/kg/d IV as a continuous infusion; *or* cisapride, 0.1-0.5 mg/kg PO q 8 h) if recurrent bloating occurs after gastropexy, without evidence of gastric outflow obstruction.
- Pain management

NUTRITION/DIET

- Enteral/oral feeding can begin the day after surgery if the patient is not vomiting.
- Several recommendations are made to prevent gastric bloat after discharge or to prevent GDV in dogs that have not had a gastropexy:
  - Divide feedings into several small meals a day.
  - Do not feed dry foods that contain an oil or fat ingredient listed as one of the first four ingredients.
  - Avoid stress during feeding.
  - Do not elevate feeding bowl during eating.
  - Restrict exercise before and after meals.

POSSIBLE COMPLICATIONS

- Cardiac arrhythmias
- Reperfusion injury
- Gastric necrosis with peritonitis if devitalized tissue not removed
- Gastric ulceration
- Esophagitis and regurgitation
- Gastroparesis and ileus
- Disseminated intravascular coagulation
- Aspiration pneumonia
- Recurrence of dilation
- Recurrence of volvulus if inadequate gastropexy

RECOMMENDED MONITORING

- ECG: ventricular arrhythmias common within 36 hours of surgery
- Electrolyte concentrations: hypokalemia
- Blood glucose concentration: hypoglycemia
- PCV/TS: hemoconcentration indicates need for increased fluid therapy. Anemia can occur from bleeding of torn short gastric vessels.
- Physical parameters: mucous membrane color, capillary refill, pulse quality, temperature, respiratory effort, lung auscultation, abdominal distension, bruising

PROGNOSIS AND OUTCOME

- Approximately 15% mortality rate for patients with GDV treated surgically
- Gastric necrosis and need for gastric resection are associated with >30% mortality
- Increased risk of death if ≥5 hours time lag from onset of clinical signs to admission, hypothermic at admission, or if hypotension occurs at any time during hospitalization
- Serum lactate level in dogs with GDV:
  - 99% survival if <6 mmol/L
  - 58% survival if >6 mmol/L

PEARLS & CONSIDERATIONS

COMMENTS

- Begin fluid resuscitation before abdominal radiography.
- Do not assume the stomach is not rotated just because a stomach tube can be passed.
- Assess suspect areas of stomach for viability 10-15 minutes after derotation by palpation, evaluating blood flow and stomach wall color. If stomach wall is green or gray, this area will need to be resected.
- Ventricular arrhythmias have not been shown to worsen prognosis. Rather, they may identify arrhythmogenic disturbances (commonly in GDV: hypokalemia, anemia, or acidosis) that must be corrected for the arrhythmia to resolve.

PREVENTION

- See Nutrition/Diet
- Do not breed dogs if history of GDV
- Prophylactic gastropexy in breeds at high risk for GDV
    - Performed during ovariohysterectomy, during splenectomy, or as an elective procedure
    - Commonly performed with the aid of laparoscopy

SUGGESTED READING

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Garbage Toxicosis

BASIC INFORMATION

DEFINITION

Gastroenteritis or hemorrhagic gastroenteritis caused by ingestion of food or garbage contaminated with bacteria or preformed bacterial toxins. Tremors or seizures can occur secondary to presence of tremorgenic mycotoxins. Garbage toxicosis is a common occurrence in dogs but less commonly seen in cats, owing to their more discriminating dietary habits.

SYNONYMS

Bacterial food poisoning, carrion toxicosis, garbage gut, songbird fever

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Potentially all animals; dogs are more likely to ingest spoiled foods.
- Cats that hunt and consume birds may develop this disorder.

RISK FACTORS

- Roaming animals
- Dogs fed food considered unfit for human consumption
- Raw food diets

CONTAGION & ZOONOSIS

- Disease is transmissible between animals because of habits of licking and sniffing.
- Dogs also might eat vomitus or feces containing bacteria or bacterial toxins.
- Zoonotic transmission possible, especially in young children or people with compromised immune systems.

GEOGRAPHY AND SEASONALITY: Disease common during warmer months, or year round in tropical and subtropical regions.

ASSOCIATED CONDITIONS & DISORDERS

- Botulism
- Tremorgenic mycotoxicosis

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- History of exposure to carrion or garbage or raw food diets
- Clinical signs within 15 minutes to 6 hours post ingestion; diarrhea can be delayed for 48 hours
- Severe vomiting, diarrhea, lethargy, anorexia

PHYSICAL EXAM FINDINGS

- Signs of abdominal pain
- Abdominal distension from gas
- Foul smelling feces; watery or bloody diarrhea
- Fever
- Ataxia
- Weak pulse, muddy mucous membranes, increased capillary refill time, hypovolemic shock
- Hypothermia as the shock state progresses

ETIOLOGY AND PATHOPHYSIOLOGY

Source:

- *Streptococcus* spp., *Salmonella* spp., *Bacillus* spp., *Escherichia coli,* and *Clostridium perfringens* are the most common bacteria involved.
- Endotoxemia and enterotoxemia are possible.

Mechanism of Toxicosis

- Via different mechanisms; endotoxins produce hypovolemic shock, collapse, and death.
- Tremors, seizures, hyperthermia may occur from tremorgenic mycotoxins.
- Gastrointestinal (GI) epithelial cells irritated/eroded:
    - Permeability disturbed, initiating vomiting, GI hemorrhage, fluid and electrolyte loss
    - Normal absorptive capabilities of the GI tract may be disrupted.
    - Stasis and GI dilation with gas accumulation follows.
    - GI stasis encourages growth of gram-negative bacteria which liberate endotoxin.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is based on a history of ingesting garbage, spoiled food, carrion, songbirds (cats), and the like and typical clinical signs of gastroenteritis or tremors/seizures (with tremorgenic mycotoxins). The disorder is different from benign self-resolving gastroenteritis in the following ways: known ingestion of contaminated substances and/or presence of systemic signs (endotoxemia, neurologic dysfunction, other). In the absence of historical evidence of ingestion, other causes of gastroenteritis must be ruled out with appropriate testing.

DIFFERENTIAL DIAGNOSIS

Toxicologic:

- Plants: castor beans, sago palm, ornamental bulbs, autumn crocus, etc.
- Metals: arsenic, antimony, iron, etc.
- Others: disulfoton (an organophosphate pesticide), gastrointestinal-irritant mushrooms

Nontoxicologic, Spontaneous:

- Viral gastroenteritis
- Hemorrhagic gastroenteritis
- Acute pancreatitis
- Acute hepatopathies
- “Salmon poisoning”

INITIAL DATABASE

- CBC and serum biochemistry profile: nonspecific changes
- Abdominal radiographs: to identify abnormal ingesta or rule in/rule out other disorders
- Monitor blood glucose (hypoglycemia associated with endotoxemia)

ADVANCED OR CONFIRMATORY TESTING

- Bacterial fecal culture is of mixed value (healthy animals often have cultures that are positive for “pathogenic” bacteria).
- Blood culture if sepsis is suspected
- Serologic identification of staphylococcal or clostridial toxins
- Penitrem A or roquefortine (tremorgenic mycotoxins) can be analyzed in the contaminated food or stomach contents (through a diagnostic laboratory).

TREATMENT

TREATMENT OVERVIEW

Treatment is aimed at limiting absorption of bacterial toxins by inducing emesis and administering activated charcoal, controlling vomiting, correcting fluid and electrolyte disorders, and other supportive measures (preventing shock and preventing secondary infection). Initial approach is similar to any general intoxication, and specific treatments are indicated if systemic signs arise.

ACUTE GENERAL TREATMENT

- In animals with a known recent exposure but no clinical signs, induction of vomiting is indicated: hydrogen peroxide 3%: 1-2 mL/kg (maximum 45 mL total) PO once; *or* apomorphine, 0.04 mg/kg IV or instilled in conjunctival sac and rinsed out when vomiting begins (dogs); *or* xylazine, 0.44 mg/kg IM (cats).
- Activated charcoal, 1-3 g/kg PO (dose according to packaging label of product; e.g., 10 mL/kg of activated charcoal suspension PO made from 2 g/kg activated charcoal suspended in 10 mL/kg tap water)
- Appropriate fluid and electrolyte therapy
- Antibiotics
    - Injectable aminoglycosides generally contraindicated because of synergistic action with endotoxins in depressing the myocardium and risk of nephrotoxicosis in hypovolemia.
    - Oral aminoglycosides (streptomycin, 5-10 mg/kg PO q 12 h; *or* neomycin 10-20 mg/kg PO q 8-12 h) work well.
    - Metronidazole, 25 mg/kg PO q 12 h (for a maximum of 5 days at this dosage) can also be used.
    - If a cat has known songbird fever, routine antibiotics are not recommended, as this tends to alter normal GI flora, allowing colonization by *Salmonella*.
- Gastrointestinal protectants such as sucralfate ¼ to a whole 1-gram tablet PO q 8 h
- Treatment for shock as needed (see p. 585)
- Appropriate treatment if disseminated intravascular coagulation occurs (e.g., including heparin 75 IU SQ q 8 h (see p. 315)
- Control tremors and seizures with methocarbamol (55-220 mg/kg IV, repeat as needed; max dose 330 mg/kg/day) or diazepam (0.5-2 mg/kg IV, repeat as needed) in cases involving tremorgenic mycotoxins.
- Profuse, persistent vomiting after the toxin has been expelled may be controlled with maropitant, 1 mg/kg SQ q 24 h; dolasetron mesylate, 0.6 mg/kg IV q 24 h; or metoclopramide, 0.2-0.4 mg/kg IM or SQ q 8 h.

NUTRITION/DIET

- Bland diet
    - Canned prescription gastrointestinal therapeutic diets
    - Low-fat, low-spice homemade diet (e.g., boiled white rice with either boiled skinless/boneless chicken breast or 2% cottage cheese)

POSSIBLE COMPLICATIONS

- Chronic diarrhea with clostridial enteritis
- Pancreatitis, malabsorption syndromes with repeated episodes of garbage toxicosis

RECOMMENDED MONITORING

- Temperature
- Heart rate
- Blood pressure
- Glucose
- CBC

PROGNOSIS AND OUTCOME

- Prognosis good provided shock does not occur
- Poor or guarded if endotoxemic shock

PEARLS & CONSIDERATIONS

COMMENTS

- Clinical signs generally resolve in 3-5 days.
- The term *songbird fever* arises from the source of intoxication, namely the decayed carcasses of songbirds that cats hunt.
- Consumption of decomposing organic material, moldy refrigerated foods, cottage cheese, cream cheese, or moldy walnuts can cause tremors and seizures due to contamination with tremorgenic mycotoxins such as penitrem A and roquefortine.

PREVENTION

- Prevent roaming and scavenging.
- Feed fresh, high-quality food.

CLIENT EDUCATION

- Discuss nutrition.
- Discuss potentially zoonotic aspects of raw diets.

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EDITOR: SAFDAR A. KHAN

1ST EDITION AUTHOR: CHARLOTTE MEANS

Gallops and Other Extra Heart Sounds

BASIC INFORMATION

DEFINITION

Extra heart sounds are classified as sounds or vibrations other than the normally ausculted first and second heart sounds. They alter the sound of a heartbeat but not the rhythm of the heartbeat. Gallops and extra heart sounds are different from premature cardiac beats and arrhythmias.

SYNONYMS

Third heart sound, fourth heart sound, diastolic heart sound, protodiastolic heart sound, presystolic heart sound, summation diastolic heart sound

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs and cats of any age and either sex, in the presence of heart disease/failure (gallop sounds)

RISK FACTORS

- Gallop sounds: congestive heart failure, systolic and diastolic ventricular dysfunction
- Systolic clicks: early mitral valvular insufficiency or flail leaflet
- Split heart sounds: increased ventricular pressures (causing splitting sounds due to delayed aortic or pulmonic valve closure under specific circumstances)
- Pericardial friction rubs: pericarditis, inflammation of the external pericardial lining

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Clinical signs relating to heart failure of virtually any etiology (see p. 468) are associated with gallop sounds. Splitting sounds may be normal or an indication of delay in valvular closure due to increased pressures on one or both sides of the heart or due to high pressure delaying valvular opening. Systolic clicks are not associated with clinical signs. Pericardial rubs are associated with pericardial diseases and their associated clinical signs.

PHYSICAL EXAM FINDINGS: A triple heart sound sequence with accentuated low-frequency sounds mimicking a cantering horse best describes a gallop sound. This sound is of low frequency, heard best with the bell of the stethoscope and usually over the mitral and or tricuspid valve area. The sound is likely to be associated with other signs of heart failure such as dyspnea, tachypnea, heart murmurs, and an increase in the heart rate.

ETIOLOGY AND PATHOPHYSIOLOGY

- Normally, only the S1 and S2 sounds are heard when auscultating the heart of the dog or cat.
- When the usually inaudible third or fourth sounds are so loud that they can be heard (gallops), they are an indication of the presence of ventricular systolic and/or diastolic dysfunction and are usually an indication of heart failure. By definition they occur during diastole and are generated by the vibration of ventricular walls during active ventricular filling (S3) or final ventricular filling by atrial contraction (S4) in a poorly compliant ventricle.
- Other additional sounds within the normal cardiac cycle can include:
    - Splitting of the normal heart sounds: either split S1, due to the asynchronous closure of AV valves, or split S2, due to asynchronous closure of aortic and pulmonic (semilunar) valves; caused by alterations in pressures within the heart and great vessels causing early or delayed valve closure
    - Extracardiac rubbing sounds
    - Systolic clicks: etiology unidentified, possibly caused by the warping/snapping of a diseased, prolapsed mitral valve. They are usually heard best with the diaphragm of the stethoscope, in contrast to the gallop sound which is a lower frequency sound heard better with the bell. The systolic click may be single or multiple. It also may come and go between consecutive cardiac cycles.
    - Opening snaps: heard in diastole and indicative of a calcified or hardened valve leaflet making a snapping sound when the valve opens during that phase of the cardiac cycle. These are unusually heard in dogs and cats, and they may be demonstrated by phonocardiography.

- Friction rubs: due to rubbing of a diseased pericardium against portions of the thorax

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Triple heart sounds occurring at a slow rate are not likely to be gallop rhythms and must be differentiated from extra beats, heart block, systolic clicks, split heart sounds, and opening snaps. Systolic clicks are higher-frequency sounds heard with the diaphragm of the stethoscope and usually are heard at the point of maximal intensity on the thorax. The sound may be consistent or variable and may be single or multiple. It can easily mimic a gallop sound except in the frequency of the ausculted sound. Split heart sounds are usually heard cranially and left over the aortic and pulmonic valve regions. They tend to be higher-frequency sounds heard best with the diaphragm of the stethoscope.

INITIAL DATABASE

Cardiac evaluation in the form of auscultation, radiography of the thorax, laboratory analyses, and echocardiographic examination usually are sufficient to identify the specific abnormality present.

TREATMENT

TREATMENT OVERVIEW

Extra heart sounds in and of themselves are NOT treated. Attention is directed to identifying the underlying cause and determining whether treatment is required for the primary etiology.

PROGNOSIS AND OUTCOME

Variable, depending on cause

PEARLS & CONSIDERATIONS

COMMENTS

The bell of the stethoscope is useful for differentiating low-frequency sounds such as gallop sounds (bell disproportionately enhances the third heart sound) from other heart sounds of higher frequency such as split heart sounds and systolic clicks (heard more clearly with the diaphram of the stethoscope).

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AUTHOR: STEPHEN J. ETTINGER

EDITOR: ETIENNE CÔTÉ

Gallbladder Rupture

BASIC INFORMATION

DEFINITION

Loss of gallbladder wall integrity

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs:

- Associated with trauma: younger dogs (mean 2.8 years)
- Associated with intrinsic gallbladder disease: middle-aged dogs (mean 8.1 years)

GENETICS & BREED PREDISPOSITION

- Shetland sheepdogs and possibly cocker spaniels are overrepresented.

ASSOCIATED CONDITIONS & DISORDERS

Dogs:

- Cholelithiasis, cholecystitis, bile peritonitis, sepsis
- Associated with gallbladder mucocele
- Gallbladder infarction
- Hypothyroidism and hyperadrenocorticism may predispose a subset of dogs to gallbladder infarction/rupture.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Gallbladder infarction/necrotizing cholecystitis:
  - Without rupture
  - With hepatic and omental adhesions and possibly fistulae to other abdominal structures
  - With gallbladder perforation and diffuse peritonitis
- Gallbladder perforation associated with penetrating trauma and subsequent bile peritonitis

HISTORY, CHIEF COMPLAINT

- Nonspecific signs: vomiting, anorexia, weakness, polydipsia, polyuria, weight loss. Often chronic (duration from onset of signs to presentation: up to 1 month; mean = 12 days)
- Some owners may notice icterus, discolored urine (bilirubinuria).

PHYSICAL EXAM FINDINGS

- Icterus: very common (77% of bile peritonitis cases)
- Abdominal distension: common (65% of bile peritonitis cases), may be subtle
- Signs of abdominal pain
- Pyrexia
- Shock

ETIOLOGY AND PATHOPHYSIOLOGY

- Causes of gallbladder rupture:
  - Necrotizing cholecystitis

- Gallbladder infarction
- Penetrating trauma
- Inadequate choleresis due to excessively thick bile, defective gallbladder contractility, and/or altered outflow

- Gallbladder rupture may result in the development of septic or nonseptic peritonitis (see p. 865).
- Lack of bile secretion into the intestine results in:
  - Lack of digestion and absorption of fat and fat-soluble vitamins, most importantly vitamin K (coagulopathy)

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on nonspecific history and physical examination finding of icterus +/− abdominal signs. Confirmation requires abdominal ultrasound examination and peritoneal fluid analysis.

DIFFERENTIAL DIAGNOSIS

- Icterus:
  - Hyperbilirubinemia due to hemolysis: immune-mediated hemolytic anemia and other diseases causing severe intravascular hemolysis
  - Hepatic diseases: cholangiohepatitis, cirrhotic/fibrosing liver disease, neoplasia, copper and other toxins
  - Extrahepatic biliary obstruction: choleliths, pancreatitis, cholangitis, neoplasia, stricture
  - Biliary leakage from other parts of the biliary system:
    - Traumatic rupture of the common or hepatic ducts
- Abdominal distension (if icterus not apparent):
  - Septic peritonitis: gastrointestinal perforation, penetrating trauma
  - Uroabdomen
  - Hemoabdomen: ruptured mass/viscus, bleeding disorder
  - Abdominal organ dilation/enlargement: gastric dilation/volvulus, mesenteric volvulus, splenic torsion, overeating, hyperadrenocorticism
  - Intraabdominal abscess: severe pancreatitis, hepatic abscess, ruptured prostatic abscess, ruptured pyometra
  - Portal hypertension
  - Congestive heart failure (right-sided)

INITIAL DATABASE

- CBC:
  - Inflammatory leukogram
  - Degenerative left shift with toxic changes:
    - Septic bile peritonitis
- Serum biochemistry profile:
  - Elevated bilirubin concentration (virtually all cases)
  - Elevated liver enzymes concentration (virtually all cases)
  - Hypokalemia
- Survey abdominal radiographs:
  - Increased opacity/loss of detail in anterior abdomen
  - Cholelithiasis (in dogs, 14%-48% are radiopaque)
  - Generalized loss of abdominal detail/fluid:
    - Bile peritonitis

ADVANCED OR CONFIRMATORY TESTING

- Abdominal ultrasound examination:
  - Evaluate gallbladder wall thickness and integrity (cholecystitis); contents (choleliths, mucocele), presence of attached omentum, and surrounding fluid, suggesting either bile peritonitis or unrelated (e.g., other differential diagnoses)
- Peritoneal fluid analysis (obtained during abdominal ultrasound examination):
  - Bilirubin concentration: > twice that of serum bilirubin is diagnostic of bile peritonitis
  - Cytologic evaluation and bacterial culture and sensitivity testing (aerobic and anaerobic): septic peritonitis
- Coagulation profile (prothrombin time is first to be abnormal with vitamin K deficiency/malabsorption)

TREATMENT

TREATMENT OVERVIEW

Treatment consists of patient stabilization followed by surgical exploration of the abdomen, with removal of the ruptured gallbladder and treatment of associated bile peritonitis; adjunctive pain control is important.

ACUTE GENERAL TREATMENT

- Rehydration: intravenous administration of balanced electrolyte solution
  - Normalization of serum electrolyte concentrations
- Parenteral antibiotics effective against gram-negative bacteria and anaerobes
  - Empirical therapy:
    - Cefoxitin, 22 mg/kg IV q 2 h peri-operatively, then q 6 h; *or*
    - Metronidazole, 10-15 mg/kg IV q 12 h *with:*
    - Enrofloxacin, 2.5-5 mg/kg IV q 12 h (maximum 5 mg/kg q 24 h in cats)
  - Specific long-term therapy based on culture and sensitivity test results
- Possible administration of fresh frozen plasma: (see p. 1347)
  - Hypoproteinemia
  - Possible coagulopathy
- Vitamin K administration: 2.5 mg/kg SQ q 12 h × 3 days, then weekly
- Exploratory laparotomy once animal is stabilized:
  - Cholecystectomy
  - Ensure patency of biliary system
  - Aerobic and anaerobic microbiologic culture of peritoneal fluid
  - Treatment of bile peritonitis: consider open peritoneal drainage

CHRONIC TREATMENT

Maintenance of bile flow: ursodeoxycholic acid 10-15 mg/kg/day PO—only after biliary obstruction is definitively ruled out/corrected, because stimulates gallbladder contraction

NUTRITION/DIET

Nutritional support via placement of feeding tube if indicated (see pp. 1322 and p. 1267)

POSSIBLE COMPLICATIONS

- Ongoing/recurrent bile leakage
- Failure to resolve septic bile peritonitis:
  - Endotoxemia
  - Sepsis
- Biliary obstruction:
  - Recurrence of cholelithiasis
- Pancreatitis

RECOMMENDED MONITORING

- Clinical and laboratory parameters assessing perfusion, including capillary refill time, pulse rate and quality, blood pressure, urine output, arterial pH, and lactate concentrations
- Respiratory function
- Serum liver enzymes and bilirubin concentrations
- Coagulation profile

PROGNOSIS AND OUTCOME

- Guarded to fair in animals with aseptic bile peritonitis
- Poor to guarded in animals with septic bile peritonitis

PEARLS & CONSIDERATIONS

COMMENTS

In dogs and cats with bile peritonitis:

- Peripheral white blood cell count is significantly lower in survivors (mean = 20,608/µL) compared with nonsurvivors (mean = 35,715/µL).
- The immature neutrophil count is significantly lower in survivors (mean = 686/µL) than in nonsurvivors (mean = 4852/µL).

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Gallbladder Mucocele

BASIC INFORMATION

DEFINITION

An abnormal accumulation of bile-laden mucus within the gallbladder (GB) lumen; the mucosa of the GB wall is characterized histologically by glandular hyperplasia. Once a rare condition, GB mucocele has recently been reported as the most common cause of canine extrahepatic biliary obstruction (EHBO).

SYNONYMS

Kiwi GB, cystic mucinous hyperplasia of the GB

EPIDEMIOLOGY

SPECIES, AGE, SEX: Older small or medium-size dogs usually affected, with no sex predilection reported. GB mucocele formation in humans is the result of cystic duct obstruction and not cystic mucinous hyperplasia.

GENETICS & BREED PREDISPOSITION: Cocker spaniels and Shetland sheepdogs are predisposed. In recent reports, miniature schnauzers are overrepresented.

ASSOCIATED CONDITIONS & DISORDERS: A weak association exists between hyperadrenocorticism and GB mucocele.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- GB mucocele can be an incidental finding or it can be responsible for the presenting complaint (approximately 75% of patients diagnosed with GB mucocele show overt signs of illness).
- Inflammation and necrosis of the GB wall can lead to rupture and peritonitis (focal or diffuse).

HISTORY, CHIEF COMPLIANT: Vomiting, inappetence, and lethargy are the most common presenting complaints. Other complaints include weight loss, diarrhea, ptyalism, and polyuria/polydipsia.

PHYSICAL EXAM FINDINGS: Abdominal pain, ascites, tachypnea, tachycardia, fever, hepatomegaly, and icterus

ETIOLOGY AND PATHOPHYSIOLOGY

- Abnormal accumulation of intraluminal mucus and inspissated bile
- Potential mechanisms for mucocele formation include progressive biliary sludging and alterations in water absorption across the GB mucosa.
- Histologic evidence of GB wall inflammation is not present in the majority of cases.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

GB mucocele diagnosis requires abdominal ultrasound. The stellate intraluminal pattern and non–gravity-dependent GB contents are considered pathognomonic. Less organized mucoceles can be more challenging to confirm.

DIFFERENTIAL DIAGNOSIS

- Cholecystitis (acute, chronic or necrotizing)
- Cholelithiasis
- Biliary sludge

INITIAL DATABASE

- CBC: most common abnormalities reported are leukocytosis characterized by a mature neutrophilia and monocytosis. In dogs, leukocytosis is significantly higher (21,200 cells/µL) with GB rupture than when the GB is intact (12,500 cells/µL).
- Serum biochemistry profile: common abnormalities include elevated serum alanine transaminase (ALT), alkaline phosphatase (ALP), aspartate transaminase (AST), and gammaglutamyl transpeptidase (GGT) activities. Increasing serum GGT activity may be associated with increased risk for mortality. Total bilirubin concentration is elevated in 63%-77% of cases. Hypercholesterolemia, hyperglobulinemia, and hypoalbuminemia are less common findings.
- Urinalysis: generally unremarkable; bilirubinuria may be noted.
- Abdominal radiography: generally unremarkable. In cases with GB rupture, decreased serosal detail may be noted if ascites is present.
- Abdominal ultrasonography: characteristic stellate/striated intraluminal GB contents. Increased GB volume/subjective distension can be noted. Other potential findings include common bile duct (BD) distension and ascites. The pancreas should be evaluated for ultrasonographic evidence of pancreatitis.

TREATMENT

TREATMENT OVERVIEW

Surgical intervention is indicated, with cholecystectomy generally considered the treatment of choice.

ACUTE GENERAL TREATMENT

- Emergency surgery is indicated for cases of suspected GB rupture. If present, ascitic fluid should be evaluated to determine whether the effusion is septic.
- GB rupture is suspected if (1) GB wall continuity can not be confirmed, (2) hyperechoic cranial abdominal fat is noted, (3) free abdominal fluid is present, and/or (4) stellate echogenic material is present within the peritoneal cavity.
- Patients with GB rupture are often hemodynamically unstable and require aggressive perioperative supportive care.
- Initial presurgical therapy generally includes fluid therapy, intravenous antibiotics (gram-negative anaerobes are the most common isolate), antiemetics, and analgesics.
- Cholecystectomy, cholecystoenterostomy, and cholecystotomy have been described for the treatment of GB mucoceles. Given that GB wall dysfunction appears to be associated with the etiopathogenesis of mucocele formation, the author believes that cholecystectomy is the treatment of choice.
- During surgery, confirmation of patency of the common BD is imperative. Gastrointestinal and hepatic biopsies should be considered.
- Samples of the GB wall and/or intraluminal contents should be collected for aerobic and anaerobic culture.
- Laparoscopic cholecystectomy has been reported for the treatment of uncomplicated cases of GB mucocele.

CHRONIC TREATMENT

- The nonsurgical resolution of GB mucocele has been reported in two dogs; however, the current literature is lacking adequate numbers to validate medical treatment.
- Patients with biliary sludge without mucocele formation generally do not require therapy unless clinical findings suggest GB disease. In these rare cases, medical management with antibiotic therapy, choleretics, and hepatoprotectants may prove helpful.

NUTRITION/DIET

- Esophagostomy, gastrostomy, or nasogastric tube placement should be encouraged, as postoperative inappetence is common in the author's experience (see pp. 1267, p. 1269, p. 1270).

POSSIBLE COMPLICATIONS

- The most commonly reported postoperative complications include pancreatitis and bile peritonitis. Aspiration pneumonia has also been reported.
- Postoperative common BD obstruction has been reported, emphasizing the need to confirm patency of the common BD at the time of cholecystectomy.

PROGNOSIS AND OUTCOME

- Perioperative mortality ranges from 21.7%-32%.
- The long-term prognosis for patients surviving to release from hospital is excellent.

- Mortality rates do not differ significantly between ruptured or intact mucoceles.
- If GB rupture results in diffuse bile peritonitis, mortality rates are as high as 68%-100%.

PEARLS & CONSIDERATIONS

COMMENTS

- Mucocele rupture does not preclude a successful outcome.
- Diffuse bile peritonitis with mucocele rupture is unlikely, owing to containment of bile salts within a solid mucinous matrix that limits exposure of bile salts to the peritoneal surface.
- To prevent reobstruction with mucocele material within the common BD and hepatic ducts, confirmation of patency of the common BD is imperative following cholecystectomy.
- Intestinal biopsies should be considered in patients with a history of chronic gastrointestinal disease.

SUGGESTED READING

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Pike FS, Berg RJ, King NW, et al: Gallbladder mucocele in dogs: 30 cases (2000-2002). J Am Vet Med Assoc 224(10):1615–1622, 2004.

AUTHOR: FRED S. PIKE

EDITOR: KEITH RICHTER

Hypothyroidism

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

The clinical syndrome that occurs as a result of decreased circulating levels of serum thyroid hormones (thyroxine [T4] and triiodothyronine [T3])

SYNONYM

Congenital hypothyroidism: cretinism

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs:

- Middle-aged at onset (2-9 years of age)
- No sex predilection

Cats

- Spontaneous hypothyroidism is very rare.
- Iatrogenic disease: middle-aged or older

GENETICS & BREED PREDISPOSITION

Dogs:

- Can occur in any breed, including mixed breeds
- Reported to be more prevalent in boxers, dachshunds, Doberman pinschers, golden retrievers, Great Danes, Irish setters, miniature schnauzers, poodles, and a number of other breeds

ASSOCIATED CONDITIONS & DISORDERS

Can occur as part of an autoimmune polyglandular syndrome (rare) along with hypoadrenocorticism or diabetes mellitus

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Congenital hypothyroidism (cretinism); rare
- Primary hypothyroidism (most common): disruption or atrophy of the thyroid glands
- Secondary hypothyroidism (rare): inadequate pituitary secretion of thyroid-stimulating hormone (TSH)

HISTORY, CHIEF COMPLAINT

- Acquired disease:
  - Signs are often nonspecific and gradual in onset.
  - Metabolic: weight gain, lethargy, mental dullness, exercise intolerance/inactivity, and cold intolerance are common.
  - Dermatologic: alopecia (bilaterally symmetric truncal) or thin hair, hyperkeratosis, seborrhea, hyper-pigmentation, otitis, “rat tail,” and pyoderma are often present, with alopecia or thin hair most common.
  - Reproductive (uncommon): persistent anestrus, infertility, and decreased libido
  - Neuromuscular: weakness/exercise intolerance are sometimes seen; other signs (ataxia, seizures, facial drooping/paralysis, head tilt/circling [vestibular signs], and stridor/change in bark [laryngeal paralysis]) are uncommon.
- Cretinism: disproportionate dwarfism, short limbs, persistent “puppy coat” or alopecia/thin dull hair, broad head, thick protruding tongue, mental dullness/retardation, delayed dental eruption, constipation

PHYSICAL EXAM FINDINGS

- Exam findings are similar to signs described by the owners.
- Additional findings (uncommon) may include ocular changes (corneal lipid deposits most common), bradycardia or other arrhythmias, constipation, decreased spinal reflexes, and decreased conscious proprioception.

ETIOLOGY AND PATHOPHYSIOLOGY

- Primary hypothyroidism is the most common form and is usually due to lymphocytic thyroiditis or idiopathic thyroid gland atrophy. Less common causes include follicular cell hyperplasia and infiltrative neoplasia.
- Secondary hypothyroidism is rare. Decreased TSH secretion leads to atrophy of the follicular cells of the thyroid gland. Loss of normal TSH secretion can occur as a result of a congenital pituitary malformation, pituitary neoplasia, or suppression of pituitary thyrotropic cells (most commonly from excess glucocorticoids [exogenous or endogenous hyperadrenocorticism]). Reversibility is possible if glucocorticoid concentrations are returned to normal.
- Tertiary hypothyroidism (decreased secretion of thyrotropin-releasing hormone [TRH]) has not been reported in the dog.
- Iatrogenic hypothyroidism can occur as a result of antithyroid medications (e.g., methimazole), bilateral thyroidectomy, or 131 radioiodine therapy (see p. 562).
- Clinical signs reflect the widespread metabolic effects of thyroid hormones.
- Surgery or anesthesia, a wide range of concurrent illnesses, and various nonthyroidal medications (e.g., glucocorticoids, phenobarbital, sulfonamides, carprofen, clomipramine) also affect circulating thyroid hormone concentrations, but not to the extent of producing clinical hypothyroidism.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected in a middle-aged dog presenting one or more of the common clinical signs. Confirmation is not always straightforward, but the presence of typical clinical signs in conjunction with a decreased serum FT4 ED value and an increased serum TSH value can be considered diagnostic.

DIFFERENTIAL DIAGNOSIS

- Alopecia (see p. 58)
- Seborrhea (see p. 255)
- Obesity/weight gain (see p. 773)

INITIAL DATABASE

- CBC, serum biochemical profile, urinalysis: hypercholesterolemia is most common and must be differentiated from normal postprandial hypercholesterolemia. A mild normocytic, normochromic, nonregenerative anemia; fasting hyperlipidemia/hypertriglyceridemia; mild increases in liver enzymes; and a mild increase in creatine kinase may also be seen.
- Basal serum total thyroxine concentration (T4):
  - Includes both free (<1%) and protein-bound (>99%) T4
  - Low levels in hypothyroid dogs: sensitivity: 89%-100%; specificity: 75%-82%; accuracy: 85%
  - If T4 is in the middle or upper end of the reference range, hypothyroidism is generally ruled out.
    - An exception is the presence of antithyroid antibodies that interfere with the assay.
    - If clinical signs strongly suggest hypothyroidism and T4 is normal, free thyroxine concentration by equilibrium dialysis (FT4ED), anti-T4 antibody, and thyroglobulin autoantibody concentrations should be measured.
  - If T4 is low or is at the low end of the reference range, it may be due to hypothyroidism, concurrent illness, medications, or may be normal (euthyroid).
- Basal serum free thyroxine concentration by equilibrium dialysis (FT4ED):
  - Measures just the free (i.e., metabolically available) T4
  - An assay based on equilibrium dialysis should be used; it is more time intensive and expensive than radio-immunoassay but much more accurate.
  - Low levels in hypothyroid dogs: sensitivity: 80%-98%; specificity 93%-94%; accuracy: 95%
  - Most accurate single hormone test for the diagnosis of hypothyroidism
- Basal serum TSH concentration:
  - A validated canine TSH assay should be used.
  - The test should not be evaluated alone but is best used in conjunction with T4 and/or FT4ED results.
    - High TSH with low T4: sensitivity: 63%-67%; specificity: 98%-100%; accuracy: 82%-88%
    - High TSH with low FT4ED: sensitivity: 74%; specificity: 98%; accuracy: 86%
    - Increased TSH with decreased T4 or FT4ED is strongly supportive of hypothyroidism.

        - A normal TSH in conjunction with decreased T4 or FT4ED does not rule out hypothyroidism.
- Also see the Hypothyroidism algorithm, .

ADVANCED OR CONFIRMATORY TESTING

If basal thyroid hormone concentrations do not rule in/out hypothyroidism, a few options exist:

- TSH stimulation test.
    - Protocol:
        - Many protocols reported; consult the laboratory performing the thyroid assays for the desired protocol and reference ranges for resting and poststimulation T4 concentrations.
        - 0.1 units/kg (maximum 5 units) medical-grade bovine TSH IV; evaluate serum T4 concentrations in preadministration and 6-hour postadministration samples.
        - Dogs <20 kg: 50 mcg recombinant human TSH IV; dogs >20 kg: 50 or 100 mcg recombinant human TSH IV; evaluate serum T4 concentrations in preadministration and 6-hour postadministration samples.
    - Interpretation:
        - If both results are below the reference range, hypothyroidism is present.
        - If post-TSH T4 concentration is >3 mcg/dL, the dog is not hypothyroid.
        - Results in between these parameters are equivocal; consider retesting 1-2 months later.
        - Medical-grade, bovine TSH is no longer available in most places.
- TRH stimulation test
    - Originally designed to identify secondary hypothyroidism. When the availability of bovine TSH became very limited, this test was used as a replacement. However, it is less reliable and so is uncommonly used.
- Response to therapy
- Serum thyroglobulin antibodies: increased levels suggest lymphocytic thyroiditis. However, lymphocytic thyroiditis does not always lead to or correlate with the presence of hypothyroidism.
- Serum thyroid hormone antibodies: if present, can interfere with testing and lead to spuriously high or low T4 results, depending on the T4 assay used.
- Thyroid scintigraphy may be useful for differentiation between hypothyroidism and nonthyroidal illness but is limited by cost and availability.
- Histopathologic evaluation of skin biopsies: vacuolated or hypertrophied erector pili muscles, increased dermal mucin, and a thickened dermis are consistent with hypothyroidism. A variety of other nonspecific changes supportive of an endocrinopathy may also be present.

TREATMENT

TREATMENT OVERVIEW

The mainstay of treatment is oral thyroid hormone replacement. Therapy should be designed to raise serum TT4 values to the normal range and eliminate clinical signs. Therapy is lifelong.

ACUTE GENERAL TREATMENT

- Hypothyroidism is generally a chronic condition that does not require acute therapy.
- Myxedema coma (rare): levothyroxine for injection 5 mcg/kg IV q 12 h until oral administration possible.

CHRONIC TREATMENT

Oral thyroid supplementation:

- Levothyroxine sodium (synthetic T4):
    - Initial dose (tablets): 0.02 mg/kg PO q 12 h. Maximum dose: 0.8 mg/dog q 12 h.
    - A novel liquid formulation of L-thyroxine available in Europe is often effective with once-daily dosing (0.02 mg/kg PO q 24 h).
    - If concurrent heart failure, renal failure, liver disease, hypoadrenocorticism, or diabetes is present, the initial dose should be decreased by 25%-50%, then slowly increased over the following 2-4 months. Also, hypothyroidism is rarely life threatening, so the concurrent disease should be controlled first before treatment of the hypothyroidism is pursued.
    - A brand-name preparation for animal use should be used, as bioavailability of generic forms can vary.
    - Adjust dose based on clinical response and serum T4 concentrations (see Recommended Monitoring below).
    - Absorption kinetics vary between brands, so serum concentrations should be reassessed if the levothyroxine brand is changed.

- Liothyronine sodium (synthetic T3):
  - Very rarely indicated
  - Consider only if a dog with confirmed hypothyroidism has failed to respond clinically, has normalized serum T4 concentrations, and at least two brands of levothyroxine have been tried.
  - Initial dosage is 4-6 mcg/kg PO q 8 h.
- Combination products (levothyroxine and liothyronine) are not recommended.

POSSIBLE COMPLICATIONS

Iatrogenic hyperthyroidism

RECOMMENDED MONITORING

- A physical examination and serum thyroxine concentration (4-6 hours post-pill) should be evaluated at 4 weeks, then q 6-8 weeks for 6-8 months, then q 6-12 months.
  - Serum T4 concentrations (4-6 hours post-pill) should be in the upper half of the normal range.
- Monitoring clinical signs: expected evolution of response.
  - An increase in alertness and activity commonly is seen within 1-2 weeks.
  - Neurologic improvement may begin within the first month, but several months may be needed for full resolution.
  - Dermatologic improvement often takes 1-4 months
  - Resolution of reproductive manifestations may take several months.
- If major clinical improvement is not seen in 3 months despite normal serum T4 concentrations, a concurrent as yet unidentified disease should be considered.

PROGNOSIS AND OUTCOME

- Primary hypothyroidism: long-term prognosis is good to excellent for return to function.
- Secondary hypothyroidism: long-term prognosis is usually guarded, since pituitary neoplasia is the most common underlying cause.

PEARLS & CONSIDERATIONS

COMMENTS

- The presence of nonthyroidal illness can make it difficult to obtain a definitive diagnosis of hypothyroidism. “Sick euthyroid syndrome” describes the condition that occurs when nonthyroidal illness results in a decrease in the basal T4 (and less commonly, FT4ED) concentrations.
- Subnormal T4 concentrations are not an immediate indication for supplementation with levothyroxine, which may at times be deleterious. The history and physical exam must be critically evaluated both for features supportive of hypothyroidism and for signs of other illness that could be causing the sick euthyroid syndrome. In the latter case, resolution/treatment of nonthyroidal illness returns T4 concentrations to normal.
- Obesity is much more prevalent (21%-40% of the North American pet dog population is or may become obese) than hypothyroidism (0.2% of dog population, possibly higher). Therefore, obese body condition can only be attributed to hypothyroidism in a small fraction of cases.

TECHNICIAN TIP

- Avoid lipemia and hemolysis when obtaining samples for diagnosis and therapeutic monitoring; fasted sample recommended.
- An artifactual increase in T4 and FT4ED occurs if the blood or serum sample is not kept cold.

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EDITOR: SHERRI IHLE

Hypothermia

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Body temperature below 99.5°F (37.5°C) in the dog and 100°F (37.8°C) in the cat

EPIDEMIOLOGY

SPECIES, AGE, SEX

Any species, any age, and either sex can be affected.

RISK FACTORS

- Very old, very young animals
- Short-haired animals
- General anesthesia
- Cold environment
- Cardiac disease

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Mild hypothermia: 90°F-99.5°F (32.2°C-37.5°C)
- Moderate hypothermia: 82°F-90°F (27.8°C-32.2°C)
- Severe hypothermia: <82°F (27.8°C)

HISTORY, CHIEF COMPLAINT

- Weak or collapsed patient
- Exposure to cold environmental temperatures or general anesthesia

PHYSICAL EXAM FINDINGS

- Shivering
- Weakness
- Ataxia
- Cardiac arrhythmia
- Coma

ETIOLOGY AND PATHOPHYSIOLOGY

- Initial compensation for hypothermia: peripheral vasoconstriction, shivering, piloerection
- Respiratory rate and effort:
  - Increased with mild hypothermia
  - Decreased with moderate to severe hypothermia (central and reflex-mediated respiratory depression)
- Cardiovascular effects:
  - Mild hypothermia initially increases heart rate and cardiac output.
  - Moderate hypothermia may produce bradycardia and (rarely) Osborn waves (positive electrocardiographic [ECG] deflection after S wave).
  - Severe hypothermia can cause cardiac arrest from ventricular fibrillation.
- Central nervous system:
  - Muscle shivering, stupor, unconsciousness, and coma
- Gastrointestinal effects:
  - Ulceration
  - Mild to severe pancreatitis

- Renal effects:
  - Cold-induced diuresis can result in severe hypovolemia.
  - Severely decreased renal perfusion can lead to ischemic tubular necrosis.
- Clinicopathologic changes:
  - Lactic acidosis due to tissue ischemia
  - Leukopenia and thrombocytopenia (splenic sequestration)
  - Hyperglycemia
  - Glucosuria
  - Hyperkalemia
  - Disseminated intravascular coagulopathy

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is concluded by measuring body temperature. Historical features (e.g., exposure to cold weather, general anesthesia) can increase the index of suspicion and are important for early recognition and treatment.

DIFFERENTIAL DIAGNOSIS

- Exposure to cold environment
- Pathologic hypothermia:
  - Hypoglycemia (puppies and kittens, endocrine diseases)
  - Hypothyroidism
  - Anesthesia
  - Severe, advanced cardiac disease (malperfusion)
  - Head trauma, brain disease

INITIAL DATABASE

- Documentation of rectal temperature <99.5°F (37.5°C)
- Packed cell volume, total solids, serum electrolytes

ADVANCED OR CONFIRMATORY TESTING

ECG:

- Sinus bradycardia: common, usually not treated beyond rewarming
- Ventricular arrhythmias are common (see p. 1165).
- Mild changes (PR, QT, QRS prolongation). Osborn waves possible but less commonly observed.

TREATMENT

TREATMENT OVERVIEW

- Restoring of core body temperature to normal range
- Treatment of hypothermia varies with:
  - Degree of hypothermia
  - Underlying systemic diseases (cardiovascular, neurologic)

ACUTE GENERAL TREATMENT

- Place intravenous catheter.
- In the unconscious patient, endotracheal intubation and oxygen supplementation (reduce risk of aspiration pneumonia and arrhythmias)
- Monitor urine output.
- Continuous ECG: to monitor for ventricular arrhythmias
  - If unconscious patient and ventricular arrhythmias, prepare for ventricular fibrillation (requires defibrillation). The cold heart is relatively resistant to defibrillation. Rewarm patient and retry defibrillation.
  - The hypothermic heart does not respond well to antiarrhythmic drugs until a temperature of >86°F (30°C) is reached.

Lidocaine is generally ineffective, and procainamide is associated with increased ventricular fibrillation in humans.
    - Bradyarrhythmia does not respond reliably to atropine but resolves with rewarming.
- After addressing acute life-threatening problems, the patient needs to be assessed for the predisposing cause of hypothermia.
- Many hypothermic patients are dehydrated. Administer warm (body temperature) intravenous fluids. Fluid rate needs to be monitored closely owing to decreased heart function and severe peripheral vasoconstriction. Start as a bolus of 5-11 mL/kg and titrate up as needed. DO NOT administer fluids to cats with hypothermia due to severe heart failure.
- Rewarming:
    - Depending on severity of hypothermia, three methods are useful:
        - Passive external rewarming. Use in mild to moderate hypothermia. Animal is wrapped in blankets to prevent further loss of heat.
        - Active external rewarming. Use for moderate to severe hypothermia. Apply heat (warm water bags, heating pads, warm incubator, bair hugger) to patient's torso.
        - Active internal rewarming. Generally used in severe hypothermia with temperature <86°F (30°C) or for animals that did not respond to other treatments.
            - Gastric, colon, and urinary bladder lavage with 109°F (42.8°C) warm 0.9% NaCl
            - Peritoneal dialysis with warm 0.9% NaCl at a rate of 10-20 mL/ kg and an exchange rate of every 30 minutes
            - Increase inspired air temperature for animals on a ventilator.

POSSIBLE COMPLICATIONS

During the rewarming process, the extremities reduce vasoconstriction, and sequestered cold blood mixes with the central circulation. Relatively warm core blood now perfuses the cold peripheral tissues. These two mechanisms cause “afterdrop,” a decrease in body temperature during the rewarming process.

RECOMMENDED MONITORING

- ECG for ventricular arrhythmias during rewarming
- Serum potassium levels during rewarming
- Neurologic status during rewarming. Increased intracranial pressure may develop secondary to ischemic injury, cold-induced edema, or from osmotic gradients.
- Monitor fluid administration with urine output, blood pressure, central venous pressure, and respiratory effort.
- Monitor serum creatinine and blood urea nitrogen to ensure normal kidney function.

PROGNOSIS AND OUTCOME

Depending on severity of hypothermia, good to guarded prognosis

PEARLS & CONSIDERATIONS

COMMENTS

- Rewarming procedures should be tapered when the body temperature is still slightly below normal, to avoid overshooting (causing hyperthermia).
- Unconscious or debilitated patients are unable to move away from a heat source, so meticulous monitoring (e.g., body temperature q 15-60 min) is essential during initial rewarming of these individuals. Burns and hyperthermic deaths have been recorded as a result of inadequate monitoring.

PREVENTION

- Avoid exposure to low environmental temperature.
- Avoid prolonged general anesthesia.

TECHNICIAN TIPS

- Avoid prolonged anesthesia.
- Monitor rectal temperature closely in pets at risk.

CLIENT EDUCATION

Keep pets indoors or in a protected environment during cold weather.

SUGGESTED READING

Ahn AH: Approach to the hypothermic patient. In Bonagura JD, editor: Kirk' s current veterinary therapy XII. Philadelphia, 1995, WB Saunders, pp 157–161.

AUTHOR: CARSTEN BANDT

EDITOR: ELIZABETH ROZANSKI

Hypotension, Systemic

BASIC INFORMATION

DEFINITION

A mean systemic arterial pressure <60 mm Hg and a systolic pressure <80-90 mm Hg

EPIDEMIOLOGY

SPECIES, AGE, SEX

Affects all species, ages, and sexes. The underlying disease may have a breed, sex, or age predilection.

RISK FACTORS

Hypotension is a clinical manifestation associated with numerous underlying disease processes (see Etiology and Pathophysiology below).

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

Signs of hypotension are typically vague and may include lethargy, depressed mentation, collapse, weakness, vomiting, and/or inappetence. Specific clinical signs related to the causative disorder may be present, such as cough and respiratory distress in a dog with hypotension due to primary cardiogenic causes, and overlap often occurs between signs of hypotension and signs due to its underlying cause.

PHYSICAL EXAM FINDINGS

- General: as above
- Circulatory: weak or thready pulses, pale mucous membranes, delayed capillary refill time
- Dogs will likely be tachycardic, whereas cats may display tachycardia or bradycardia.
- Findings related to an underlying disease, such as heart murmur, external/internal hemorrhage, or evidence of infection (fever or injected mucous membranes)

ETIOLOGY AND PATHOPHYSIOLOGY

There are numerous primary diseases that cause secondary hypotension:

- Cardiogenic:
  - Cardiomyopathies (dilated, hypertrophic, unclassified)
  - Pericardial effusion
  - Arrhythmias
  - Drug suppression of cardiac contractility (e.g., anesthetics, P-blockers)
- Hypovolemia:
  - Hemorrhage
  - Gastrointestinal fluid losses
  - Burns
  - Urinary loss
  - Hypoadrenocorticism
- Decreased vascular tone:
  - Sepsis
  - Anaphylaxis
  - Drugs (e.g., phenothiazines, angiotensin-converting enzyme (ACE) inhibitors, calcium channel blockers, nitroprusside)
- The body responds to a decrease in blood pressure in much the same way irrespective of cause.
- Decreased blood pressure causes the carotid sinus and aortic body receptors to respond, resulting in stimulation of the sympathetic nervous system, release of antidiuretic hormone (vasopressin) and adrenocorticotropic hormone from the pituitary, and release of catecholamines from the adrenal medulla.

- The renin-angiotensin-aldosterone system is stimulated: decreased arterial blood pressure elicits renin release from the juxtaglomerular cells of the kidney. In turn, renin transforms circulating angiotensinogen (α-2 macroglobulin from liver) to angiotensin I, which is activated to the powerful vasoconstrictor angiotensin II by the ACE in multiple tissues including the lung.
- These mechanisms lead to retention of sodium and water, vasoconstriction, and increased cardiac output, which all help to maintain blood pressure.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis of systemic hypotension involves recognition of the clinical signs and physical exam findings consistent with hypotension and subsequent measurement of arterial blood pressure. Many clinicians have argued to make blood pressure measurement part of routine physical exams, which could be appropriate in severely ill patients but is not currently justified for outpatient or routine visits. A repeatable finding of systemic hypotension in a patient showing overt signs of illness justifies a full diagnostic workup to identify an underlying cause and initiate treatment to correct both the hypotension and the underlying disease.

DIFFERENTIAL DIAGNOSIS

See Etiology and Pathophysiology above. Also, need to rule out inaccurate measurement (recommend recheck measurement if reading does not fit the clinical picture).

INITIAL DATABASE

Indirect or direct arterial blood pressure: diagnostic test of choice for confirming and monitoring hypotension (see p. 1209). As part of evaluating patient for underlying disorders:

- CBC (e.g., high or low white cell count if patient has underlying sepsis)
- Serum biochemistry profile: azotemia is common and may be renal or prerenal. Other abnormalities (e.g., liver enzyme elevations) may similarly be related to the causes or may be the effects of hypotension.
- Urinalysis: evidence of primary renal disease (low specific gravity with azotemia or dehydration) or infection
- Thoracic and abdominal radiographs (evidence of pulmonary infiltrates [edema, hemorrhage, metastases], pneumonia, trauma, or effusions)
- Ultrasonography: to assess for effusions, cardiac function and chamber size, and assist in diagnostic paracentesis if indicated
- Paracentesis (abdominal, pleural, pericardial): to assess the nature of a patient's effusion (e.g., hemorrhage) if indicated

ADVANCED OR CONFIRMATORY TESTING

- Cytologic and microbiologic testing of effusions as needed
- Additional tests as mandated by results to date

TREATMENT

TREATMENT OVERVIEW

The primary goal is to treat the underlying disease. If this goal cannot be achieved promptly or if results of treatment may not be immediate, restoration of blood pressure using other intravenous fluids or vasoactive medications may be necessary. Prior to initiating these treatments, cardiogenic causes of hypotension must be ruled out, as the goal with cardiogenic shock may involve opposite targets relative to intravascular volume (e.g., diuretic and possibly positive inotrope administration if congestive heart failure is present). Treatment of hypotension is not justified when it is found incidentally in an otherwise well patient (rule out artifact or occult disorder needing to be identified first).

ACUTE GENERAL TREATMENT

Volume replacement selected according to type of fluid lost:

- Crystalloids (lactated Ringer's solution, 0.9% NaCl): 40-90 mL/kg IV to effect
- Synthetic colloids: 5-20 mL/kg IV to effect
- Hypertonic saline: 4-6 mL/kg IV to effect (avoid if patient is dehydrated or hypernatremic)
- Blood, plasma transfusions (see p. 1347)
- Positive inotropic support (only after adequate volume resuscitation, if low cardiac contractility is documented or highly

suspected, and typically for short-term use only while underlying disease is addressed):
    - Dobutamine IV:
        - Dogs: 5-20 mcg/kg/min
        - Cats: 2.5-15 mcg/kg/min
- Vasopressors IV (only after adequate volume resuscitation and if hypotension is suspected to be due to systemic vasodilation; see):
    - Dopamine: 7-20 mcg/kg/min; *or*
    - Norepinephrine: 0.05-1 mcg/kg/min; *or*
    - Epinephrine: 0.1-1 mcg/kg/min; *or*
    - Vasopressin: 0.1-1 mU/kg/min
- Pericardiocentesis if pericardial effusion with tamponade is present.

CHRONIC TREATMENT

Treatment of the underlying cause (e.g., locate and stop source of hemorrhage, IV antibiotics for sepsis).

DRUG INTERACTIONS

- Use of high-dose or multiple vasopressors may lead to intense vasoconstriction that could result in organ ischemia.
- Catecholamines may precipitate cardiac arrhythmias.
- Cardiogenic causes of hypotension must be ruled out prior to IV fluid or vasopressor therapy, as these treatments may further decrease oxygen delivery and dramatically worsen patient condition.

POSSIBLE COMPLICATIONS

Complications related to severe or protracted hypotension include renal failure, loss of gastrointestinal integrity with absorption of bacteria and bacterial toxins, myocardial dysfunction, brain ischemia, and loss of vascular tone.

RECOMMENDED MONITORING

- Monitor blood pressure either indirectly (cuff) or directly (arterial line) until blood pressure has normalized. Direct monitoring is technically challenging and has possible minor complications, but it has the benefit of more accurate, continuous measurements and arterial blood sampling for acid-base and ventilation/perfusion analysis.
- Central venous pressure (CVP) can be utilized as an indicator of volume status (see p. 1227). If the CVP is low (<5 cm H2O), more fluids should be given. Adequate fluid resuscitation is present if the CVP is between 5 and 10 cm H2O. However, if left-sided heart disease is present, volume-overload pulmonary edema can occur despite normal CVP.
- Monitor for signs of end-organ damage (e.g., urine output, mentation).
- If hemorrhage is suspected, monitor hematocrit and total solids.
- Monitor ECG if arrhythmias are present.

PROGNOSIS AND OUTCOME

- Prognosis depends largely on the underlying cause, as well as initial response to supportive treatment.
- In most patients, hypotension will respond to intravenous fluid therapy.
- The need for high-dose or multiple vasoactive or inotropic medications may imply a worse overall prognosis.
- Nonresponsive hypotension implies a poor prognosis, with multiple organ dysfunction a likely outcome.

PEARLS & CONSIDERATIONS

COMMENTS

- Hypotension is a serious consequence of numerous disease processes.
- Prompt identification and treatment of the underlying cause is essential to a successful outcome.
- Persistent hypotension implies ongoing hemorrhage, systemic vasodilation, decreased cardiac function, or capillary leakage.

TECHNICIAN TIPS

- When any of the above historical or physical findings are present, obtaining a blood pressure measurement can identify systemic hypotension and greatly assist in determining the primary underlying cause.
- When using an indirect, cuffed technique, the width of the cuff should be approximately 40% of the circumference of the area

of the limb the cuff will be applied (see p. 1209).
- The Doppler technique only reliably measures the systolic arterial pressure.
- Most oscillometric machines measure systolic, mean, and diastolic pressures but are inaccurate on small patients or with significant vasoconstriction or arrhythmia.

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Hypospadias

BASIC INFORMATION

DEFINITION

A rare condition in which the penile urethra terminates proximal to the tip of the penis

SYNONYM

Pseudohermaphrodite

EPIDEMIOLOGY

SPECIES, AGE, SEX

Hypospadias has been reported in both dogs and cats. Affected animals can be genetically male (XY), female (XX), or some form of intersex (XX, XY, XX sry positive).

GENETICS & BREED PREDISPOSITION

Most commonly reported in Boston terriers; the genetic basis of the condition is unknown.

RISK FACTORS

Administration of progestins or androgens to pregnant dams prior to sexual differentiation of the external genitalia will result in partial masculinization (increased anogenital distance, elongation of the vulva, and clitoral hypertrophy).

ASSOCIATED CONDITIONS & DISORDERS

Urine dribbling and scalding, ascending urinary tract infection (cystitis)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Subtypes are based upon location of urethral opening: penile, scrotal, and perineal.

HISTORY, CHIEF COMPLAINT

Affected animals may show no clinical signs if the urethral orifice is located in the distal penis. Animals with the urethral orifice terminating at the scrotum or perineum may have urinary incontinence and inguinal dermatitis due to urine dribbling and scalding.

PHYSICAL EXAM FINDINGS

The severity of the lesion varies from a slight deviation of the urethral orifice in the distal glans penis to a ventral cleft along the entire length of the penis, prepuce, and scrotum, with the urethral orifice located in the perineum.

ETIOLOGY AND PATHOPHYSIOLOGY

Most likely due to a defect in masculinization and incomplete fusion of the ventral raphe of the penis. May be due to a defect in androgen receptors with the urogenital tubercle.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is made by physical examination.

DIFFERENTIAL DIAGNOSIS

This is a unique disorder.

INITIAL DATABASE

Physical examination

ADVANCED OR CONFIRMATORY TESTING

Urinalysis to identify cystitis if present (ascending infection)

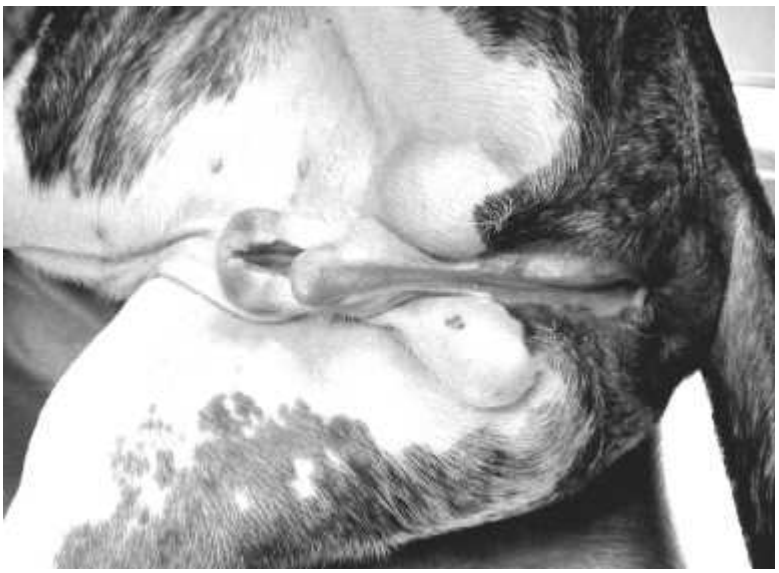
TREATMENT

TREATMENT OVERVIEW

Treatment is necessary in severe cases to prevent urine dribbling due to proximal termination of the penile urethra.

ACUTE GENERAL TREATMENT

Depends on the location of the urethral termination. Surgical apposition of the ventral penile urethral mucosa and tunica around a urethral catheter may be sufficient in some cases. For those cases in which the urethra terminates at the scrotum or the perineum, a scrotal or perineal urethrostomy may be possible, with amputation of the distal penis.



HYPOSPADIAS Inguinal region of a male dog, cranial is to the left. A severe hypospadias lesion is seen with the urethral orifice opening as a ventral cleft along the entire length of the penis, prepuce, and scrotum.

PROGNOSIS AND OUTCOME

Good if a mild abnormality, fair for surgical repair

PEARLS & CONSIDERATIONS

COMMENTS

Examination of the penis (exteriorized from the prepuce) to identify defects such as hypospadias is essential in any case of urinary incontinence in puppies.

PREVENTION

Hypospadias is considered to be a form of male pseudohermaphroditism and may be heritable. However, hypospadias can be caused by administration of progestins or androgens and certain teratogens during pregnancy (resulting in female pseudohermaphroditism) as well as by feeding the dam a diet low in vitamin A. Castration is recommended unless known steroid administration to the dam during pregnancy can be confirmed.

SUGGESTED READING

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AUTHOR: JAMES FLANDERS

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Hypopyon

BASIC INFORMATION

DEFINITION

The gross accumulation of leukocytes in the anterior chamber

SYNONYM

Pus in the anterior chamber

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs and cats, either sex, all ages

RISK FACTORS

Anterior uveitis, endophthalmitis, panophthalmitis, and corneal ulceration

CONTAGION & ZOONOSIS

Some forms of uveitis may be due to infectious agents and also zoonotic (see p. 1151)

GEOGRAPHY AND SEASONALITY

In general none, although some forms of infectious uveitis may have geographic predispositions

ASSOCIATED CONDITIONS & DISORDERS

Anterior uveitis is usually present and may produce systemic signs. Ocular lymphoma, infected corneal ulcers, and post-surgical invasion of the anterior chamber may result in hypopyon.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Early forms of incipient hypopyon may be recognized by cells floating in the anterior chamber. Keratic precipitates are forms of leukocyte aggregation on the posterior cornea.

HISTORY, CHIEF COMPLAINT

White to yellow opacity noted in the ventral anterior chamber, conjunctival hyperemia and uveitis signs

PHYSICAL EXAM FINDINGS

- Varying degrees of a creamy white “keel boat” opacity in the anterior chamber. Most hypopyons do not occupy more than the ventral 20% of the anterior chamber. Easily overlooked when mild, as the third eyelid may hinder visualization.
- The eye usually has other signs of anterior uveitis such as conjunctival/episcleral vascular injection, aqueous flare (visible turbidity instead of transparency; suggests increased protein, cellularity, or both) in the anterior chamber, and a tonic (relatively or absolutely immobile) pupil that does not dilate readily.
- Corneal ulceration may be present.

ETIOLOGY AND PATHOPHYSIOLOGY

- Hypopyon is produced by a strong leukotactic stimulus such as bacterial or fungal infection, but cultures from the anterior chamber often do not yield organisms. Negative cultures of the aqueous humor may indicate an absence of an infectious

agent, aqueous turnover diluting the organism, fastidious organisms that require special culturing techniques, or a toxin is responsible for stimulating leukotaxis.
- Corneal infections may produce inflammatory mediators that diffuse into the anterior chamber and result in hypopyon, even though the agent is not in the anterior chamber.
- Leukemias and ocular lymphoma may be associated with increased leukocytes in the anterior chamber to the point of producing hypopyon.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is made on observing a white to yellow opacity that settles ventrally within the anterior chamber. A bright focal light source and careful visualization of the ventral anterior chamber with the patient's head ventroflexed should help keep the third eyelid down and improve visualization of mild hypopyon.

DIFFERENTIAL DIAGNOSIS

- Lipids in the anterior chamber are creamy white but invariably diffuse.
- Fibrin clots in the anterior chamber. Both hypopyon and fibrin clots may occur concurrently. Fibrin clots are irregular in shape and frequently localized over the pupil. Hypopyon settles ventrally with a flat top.

INITIAL DATABASE

- History: recent intraocular surgery, systemic signs
- Thorough ocular and physical examinations (see p. 1313) to search for a source of sepsis or for a malignancy, either locally (in or on the eye) or systemically.
- If local ocular causes for the leukotaxis cannot be found, perform CBC, chemistry profile, urinalysis for evidence of systemic disease.
- If hypopyon or intraocular inflammation is so severe as to preclude posterior segment examination, ocular ultrasound is indicated for prognostic and diagnostic purposes to detect evidence of endophthalmitis, foreign bodies, neoplasia.
- Aqueous centesis with a 30-gauge needle for culture and cytology. Can be performed under topical anesthesia by an experienced examiner. In eyes with mild hypopyon or those associated with corneal disease, centesis is often not performed, as the signs often are improving by the time the culture results are known, or the cornea is a better source for culturing.

ADVANCED OR CONFIRMATORY TESTING

If the cause for hypopyon is anterior uveitis, and this is thought to originate from systemic disease, appropriate infectious disease titers, chest radiographs, and other tests may be indicated.

TREATMENT

TREATMENT OVERVIEW

The hypopyon itself is not treated (i.e., aspirated or surgically removed). The underlying disease (e.g., septic uveitis, keratitis, malignancy) is treated.

ACUTE GENERAL TREATMENT

- Frequent topical broad-spectrum antibiotic such as third- or fourth-generation fluoroquinolone q 4 h. Anterior chamber sepsis may not be present, but the risk is too great to delay initiation of antibiotics.
- Systemic broad-spectrum bactericidal antibiotics
- Topical 1% atropine sufficient to maintain pupil dilation
- Topical and/or systemic nonsteroidal antiinflammatory drugs for the uveitis.

CHRONIC TREATMENT

Therapy may be modified depending on results of culture and source of inflammation. Hypopyon usually resolves within several days when inflammation is controlled.

POSSIBLE COMPLICATIONS

Topical or systemic glucocorticoids may be contraindicated with bacterial or fungal infections but indicated with viral-or lymphoma-associated hypopyon.

RECOMMENDED MONITORING

If bacterial sepsis is suspected, initial monitoring should be either daily or more frequently if significant inflammation is present.

PROGNOSIS AND OUTCOME

The prognosis is variable, depending on the underlying disease. Hypopyon improves rapidly with successful therapy of the underlying stimulus.

PEARLS & CONSIDERATIONS

COMMENTS

- Bacterial culture results are negative in most cases of hypopyon, and the risk for rapid development of structural damage to the eye is too great to withhold antibiotics until culture results are known.
- Hypopyon itself is not treated and produces minimal sequela in most cases.

CLIENT EDUCATION

If hypopyon is due to sepsis, blindness is a potential sequela.

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Hypoplastic Trachea

BASIC INFORMATION

DEFINITION

Congenital abnormal narrowing of the tracheal lumen, well-recognized in brachycephalic breeds

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs <1 year old; 2:1 males/females. Not reported in cats.

GENETICS AND BREED PREDISPOSITION

Of reported dogs, 55% are bulldogs, and 15% are Boston terriers. Also reported as a recessive trait in Husky-mix puppies with blue eyes and partially white faces.

ASSOCIATED CONDITIONS AND DISORDERS

- Brachycephalic syndrome: elongated soft palate in 43% of affected dogs, stenotic nares in 22%
- Other congenital anomalies (pulmonic or aortic stenosis, megaesophagus) or respiratory abnormalities (bronchopneumonia, laryngeal paralysis, everted laryngeal saccules, laryngeal collapse) may be present.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Incidental finding in approximately 10% of affected dogs
- Recurrent respiratory infections with poor response to treatment
- Clinical signs associated with concurrent brachycephalic syndrome such as stertor, stridor, exercise intolerance, lethargy, coughing, gagging, syncope

PHYSICAL EXAM FINDINGS

- Physical examination can be unremarkable
- Abnormalities attributable to dyspnea or bronchopneumonia:
  - Cough
  - Stridor (inspiratory, may be high-pitched or gasping sounds) if laryngeal abnormalities
  - Stertor if elongated soft palate
  - Increased lung sounds
  - Fever
  - Lethargy
  - Increased respiratory rate and effort

ETIOLOGY AND PATHOPHYSIOLOGY

- Trachea develops with the ends/tips of cartilaginous rings apposed or overlapped and dorsal membrane narrow or absent, narrowing the tracheal lumen.
- With narrowed tracheal lumen, linear air velocity and tracheal resistance increase, increasing work of respiration.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis of congenital tracheal hypoplasia is based on comparison of tracheal diameter to thoracic inlet diameter. Normal tracheal

diameter is smaller in bulldogs than in other breeds.

DIFFERENTIAL DIAGNOSIS

- Elongated soft palate
- Everted laryngeal saccules
- Stenotic nares
- Laryngeal paralysis or collapse
- Tracheal collapse
- Any cause of bronchopneumonia or tracheobronchitis

INITIAL DATABASE

- CBC: inflammatory leukogram with left shift possible if bronchopneumonia present
- Serum biochemistry panel and urinalysis: usually normal
- Thoracic radiographs:
  - Diffusely narrowed tracheal lumen
  - Bronchopneumonia in approximately 8% of cases

ADVANCED OR CONFIRMATORY TESTING

- Decrease in tracheal diameter on lateral thoracic radiograph:
  - TD:TI ratio is the ratio of tracheal diameter (TD) at the level of the thoracic inlet to the thoracic inlet diameter (TI, distance from the ventral aspect of the vertebral column at the midpoint of the first rib to the closest point on the inner surface of the manubrium).
  - For dogs older than 6 months, normal TD:TI = 0.2 for nonbrachycephalic breeds and non-bulldog brachycephalic breeds, and 0.14 for bulldogs.
  - Ratios lower than these indicate tracheal hypoplasia (assuming a diffuse, not focal, narrowing).
- Tracheoscopy/bronchoscopy or trans-tracheal wash for cytology, culture and sensitivity in dogs with nonresponsive bronchopneumonia.
- Histopathologic evaluation: generally not beneficial
  - Overlap or apposition of tips/ends of tracheal rings
  - Dorsal membrane folded, narrowed, or absent

TREATMENT

TREATMENT OVERVIEW

Since animals with tracheal hypoplasia usually present with signs caused by other abnormalities (e.g., elongated soft palate, stenotic nares, pneumonia), treatment is directed toward correction of the abnormality that is the primary cause of clinical signs and treatment of secondary infections when present. Surgery for stenotic nares and elongated soft palate should be delayed in animals with pneumonia until the lungs have improved radiographically.

ACUTE GENERAL TREATMENT

- Oxygen Supplementation (see p. 1318)
- Sedation
  - Acepromazine, 0.03-0.05 mg/kg IV (e.g., 0.25-0.5 mg total dose for medium-size dog) with butorphanol (0.2-0.4 mg/kg IV q 2-4 has needed) if dyspneic or hyperpneic
- If bronchopneumonia is present, broad-spectrum antibiotic treatment based ideally on results of culture and sensitivity

CHRONIC TREATMENT

- Reduce weight if obese.
- Limit exercise, reduce stress.
- Correct associated respiratory defects (see pp. 151 and p. 635)

POSSIBLE COMPLICATIONS

Death from severe respiratory distress or bronchopneumonia

RECOMMENDED MONITORING

Repeat thoracic films in 1-2 weeks in dogs with bronchopneumonia. Radiographic improvement of bronchopneumonia can lag several days behind clinical improvement.

PROGNOSIS AND OUTCOME

In the absence of concurrent respiratory disease, hypoplastic trachea is well tolerated. Mortality rate (death or euthanasia) of 50% reflects associated respiratory disease or other defects (megaesophagus, cardiac disease).

PEARLS & CONSIDERATIONS

COMMENTS

- Dyspnea is not related to the degree of tracheal lumen diameter narrowing but to presence of other diseases.
- Presence of hypoplastic trachea does not affect outcome of animals undergoing surgery for elongated soft palate or stenotic nares.
- Some degree of diffuse increase in tracheal diameter may be seen after clinical improvement; this increase in diameter is attributed to reduced tracheal mucosal edema.
- Of dogs with hypoplastic trachea, 60% are clinically normal at recheck >6 months after diagnosis.

PREVENTION

There are no means of preventing this disease. Affected animals should not be bred.

TECHNICIAN TIP

Normal bulldogs have a smaller-diameter trachea than other breeds and therefore will need smaller endotracheal tubes when undergoing general anesthesia.

CLIENT EDUCATION

- Consider thoracic radiographs of bulldogs, Boston terriers before breeding.
- Affected dogs have lifelong risk of respiratory infections and dyspnea.

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Riecks TW, et al: Surgical correction of brachy-cephalic syndrome in dogs: 22 cases (1991-2004). J Am Vet Med Assoc 230:1324–1328, 2007.

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Hypoparathyroidism, Primary

BASIC INFORMATION

DEFINITION

An absolute or relative deficiency of parathyroid hormone (PTH) from parathyroid gland destruction or atrophy, causing hypocalcemia

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Uncommon disorder in dogs and cats
- Dogs: any age, breed, or sex may be affected
- Cats: young to middle-aged, any breed; male predominance

CLINICAL PRESENTATION

HISTORY/CHIEF COMPLAINT

- Sporadic or episodic signs, all related to hypocalcemia (see p. 576)
- Most common:
  - Muscle tremors or twitching that may be focal or diffuse and may worsen with exercise or excitement
  - Seizures
  - Stiff gait, muscle pain/cramping
  - Weakness, decreased activity (more common in cats)
- Less common:
  - Facial rubbing
  - Biting or licking paws
  - Behavior changes (restless, nervous, anxious, aggressive, reluctant to be touched)
  - Excessive panting
  - Vomiting, diarrhea, weight loss

PHYSICAL EXAM FINDINGS

- Neuromuscular signs (see above); raised nictitating membranes possible (cats)
- Additional findings may include hyperthermia (from muscle fasciculations), tense abdomen, thin body condition, or cataracts.
- Physical examination may be normal.

ETIOLOGY AND PATHOPHYSIOLOGY

- Naturally occurring disease is suspected to be due to immune-mediated destruction or idiopathic atrophy of the parathyroid glands.
- In normal animals, PTH secretion is controlled by ionized calcium concentrations via negative feedback, but with hypoparathyroidism the parathyroid glands are unable to respond to hypocalcemia.
- Loss of PTH results in sustained, potentially severe hypocalcemia and hyperphosphatemia.
  - Hypocalcemia results from decreased resorption of calcium from bone, decreased intestinal absorption of calcium, and increased renal excretion of calcium.
  - Hyperphosphatemia occurs due to decreased renal phosphate excretion.
- Loss of the normal membrane-stabilizing effect of ionized calcium on nerve cells causes increased excitability of central and peripheral nervous tissue.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Concomitant hypocalcemia and hyperphosphatemia in a patient with normal renal function strongly suggests primary hypoparathyroidism. The diagnosis is confirmed by evaluating concurrent serum ionized calcium and PTH concentrations.

DIFFERENTIAL DIAGNOSIS

Hypocalcemia (see p. 576)

INITIAL DATABASE

- CBC: unremarkable. Serum biochemical profile, urinalysis: hypocalcemia and hyperphosphatemia, normal renal parameters
- Confirm hypocalcemia:
  - Repeat calcium measurement on a separate blood sample.
  - Measure serum ionized calcium concentration.
  - Formulas to "correct" serum calcium to account for changes in total calcium due to serum albumin values do not account for much of the variability in serum calcium and are no longer recommended.

ADVANCED OR CONFIRMATORY TESTING

- Primary hypoparathyroidism is confirmed by evaluating concurrent serum ionized calcium and PTH concentrations; both will usually be decreased.
- A low-normal serum PTH concentration is inappropriate if ionized calcium concentration is low; thus in a patient with low ionized calcium, a serum PTH concentration that is either decreased or low normal is compatible with a diagnosis of primary hypoparathyroidism.

TREATMENT

TREATMENT OVERVIEW

- The goal of therapy is to increase serum calcium concentration above the threshold for clinical signs and maintain it just below or at the low end of the reference range (i.e., 8-9.5 mg/ dL [2-2.4 mmol/L]). Lifelong therapy is required.
- Therapy must be individualized, and frequent monitoring for appropriate adjustment of drug dosages is required. "Overtreatment" resulting in hypercalcemia must be avoided.
- The need for acute emergency therapy will vary depending on the severity of presenting signs.
- Referral is indicated if 24-hour care and in-house serum calcium monitoring cannot be provided during the immediate posttetanic period.

ACUTE GENERAL TREATMENT

For hypocalcemic tetany: see p. 576.

CHRONIC TREATMENT

- Subacute/early chronic treatment:
  - Oral vitamin D (see table, below):
    - Calcitriol is preparation of choice
    - Quicker- and shorter-acting forms (and therefore easier to use for dosage adjustments) are more expensive.
  - Oral calcium:
    - Dose: 25 mg/kg elemental calcium q 8-12 h
    - The amount of elemental calcium per tablet varies with the preparation/salt.
    - Once the serum calcium concentration is stable and the dog or cat is eating well, oral calcium supplementation can be tapered over 2-3 weeks and then discontinued, as dietary calcium is adequate for most.
  - Parenteral calcium administration is usually needed during the time it takes for oral vitamin D and oral calcium supplementation to take effect:
    - Calcium gluconate IV via continuous rate infusion (60-90 mg/kg q 24 h; do not add to bicarbonate-containing fluids) or SQ q 6-8 h (see p. 576); dilute one part calcium to 2-4 parts saline). Do NOT give calcium chloride SQ, as perivascular administration can cause tissue necrosis and sloughing.
    - Monitor serum calcium concentrations q 12-24 h and adjust dose to maintain serum calcium concentration between 8-9.5 mg/dL (2.0-2.4 mmol/L). When serum calcium concentrations have been consistently above 8 mg/dL (2 mmol/L) for 48 hours, parenteral calcium can be tapered and discontinued over 3–7 days by increasing the dosing interval.

Vitamin D Preparations

Preparation	Daily Dose	Time to Maximal Effect	Time Required for Toxicity Relief

Calcitriol (1,25-dihydroxy-cholecalciferol, vitamin D3)	■ Initial: 0.01-0.015 mcg/kg PO q 12 h × 3-4 days (dog); 0.01-0.04 mcg/kg PO q 24 h (cat) ■ Maintenance: 0.005-0.015 mcg/kg PO q 24 h	1-4 days	1-14 days
Dihydrotachysterol	■ Initial: 0.02-0.03 mg/kg PO q 24 h × 2 days or to effect ■ Maintenance: 0.01-0.02 mg/kg PO q 24-48 h	1-7 days	1-3 weeks

- Maintenance/long-term chronic treatment:
  - Vitamin D should be slowly tapered to the lowest dose possible to maintain stable serum calcium concentrations. Lifelong therapy is required.

POSSIBLE COMPLICATIONS

- Overzealous treatment with vitamin D may result in hypercalcemia. Hypercalcemia in conjunction with hyperphosphatemia puts animals at risk for soft tissue (including renal) mineralization.
- Although SQ calcium gluconate is generally deemed safe, there are multiple case reports describing severe, extensive calcinosis cutis and epidermal necrosis following SQ administration of calcium gluconate for primary hypoparathyroidism in both dogs and a cat.

RECOMMENDED MONITORING

- During the immediate posttetanic phase, patients should be observed 24 hours/day for seizures and other clinical signs of hypocalcemia.
- Serum calcium and phosphorus concentrations should initially be measured at least q 12-24 h, then with decreasing frequency as serum calcium concentration stabilizes. When patients are stable with maintenance oral vitamin D therapy, evaluation of serum calcium and phosphorus concentrations is recommended q 3-6 months.

PROGNOSIS AND OUTCOME

With careful treatment and monitoring, prognosis is good.

PEARLS & CONSIDERATIONS

COMMENTS

- Treatment with synthetic human PTH is being evaluated in human patients and may be a future treatment option for veterinary patients.
- Because of the risk of induction of hypercalcemia, use of ergocalciferol (Vitamin D2) is not recommended.

SYNONYMS:

- Vitamin D1: lamisterol (forms calciferol); vitamin D2: ergocalciferol/viosterol/activated ergosterol; vitamin D3: cholecalciferol/ergosterol/activated 7-dehydrocholesterol; vitamin D4: dihydrotachysterol/22:23-dihydrovitamin D2; vitamin D5: irridated 7-dehydrositosterol; calcitriol: 1,25-dihydroxycholecalciferol/1,2 5-dihydroxyvitamin D

TECHNICIAN TIP

Hyperthermia in hypocalcemic patients generally results from muscle fasciculations, not true fever. Therefore, cooling measures (moistening paw pads, fan/air circulation) may be appropriate, but antipyrexic drugs (e.g., nonsteroidal antiinflammatories) are not.

CLIENT EDUCATION

- Appropriate therapy requires repeated evaluation of serum calcium concentrations. Monitoring will become less intensive as serum calcium concentrations stabilize, but clients should be prepared for frequent rechecks.
- Treatment must be lifelong for dogs with naturally occurring hypoparathyroidism.

SUGGESTED READING

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Hyponatremia

BASIC INFORMATION

DEFINITION

Low serum sodium (<125 mEq/L) with plasma hypoosmolality; it may be associated with low, normal, or high plasma tonicity.

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs and cats: no breed or sex predilection

RISK FACTORS

- Renal insufficiency
- Excessive water intake
- Hypoadrenocorticism
- Severe liver disease or end-stage heart failure

ASSOCIATED CONDITIONS & DISORDERS

Osmotic demyelination syndrome (neurologic signs)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Clinical signs are related to the rapidity of onset rather than to severity of hyponatremia or hypoosmolality.
- Signs in humans are often seen with acute levels less than 120 mEq/L or a drop at a rate greater than 0.5 mEq/L/h
- Can lead to cerebral edema
- Clinical signs may be absent in chronic cases.

HISTORY, CHIEF COMPLAINT

- Mild lethargy
- Nausea and vomiting
- Abdominal distention
- Weight gain
- Seizures, incoordination, and coma

PHYSICAL EXAM FINDINGS

- Patient can exhibit signs of dehydration, including decreased skin turgor and tacky mucous membranes.
- Signs of third spacing such as ascites or edema
- Hypovolemia with weak pulses, tachycardia, prolonged capillary refill time

ETIOLOGY AND PATHOPHYSIOLOGY

- Hypotonic (dilutional) hyponatremia:
  - Excess of water relative to existing sodium stores
  - Most commonly due to impaired renal excretion of water
  - Other causes include congestive heart failure, severe liver disease, nephrotic syndrome.
  - Except for renal disease, characterized by high plasma concentrations of arginine vasopressin (antidiuretic hormone) despite hypotonicity
  - Ascites or edema is common.
  - Excessive water intake may also be a cause.
- Isotonic hyponatremia:

    - Associated with volume depletion (hypovolemia)
    - Causes include loss of fluid via gastrointestinal tract, loss into third spaces (peritoneal effusion, pleural effusion), and renal loss.
    - Hypotonicity with loss of hypotonic fluid results from:
        - A decrease in glomerular filtration rate increases isosmotic resorption of sodium and water in the proximal tubules and decreases delivery of tubular fluid to the distal diluting sites.
        - Volume depletion causes vasopressin release, which impairs water excretion.
        - Stimulation of thirst due to the volume depletion, which causes the animal to drink water.
- Hypertonic (translocational) hyponatremia:
    - Hyperglycemia
    - Retention of hypertonic mannitol in patients with renal insufficiency
- Pseudohyponatremia

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The clinical signs of hyponatremia are nonspecific, but a simple serum electrolyte measurement is confirmatory.

DIFFERENTIAL DIAGNOSIS

Pseudohyponatremia:

- Obtain plasma osmolality; hypernatremic patients with normal osmolality have pseudohyponatremia.
- Pseudohyponatremia is a laboratory artifact that may be seen with hyperlipidemia and severe hyperproteinemia.

INITIAL DATABASE

- CBC
- Serum biochemistry profile and urinalysis
- Abdominal and thoracic radiographs
- Abdominal ultrasound
- Calculated serum osmolality

ADVANCED OR CONFIRMATORY TESTING

- Thyroid panel
- Adrenocorticotropic hormone stimulation
- Abdominocentesis or thoracocentesis with fluid analysis

TREATMENT

TREATMENT OVERVIEW

Goals are to diagnose and manage underlying disease. If clinical signs are present, increase sodium concentration and osmolality gradually.

ACUTE GENERAL TREATMENT

- Aim to increase serum sodium concentrations by a maximum of 2-3 mEq/h.
- The use of conventional crystalloids such as lactated Ringer's solution or 0.9% saline is recommended.
- Restore volume if patient is hypovolemic.
- Treatment of underlying cause if systemic disorder

CHRONIC TREATMENT

- Aim to increase serum sodium concentration by 0.7 mEq/h.
- Management/resolution of systemic disorder if present
- Mild water restriction, with serum sodium concentration monitoring, can be effective.
- Edematous patients should be treated with a combination of sodium-restricted diet, saline, and diuretics.

- Do not correct at a rate of greater than 12-15 mEq/L/d.

POSSIBLE COMPLICATIONS

- Correcting a sodium deficit faster than the body can compensate by restoring organic osmolytes can lead to brain dehydration (rapid shifts in osmolality will cause disorders of the central nervous system secondary to dehydration of the brain).
- Brain injury causes osmotic demyelination syndrome, which leads to cerebral edema, seizures, and other neurologic signs.

RECOMMENDED MONITORING

Frequent monitoring of electrolytes including serum sodium and potassium concentrations

PROGNOSIS AND OUTCOME

Good, provided underlying problem can be reversed or eliminated and overly rapid correction is avoided

PEARLS & CONSIDERATIONS

COMMENTS

When treating acute hyponatremia, correction can be made as quickly as the hyponatremia developed (i.e., if the sodium dropped in 24 hours, it can be entirely corrected in 24 hours).

CLIENT EDUCATION

Related to underlying disease

SUGGESTED READING

DiBartola S: Disorders of sodium and water: hypernatremia and hyponatremia. In DiBartola S, ed: Fluid therapy in small animal practice, ed 3, St Louis, 2006 Saun-ders Elsevier.

AUTHORS: YONAIRA CORTÉS, ANN MARIE MANNING

EDITOR: ETIENNE CÔTÉ

Hypokalemia

BASIC INFORMATION

DEFINITION

Serum potassium concentration <3.5 mEq/L

EPIDEMIOLOGY

SPECIES, AGE, SEX

Cats are more likely to show clinical signs than dogs: signs may be seen when serum potassium is between 3 and 3.5 mEq/L. Dogs: signs may not be evident until serum potassium is <2.5 mEq/L.

GENETICS & BREED PREDISPOSITION

A familial inherited (assumed autosomal recessive) hypokalemic myopathy has been reported in 2- to 12-month-old Burmese kittens.

RISK FACTORS

Cats: dietary factors such as potassium-depleted, acidifying, magnesium-restricted, and/or high-protein diets. Canned feline diets have now been modified to reduce this risk.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Musculoskeletal:
  - Generalized muscle weakness
  - Polymyopathy: increased serum creatine kinase, electromyographic abnormalities (most notable in cats)
- Cardiovascular:
  - Variable clinical expression
- Renal:
  - Chronic tubulointerstitial nephritis, impaired renal function, azotemia (most notable in cats)
- Gastrointestinal (GI): paralytic ileus

HISTORY, CHIEF COMPLAINT

- Many dogs and cats have no obvious signs.
- Generalized skeletal muscle weakness: most common complaint
- Hypokalemic polymyopathy in cats: flaccid ventroflexion of neck (see online chapter: Neck Ventroflexion), forelimb hypermetria, broad-based stance in hind limbs
- Polyuria, polydipsia, decreased urine concentrating ability
- Vomiting; diarrhea, or constipation

PHYSICAL EXAM FINDINGS

- Musculoskeletal
  - Generalized skeletal muscle weakness
  - Cats with polymyopathy: flaccid ventroflexion of neck, forelimb hypermetria, broad-based stance in hind limbs
- Cardiovascular
  - Arrhythmias, especially premature ventricular complexes
  - Abnormalities often only detectable by electrocardiography
- GI (paralytic ileus)
  - Rare in dogs and cats
  - Abdominal distention
  - Constipation

ETIOLOGY AND PATHOPHYSIOLOGY

- Increased potassium loss in urine:
  - Chronic kidney disease (cats)
  - Diet-induced hypokalemic nephropathy (cats)
  - Renal tubular acidosis
  - Postobstructive diuresis (cats with urethral obstruction)
  - Diuretic administration
  - Dialysis
  - Hyperaldosteronism
  - Hyperadrenocorticism
- Increased potassium loss via GI tract:
  - Vomiting
  - Diarrhea
- Increased potassium sequestration into cells (translocation from extracellular to intracellular fluid) may occur with alkalemia, insulin release, catecholamine release:
  - Alkalemia: potassium ions enter cells in exchange for hydrogen ions.
  - Insulin: promotes uptake of glucose and potassium by hepatocytes and skeletal muscle cells.
  - Severe illness: stress leads to epinephrine release, which contributes to hypokalemia.
- Decreased potassium dietary intake:
  - Uncommon; may be a contributing factor
- Iatrogenic:
  - Fluid therapy, insulin therapy, bicarbonate therapy, loop and thiazide diuretics, enemas, parenteral nutrition
- Combinations of factors:
  - Diabetic ketoacidosis

DIAGNOSIS

OVERVIEW STATEMENT

A diagnosis of hypokalemia should be suspected when a patient presents with signs of profound muscle weakness. This is especially true if the patient has a history of predisposing risk factors, such as chronic kidney disease (primarily in cats) or diabetes mellitus.

INITIAL DATABASE

- CBC: no specific abnormality
- Serum biochemistry profile: establishes the diagnosis
- Urinalysis

ADVANCED OR CONFIRMATORY TESTING

- Do 24-hour urine potassium excretion (confirmation of excess renal potassium excretion). Rarely applied clinically.
- ACTH stimulation; low-dose dexamethasone suppression (hyperadrenocorticism)
- Serum aldosterone levels, abdominal ultrasound exam (hyperaldosteronism)
- Electrocardiography:
  - Hypokalemia delays ventricular repolarization, increases duration of action potential, increases automaticity.
  - Supraventricular and ventricular arrhythmias may be seen.
  - Decreased T-wave amplitude and ST-segment depression (often seen in human patients) are not consistent findings in dogs and cats.
- Echocardiography:
  - Decreased myocardial contractility
  - Decreased cardiac output

TREATMENT

TREATMENT OVERVIEW

The therapeutic goal is to reestablish normal serum potassium levels while avoiding hyperkalemia, as well as to maintain normal serum potassium levels long term. Therapy is indicated if serum potassium is <3 mEq/L, or if clinical signs of hypokalemia are evident, or if serum potassium loss is expected. Intravenous KCl is the drug of choice in the acute case; oral potassium gluconate is used for long-term maintenance therapy.

ACUTE GENERAL TREATMENT

- Potassium chloride (KCl) administered IV at a rate not to exceed 0.5 mEq/ kg/h
- In dogs and cats with normal renal function, maintenance potassium concentration should be approximately 20 mEq/L of fluids, given at a rate of 40 mL/kg/d IV.
- Concentration of potassium in IV fluids should not exceed 60 mEq/L (in most cases); higher concentrations can cause pain and sclerosis of peripheral veins.
- Although IV administration is preferred, KCl can be given subcutaneously so long as potassium concentration in fluids is less than 30 mEq/L.
- In mildly affected patients, oral potassium gluconate (Kaon Elixir, Tumil-K) may be the only therapy required; starting dose is 0.33 mEq/kg PO q 8 h.

CHRONIC TREATMENT

Once serum potassium is in normal range, oral potassium gluconate is continued at a maintenance dosage of 0.5 mEq/kg PO q 12 h until inciting cause is eliminated.

DRUG INTERACTIONS

Using potassium supplementation along with angiotensin-converting enzyme inhibitors, potassium-sparing diuretics (e.g., spironolactone), prostaglandin inhibitors, or β-blockers may result in hyperkalemia.

POSSIBLE COMPLICATIONS

Cardiac arrhythmias

RECOMMENDED MONITORING

During acute treatment phase, adjustments in IV potassium therapy should be based on serum potassium concentration measured once or twice a day.

PROGNOSIS AND OUTCOME

- Clinical signs usually resolve within 1-5 days after correction of hypokalemia.
- Depending on cause, long-term oral potassium supplementation may be required.

PEARLS & CONSIDERATIONS

COMMENTS

- Clinical signs associated with hypokalemia are seen more commonly in cats than in dogs.
- Chronic kidney disease is the most common condition associated with hypokalemia in cats; approximately 20%-30% of cats with chronic kidney disease are hypokalemic at presentation.
- Most dogs with chronic kidney disease have normal serum potassium concentrations.
- A common iatrogenic cause of hypokalemia is IV administration of potassium-deficient fluids to anorectic patients; solutions used for maintenance fluid therapy should contain 15-30 mEq potassium/L to avoid this complication.

SUGGESTED READING

Riordan LL, Schaer M: Potassium disorders. In Silverstein CS, Hopper K, editors: Small animal critical care medicine. St Louis, 2009, Saunders Elsevier, pp 229–233.

AUTHOR: MICHAEL BERNSTEIN

EDITOR: ETIENNE CÔTÉ

Hypocalcemia

BASIC INFORMATION

DEFINITION

A reduction of blood calcium concentration below normal. Uncommon occurrence except in cats following thyroidectomy.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs and cats of either sex and any age can be affected; exact predispositions depend on underlying causes.
- Hypoparathyroidism occurs mainly in female (65%), middle-aged dogs.
- Puerperal tetany (eclampsia) occurs in small lactating bitches.
- Older cats undergoing thyroidectomy are at risk of iatrogenic parathyroidectomy.

GENETICS & BREED PREDISPOSITION

Hypoparathyroidism in dogs: toy poodles, miniature schnauzers, Labrador retrievers, German shepherds, dachshunds, terriers

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Animal presented with signs relating to hypocalcemia
- Incidental finding on blood work, animal presented for another problem

HISTORY, CHIEF COMPLAINT

- Abrupt onset of neurologic and/or neuromuscular signs
- Signs may be intermittent despite persistent hypocalcemia:
  - Focal/generalized muscle tremors
  - Stiff, stilted, rigid gait
  - Nervousness, excessive panting
  - Generalized seizures, tetany
  - Facial rubbing
  - Ear twitching (common in cats)

PHYSICAL EXAM FINDINGS

- Muscle rigidity, tremors
- Tense abdomen
- Stiff gait
- Tachyarrhythmias, soft heart sounds, weak pulse
- Raised nictitating membranes (cats)
- Physical exam can be normal

ETIOLOGY AND PATHOPHYSIOLOGY

- Calcium homeostasis: 50% of total circulating calcium is ionized (biologically active form), 40% is bound to albumin (storage form), 10% is complexed to anions (storage form).
- Clinical signs of hypocalcemia will occur *only* when the ionized form is decreased.
- Serum calcium is tightly regulated by parathyroid hormone (PTH), vitamin D, and calcitonin.
- PTH increases serum calcium by:
  - Increasing osteoclastic bone resorption of calcium and phosphorus
  - Increasing calcium and decreasing phosphorus resorption from renal tubules
  - Stimulating conversion of vitamin D to its active form by the renal enzyme 1-a-hydroxylase
- Inactive vitamin D is absorbed in the intestine, transported to the liver where it is hydroxylated to 25-dihydroxy vitamin D, then

transported to the kidney where it is hydroxylated by 1-a-hydroxylase to the active metabolite 1,25-dihydroxy vitamin D (calcitriol).

- Vitamin D increases serum calcium and phosphorus by:
  - Increasing intestinal absorption of calcium, phosphorus and magnesium from the intestine
  - Facilitating PTH-induced bone resorption
  - Increasing renal tubular resorption of calcium and phosphorus
- Calcitonin decreases serum calcium and phosphorus by:
  - Blocking bone resorption
  - Decreasing renal tubular resorption of calcium and phosphorus

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The most common causes of clinical hypocalcemia are puerperal tetany in the lactating bitch and thyroidectomy in the cat. Hypoalbuminemia is a common cause of nonclinical hypocalcemia.

DIFFERENTIAL DIAGNOSIS

- Parathyroid-related:
  - Primary hypoparathyroidism (immune-mediated, idiopathic, surgical complication post thyroidectomy in cats)
- Acute renal failure/chronic kidney disease
- Puerperal tetany (eclampsia)
- Acute pancreatitis
- Ethylene glycol toxicity
- Hypomagnesemia
- Vitamin D deficiency
- Hypoalbuminemia (total serum [calcium] is low but ionized serum [calcium] is normal)
- Phosphate-containing enemas (especially in cats)
- Laboratory error

INITIAL DATABASE

- Complete serum biochemistry profile: identifies hypocalcemia
- Serum ionized calcium: differentiates between absolute hypocalcemia and relative (i.e., metabolically insignificant) hypocalcemia
- Serum magnesium: identifies hypomagnesemia
- Electrocardiogram

ADVANCED OR CONFIRMATORY TESTING

- Serum parathyroid hormone concentration: low in hypoparathyroidism
- Serum vitamin D concentration: low if the cause of the hypocalcemia

TREATMENT

TREATMENT OVERVIEW

In the patient presenting clinical signs, administration of calcium can be lifesaving. Increase serum calcium concentration above the threshold responsible for clinical signs:

- Total calcium above 6-7 mg/dL (1.5-1.75 mmol/L)
- Ionized calcium above 2.4-2.8 mg/dL (0.6-0.7 mmol/L)

ACUTE GENERAL TREATMENT

- Intravenous calcium infusion:
  - Administer 10% calcium gluconate IV at a dose of 0.5-1.5 mL/kg or 5-15 mg/kg slowly to effect over 15-30 minutes.
  - Electrographic monitoring is recommended during IV calcium administration.
  - The infusion should be slowed/discontinued if bradycardia, ventricular premature complexes, or shortening of the Q-T

interval is observed.
- Once clinical signs have improved, continue parenteral calcium administration. Calcium can be given as a continuous intravenous infusion at 60-90 mg/kg/d of elemental calcium (10% calcium gluconate contains 9.3 mg/mL of elemental calcium). Subcutaneous administration may be considered if venous access is not possible, but probably should be avoided in general (cases of severe, extensive calcinosis cutis and epidermal necrosis in some dogs and a cat treated with calcium gluconate).

CHRONIC TREATMENT

- Vitamin D: calcitriol is the form of vitamin D recommended for maintenance therapy (rapid onset of action, short half-life, does not require hepatic/renal transformation).
  - Loading dose: 0.01-0.015 mcg/kg q 12 h PO for 4 days
  - Maintenance dose: 0.0025-0.0075 mcg/kg q 12 h
  - Maximal effect is seen 1-4 days after initiation of treatment. Maintenance dose should be adjusted to obtain normocalcemia.
- Calcium supplementation: calcium carbonate (1 g = 20 mEq calcium) is recommended at a dose of 25 mg/kg q 8-12 h PO. Dose should be adjusted to obtain normocalcemia.
  - Once normocalcemia is achieved, the dose of oral calcium can be slowly decreased and stopped. Vitamin D must be continued until the underlying disorder is corrected.
- Therapy with synthetic PTH is not currently available.

POSSIBLE COMPLICATIONS

Subcutaneous calcium administration has been associated with the development of calcinosis cutis, and therefore the IV route may be preferable.

RECOMMENDED MONITORING

Monitor total serum calcium: target level 8-9.5 mg/dL (2-2.4 mmol/L; just below reference range).

PROGNOSIS AND OUTCOME

Dependent on the underlying disease

PEARLS & CONSIDERATIONS

COMMENTS

- Calcium must not be measured on EDTA blood. EDTA will chelate the calcium, falsely lowering its value, so avoid lavender-top tubes for serum calcium measurement.
- Avoid the use of calcium chloride for injections or infusions, as it is very caustic.
- Hypoalbuminemia may cause a mild decrease in the protein-bound fraction of calcium, thus resulting in a mildly decreased total serum calcium. Ionized calcium remains normal.
- Correcting the calcium value to compensate for albumin is not valid in dogs or cats; ionized calcium measurement is accurate.

CLIENT EDUCATION

The owner should be informed of clinical signs associated with hypocalcemia to ensure early and rapid detection.

SUGGESTED READING

Feldman EC, Nelson RW: Hypocalcemia and primary hypoparathyroidism. In Canine and feline endocrinology and reproduction, ed 3, St Louis, 2004, Saunders Elsevier, pp 716–741.

AUTHOR: MARILYN DUNN

EDITOR: ETIENNE CÔTÉ

Hypoadrenocorticism

Additional Images Available on Website

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

An endocrine disorder in dogs (rare in cats) caused by adrenocortical insufficiency

SYNONYM

Addison's disease

Glucocorticoid-deficient hypoadrenocorticism: “atypical” hypoadrenocorticism

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Most common in young/middle-aged female dogs, but any age, gender, or breed may be affected
- “Atypical” hypoadrenocorticism: dogs tend to be older at time of diagnosis.
- Nova Scotia Duck Tolling Retrievers (NSDTR) tend to be younger at time of diagnosis
- Affected cats are typically young/middle-aged, although any age may be affected; no apparent sex predilection

GENETICS & BREED PREDISPOSITION

- Increased risk: Great Danes, Portuguese water dogs, West Highland white terriers, bearded collies, poodles, rottweilers, soft-coated wheaten terriers, NSDTR, and Leonbergers.
- Heritable disease in standard poodles, bearded collies, Portuguese water dogs, and NDSTR; no sex predilection in these breeds
    - Standard poodles, Portuguese water dogs, NSDTR; appears to be autosomal recessive mode of inheritance; mode of inheritance not clearly defined in bearded collies

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- “Typical” hypoadrenocorticism: signs of both glucocorticoid and mineralocorticoid deficiency
- “Atypical” hypoadrenocorticism: only signs of glucocorticoid deficiency are present.

HISTORY/CHIEF COMPLAINT

- Clinical signs classically are notoriously vague and often wax and wane over weeks or months (sometimes only apparent to owners in retrospect); worsening in stressful situations (e.g., travel, boarding) is possible. Severity of signs ranges from a mild, progressive, intermittent course to an acute, life-threatening crisis.
- Dogs:
    - Most common: weakness, lethargy, anorexia, vomiting
    - Less common: diarrhea (possibly with melena or hematochezia), weight loss, trembling, polyuria/polydipsia (PU/PD), regurgitation (due to megaesophagus), and collapse. Rarely, seizures may occur secondary to hypoglycemia.
- Cats: anorexia, weight loss, lethargy; vomiting and PU/PD are uncommon.

PHYSICAL EXAM FINDINGS

- As described (History/Chief Complaint, above)
- In crisis, aforementioned signs may be present and severe. Mental depression/moribund state, bradycardia (from hyperkalemia) and signs of hypovolemic shock are possible.

ETIOLOGY AND PATHOPHYSIOLOGY

- Primary hypoadrenocorticism (typical and atypical): most commonly due to idiopathic or immune-mediated destruction of the

adrenal cortices. Other uncommon causes of adrenocortical destruction: granulomatous disease (histoplasmosis, blastomycosis, tuberculosis); infarction; neoplasia; adrenocortical amyloidosis; drugs (e.g., mitotane).

- Secondary hypoadrenocorticism (spontaneous): destructive lesions or congenital defects of the hypothalamus or pituitary result in decreased secretion of corticotropin-releasing factor or adrenocorticotropic hormone (ACTH), respectively. Very rare.
- Secondary hypoadrenocorticism (iatrogenic): administration of exogenous corticosteroids suppresses normal ACTH production, resulting in adrenal gland atrophy; sudden cessation of exogenous corticosteroid administration then produces hypoadrenocorticism.
- Clinical signs and laboratory findings reflect the absence of normal activities of glucocorticoids and mineralocorticoids.
- Hypoadrenocorticism affecting all layers of the adrenal cortex ("typical;" electrolytes are abnormal) is much more common than hypoadrenocorticism affecting only glucocorticoid synthesis ("atypical;" electrolytes are normal)
- Consequences of glucocorticoid deficiency:
  - Malaise, lethargy
  - Gastrointestinal (GI) signs (anorexia, vomiting, diarrhea, abdominal pain, melena, weight loss, regurgitation)
  - Hypoglycemia
  - Absence of a stress leukogram in an ill patient (failure of glucocorticoid-induced neutrophil release and lymphocyte reduction), mild anemia
- Consequences of mineralocorticoid (aldosterone) deficiency:
  - Decreased renal sodium, chloride (and consequently water) resorption, resulting in hyponatremia, hypochloremia, and volume depletion/dehydration
  - Hyponatremia (see p. 578) results in hypovolemia, hypotension, decreased cardiac output and poor tissue perfusion, solute diuresis and medullary solute washout. Consequences include prerenal azotemia, metabolic acidosis, weakness, microcardia, depression, decreased urine concentrating ability, and PU/PD.
  - Decreased renal potassium excretion resulting in hyperkalemia (see p. 556)
  - Metabolic acidosis due to decreased renal hydrogen ion excretion and poor tissue perfusion
- Additional reported findings for which a mechanism is not clearly defined include hypercalcemia (total and/or ionized calcium), hypoalbuminemia, hypocholesterolemia, and mega-esophagus.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

"Typical" hypoadrenocorticism is suspected based on compatible historical/ clinical findings in conjunction with hyponatremia and hyperkalemia. Bradycardia with concurrent hypovolemia and/or absence of a stress leukogram in an ill patient increase the likelihood of the diagnosis. "Atypical" hypoadrenocorticism should be considered in dogs with historical/clinical signs of nonspecific illness (particularly gastrointestinal signs) and compatible laboratory findings, including absence of a stress leukogram, anemia, hypoalbuminemia, hypoglycemia, or hypocholesterolemia. The diagnosis (typical or atypical) is confirmed with an ACTH stimulation test.

DIFFERENTIAL DIAGNOSIS

- History/chief complaint: primary gastrointestinal disease, intoxication, pancreatitis, renal disease, liver disease
  - The presence of prerenal azotemia and isosthenuria can make it difficult to distinguish between hypoadrenocorticism and acute renal failure. Differentiation is important because hypoadrenocorticism carries an excellent long-term prognosis. Initial treatment for both is similar, and the disorders can be distinguished using the ACTH stimulation test.
- Hyperkalemia (see p. 556)
- Hyponatremia (see p. 578)
- Hypercalcemia (see p. 553)
- Hypoglycemia (see p. 1401)

INITIAL DATABASE

- CBC, serum biochemical profile, urinalysis:
  - "Typical" hypoadrenocorticism: common findings include normocytic, normochromic nonregenerative anemia; absence of stress leukogram; hyponatremia; hypochloremia; hyperkalemia; metabolic acidosis; prerenal azotemia. Hypoglycemia, hypercalcemia, hypoalbuminemia, and isosthenuria are also possible. A decreased Na:K ratio (<27) supports a tentative diagnosis but is not pathognomonic and cannot be used for making a definitive diagnosis. Likewise, the diagnosis should not be excluded in dogs with a Na:K ratio of up to 30 in the presence of compatible clinical signs.
  - "Atypical" hypoadrenocorticism: normocytic, normochromic anemia; no stress leukogram, possible hypoglycemia hypoalbuminemia, hypocholesterolemia. Electrolyte levels are normal.
- In cats, a decreased Na:K ratio may be associated with many disorders other than hypoadrenocorticism.
- Electrocardiogram: changes consistent with hyperkalemia possible
- Thoracic radiographs: microcardia common; signs of megaesophagus ± aspiration pneumonia possible.

- Abdominal ultrasound: adrenal glands may be normal in size or slender; whereas slender adrenal glands are supportive of hypoadrenocorticism, normal adrenal gland size does not rule out the diagnosis.
- Basal serum cortisol level: if normal, hypoadrenocorticism is highly unlikely. If low, uncertainty persists.

ADVANCED OR CONFIRMATORY TESTING

- ACTH stimulation test is the definitive diagnostic test for hypoadrenocorticism. Basal serum cortisol concentration may be low-normal to low and fails to increase after ACTH administration.
- Dogs:
  - Protocol 1 (preferred): (a) Collect blood sample for pre-ACTH cortisol level; (b) Administer synthetic aqueous ACTH (cosyntropin) 5 mcg/ kg up to 250 mcg/dog IV; (c) Collect blood sample 60 minutes later (post-ACTH cortisol level).
  - Protocol 2: Collect blood sample for pre-ACTH cortisol level; (b) Administer ACTH gel 2.2 IU/kg IM; (c) Collect blood sample 2 hours later (post-ACTH cortisol level). Anecdotal reports indicate sporadic variability in ACTH gel efficacy.
- Cats:
  - (a) Collect blood sample for pre-ACTH cortisol level; (b) Administer synthetic aqueous ACTH 125 mcg/cat IV or IM; (c) Collect blood samples 30 and 60 minutes later (post-ACTH cortisol level).
- Endogenous ACTH can be measured to differentiate secondary (decreased ACTH) from early primary hypoadrenocorticism (increased ACTH) if atypical hypoadrenocorticism is present.

TREATMENT

TREATMENT OVERVIEW

Extent of initial therapy will depend on severity of clinical signs. For animals in an Addisonian crisis, initial therapy is directed toward correcting life-threatening conditions (hypotension, hypovolemia, hyperkalemia, acidosis, hypoglycemia). The cornerstone of therapy is IV fluid therapy. Patients with severe, typical clinical and laboratory abnormalities should be treated as if they have hypoadrenocorticism; delaying treatment until ACTH stimulation results are available may result in death of the patient. Chronic therapy involves physiologic replacement of deficient hormones. Lifelong hormone therapy is required.

ACUTE GENERAL TREATMENT

- Normal saline (0.9% NaCl) IV:
  - Critical component of therapy
  - Dogs: 40-80 mL/kg/h IV for ~1 to 2 hours, then 90-120 mL/kg/d for 1-2 days; switch to a balanced electrolyte solution (e.g., lactated Ringer's solution) when serum electrolyte levels are within reference ranges.
  - Cats: administer 40 mL/kg IV over 2-4 hours to rehydrate, then 65 mL/ kg/d
- Fluid therapy is the primary treatment for hyperkalemia and acidosis.
  - If hyperkalemia is life threatening (serum concentration >8 mEq/L and/or electrocardiographic findings), may need sodium bicarbonate, insulin/glucose or calcium gluconate (see p. 556).
  - If acidosis is severe (serum bicarbonate <12 mEq/L), consider bicarbonate therapy:
    - Base deficit (mEq/L) = 25 - patient's blood [$Hco3^{-}$]. If blood gas results are not available and patient is severely ill, assume base deficit = 10 mEq/L: Total dose NaHco3 (mEq/L) = body weight in kg × 0.3 × base deficit. Give 25% of total dose in IV fluids over first 6-8 hours, then reassess and repeat if blood $Hco3^{-}$ still <12 mEq/L.
- Glucocorticoid administration:
  - Dexamethasone sodium phosphate (preferred): rapid-acting and is not detected by cortisol assay (ACTH stimulation test). Initially administer 0.5-1 mg/kg IV once, then 0.05-0.1 mg/kg q 12 h in IV solution.
  - Alternatively, prednisone sodium succinate (4-20 mg/kg over 2-4 minutes initially, then q 2-6 h) can be administered but only after completion of the ACTH stimulation test.
- Hypoglycemia: add dextrose to IV fluids to make 2.5%-5% dextrose concentration.
- Once life-saving treatment has been initiated, perform ACTH stimulation test (as above).
- Monitor urine production.
- Monitor electrolytes and glucose q 8-12 h until normal.
- Maintain fluid therapy until patient is eating.
- Use injectable dexamethasone until oral prednisone can be instituted.
- Mineralocorticoid administration: can be initiated immediately *after* completion of ACTH stimulation test or following correction of electrolyte imbalances with fluid therapy.

CHRONIC TREATMENT

- Lifelong supplementation with glucocorticoids and mineralocorticoids (primary hypoadrenocorticism) or with glucocorticoids alone (secondary or atypical hypoadrenocorticism) is required.

- Glucocorticoid supplementation: prednisone, 0.22 mg/kg PO q 12 h initially then taper to 0.2-0.25 mg/kg PO q 24 h depending on individual needs
    - Increased prednisone (0.25-1 mg/kg PO q 12 h) may be required during times of stress (e.g., travel, new pet or child). Taper to usual maintenance dose once the event has resolved.
    - Patients receiving fludrocortisone acetate may not require additional daily glucocorticoid therapy, but those receiving deoxycorticosterone pivalate (DOCP) almost always do.
- Mineralocorticoid supplementation: either DOCP injection or oral fludrocortisone
    - DOCP
        - Initial dose is 2.2 mg/kg SQ or IM q ~25 days
        - Measure serum electrolytes on days 12 and 25 after treatment and adjust dosing based on results
        - If hyperkalemia and hyponatremia exist on day 12, increase the next dose by 5%-10%. If electrolytes are normal at 12 days but abnormal at 25 days, shorten the dosing interval by 48 hours.
        - Once dosage and dosing interval are determined, clients can be taught to give DOCP at home.
    - Fludrocortisone acetate
        - Dogs: 0.01 mg/kg PO q 12 h initially; dose often needs to be increased over first 6-18 months to maintain normal serum electrolyte concentrations.
        - Cats: 0.05-0.1 mg PO q 12 h initially; adjust based on serum electrolyte concentrations.
    - Salt supplementation: indicated if high fludrocortisone doses are required for normal serum sodium concentrations

POSSIBLE COMPLICATIONS

- With Addisonian crises, death can occur if treatment is not prompt and intensive.
- Overly rapid correction of hyponatremia can result in demyelinosis (see p. 559).
- Side effects of prolonged excessive prednisone and/or fludrocortisone treatment can include PU/PD and other mild signs of iatrogenic hyperadrenocorticism. In animals receiving fludrocortisone, if PU/PD cannot be resolved by eliminating salt supplementation and tapering prednisone (to lowest dose needed to prevent signs of hypocortisolism) then switching to DOCP should be considered.

RECOMMENDED MONITORING

- Serum electrolytes, BUN, glucose: 7 and 14 days after diagnosis (can coincide with day 12 after DOCP injection)
- Once electrolytes stabilize, recheck monthly for 3-6 months, then q 3-6 months.
- Once the treatment regimen is established and the dog is well, recheck electrolytes q 6-12 months for dose adjustments based on changing body weight.
- Subsequent ACTH stimulation testing is of no use (glucocorticoid interference).

PROGNOSIS AND OUTCOME 

- With treatment and monitoring, prognosis is excellent and a normal lifespan is expected.
- BUN and creatinine elevations with concurrent isosthenuria should not be taken to indicate renal failure and thus do not necessarily influence the prognosis (see Pearls & Considerations below).

PEARLS & CONSIDERATIONS 

COMMENTS

This disease can mimic others that are more common (acute renal failure, hepatic disease, GI disease), and the diagnosis of hypoadrenocorticism is commonly missed initially. The CBC can provide a valuable clue: absence of a stress leukogram in an ill animal is inappropriate and suggests hypoadrenocorticism.

TECHNICIAN TIP

A common cause of pseudohyperkalemia is normal in vitro blood clotting (platelet activation releases potassium); it is easily ruled out by remeasuring blood potassium on a sample drawn into a green-top tube (heparin).

CLIENT EDUCATION

It is important to educate clients that this disease requires lifelong treatment, and that failure to administer therapy may result in a life-threatening crisis.

SUGGESTED READING

Adler JA, Drobatz KJ, Hess RS: Abnormalities of serum electrolyte concentrations in dogs with hypoadrenocorticism. J Vet Intern Med 21:1168–1173, 2007.

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EDITOR: SHERRI IHLE

Hyphema

BASIC INFORMATION

DEFINITION

Blood in the anterior chamber of the eye

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs and cats; any age, either sex

GENETICS & BREED PREDISPOSITION

Dependent on the cause:

- Hereditary coagulopathies
- Breed predisposition to retinal detachments (see p. 985)
- Inherited congenital ocular defects (e.g., collie eye anomaly in rough and smooth collies, border collies, Australian shepherds, Lancashire heelers, and Shetland sheepdogs; persistent hyperplastic primary vitreous syndromes in Doberman pinschers, miniature schnauzers, and Staffordshire bull terriers)

RISK FACTORS

- Stimuli for ocular vascularization:
  - Chronic retinal detachments (see p. 985)
  - Intraocular neoplasia (see p. 620)
  - Glaucoma (see p. 448)
- Animals at increased risk of ocular trauma (e.g., blind animals, hunting dogs, exophthalmic dogs, puppies exposed to cats)
- Systemic diseases causing vasculopathies and/or coagulopathies:
  - Systemic hypertension (see p. 1068)
  - Leukemias
  - Hyperviscosity syndromes such as with multiple myeloma
  - Severe liver disease
  - Infectious diseases:
    - Feline leukemia virus (FeLV) infection and feline coronavirus/feline infectious peritonitis infection (FIP) in cats (see pp. 385 and p. 383)
    - Rickettsial diseases (see pp. 334 and p. 994)
  - Immune-mediated diseases:
    - Thrombocytopenia (see p. 1091)
    - Anemia (see p. 73)
  - Toxicosis:
    - Anticoagulant (see p. 83)
    - Complication of ciliary body cysts

CONTAGION & ZOONOSIS

Depends on underlying cause (e.g., FeLV and FIP transmitted cat to cat). *Brucella cants* infection with uveitis/hyphema: one of the few zoonotic diseases.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Acute:
  - Varying degrees of blood are present in the eye
  - When the blood is unclotted and the animal is quiet (often in the morning), blood settles ventrally producing a

meniscus.
    - Appearance may change rapidly. When activity level is increased during the day, settled blood may disperse and appear worse, or rebleeding may occur.
- Chronic:
    - Clot formation may become dark or black/brown (“eight ball hemorrhage”).
    - If glaucoma occurs, blood staining of the cornea may develop.

HISTORY, CHIEF COMPLAINT

- Reflective of underlying cause (see Risk Factors above)
- Blood or redness in the eye

PHYSICAL EXAM FINDINGS

- Ocular:
    - Varying degrees of blood in the anterior chamber
    - May see fibrin clots with erythrocyte entrapment +/−
    - Hypopyon +/−
    - Conjunctival injection is often present, indicating an associated anterior uveitis (see p. 1151)
    - Corneal edema +/−
    - Intraocular pressure (IOP):
        - May be reduced (<10 mm Hg) (i.e., acute; uveitis)
        - May be elevated (>30 mm Hg = glaucoma) (i.e., chronic; secondary glaucoma)
- General physical examination:
    - Search for evidence of systemic disease.

ETIOLOGY AND PATHOPHYSIOLOGY

- Neovascularization in the eye is fragile and often results in spontaneous hyphema.
- Blood in the anterior chamber is immediately diluted with aqueous humor and usually undergoes rapid fibrinolysis from tissue plasminogen activator that is produced by the iris. This may lyse the clot adjacent to the iris but leave a clot in the pupil.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

For all cases of hyphema, it is critical to determine whether the cause is strictly eye related (e.g., persistent hyperplastic primary vitreous, primary intraocular neoplasia) or systemic (bleeding disorder). Determining whether or not the affected globe has vision or the potential for vision is important for prognosis for vision.

DIFFERENTIAL DIAGNOSIS

- Intense corneal vascularization (see p. 254)
- Rubeosis iridis: new blood vessel growth on the surface of the iris (see p. 1151)

INITIAL DATABASE

- Ophthalmic examination (see p. 1313):
    - Examine periocular region for evidence of trauma; examine contralateral eye for lesions in both anterior and posterior segments.
    - Pupillary light and dazzle reflexes, menace response, for vision prognosis
    - Fluorescein stain and examine cornea/sclera for evidence of perforating injury.
    - If possible, examine iris for evidence of inflammation and assess pupil size.
    - Measure IOP to assess for signs of uveitis (i.e., hypotony or low IOP [IOP <10 mm Hg]) versus glaucoma (IOP >30 mm Hg).
- General physical examination:
    - Examine mucous membranes and skin for petechiae.
    - Palpate abdominal organs and lymph nodes for organomegaly and/ or lymphadenopathy suggestive of neoplastic and/or infectious diseases.
    - Auscult chest (pulmonary hemorrhage).
- Ocular ultrasound: for cause of bleeding such as retinal detachment, intraocular neoplasia, or intraocular foreign body
- Radiograph of head to detect metallic foreign body (pellet) in hunting dogs or if possibility of malicious cause

- CBC, chemistry profile, and urinalysis for evidence of systemic disease
- Systemic blood pressure to test for hypertension

ADVANCED OR CONFIRMATORY TESTING

- Coagulation profile
- Infectious disease titers or tests
- Fine-needle aspirates/biopsy of organomegaly or enlarged lymph nodes

TREATMENT 

TREATMENT OVERVIEW

While investigating the underlying cause, prompt initiation of therapy is recommended to begin resorption of erythrocytes and fibrin from the anterior chamber and help prevent secondary glaucoma. With systemic disorders, treatment centers on hemostasis and optimal blood volume and blood pressure. In cases of uncontrollable uveitis and/or secondary glaucoma, enucleation or evisceration and prosthesis (globe salvage) should be considered once the underlying cause has been determined and addressed.

ACUTE GENERAL TREATMENT

- Treat anterior uveitis with topical corticosteroids (e.g., prednisolone acetate 1% or dexamethasone 0.1% q 6-8 h).
  - *Only* if no lesions of the corneal surface
- If pupil is not dilated and IOP is normal or low (<15-20 mm Hg), topical atropine 1% solution q 12 h
- If IOP >20 mm Hg, topical or systemic carbonic anhydrase inhibitors (see p. 448)
- Trauma: surgery to repair corneal and/ or scleral defects (see p. 249)

CHRONIC TREATMENT

- Traumatic hyphema:
  - *Clotted* hyphema may be dissolved with injection of 25 mcg of tissue plasminogen activator into the anterior chamber (referable procedure) within 3-4 days of the hemorrhage; risk of rebleeding.
- Uncontrollable uveitis and/or secondary glaucoma:
  - Enucleation (globe removal) or evisceration and prosthesis (globe salvage)
- Surgical removal of blood from anterior chamber rarely indicated (referable procedure)

BEHAVIOR/EXERCISE

Restricted activity in acute cases of clotting disorders or trauma. In acute severe hyphema, cage rest with sedation if necessary to keep patient quiet.

DRUG INTERACTIONS

Nonsteroidal antiinflammatory drugs are usually avoided to prevent secondary bleeding.

POSSIBLE COMPLICATIONS

Rebleeding, glaucoma, vision loss, phthisis bulbi with ruptured globes, severe uveitis

RECOMMENDED MONITORING

Reexamine in 48-72 hours for resorption of blood and changes in IOP.

PROGNOSIS AND OUTCOME 

- Dependent on removal or control of underlying cause
- Traumatic hyphema < half of the anterior chamber typically improves spontaneously.
- Hyphemas > three-fourths of the chamber have guarded prognosis.
- Prognosis for vision in traumatic hyphema is usually determined by the initial trauma and the associated ocular injury.
- Globes with chronic uveitis and/or glaucoma require enucleation or evisceration and prosthesis.

PEARLS & CONSIDERATIONS

COMMENTS

- Almost every instance of hyphema is thought by the owner to be caused by trauma.
- Unless obvious abrasions and contusions exist around the eye, rule out other causes before confirming traumatic hyphema.

PREVENTION

- Avoid situations that predispose the animal to trauma (i.e., puppies interacting with feisty cats).
- Ensure toxins such as warfarin are out of reach of animals.
- Tick control.
- Avoid breeding dogs and cats with predisposing genetic diseases.

CLIENT EDUCATION

Resorption of hyphema is highly variable and difficult to predict.

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Hyperviscosity Syndrome

BASIC INFORMATION

DEFINITION

An uncommon sequela of some disease processes that may result in elevated viscosity of the blood. A constellation of clinical signs can occur secondarily.

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs more frequently than cats; middle-aged to older

ASSOCIATED CONDITIONS & DISORDERS

Hyperviscosity syndrome can cause several sequelae:

- Volume overload and congestive heart failure
- Azotemia from decreased renal perfusion, infiltrative renal lesions, or associated hypercalcemia
- Immune suppression and secondary infection
- Pathologic fractures from infiltrative bone lesions
- Neurologic signs from sludging of blood
- Bleeding disorder from platelet and coagulation factor inhibition

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

Variable combinations and severity of nonspecific signs: lethargy, weakness, weight loss, polyuria/polydipsia, neurologic deficits, and blindness. Occasionally a patient will be noted to manifest a bleeding disorder, or blood is noted to be thick and difficult to draw via phlebotomy.

PHYSICAL EXAM FINDINGS

Ocular changes (retinal vessel engorgement/tortuosity, retinal hemorrhage or detachment, papilledema), neurologic deficits (blindness, dementia), epistaxis, mucosal hemorrhage or ecchymoses, or lymphadenopathy may be present.

ETIOLOGY AND PATHOPHYSIOLOGY

Hyperviscosity syndrome may be caused by one of several hematologic conditions:

- Multiple myeloma (IgG or IgA)
- Waldenström's macroglobulinemia (IgM)
- Plasma cell leukemia
- Lymphoma
- Chronic lymphocytic leukemia
- Feline infectious peritonitis
- Amyloidosis
- Ehrlichiosis
- Primary polycythemia
- Secondary polycythemia:
  - Hypoxemia (right-to-left patent ductus arteriosus, elevated altitude, pulmonary disease)
  - Neoplasia (renal tumors, rarely sarcomas)
- Blood viscosity is a function of the concentration and composition of its components.
- A marked increase in plasma proteins or cellular constituents raises blood viscosity. This leads to sludging in the microcirculation, which is the mechanism for clinical manifestations.
- Hyperviscosity may present insidiously with vague, nonspecific signs or acutely with neurologic and/or ophthalmic deficits.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

History and physical exam findings should trigger an index of suspicion for the diagnosis, which is further supported by routine CBC and serum biochemistry profile showing severe leukocytosis, erythrocytosis/polycythemia, or hyperglobulinemia. Identifying any of these lab test abnormalities warrants a complete diagnostic evaluation to identify the underlying condition. Establishing a diagnosis of the underlying cause (see list above) is essential for optimal treatment. Serum viscosity can occasionally be measured by a reference laboratory, but the clinical utility is low because treatment will still depend on the underlying cause.

DIFFERENTIAL DIAGNOSIS

- Lethargy, weakness, weight loss, polyuria/polydipsia: these nonspecific signs are generally investigated with at least a CBC, serum biochemical profile, and urinalysis, which are the screening tests of choice for identifying abnormalities responsible for hyperviscosity.
- Acute visual deficits: retinal detachment, retinal hemorrhage, sudden acquired retinal degeneration, other
- Acute neurologic deficit: encephalitis, intracranial hemorrhage, hepatic encephalopathy, other
- Difficult phlebotomy: hypovolemia, technical difficulties

INITIAL DATABASE

- CBC: markedly elevated hematocrit (i.e., >60%) suggests erythrocytosis/ polycythemia as cause of hyperviscosity; abnormal lymphocyte count and/ or morphology may be apparent with chronic lymphocytic leukemia.
- Serum biochemistry profile: hyperglobulinemia if hyperviscosity caused by Waldenström's macroglobulinemia, multiple myeloma, feline infectious peritonitis, amyloidosis, or ehrlichiosis; possibly present with chronic lymphocytic leukemia.
- Urinalysis: no specific findings. Bence Jones proteins are not detected on routine urinalysis.
- Retinal exam: retinal arteries may be enlarged or tortuous; signs of uveitis or chorioretinitis may be present in feline infectious peritonitis.

ADVANCED OR CONFIRMATORY TESTING

- Arterial blood pressure: systemic hypertension may be a sequela of hyperglobulinemia.
- Chest radiographs: lytic bone lesions can be observed with multiple myeloma or metastatic disease in lymphoma; heavy interstitial or bronchiolar patterns possible in secondary polycythemia.
- Abdominal ultrasound:
    - Diffuse hepatosplenomegaly or lymphadenopathy may be present with lymphoma, ehrlichiosis, multiple myeloma (mainly splenomegaly)
    - Renal neoplasm (source of excess erythropoietin) possibly identified as source of secondary polycythemia
- Serum protein electrophoresis: monoclonal protein spike common with chronic lymphocytic leukemia, Waldenström's macroglobulinemia, multiple myeloma or plasma cell leukemia. More often polyclonal with feline infectious peritonitis, amyloidosis, or ehrlichiosis but occasionally can be monoclonal. Urine electrophoresis may reveal monoclonal spike for the neoplastic disorders (less commonly used).
- Bence-Jones proteinuria expected if hyperglobulinemia is cause of hyperviscosity
    - Excessive immunoglobulin light chains excreted in urine
    - May be present with multiple myeloma, chronic lymphocytic leukemia, Waldenström's macroglobulinemia, or plasma cell leukemia
- Coagulation profile: bleeding disorder, especially platelet dysfunction (elevated buccal mucosal bleeding time; normal PT, APTT) may occur with hyperglobulinemia. Indicated in cases with signs of bleeding (e.g., hyphema).
- Bone marrow aspirate ± core biopsy: >20% plasma cells in multiple myeloma or plasma cell leukemia
- Echocardiogram (with microbubble contrast): to identify right ventricular hypertrophy and right-to-left cardiac shunt if present
- *Ehrlichia canis* titer, *Leishmania* direct agglutination test, others: as indicated by geographic exposure and other features of case

TREATMENT

TREATMENT OVERVIEW

As hyperviscosity syndrome is a secondary condition, it is imperative to recognize that patients may present with chief complaints that are actually sequelae (i.e., epistaxis, blindness, retinal hemorrhage) of the underlying condition. Identifying and treating the primary disease process is the cornerstone of long-term care. Acutely, the most important treatment interventions are to ensure the patient is adequately hydrated, oxygenated, and producing urine. Phlebotomy or other treatments to reduce circulating blood components may

be used immediately if clinical signs are severe and clinical improvement is needed prior to the onset of benefit of treating the underlying cause.

ACUTE GENERAL TREATMENT

Plasmapheresis or phlebotomy to decrease Hct to <60% (e.g., remove 10-20 mL/kg whole blood, with replacement of equivalent volume of isotonic crystalloid fluids) to decrease blood viscosity and alleviate neurologic or ophthalmic signs. When hyperglobulinemia is the cause of hyperviscosity, the withdrawn blood can be centrifuged, and autologous red cells may be autotransfused.

CHRONIC TREATMENT

- Treatment of the underlying disorder (e.g., chemotherapy for leukemias, lymphoma, multiple myeloma; doxy-cycline for ehrlichiosis)
- Repeated plasmapheresis for Waldenström's macroglobulinemia
- Polycythemia, two options:
    - Phlebotomy. A total of 10-20 mL/kg in one day, repeated on an as-needed basis as clinical signs and polycythemia recurrence dictate; *or*
    - Anti-RBC-precursor drugs. First decrease the Hct to <60% using phlebotomy, then hydroxyurea 30-50 mg/kg PO q 24 h initially for 7-10 days followed by 30-50 mg/kg 2 or 3 times weekly as needed to maintain Hct <60%. Monitor CBC for signs of myelotoxicity.

RECOMMENDED MONITORING

- For hyperviscosity caused by polycythemia: monitor hematocrit.
- For hyperviscosity caused by hyperglobulinemia, monitor total protein, albumin, and globulin; repeated serum electrophoresis can be used for monitoring multiple myeloma.

PROGNOSIS AND OUTCOME

Guarded, dependent on underlying disease process

PEARLS & CONSIDERATIONS

COMMENTS

- Use corticosteroids cautiously prior to establishing a diagnosis, as biopsy or bone marrow results may be affected.
- Patients with hyperglobulinemia are predisposed to infection, and corticosteroids suppress the immune system.

SUGGESTED READING

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Hypertrophic Osteopathy

BASIC INFORMATION

DEFINITION

A periosteal reaction in the distal extremities of the limbs secondary to a mass in the thorax or abdomen

SYNONYMS

HO, hypertrophic pulmonary osteoarthropathy (HPOA), hypertrophic pulmonary osteopathy, Marie's disease, pulmonary osteoarthropathy

EPIDEMIOLOGY

SPECIES, AGE, SEX

Mainly dogs, rare in cats. Older animals, since this disorder is often associated with neoplasia.

GENETICS & BREED PREDISPOSITION

Large breeds of dogs

RISK FACTORS

- Thoracic mass (e.g., primary pulmonary neoplasia, metastatic pulmonary neoplasia, pulmonary abscess, esophageal carcinoma, *Spirocerca lupi* granuloma)
- Heartworm disease
- Canine tuberculosis
- Abdominal mass (e.g., rhabdomyosarcoma of the bladder, liver adenocarcinoma, prostatic adenocarcinoma)

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Acute or gradual swelling of limbs, especially forelimbs
- Lethargy, low-grade lameness or reluctance to move
- Incidental finding secondary to a thoracic or abdominal mass

PHYSICAL EXAM FINDINGS

- Swollen, hard extremities (e.g., distal long bones)
- Occasional pitting edema
- Decreased movement in joints secondary to soft-tissue swelling

ETIOLOGY AND PATHOPHYSIOLOGY

- Etiology unknown
- Autonomic neurovascular reflex increasing peripheral blood flow and causing periosteal congestion and new bone formation is speculated.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The combination of a limb lesion and radiographic appearance of a lung or abdominal mass defines hypertrophic osteopathy.

DIFFERENTIAL DIAGNOSIS

Radiographic:

- Primary bone neoplasia
- Secondary bone neoplasia
- Fungal bone disease
- Panosteitis

INITIAL DATABASE

- CBC: thrombocytopenia occasionally seen, unknown cause
- Serum biochemistry profile and urinalysis unremarkable or related to thoracic or abdominal mass
- Plain radiographs of extremities: palisades of periosteal new bone on phalanges, metacarpi, metatarsi progressing to tibia/fibula, radius/ulna
- Thoracic radiographs
- Abdominal radiographs

ADVANCED OR CONFIRMATORY TESTING

- Thoracic ultrasonography
- Abdominal ultrasonography
- Biopsy of inciting (e.g., pulmonary) lesion for histologic diagnosis

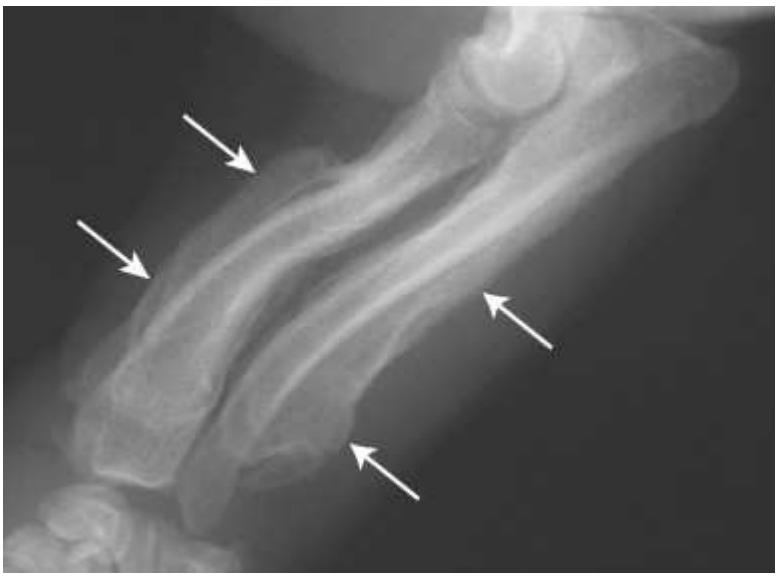
TREATMENT

TREATMENT OVERVIEW

Treat the underlying thoracic or abdominal disease.

ACUTE GENERAL TREATMENT

Definitive thoracic or abdominal surgery to treat the primary disease



HYPERTROPHIC OSTEOPATHY Lateral radiograph of the radius and ulna of a 9-year-old female spayed Dachshund dog with pulmonary carcinoma. Note the exuberant periosteal reaction *(arrowheads)* typical of hypertrophic osteopathy.

RECOMMENDED MONITORING

Follow-up radiographs of extremities to evaluate bone remodeling

PROGNOSIS AND OUTCOME

- Determined by the underlying thoracic or abdominal mass
- After treatment of the primary disease, clinical signs may continue for 1-2 weeks. Bone lesions can take months to remodel, even with correction of the underlying disorder, and are not known to be fully reversible.

PEARLS & CONSIDERATIONS

COMMENTS

Swelling of the distal extremities of an older dog with radiographic evidence of characteristic palisading periosteal reaction calls for thoracic and abdominal radiographs in search of an underlying primary lesion.

SUGGESTED READING

Halliwell WH: Tumorlike lesions of bone. In Bojrab MJ, editor: Disease mechanisms in small animal surgery. Philadelphia, 1993, Lea & Febiger, pp 933–934.

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EDITOR: ETIENNE CÔTÉ

Hypertrophic Osteodystrophy

BASIC INFORMATION

DEFINITION

A disease of the long bones of young, rapidly growing dogs, causing disruption of metaphyseal trabeculae

SYNONYMS

Barlow's disease, canine skeletal scurvy, HOD, hypovitaminosis C, idiopathic osteodystrophy, metaphyseal osteopathy, Moeller-Barlow disease, osteodystrophy types I and II

EPIDEMIOLOGY

SPECIES, AGE, SEX

Canine, range 2-8 months; males more commonly affected

GENETICS & BREED PREDISPOSITION

Large breeds

RISK FACTORS

Rapid rate of growth

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Acute
- Occasionally peracute

HISTORY, CHIEF COMPLAINT

- An acute onset of soft-tissue swelling of the distal forelimbs or occasionally of the distal hind limbs
- Low-grade lameness of short duration
- Peracute refusal to stand, anorexia, signs of pain

PHYSICAL EXAM FINDINGS

- Febrile, 104°F (40°C) or higher
- Swollen, hot limb with moderate pain
- Peracute cases can show lethargy, dehydration, and severe pain on palpation of the swollen extremities.

ETIOLOGY AND PATHOPHYSIOLOGY

- Unknown
- Definitely not a deficiency of vitamin C or an excess of vitamin D, dietary minerals, or caloric intake
- Unproven link to canine distemper virus
- Disturbance of metaphyseal blood supply, causing delayed ossification of the physeal hypertrophic zone

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The presentation of acute warm diaphyseal regions of the long bone(s) in a growing dog is highly suggestive. Radiographs of the affected region are warranted because they may support the diagnosis and rule out other possible disorders.

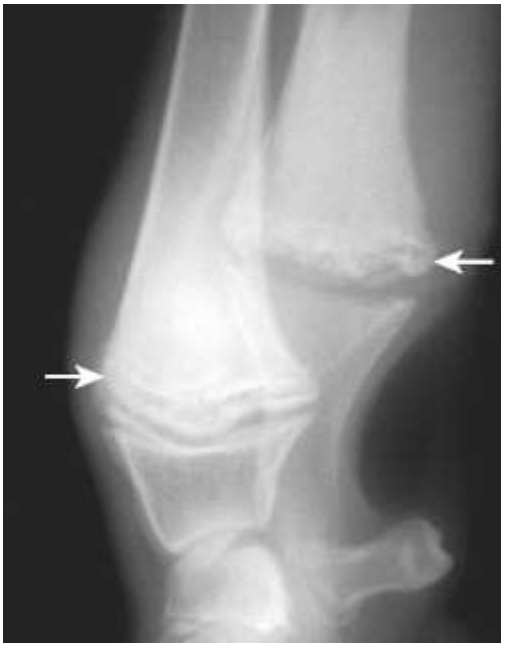
DIFFERENTIAL DIAGNOSIS

Radiographic:

- Panosteitis
- Septic arthritis
- Rickets (failure to calcify the cartilaginous matrix of the growth plate)

INITIAL DATABASE

- Plain radiographs; pathognomonic pseudophyseal line adjacent to the physis on the metaphyseal side (“scorbutic line”)
- CBC, biochemistry profile, and urinalysis are invariably unremarkable.
- Rare hypocalcemia of unknown significance



HYPERTROPHIC OSTEODYSTROPHY Lateral radiographic view of the distal radius and ulna of a 4-month-old Great Dane puppy with hypertrophic osteodystrophy (HOD). Note the radiolucent lines (“scorbutic lines” *[arrows])* parallel to the epiphyseal growth plates and antebrachiocarpal joint, characteristic of HOD.

ADVANCED OR CONFIRMATORY TESTING

Arthrocentesis (usually performed if physical exam and/or radiographs suggest a different or concurrent diagnosis): increased volume of transparent, straw-colored fluid with normal viscosity and increased numbers of neutrophils; otherwise normal

TREATMENT

TREATMENT OVERVIEW

Pain relief and supportive care; the disorder self-resolves with time.

ACUTE GENERAL TREATMENT

- Nonsteroidal antiinflammatory medication (e.g., carprofen, meloxicam, or deracoxib)
- Rest, confinement, soft bedding, turning every 4-6 hours if nonambulatory
- Severe cases require more intensive management, including the use of intravenous glucocorticoids (rule out possibility of bacterial infection first), intravenous fluids, and nutritional support.

CHRONIC TREATMENT

- Do not supplement with vitamin C, D, or minerals.
- Correct the use of inappropriate diet:
  - Use a lower-calorie puppy food.
  - Feed an amount that will achieve a thin or lean body condition score so as to minimize load on the developing skeleton until the dog reaches skeletal maturity.

POSSIBLE COMPLICATIONS

Relapses can occur until the patient reaches skeletal maturity.

PROGNOSIS AND OUTCOME

- Good
- Despite expected complete resolution, some owners may elect euthanasia in severe cases or following multiple relapses.
- Diaphyseal deformities of the affected long bones may persist.

PEARLS & CONSIDERATIONS

COMMENTS

- Radiographic changes are pathognomonic.
- Relapses and permanent bone deformities can occur.

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AUTHOR: NICHOLAS J. TROUT

EDITOR: ETIENNE CÔTÉ

Hypertrophic Cardiomyopathy

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Hypertrophic cardiomyopathy (HCM) is a common, primary myocardial disease characterized by presence of increased left ventricular wall thickness (concentric hypertrophy) in the absence of secondary causes of hypertrophy such as systemic hypertension, aortic stenosis, or hyperthyroidism.

SYNONYMS

Idiopathic hypertrophic cardiomyopathy (HCM). Hypertrophic obstructive cardiomyopathy (HOCM): if systolic anterior motion of the mitral valve is present, obstructing the left ventricular outflow tract

EPIDEMIOLOGY

SPECIES, AGE, SEX

Juvenile (4 months) to aged routinely recognized; average age ≈6 yrs. Purebred cats often younger: average age of diagnosis in Ragdoll cats is 15 months. Males tend to be more severely affected, but there is no sex-linked heritability.

GENETICS & BREED PREDISPOSITION

- Autosomal-dominant heritability with incomplete penetrance in Maine coon cats and Ragdoll cats. Two different missense mutations of the sarcomeric protein, myosin-binding protein C, are causative of HCM in these two breeds, although there is suspicion that there are additional mutations yet to be discovered in the Maine coon cat.
- Autosomal-dominant heritability in a family of American shorthair cats.
- Other breeds predisposed: British shorthair, Norwegian forest cat, Turkish van, Scottish fold, Sphynx, and Rex. However, domestic shorthair cats remain the most common type of cat diagnosed with HCM.

RISK FACTORS

Precipitating events commonly lead to congestive heart failure (CHF) in cats with previously compensated (“asymptomatic”) HCM. Intravenous fluid administration, recent corticosteroid administration (methylprednisolone acetate), or recent anesthesia/ surgery are common triggers.

ASSOCIATED CONDITIONS & DISORDERS

Congestive heart failure (CHF), aortic thromboembolism, sudden cardiac death

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Often, cats show no clinical signs, and HCM is discovered incidentally (e.g., murmur on physical exam).
- Respiratory abnormalities (CHF): tachypnea, dyspnea, orthopnea, open mouth breathing, uncommonly cough
- Nonspecific: lethargy, anorexia, vomiting
- Lameness or inability to move limb (aortic thromboembolism)
- Sudden death

PHYSICAL EXAM FINDINGS

- Systolic murmur (30%-80% of cases)
- Gallop heart sound (S4 heart sound) variably present (≈30%)
- Arrhythmia: premature beats, irregular rhythm (20%-70% of cats)
- Respiratory abnormalities common if heart failure: tachypnea, dyspnea, increased adventitious lung sounds, ventrally dampened lung sounds if pleural effusion
- If arterial thromboembolism: cyanotic nail beds and toe pads, absent pulses of that limb, contracted and painful muscles,

paresis or plegia of limb

ETIOLOGY AND PATHOPHYSIOLOGY

- Initial defect is myocyte dysfunction due to primary sarcomeric defect; remaining sarcomeres develop compensatory concentric hypertrophy. Myocardial fibrosis consists of replacement fibrosis of dead myocardial cells and interstitial fibrosis likely due to elevated angiotensin II and aldosterone levels.
- Diastolic dysfunction (impaired relaxation and increased myocardial stiffness) caused by altered calcium handling, concentric hypertrophy, myofiber disarray, and myocardial fibrosis.
- Elevated left ventricular filling pressure leads to elevated left atrial and pulmonary venous pressure and development of left sided CHF (pulmonary edema +/− pleural effusion).
- Left atrial thrombus may form secondary to sluggish blood flow in the dilated left atrium and can lead to arterial thromboembolism.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is made by echocardiographic measurement of increased left ventricular wall or interventricular wall thickness of 6 mm or greater in the absence of systemic causes such as hyperthyroidism or systemic hypertension. Thoracic radiographs are necessary to evaluate for presence of congestive heart failure but radiographs alone cannot specify the type of cardiac disease present.

DIFFERENTIAL DIAGNOSIS

Echocardiographically, hypertrophic cardiomyopathy is a diagnosis of exclusion after other causes of increased left ventricular wall thickness have been ruled out:

- Hyperthyroidism
- Systemic hypertension
- Subaortic stenosis
- Acromegaly

INITIAL DATABASE

- Echocardiogram: interventricular septum or left ventricular free wall end diastolic thickness 6 mm or greater. Papillary hypertrophy often present (subjective or quantitative). End-systolic cavity obliteration may be seen. Systolic anterior motion (SAM) of the mitral valve may be seen, confirming HOCM; with HOCM, color-flow Doppler shows left ventricular outflow tract/aortic turbulence and mitral regurgitation. Degree of obstruction caused by SAM is determined by continuous-wave Doppler measurement of the aortic blood flow velocity, using the left apical five-chamber view. Left atrial enlargement is determined by two-dimensional measurements of left atrial diameter and aortic diameter in diastole, using the right parasternal short-axis view at the level of the aortic valve. Left atrial to aortic ratio greater than 1.5 or left atrial diameter >16 mm in the cat denotes left atrial enlargement.
- Electrocardiogram (ECG): supra ventricular or ventricular premature complexes possible. Atrial fibrillation is rare but may be seen with severe left atrial dilation. Left axis deviation (mean electrical axis 0 to −90 degrees) or increased QRS amplitude >1 mV may indicate left ventricular hypertrophy.
- Clinicopathologic evaluation: CBC, serum biochemistry profile, urinalysis unremarkable unless arterial thromboembolism (see p. 88).
- Serum T4 and systolic blood pressure are important to evaluate for secondary causes of concentric left ventricular hypertrophy.
- Thoracic radiographs: Often normal if no left atrial enlargement. More severe cases may show left atrial enlargement, distended pulmonary veins, and if CHF is present, patchy interstitial to alveolar infiltrates often of caudal lung lobes and accessory lung lobe, although no pattern of distribution is typical; pleural effusion also is possible.

ADVANCED OR CONFIRMATORY TESTING

- Tissue Doppler imaging (TDI) echocardiography (pulsed-wave Doppler or color Doppler) to identify diastolic dysfunction and monitor therapeutic effects or progression of disease.
- Plasma brain natriuretic peptide (BNP) often is markedly elevated in cats with severe HCM and CHF and may be elevated in asymptomatic cats. The inactive fragment, NT-proBNP, may be measured using a commercially available test (Cardiocare [IDEXX Laboratories]), but no point-of-care test is yet available.

TREATMENT

TREATMENT OVERVIEW

- Treatment of CHF: reduce the accumulation of pleural effusion or pulmonary edema.
- Antihypertrophic treatment in attempts to reduce the concentric hypertrophy of the left ventricle and decrease myocardial stiffness; consider if wall thickness >7 mm; unproven efficacy.
- Reduce SAM if moderate or severe (pressure gradient >50 mm Hg), which will reduce the pressure overload of the left ventricle, reduce mitral regurgitation, and potentially reduce concentric hypertrophy in severe obstructions.
- Antiarrhythmic treatment if severe tachyarrhythmias such as ventricular tachycardia, supra ventricular tachycardia, or atrial fibrillation
- Anticoagulant therapy in animals with high risk of arterial thromboembolism (spontaneous contrast, severe left atrial dilation, or a left atrial thrombus present on echocardiogram) or in animals having suffered arterial thromboembolism

ACUTE GENERAL TREATMENT

Acute decompensated CHF (see p. 468):

- Thoracocentesis
- Oxygen therapy in oxygen cage, minimize stress
- Furosemide (1-4 mg/kg IV)
- Nitroglycerin
- Concurrent fluid therapy is contraindicated.
- Avoidance of β-blocker therapy during the initial decompensated stage (unless severe tachyarrhythmia also present), controversial whether to start once heart failure is resolved.

CHRONIC TREATMENT

- Reduce SAM if moderate or severe: atenolol or diltiazem
  - Atenolol, 6.25-12.5 mg per cat PO q 12 h. Start at the low dose (typically when asymptomatic), recheck heart rate (HR) and murmur intensity in 1-2 weeks, then increase to 12.5 mg PO q 12 h if HR remains >170 bpm or if SAM severity by continuous-wave Doppler echocardiography or murmur intensity not improved. Do not increase atenolol if HR< 130 bpm.
  - Diltiazem: less effective than atenolol in reducing SAM and preventing sinus tachycardia.
    - Diltiazem, 7.5 mg per cat PO q 8 h
    - Sustained release diltiazem:
  - Dilacor XR, 30 mg PO q 12 h (60-mg tablets)
  - Cardizem CD (180-mg capsules), 10 mg/kg PO q 24 h
  - Consider antihypertrophic treatment for moderate to severe left ventricular hypertrophy (wall thickness >7 mm).
    - Atenolol or diltiazem at doses written previously; may reduce hypertrophy in some cases; controversial.
    - Angiotensin-converting enzyme (ACE) inhibitors or aldosterone antagonist (spironolactone) not likely to be of benefit in early compensated HCM; controversial.
- Chronic CHF: see p. 470
- Chronic refractory CHF:
  - Addition of second diuretic: hydrochlorothiazide (1-4 mg/kg PO q 12 h) ± spironolactone (1-2 mg/kg PO q 12 h)
  - ± Potassium supplement if hypokalemic (2-4 mEq PO q 12 h)
  - Consider SQ administration (increased bioavailability compared to oral) of furosemide 1-2 times a week if maximized on 4 mg/kg PO q 8 h in the face of active heart failure.
- Anticoagulation for prevention of arterial thromboembolism:
  - One baby aspirin (81 mg ASA) or 5 mg PO q 3 d
  - Low-molecular-weight heparin (Enoxaparin): 1.5 mg/kg SQ q 12 h; pharmacokinetics and optimal dosing are still under investigation.
  - Clopidogrel as a potent platelet inhibitor (18.75 mg PO q 24 h)
  - Combination therapy is controversial but has been done in cats with persistent spontaneous contrast on echocardiography or recurrent arterial thromboembolism.
- Antiarrhythmic therapy if supraventricular tachycardia, ventricular tachycardia, or atrial fibrillation with rapid ventricular response rate (see pp. 1165 and p. 108)

NUTRITION/DIET

Sodium restriction only if palatable and only with congestive heart failure; diuretic administration is ongoing (sodium restriction may decrease required dosage of diuretic [s]).

BEHAVIOR/EXERCISE

Avoidance of eliciting intense physical activity (e.g., laser pointer, feather on end of string and wire), which increases heart rate and myocardial oxygen demand

DRUG INTERACTIONS

- Diuretics and ACE inhibitors may exacerbate renal dysfunction.
- Concurrent use of β-blockers and calcium channel blockers is generally contraindicated, as they may cause profound negative chronotropic ± negative inotropic effects.

POSSIBLE COMPLICATIONS

- Prerenal/renal azotemia and hypokalemia during treatment with diuretics
- Cats receiving high doses of diuretics are often mild to moderately azotemic but often maintain reasonable quality of life without requirement for concurrent fluid administration.
- ACE inhibitors occasionally may cause acute renal azotemia, which may reverse after discontinuation of the ACE inhibitor and supportive care.

RECOMMENDED MONITORING

- Baseline serum renal panel and urinalysis; repeat renal panel q 12 h during acute CHF treatment.
- Repeat renal panel 1-2 weeks after initiation of treatment with ACE inhibitor. If significant azotemia occurs, decrease or discontinue the ACE inhibitor, and if possible decrease the diuretic and recheck renal panel.
- Thoracic radiographs to assess therapeutic efficacy of diuretics in resolving the CHF; intermittent recheck radiographs q 2-4 months once stabilized.
- Echocardiogram: depending on severity of HCM q 3-12 months. If recent pulmonary edema or pleural effusion, recheck echocardiogram to assess for left atrial dilation to support the diagnosis of CHF. Monitor left atrial size as risk factor for development of CHF or arterial thromboembolism. Monitor left ventricular (LV) hypertrophy to assess possible progression of disease or assess potential antihypertrophic therapeutic effects. To evaluate for therapeutic reduction in SAM, repeat echocardiogram 1-2 weeks after therapy.
- If systemic hypertension or hyperthyroidism is present, a recheck echocardiogram 3-4 months after cat is normotensive or euthyroid should show regression of LV hypertrophy. If hypertrophy is still present, the cat has concurrent HCM or there is incomplete control of the systemic disorder.
- If arrhythmia is present, recheck ECG to assess response to antiarrhythmic therapy.

PROGNOSIS AND OUTCOME 

- Fair to good prognosis for cats with mild nonprogressive HCM. Cats with HCM and no clinical signs have a median survival >5 years.
- Young male cats and Ragdoll cats with significant left ventricular hypertrophy often progress more rapidly and die from their disease, and often die by 4 years of age.
- Severe HCM and CHF: poor long-term prognosis, median survival of 3 months, although highly variable with survival times over 2 years in some individuals.
- Severe HCM and arterial thromboembolism: poor prognosis, median survival of 2 months but highly variable.

PEARLS & CONSIDERATIONS 

COMMENTS

- Wide range of severity and progression of HCM in individual cats
- In a multicenter, prospective, randomized and blinded study, neither ACE inhibitors, atenolol, nor diltiazem were shown to improve survival over furosemide alone in cats with severe HCM and CHF or arterial thromboembolism.
- Avoidance of long-acting corticosteroid injections
- Anesthetic considerations: avoidance of high fluid rates and drugs that cause tachycardia. Consider induction with midazolam and propofol or with etomidate; maintenance with isoflurane or propofol.

PREVENTION

Genetic screening tests are available for Maine coon cats and Ragdolls, and breeding programs should be aimed at eliminating

genotypically affected cats. Echocardiograms are necessary to screen potential breeding candidates in all breeds, including Maine coon cats, since some Maine coon cats may have HCM despite a normal genotype.

TECHNICIAN TIPS

- Cats with HCM and heart failure tend to be very fragile and require careful handling to minimize stress. For thoracocentesis, cats may be maintained in a comfortable sternal position with gentle and as minimal as possible restraint.
- Blood pressure measurement should also be done prior to other diagnostic tests, with as minimal restraint or stress as possible

CLIENT EDUCATION

- In cats with CHF, teaching clients to monitor resting respiratory rate and respiratory effort is helpful, and to contact the doctor when rates are consistently >40 breaths per minute.
- Risk of sudden death and arterial thromboembolism. Difficulty in preventing arterial thromboembolism when severe underlying cardiac disease is present.

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Hyperthyroidism

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

The clinical condition that results from continued excessive secretion of thyroid hormones (thyroxine and triiodothyronine) by the thyroid gland.

SYNONYM

Thyrotoxicosis

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Older cats; range is 4-20+ years, but 95% of cats diagnosed with hyperthyroidism are >8 years old.
- No sex predilection

GENETICS & BREED PREDISPOSITION

Purebred cats are significantly less likely to be hyperthyroid than domestic/mixed breeds.

RISK FACTORS

Possibly canned food or ectoparasiticide exposure

ASSOCIATED CONDITIONS & DISORDERS

- Concentric cardiac hypertrophy (ventricular thickening)
- Systemic hypertension
- Hyperthyroidism may mask underlying renal dysfunction

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Apathetic hyperthyroidism (10% of cases): cat has decreased appetite, lethargy, and occasionally weight gain.

HISTORY, CHIEF COMPLAINT

- Polydipsia and polyuria
- Polyphagia
- Weight loss despite good appetite
- Hyperactivity, nervousness
- Vomiting and/or diarrhea
- Tachypnea/panting
- Weakness, lethargy
- Decreased grooming activity
- Heat avoidance or seeking cool areas

PHYSICAL EXAM FINDINGS

- Poor body condition
- Unkempt haircoat
- Dehydration
- Cardiac changes
    - Sinus tachycardia

  - Systolic heart murmur
  - Arrhythmia
- Abnormal retinal examination (tortuous retinal blood vessels, retinal tears, retinal detachment)
- Palpable thyroid gland(s)

ETIOLOGY AND PATHOPHYSIOLOGY

- Benign thyroid neoplasia or adenomatous hyperplasia of one (30%) or both (70%) thyroid lobes is most common.
- Thyroid carcinoma is found in <2% of hyperthyroid cats.
- Although many theories have been proposed, no studies have adequately demonstrated an etiology for feline hyperthyroidism.
- Canine hyperthyroidism is the result of a functional thyroid carcinoma (see p. 1095).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected in a middle-aged to older cat with clinical signs of weight loss, polyphagia, polyuria, polydipsia, and/or poor grooming habits. Confirmation is usually based on a high serum total thyroxine (T4) concentration. In rare cases when the serum T4 does not correlate with the clinical signs, further evaluation of the thyroid status is necessary.

DIFFERENTIAL DIAGNOSIS

- For polyphagia with weight loss in an adult/geriatric cat: diabetes mellitus, inflammatory bowel disease, gastrointestinal lymphoma. Rarely in cats: hyperadrenocorticism, glomerulonephritis/protein-losing nephropathy.
- For polyuria/polydipsia, see p. 902
- For polyphagia, see p. 899
- For weight loss, see p. 1181
- For vomiting, chronic, see p. 1175
- For diarrhea, chronic, see p. 305
- For arrhythmias/tachycardia/murmur:
  - Primary idiopathic hypertrophic cardiomyopathy (see p. 565)
  - Restrictive cardiomyopathy (see p. 981)

INITIAL DATABASE

- CBC, serum biochemical profile, urinalysis: possible stress leukogram and mild erythrocytosis; increase in liver enzymes common; increased blood urea nitrogen (BUN) and creatinine, phosphorus, and bilirubin less common; urine specific gravity results vary.
- Serum total thyroxine (T4) measurement: usually increased, although values are sometimes in the upper half of the reference range, especially if concurrent disease is present (“euthyroid sick”–like effect).
- Thoracic radiographs: cardiomegaly common; possible pulmonary edema, and/or pleural effusion
- Systemic blood pressure measurement (see p. 1209): hypertension (systolic blood pressure repeatedly >180 mm Hg in calm environment) is common.
- Electrocardiogram if an arrhythmia or other signs of heart disease are present: sinus tachycardia is most common; atrial or ventricular arrhythmias are possible but uncommon.

ADVANCED OR CONFIRMATORY TESTING

- Serum T4 (increased) alone is often diagnostic. If T4 is in the normal range, but the thyroid gland is palpable and/or signs suggestive of hyperthyroidism are present, one of the following tests can be considered:
  - Reevaluate the T4 in a few weeks (if clinical signs are mild).
  - Serum free T4 by equilibrium dialysis (FT4ED): increased FT4ED in conjunction with a high normal total T4 supports a diagnosis of hyperthyroidism.
- T3 suppression test: generally replaced by FT4ED
- Thyroid-stimulating hormone (TSH) and thyrotropin-releasing hormone (TRH) response tests have also been used but are of more limited diagnostic use owing to poor differentiation of hyperthyroid and euthyroid cats, especially if concurrent disease is present.
- Radionuclide (99m-technetium) thyroid scan can be used for determining whether one or both thyroid glands is/are involved, and whether ectopic functional thyroid tissue is present. These points are perhaps of greatest concern if surgical thyroidectomy is contemplated (completeness of excision).
- Echocardiography (cats): can identify left ventricular thickening. If it is symmetric (whole left ventricle is thickened), either

hyperthyroidism or unrelated idiopathic hypertrophic cardiomyopathy (HCM) may be the cause. If it is asymmetric (e.g., interventricular septum is thicker than left ventricular free wall), or hypertrophy is severe, then idiopathic HCM is contributory, and hyperthyroidism alone cannot be causative.

TREATMENT

TREATMENT OVERVIEW

- Three treatment options are available, including daily antithyroid medication, surgical thyroidectomy, and radioactive iodine therapy. The clinical status of the patient will dictate which treatment option is best for an individual. Therapy of concurrent medical conditions such as cardiac hypertrophy and systemic hypertension may be necessary, especially in the early stages of therapy.
- Ideally, therapy will restore serum T4 to normal levels and eliminate clinical signs.
- The clinical therapeutic goal is to encourage weight gain and improve body condition and haircoat, as well as decrease polyuria, polydipsia, and polyphagia, with the overall goal of maximizing quality of life. Depending on renal function, achieving this goal may or may not include returning the serum thyroid hormone levels to normal.

ACUTE GENERAL TREATMENT

- Hyperthyroidism is a chronic disease, so urgent acute treatment usually is not needed.
- Concurrent congestive heart failure may require immediate intervention (see p. 468).
- "Thyroid storm": intense sympathetic discharge usually in response to restraint or other stressful trigger.
    - Managed most effectively through prevention (calm environment, cautious/gentle restraint)
    - If thyroid storm occurs, immediately ensure as calm and quiet an environment as possible while initiating supportive management of complications that occur. May include any or all of the following: acute/decompensated heart failure, severe tachycardia (best treated through calming environment, possibly mild sedation but not with acepromazine), severe bradycardia (very conservative doses of atropine, e.g., 0.01-0.02 mg/kg IV once), severe systemic hypertension (calming environment).
    - Thyroid storm may be acutely fatal and must be prevented through gentle handling of hyperthyroid cats, who often are hyperesthetic and fractious.
    - Prevention through beta-blockade (atenolol, 6.25 mg PO q 12 h, provided medication administration can be accomplished with minimal stress to the cat) has been advocated.

CHRONIC TREATMENT

See Hyperthyroidism algorithm,

- Cats often have renal dysfunction that is not identifiable at the time of diagnosis of hyperthyroidism. Once antithyroid therapy is initiated, the renal dysfunction is unmasked. Therefore a trial of oral antithyroid medication (10-14 days or longer), with monitoring of renal parameters, is recommended before treatment with a more permanent and costly modality (i.e., surgery or radioactive iodine).
- Medical treatment:
    - Thioureylene antithyroid drugs suppress thyroid hormone production.
        - Methimazole (2.5-5 mg/cat PO q 8-12 h) or carbimazole (5 mg/cat PO q 8 h; currently not available in North America) are most commonly used.
        - Transdermal methimazole (methimazole in pluronic lecithin organogel (PLO) from a compounding pharmacy) (2.5-5 mg/cat applied inside the ear pinna q 12 h) has been used in cats that are not amenable to pill administration. Owners should wear an examination glove or a finger cot, and should clean any residual material from the pinna using a damp cotton ball prior to methimazole dosing. Remission may take longer with this formulation. This formulation is also more costly, and longer-term stability (>a few weeks to a few months) of the drug is unproven.
        - Regardless of the formulation used, the dosage is adjusted so that serum T4 concentrations are in the lower half of the reference range.
        - Therapy is expected to be lifelong.
    - Discontinuation of the medication will result in return of clinical signs, so client compliance is essential.
    - Potential side effects of methimazole include anorexia/vomiting, lethargy, pruritus of the head and neck (and self-induced trauma), hepatoxicity (uncommon), thrombocytopenia (uncommon), agranulocytosis (uncommon), and immune-mediated hemolytic anemia (rare). If hemorrhage, icterus, or severe neutropenia occurs, drug administration must be stopped and an alternative treatment initiated. Adverse effects are generally reversible.
    - Other medical treatments that have been used include potassium iodate and calcium ipodate, but these are considered only for short-term use before a more definitive treatment in patients who cannot tolerate methimazole or carbimazole.

- A β-blocker (e.g., atenolol, 6.25 mg/cat PO q 12 h) is used if severe sinus tachycardia (>260 beats/min) persists despite euthyroidism, or if antithyroid drugs need to be stopped (e.g., in preparation for radioiodine).

- Thyroidectomy:
  - Potentially curative
  - Eliminates grossly abnormal thyroid tissue, but ectopic tissue may remain if radionuclide imaging is bypassed.
  - Unilateral thyroidectomy: contralateral thyroid gland can eventually become hyperplastic or adenomatous (recurrent hyperthyroidism).
  - Medical treatment is recommended for several weeks before surgery (assess euthyroid renal function, improve metabolic and cardiac status before administering anesthetic).
  - Bilateral thyroidectomy: may involve loss of several or all parathyroids. Postoperative monitoring of serum calcium is required; if indicated, treat as for hypoparathyroidism (see p. 580).
  - Other possible postoperative complications include Horner's syndrome (see p. 543) and laryngeal paralysis (see p. 635).
- Radioactive iodine (^{131}I) therapy:
  - This is considered the best treatment option for long-term control and possible cure of hyperthyroidism, provided that during a trial of medical antithyroid therapy, serum BUN and creatinine are normal and/or urine specific gravity > 1.035.
  - Treatment renders all hyperfunctional thyroid tissue, including ectopic tissue, nonfunctional.
  - Disadvantages: special handling facilities and posttherapy isolation for several days to weeks are required. The length of isolation is dependent upon the facility. Prior to therapy, the cat must be eating and able to tolerate the required period of time in isolation.
  - The necessity of discontinuing medical antithyroid drugs before treatment is controversial. Consult the facility administering the radiotherapy.

RECOMMENDED MONITORING

- Medical therapy: exam including body weight, CBC, serum biochemical profile, urine specific gravity, T4 at 2 weeks; if normal, reassess q 6 months or if adverse effect or recurrent signs of hyperthyroidism occur.
- Thyroidectomy: exam including body weight, postoperative monitoring of serum calcium if bilateral thyroidectomy; CBC, serum biochemical profile, urinalysis and T4 at 2 weeks, then monitor T4 q 3-6 months.
- Radioactive iodine therapy: exam including body weight, CBC, serum biochemical profile, urinalysis, and T4 2 weeks after treatment, then monitor T4 q 3-6 months.

PROGNOSIS AND OUTCOME

- With successful radioactive iodine therapy or thyroidectomy the short-term prognosis is excellent and long-term prognosis is good. Cure may be obtained in many cases.
  - These patients are older at the time of diagnosis, and other conditions may be present or soon develop; length of survival has been documented to be approximately 2 years post diagnosis regardless of the type of therapy chosen.
- With the presence of renal dysfunction the short-term prognosis is good, but the long-term prognosis is guarded to poor, as both hyperthyroidism and renal dysfunction are progressive illnesses and treatments may be mutually antagonistic.

PEARLS & CONSIDERATIONS

COMMENTS

Concurrent hyperthyroidism and chronic kidney disease should be treated according to which disorder is predominantly responsible for clinical signs:

- Hyperthyroid cats with polyphagia, weight loss, and/or hyperactivity who are also incidentally found to be azotemic should be treated for hyperthyroidism. Chronic kidney disease (see p. 205) is monitored and managed secondarily.
- Cats with chronic kidney disease and overt anorexia, dehydration, uremic oral ulcers, and/or vomiting who are also incidentally found to be hyperthyroid should be treated for chronic kidney disease. In these cases, hyperthyroidism is monitored and generally not treated unless it is causing characteristic signs.
- Cats with no clinical signs attributable to either chronic kidney disease or hyperthyroidism but who are found to have both syndromes incidentally on routine laboratory testing should be monitored periodically (see Recommended Monitoring above) and not treated specifically for either disorder, other than preventive measures (e.g., nutrition).
- Cats with clinical signs of both chronic kidney disease and hyperthyroidism may require medical treatment for chronic kidney disease and “partial treatment” of hyperthyroidism (i.e., medical treatment to lower the T4 somewhat but still above the normal range).

TECHNICIAN TIPS

- Serum submitted for T4 should be free of hemolysis.
- Serum submitted for FT4 ED should be free of hemolysis and lipemia; a fasted sample is recommended.

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Hyperparathyroidism, Primary

BASIC INFORMATION

DEFINITION

Primary hyperparathyroidism (PHPTH) is an uncommon disease of dogs caused by increased synthesis and secretion of parathyroid hormone (PTH). The source of increased PTH is autonomously functioning parathyroid cells due to parathyroid adenoma, hyperplasia, or carcinoma. For secondary causes of hyperparathyroidism, see pp. 976 and p. 770.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Older dogs predominantly; no gender predilection
- Rare in cats. Typically older cats are affected.

GENETICS & BREED PREDISPOSITION

- Any breed
- Keeshonden overrepresented. In Keeshonden, PHPTH is heritable (autosomal dominant). A genetic test is available to determine if a Keeshond patient has the affected form of the gene.
- Hereditary neonatal PHPTH has been reported in two German shepherd dogs.

CLINICAL PRESENTATION

HISTORY/CHIEF COMPLAINT

- Polyuria/polydipsia (≈50% dogs; ≈10% cats)
- Lower urinary tract signs (caused by infection or cystic calculi) including pollakiuria, stranguria, and hematuria (≈50% of dogs)
- Weakness, lethargy (≈40-50% of dogs and cats)
- Inappetence (≈25-30% of dogs; ≈40% of cats), vomiting (≈10% of dogs; ≈40% of cats)
- Some (≈30%) affected dogs have no clinical signs; hypercalcemia is an incidental finding.

PHYSICAL EXAM FINDINGS

- Physical examination is typically unremarkable.
- A parathyroid mass is not usually palpable in dogs. Parathyroid masses may be palpable in the ventral neck of cats.

ETIOLOGY AND PATHOPHYSIOLOGY

- PHPTH is most often due to a solitary parathyroid adenoma. Less common causes include hyperplasia of one or more glands or (rarely) parathyroid carcinoma.
- In normal animals, serum PTH concentration is controlled by ionized calcium via negative feedback. In PHPTH, the gland(s) function autonomously, and feedback inhibition is lost.
- Increased serum PTH concentrations cause hypercalcemia and hypophosphatemia.
- Clinical signs are due to hypercalcemia (see p. 553).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

- Concurrent hypercalcemia and low to low-normal serum phosphorus concentration suggest the possibility of PHPTH; however, these findings are also characteristic of humoral hypercalcemia of malignancy, a far more common disorder. The presence of cystic calculi and/or the absence of other historical or physical signs further increase suspicion for PHPTH.
- One or more parathyroid masses may be visible with ultrasonography; failure to visualize a parathyroid mass does not rule out the diagnosis.

- The diagnosis is established by measuring concurrent serum ionized calcium and PTH concentrations.

DIFFERENTIAL DIAGNOSIS

Hypercalcemia (see p. 553)

INITIAL DATABASE

- CBC, serum biochemical profile, urinalysis, urine culture: hypercalcemia, low or low-normal phosphorus concentration, and isosthenuria are typical. Urinary tract infection is relatively common.
- Confirm hypercalcemia by repeating the test on a new sample and/or measure serum ionized calcium concentration.
- Abdominal radiographs: possible cystic calculi
- Other tests to rule out more common of causes of hypercalcemia, particularly hypercalcemia of malignancy, may include thoracic and abdominal radiographs, abdominal ultrasound, aspiration of lymph nodes and/or bone marrow, and/or serum parathyroid hormone-related protein (PTHrP) concentration.

ADVANCED OR CONFIRMATORY TESTING

- Concurrent serum ionized calcium and PTH concentrations: A serum PTH concentration within the reference range is inappropriate with concurrent increased ionized calcium concentration; thus in a patient with increased ionized calcium, a serum PTH concentration that is either high or within the reference limits supports a diagnosis of PHPTH.
  - Elevated PTH: ≈one-fourth of cases
  - PTH within reference range: ≈three-fourths of cases; of these, over half reported in the lower half of the reference range.
- Ultrasonography of the neck to evaluate the parathyroid glands requires an experienced ultrasonographer and sensitive ultrasound equipment. Visualization of an enlarged parathyroid gland(s) in conjunction with compatible serum ionized calcium and PTH concentrations strongly supports the diagnosis of PHPTH.
- Diagnosis is confirmed by exploratory surgery of the neck or by response to ablation therapy.

TREATMENT

TREATMENT OVERVIEW

Goals of treatment are to remove or ablate affected parathyroid gland(s) and monitor/treat for postoperative hypocalcemia. Refenal is indicated if the attending clinician is unfamiliar with thyroid/parathyroid evaluation and surgery, or if 24-hour care and in-house serum calcium monitoring cannot be provided during the immediate postprocedural period. Treat urinary tract infections and remove cystic calculi.

ACUTE GENERAL TREATMENT

- +/-Nonspecific treatment of hypercalcemia (see p. 553) while awaiting a definitive diagnosis or surgery (see p. 553). Contrary to patients with other causes of hypercalcemia, animals with PHPTH rarely require treatment for hypercalcemia.
- Surgical exploration of the neck, with removal of the affected parathyroid gland(s). Most often a solitary parathyroid mass is easily identified and removed. Occasionally evaluation/identification of affected glands can be difficult. In rare instances, removal of all four parathyroid glands and both thyroid glands is considered.
- Newer therapies (percutaneous ultrasound-guided ethanol ablation or radiofrequency heat ablation) are effective and less invasive than surgery but technically challenging and still require general anesthesia (see p. 1263).

CHRONIC TREATMENT

- Surgical or ablation therapy is curative in most patients, so chronic therapy is not required.
- If all four parathyroid glands are removed, lifelong vitamin D and thyroid hormone replacement are indicated (see pp. 580 and 588).

POSSIBLE COMPLICATIONS

- The most important complication is postprocedural hypocalcemia, which may occur with parathyroidectomy or ablation.
- Unaffected glands often atrophy with prolonged increased serum PTH concentrations. After removal of the affected gland(s), serum PTH and calcium may decline more rapidly than normal glands can recover.
- Hospitalization is recommended for at least 5 days after surgery to minimize physical activity, monitor for signs of hypocalcemia, and monitor serum calcium concentrations (q 12-24 h).
- Treatment for hypocalcemia (vitamin D +/-calcium) must be individualized. The goal of therapy is to keep the serum calcium

concentration in the slightly low/low-normal range (8–9.5 mg/dL; 2-2.4 mmol/L) to prevent clinical signs of hypocalcemia while stimulating recovery of function in atrophied parathyroid glands (see p. 576 for vitamin D dosage).

- In general, if serum calcium concentration <14 mg/dL (3.5 mmol/L) before surgery, postoperative hypocalcemia is unlikely. Treatment is recommended only if total calcium falls below 8.5 mg/dL (2.1 mmol/L), if the rate of decline of calcium after surgery is very rapid (e.g., >25% in 1 day), or if clinical signs of hypocalcemia occur.
- If pretreatment serum calcium concentration >14 mg/dL (3.5 mmol/L), prophylactic treatment with vitamin D and calcium is begun the morning of surgery.
- If pretreatment serum calcium concentration >18 mg/dL (4.5 mmol/L), prophylactic treatment is begun 36 hours before surgery.
- If only 1-3 parathyroid glands were removed, vitamin D treatment can be tapered over 3-6 months based on serum calcium levels.
- Additional complications following ultrasound-guided heat or ethanol ablation occur uncommonly and include cough, voice change, and Horner's syndrome.

RECOMMENDED MONITORING

Although rare, PHPTH recurrences may be observed even longer than 12 months after successful treatment; evaluation of serum calcium is recommended every 3-6 months.

PROGNOSIS AND OUTCOME

Prognosis is excellent following successful surgery or ablation.

PEARLS & CONSIDERATIONS

COMMENTS

- Renal failure and associated azotemia occur uncommonly with PHPTH.
- A normal serum PTH level is consistent with PHPTH when there is concurrent hypercalcemia, because it should be low in response to calcium elevations.

TECHNICIAN TIP

Postoperative (parathyroid ablation/removal) patients should be monitored for the first signs of hypocalcemia (muscle fasciculations/twitching, stiff gait, eventually seizures) as immediate grounds for measuring serum calcium level.

SUGGESTED READING

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Goldstein RE, Atwater DZ, Cazolli DM, et al: Inheritance, mode of inheritance, and candidate genes for primary hyperparathyroid-ism in Keeshonden. J Vet Intern Med 21:199–203, 2007.

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EDITOR: SHERRI IHLE

Hypernatremia

BASIC INFORMATION

DEFINITION

A serum sodium concentration >158 mEq/L in dogs or >165 mEq/L in cats, which represents a deficit of water in relation to the body's sodium stores. Hypernatremia can result from a net water loss or a hypertonic sodium gain.

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs and cats of any age and either sex

GENETICS & BREED PREDISPOSITION

Primary hypodipsia in miniature schnauzers

RISK FACTORS

Inadequate access to water, fever, high ambient temperature, altered mental status

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- *Pure water deficit:* a net water loss in the absence of sodium deficit; majority of water loss is from the intracellular fluid compartment
- *Hypotonic fluid loss:* water loss along with sodium loss; most common form encountered in veterinary medicine
- Impermeant solute gain

HISTORY, CHIEF COMPLAINT

- Often discovered incidentally
- When present, signs of hypernatremia largely reflect central nervous system dysfunction.
- Severity of signs correlates positively with the degree of hypernatremia and rapidity of onset.

PHYSICAL EXAM FINDINGS

- Primarily neurologic signs: seen when plasma sodium is >170 mEq/L. Signs are due to movement of water out of brain cells.
- Tachypnea, muscular weakness, restlessness, ataxia, seizure, coma. Polydipsia may occur initially but dissipates as disease progresses.
- With hypotonic fluid loss, signs of volume depletion (hypotension, dehydration) may be present.
- With impermeant solute gain (rare), signs of volume overload (overhydration: serous nasal discharge, dyspnea from pulmonary edema) may be present.
- Other findings depend on underlying condition.

ETIOLOGY AND PATHOPHYSIOLOGY

- *Pure water deficit:* a net water loss from the body in the absence of sodium deficit; majority of water loss is from the intracellular fluid compartment. Causes include:
  - Unreplaced insensible losses
  - Hypodipsia: primary hypodipsia in miniature schnauzers
  - Neurogenic (central) diabetes insipidus: posttraumatic, neoplastic, idiopathic, meningitis, encephalitis, hypoxic or ischemic encephalopathy
  - Nephrogenic diabetes insipidus: renal disease, hypercalcemia, hypokalemia
- *Hypotonic fluid loss:* water loss along with some degree of sodium loss. Causes include:
  - Renal: loop diuretics, osmotic diuretics, postobstructive diuresis

- Polyuric phase of acute tubular necrosis, intrinsic renal disease
- Gastrointestinal: vomiting, diarrhea, osmotic cathartics
- Cutaneous: burns

- *Impermeant solute gain.* Causes include:
  - Administration of hypertonic sodium bicarbonate, sodium chloride, or hypertonic fluid
  - Ingestion of table salt or salt water
  - Hyperaldosteronism or hyperadrenocorticism

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

See Etiology and Pathophysiology above.

INITIAL DATABASE

- CBC, serum biochemistry profile, urinalysis. By definition, identifies hypernatremia. Provides further information regarding possible underlying causes (e.g., renal parameters)
- Serum osmolality (calculated or measured)
  - Elevated with hypernatremia of any cause; sodium is the main determinant of serum osmolality.
  - Serial measurement possible for monitoring response to treatment
  - Advantage of measured osmolality over calculated osmolality or serum sodium measurement alone: measurement of otherwise undetected high-osmolality molecules (e.g., ethylene glycol)

ADVANCED OR CONFIRMATORY TESTING

As dictated by history, physical exam findings, and preliminary tests. May include adrenocorticotropic hormone stimulation test, thyroid profile, imaging studies of the brain.

TREATMENT

TREATMENT OVERVIEW

- Replace water and electrolytes, restore effective circulating volume, and treat underlying cause. Rate of correction depends on whether hypernatremia was acute in onset (began within the previous 24 hours, as with recent administration of hypertonic saline) or chronic or unknown in time of onset (vast majority; hypernatremia is known or suspected to have begun >24 hours earlier, as with most naturally occurring hypernatremia).
  - Acute: replace at a rate such that the decrease in serum sodium does not exceed 1 mEq/L/h and does not exceed 24 mEq/L/day
  - Chronic or unknown: replace at a rate such that the decrease in serum sodium does not exceed 0.5 mEq/L/h and does not exceed 12 mEq/L/day
- The cornerstone of successful treatment is frequent monitoring of the patient's mentation and serum sodium concentration.

ACUTE GENERAL TREATMENT

- *Pure water loss:* calculate water deficit. Replace the deficit over 24-48 hours with 5% dextrose in water, not exceeding limit (see Pearls and Considerations below).
  - Water deficit (Liters) = body weight (kg) × 0.6 × ([present serum Na/desired serum Na]-1).
  - Administer calculated water deficit over the recommended time frame for acute or chronic hypernatremia.
  - Total body water is normally 60% of body weight. This value (0.6 in the equation) can be increased in pediatric/neonates or can be decreased in cachectic animals.
- *Hypotonic fluid loss:* replace with a limited amount of isotonic crystalloids to improve hemodynamic parameters. Once improved/stabilized, switch to a hypotonic solution and administer/titrate based on monitoring, not exceeding limit.
- *Gain of impermeant solute:* 5% dextrose diuresis and administer/titrate based on monitoring, not exceeding limit (see Pearls and Considerations below).
- Persistent hypernatremia despite fluid therapy adjustments:
  - Central diabetes insipidus: DDAVP, 1 mcg/kg SQ q 8-12 h; or aqueous vasopressin, 1-2 U/cat or 3-5 U/dog q 24-48 h (see p. 296)
  - Nephrogenic diabetes insipidus: thiazide diuretics (see p. 296)

CHRONIC TREATMENT

- Remove offending drugs.
- Treat underlying condition.

POSSIBLE COMPLICATIONS

Rapid correction of hypernatremia can lead to cerebral edema as excess water moves into brain cells. The signs of cerebral edema may not be seen for 2-3 days post correction of hypernatremia. Edema is more likely to occur in patients with prolonged hyperosmolality and aggressive hypotonic fluid replacement.

RECOMMENDED MONITORING

Check serum electrolytes q 4-8 h.

PROGNOSIS AND OUTCOME 

Mortality varies according to the severity of hypernatremia, rapidity of onset, and underlying condition

PEARLS & CONSIDERATIONS 

COMMENTS

When correcting hypernatremia, the rate of decrease of blood/serum sodium concentration must not exceed 0.5 mEq/L/h.

- Decreasing sodium concentration at a rate >0.5 mEq/L/h risks complications such as cerebral edema.
- Exception: up to 1 mEq/L/h is possible if hypernatremia is known to have begun within 24 hours (e.g., hypertonic saline administration).

PREVENTION

- Ensure adequate drinking water access. prevent excessive drinking of salt water or consumption of pure salt.
- Do not administer table salt as an emetic in cases of toxin ingestion. Use hydrogen peroxide or syrup of ipecac instead.

SUGGESTED READING

DiBartola SP: Disorders of sodium and water: hypernatremia and hyponatremia. In diBar-tola SP, de Morais HSA, eds: Fluid therapy in small animal practice, ed 3, St Louis, 2006, Saunders Elsevier, pp 47–79.

Temo K, et al: Hypernatremia in critically ill cats: pathophysiology. Compend Contin Educ Pract Vet 26:422–433, 2004.

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EDITOR: ETIENNE CÔTÉ

Hyperlipidemia

BASIC INFORMATION

DEFINITION

Increased fasting blood cholesterol and/or triglyceride (TG) concentrations; a well-recognized (dogs) to uncommon (cats) disorder in small animals.

SYNONYMS

Hyperlipoproteinemia, lipemia

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Primary: middle-aged/older (dogs); variable age of onset (cats)
- Secondary: varies with primary cause

GENETICS & BREED PREDISPOSITION

- Idiopathic hypertriglyceridemia: miniature schnauzers, Burmese cats
- Idiopathic hypercholesterolemia: Doberman pinschers, rottweilers, briards, rough collies
- Feline familial hyperlipidemia: autosomal recessive trait in domestic short-haired cats

RISK FACTORS

- Obesity (dogs)
- Drugs: glucocorticoids, phenobarbital (dogs), megestrol acetate (cats)
- High-fat diets or parenteral nutrition
- Hypothyroidism
- Hyperadrenocorticism
- Pancreatitis
- Diabetes mellitus
- Protein-losing nephropathy
- Cholestasis

ASSOCIATED CONDITIONS & DISORDERS

- Pancreatitis
- Vacuolar hepatopathy
- Gallbladder mucocele
- Seizures
- Xanthomas (intraocular or cutaneous nodules/plaques composed of lipid-containing histiocytes)
- Peripheral neuropathy
- Behavior changes

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Primary hyperlipidemia:

- Dogs:
  - Idiopathic hyperlipidemia/idiopathic hypertriglyceridemia
    - Increased very low-density lipoproteins (VLDL)
    - ± Increased chylomicra (CM)
    - ± Mild hypercholesterolemia

    - Idiopathic hyperchylomicronemia
        - Increased TG and CM
    - Idiopathic hypercholesterolemia
        - Increased low-density lipoproteins (LDL)
- Cats:
    - Familial hyperlipidemia/hyperchylomicronemia:
        - Increased CM and VLDL
        - Inactive lipoprotein lipase Secondary Hyperlipidemia: *see Risk Factors above*

HISTORY, CHIEF COMPLAINT

- Clinical signs, when present, are the result of hypertriglyceridemia; hypercholesterolemia virtually never causes clinical signs.
- Dogs: vomiting, diarrhea, abdominal discomfort (pancreatitis), seizures, anorexia, lethargy
- Cats: cutaneous/subcutaneous masses (xanthomas), lameness (neuropathy)

PHYSICAL EXAM FINDINGS

- Hypertriglyceridemia
    - Dogs: signs of abdominal discomfort, hepatosplenomegaly, lipemia retinalis, lipemic aqueous humor, intraocular xanthogranuloma
    - Cats: xanthomas, decreased reflexes (peripheral neuropathy), pale mucous membranes, lipemia retinalis, lipid keratopathy, lipemic aqueous humor
- Hypercholesterolemia
    - Dogs: lipemia retinalis, lipid keratopathy, arcus lipoides corneae

ETIOLOGY AND PATHOPHYSIOLOGY

- Lipoproteins
    - Lipids (TG and cholesterol) do not circulate free in circulation; rather, they are complexed in varying proportions as circulating particles called *lipoproteins.*
    - Four major types (listed in decreasing order of TG concentration and increasing order of cholesterol concentration in the lipoprotein particle):
        - CM
        - VLDL
        - Low-density lipoproteins
        - High-density lipoproteins
- Hyperlipidemia
    - From excessive dietary lipid, excessive endogenous lipid production/mobilization, and/or impaired lipid clearance from blood. Types:
        - Postprandial hyperlipidemia:
            - CM in circulation 2-10 hours after fatty meal
        - Primary hyperlipidemia:
            - Inborn error in lipoprotein metabolism
                - Lack of lipoprotein lipase activity
                - Absence of surface apolipo-proteins (CII)
        - Secondary hyperlipidemia:
            - Underlying disease (see Risk Factors above) causing altered lipid metabolism
            - Secondary hyperlipidemias are more common than primary.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Lipemic serum suggests hypertriglyceridemia; hypercholesterolemia alone does not cause serum to appear lipemic. Persistent increases in triglycerides or cholesterol after a 12-hour fast indicate disease and should prompt investigation for secondary causes of hyperlipidemia.

DIFFERENTIAL DIAGNOSIS

Postprandial hyperlipidemia

INITIAL DATABASE

- CBC, serum biochemical profile (including serum cholesterol and TG concentrations), urinalysis:
  - Perform after > 12-hour fast
  - Identify causes of secondary hyperlipidemia
- Subsequently, consider:
  - Tests for hypothyroidism (see p. 588)
  - Tests for hyperadrenocorticism (see p. 548)
  - Urine protein/creatinine ratio
  - Abdominal ultrasound
  - Serum trypsinlike immunoreactivity
  - Pre- and postprandial bile acids

ADVANCED OR CONFIRMATORY TESTING

- If a cause of secondary hyperlipidemia is not found, additional tests may help define the primary hyperlipidemia.
- Chylomicron (CM) test: lipemic serum is left undisturbed for 12 hours at 4°C.
  - If CM are present they will form a surface "cream layer" over a clear infranatant of serum, suggesting a disorder of CM metabolism such as idiopathic hyperchylomicronemia. A nonfasting sample is an important differential.
  - If the sample remains turbid, VLDL retention (and therefore a secondary hyperlipidemia such as that due to diabetes mellitus) is likely.
  - Formation of a "cream layer" over turbid serum suggests a combined disorder.
- Lipoprotein electrophoresis, ultracentrifugation, and precipitation tests can be useful but are not routinely available.
- Lipoprotein lipase activity can be assessed by measuring TG (± lipoprotein) concentrations before and 15 minutes after heparin (dog: 90 IU/kg IV; cat: 40 IU/kg IV) administration. If no change, lipoprotein lipase inactivity is suspected.

TREATMENT

TREATMENT OVERVIEW

Treatment primarily consists of management of secondary causes and nutritional therapy. Medications are reserved for unresponsive severe cases of hyperlipidemia (TG > 500 mg/dL or cholesterol > 800 mg/dL). Goal of treatment is to reduce fasting TG or cholesterol concentrations to < 500 mg/dL. Treatment is lifelong.

ACUTE GENERAL TREATMENT

Treat underlying diseases.

CHRONIC TREATMENT

- Hypertriglyceridemia
  - Dietary management should be the mainstay of treatment (see Nutrition, below)
  - Menhaden fish oils: 200-330 mg/kg/d PO (dogs); *or*
  - Gemfibrozil: 200 mg/kg PO q 24 h (dogs); 7.5-10 mg/kg PO q 12 h (cats); *or*
  - Niacin 100 mg PO q 24 h (dogs)
- Hypercholesterolemia
  - A primary cause is often (almost always) present, and its control resolves the hypercholesterolemia.
  - Otherwise, dietary management should be the mainstay of treatment (see Nutrition, below).
  - Cholestyramine: 1-2 g PO q 12 h (dogs); *or*
  - Lovastatin: 10-20 mg PO q 24 h (dogs)

NUTRITION/DIET

- Hypertriglyceridemia
  - Dietary fat restriction (dog: <20% metabolizable energy [ME]; cat: <25% ME)
  - If the low-fat diet is unsuccessful, then an ultralow-fat (10-12% ME) homemade diet can be designed by a nutritionist.
- Hypercholesterolemia
  - Low-fat diet with increased amounts of soluble fiber

DRUG INTERACTIONS

- Cholestyramine can interfere with the absorption of other oral medications (digoxin, ursodiol, calcitriol, dihydrotachysterol)
- Lovastatin's metabolism may be inhibited by clarithromycin and cyclosporine, and lovastatin may increase the toxicity of cyclosporine.

POSSIBLE COMPLICATIONS

- Gemfibrozil may cause abdominal discomfort, vomiting, diarrhea, and hepatopathy.
- Niacin may cause vomiting, diarrhea, erythema, pruritus, and hepatopathy.
- Cholestyramine may cause constipation and hypertriglyceridemia.
- Lovastatin may cause lethargy, diarrhea, muscle pain, and hepatopathy.

RECOMMENDED MONITORING

- Monitor plasma triglycerides 1 month after initiation of low-fat diet, then every 6-12 months.
- Monitor hematologic/biochemical parameters with gemfibrozil, niacin, or lovastatin.
- Monitor plasma TG with cholestyramine.

PROGNOSIS AND OUTCOME

- Successful management depends on adequate control of underlying diseases and reduction of plasma lipid concentrations.
- Cats with peripheral neuropathies:
    - Clinical signs generally resolve within 4-12 weeks of instituting diet change.

PEARLS & CONSIDERATIONS

COMMENTS

- Hyperlipidemia in fasted patients (>12 hours) is abnormal.
- Hypertriglyceridemia often signals underlying disease.
- Lipemic plasma is an indication of hypertriglyceridemia, not hypercholesterolemia.
- Hypercholesterolemia may indicate the presence of an underlying disorder but rarely causes significant clinical disease.

TECHNICIAN TIP

If the supernatant in a hematocrit tube is cloudy, and the patient has not eaten in >12 hours, the most likely reason is hyperlipidemia (specifically, elevated triglycerides). This valuable clue should be mentioned to the attending veterinarian, as it may influence treatment and prognosis.

PREVENTION

- Treat predisposing disorders.
- Monitor TG concentrations in susceptible breeds.

SUGGESTED READING

Johnson MC: Hyperlipidemia disorders in dogs. Compend Contin Educ Pract Vet 27(5):361, 2005.

Xenoulis PG, Steiner JM: Lipid metabolism and hyperlipidemia in dogs. Vet J 183:12–21, 2010.

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1ST EDITION AUTHOR: ANDREA NICASTRO

Hyperkalemia

BASIC INFORMATION

DEFINITION

A serum potassium concentration in excess of 5.5 mEq/L. Amounts exceeding 7.5 mEq/L are potentially harmful.

EPIDEMIOLOGY

SPECIES, AGE, SEX

Any patient can be affected.

GENETICS & BREED PREDISPOSITION

- Actual hyperkalemia: standard poodles with Addison's disease
- Pseudohyperkalemia: Akita, English springer spaniel with phosphofructokinase deficiency

RISK FACTORS

- Renal impairment
- Urinary obstruction
- Urinary bladder rupture
- Hypoadrenocorticism
- Mineral acid metabolic acidosis
- Excess intake

ASSOCIATED CONDITIONS & DISORDERS

Bradycardia

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Acute and chronic

HISTORY, CHIEF COMPLAINT

- Acute: dramatic and life threatening; produces diffuse muscle weakness, mental depression, anorexia. Stranguria accompanies lower urinary outflow obstructions. Vomiting common with acute renal failure and hypoadrenocorticism.
- Chronic: slower in onset and not as dramatic. Decreased appetite, weight loss, intermittent vomiting and diarrhea can occur.

PHYSICAL EXAM FINDINGS

- Generalized muscle weakness
- Weak pulse
- Prolonged capillary refill time
- Bradycardia, especially in setting of dehydration (where heart rate would normally be increased)
- Irregular heart rate
- Body temperature normal or hypothermia

ETIOLOGY AND PATHOPHYSIOLOGY

Etiology:

- Increased potassium intake
- Potassium translocation from intracellular to extracellular fluid space:

    - Mineral acid-caused metabolic acidosis
    - Insulin deficiency
    - Catecholamine increases
    - Hypertonicity
    - Massive tissue destruction (rare in dogs and cats)
- Decreased excretion:
    - Hypoaldosteronism
    - Acute renal failure
    - Urinary bladder rupture or outflow obstruction
    - Type 4 renal tubular acidosis
    - Certain drugs (uncommon)

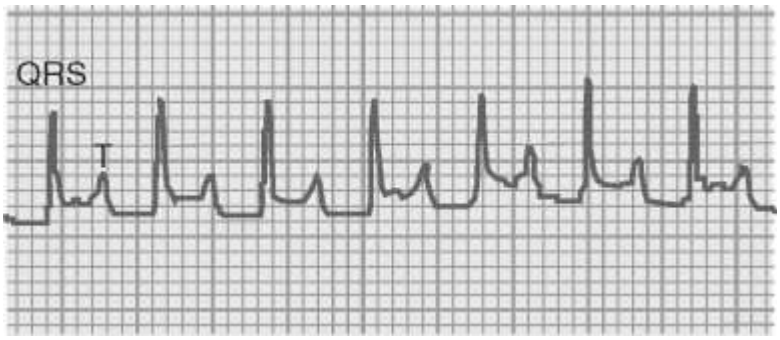
Pathophysiology:

- Affects primarily skeletal and cardiac muscle tissues
- Life-threatening effects on heart:
    - Depressed excitability and conduction velocity
    - Secondary to persistent depolarization and inactivation of the sodium channels within the cell membranes, causing cardiac conduction abnormalities
- Skeletal muscle weakness occurs.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

- Presumptive with history, physical examination, and electrocardiogram (ECG). Confirmed with specific laboratory measurement.
- Traditionally, experimentally induced hyperkalemia has been reported to cause a pattern of electrocardiogram (ECG) abnormalities that worsened in parallel to the degree of the elevated serum potassium concentration. These included peaked or depressed T wave, decreased R-wave and P-wave amplitudes, prolongation of PR interval, eventual disappearance of P-wave, widening of QRS complexes, heart blocks, aberrant atrioventricular conduction, and eventually ventricular fibrillation or asystole.
- A recent clinical study by Tag and Day shows that sick dogs and cats do not follow the predicted pattern mentioned above. Some with considerably elevated serum potassium concentrations (>7.0 mEq/L) can have either normal ECG patterns or show minimal changes that would be expected only at lower serum levels. Some patients with serum potassium levels <7.0 mEq/L had more severe ECG patterns than would be expected at those lower serum levels. However, this same article did not attempt to correlate the ECG of any particular serum potassium concentration with simultaneous serum sodium measurements.
- Confirmed with laboratory serum potassium quantitation



HYPERKALEMIA ECG from a cat with urethral obstruction and hyperkalemia (serum K^+ = 7.1 mEq/L) showing atrial standstill. No P waves are seen, but the R-R rhythm is regular, typical of atrial standstill. The heart rate is 210/min, demonstrating that in cats, unlike dogs, a rapid heart rate is still consistent with hyperkalemia. There is mild ST-segment elevation, suggesting myocardial hypoxia. Lead V2, 25 mm/sec, 1 cm = 1 mV.

DIFFERENTIAL DIAGNOSIS

- Any cause of hypovolemic shock
- Primary underlying myocardial disease

INITIAL DATABASE

- Thorough history and physical examination
- CBC
- Serum biochemistry profile:
  - Serum electrolytes: elevated potassium (by definition); sodium may be concurrently low with hypoadrenocorticism, enteritis, renal disease, or pregnancy; chloride.
  - Blood urea nitrogen, creatinine: elevated with prerenal (e.g., hypoadrenocorticism), renal, or postrenal (e.g., urethral obstruction or urinary bladder rupture) azotemia.
  - Total CO2/Hco3¯decreased with metabolic acidosis
  - Glucose: may be decreased in hypoadrenocorticism, sepsis.
- Urinalysis: isosthenuria concurrent with azotemia in renal failure or in hypoadrenocorticism.
- Blood gas: pH, Hco3¯, or Tco2 helpful
- Abdominal imaging

TREATMENT

TREATMENT OVERVIEW

- Antagonize myocardiotoxicity.
- Treat the underlying cause.
- Stop drugs known to increase serum potassium concentration.

ACUTE TREATMENT

The main object is to either antagonize the effects or decrease the serum potassium concentration.

- Calcium gluconate 10% solution (0.5-1.5 mL/kg IV) immediately antagonizes myocardiotoxicity without actually lowering serum potassium concentration
- Lowering the serum potassium:
  - Sodium bicarbonate, 1-2 mEq/kg IV bolus (minimally effective)
  - Regular insulin and glucose, give 0.25-0.5 units of insulin/kg IV, covering each unit of insulin administered with 2 g dextrose (2 g =4 mL 50% dextrose)
- ECG monitoring
- Treat the underlying cause.
- Repeat serum potassium measurement.

CHRONIC TREATMENT

Treat any underlying disease:

- Hypoadrenocorticism (see p. 548): desoxycorticosterone pivalate and prednisone
- Renal tubular acidosis type 4: furosemide
- Chronic renal disease: fluid therapy or dialysis

DRUG INTERACTIONS

- Can impair potassium excretion
- Avoid ACE inhibitors and aldosterone antagonists during the hyperkalemia or if there is a predisposition for recurrence.

POSSIBLE COMPLICATIONS

Cardiac arrest, death

RECOMMENDED MONITORING

- Periodic serum sodium and potassium monitoring with hypoadrenocorticism
- Follow-up renal evaluations

PROGNOSIS AND OUTCOME

- Guarded for renal failure
- Good for hypoadrenocorticism

PEARLS & CONSIDERATIONS

- Do a lead II ECG on all patients that are suspect for having hyperkalemia.
- Bradycardia in a dehydrated patient is inappropriate; hyperkalemia should be considered as one of the causes.
- Calcium gluconate IV works within a few minutes, sodium bicarbonate IV works within 15 minutes, and regular insulin and dextrose work within 30 minutes.
- Other causes of pseudohyperkalemia: thrombocytosis, very high white blood cell counts, blood samples put in ethylenediamine tetraacetic acid (EDTA) tubes.
- In cats, hyperkalemia does not always cause bradycardia; hyperkalemic cats may be tachycardic even with severe hyperkalemia.
- On an ECG, peaked T waves are often normal; the transition from normal T wave to peaked T wave, however, is very suggestive of evolving hyperkalemia.

PREVENTION

Timely treatment of predisposing cause

CLIENT EDUCATION

Become acquainted with the early signs of the primary disorder.

SUGGESTED READING

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Hyperemia

Additional Images Available on Website

BASIC INFORMATION

DEFINITION

- Active hyperemia: an increased volume of blood in an affected tissue or area due to arterial and arteriolar dilation
- Passive hyperemia: increased volume of blood in an affected tissue or area due to obstruction of blood outflow

SYNONYMS

- Active hyperemia: arterial hyperemia, reactive hyperemia, engorgement, flushing, erythema, injected mucous membranes
- Passive hyperemia: venous hyperemia, congestion

EPIDEMIOLOGY

SPECIES, AGE, SEX

No species, age, or sex predilection except as dependent on underlying etiology

RISK FACTORS

- Increased tissue metabolic demand (e.g., fever, physical exertion)
- Vascular occlusion: extravascular or intravascular

GEOGRAPHY AND SEASONALITY

Vasodilatory cooling related to high environmental heat is a normal manifestation of hyperemia.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Primary complaint:
  - Obvious extravascular occlusion such as limb constriction
  - Gross tissue changes
- Secondary finding:
  - Clinical sign noted in addition to other associated abnormal findings
  - Incidental finding of no clinical significance (e.g., due to anxiety, physical activity, or hot weather)
- Hyperemia may also be classified as active or passive, or as regional or generalized.

HISTORY, CHIEF COMPLAINT

- Highly variable depending on underlying cause
- Examples (generalized hyperemia):
  - Recent exposure to allergen (insect bite, vaccine, food allergen, other)
  - Exposure to infectious agent
  - Exposure to high environmental temperature (enclosed in car during hot weather, other)
  - Anxiety, restlessness (e.g., pheochromocytoma, mast cell disease, polycythemia)
  - None (incidental finding during routine examination)

PHYSICAL EXAM FINDINGS

- Since hyperemia is a clinical sign and not a disease entity, specific physical findings are dependent on the underlying etiology.
- Generalized hyperemia:
  - Tachycardia, tachypnea, hyperthermia
  - Increased respiratory effort
  - Shortened capillary refill time

    - Weakness, collapse
    - Episodic increased levels of activity
- Localized hyperemia:
    - Regional dermal redness
    - Possible swelling and/or pain in the region

ETIOLOGY AND PATHOPHYSIOLOGY

Arteriolar dilation due to sympathetic neurogenic mechanisms or exposure to or release of local or systemic vasoactive substances such as adenosine or nitric oxide in response to altered blood flow.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

As hyperemia is a clinical sign associated with a wide variety of conditions, the first step is to rule out obvious causes via a careful history and physical examination and determine whether the presence of hyperemia is clinically significant.

DIFFERENTIAL DIAGNOSIS

- Any condition causing redness, swelling, or inflammation such as infectious, inflammatory, immune-mediated, neurogenic, toxic, allergic
- Any cause of hyperthermia such as environmental, exercise, infectious, inflammatory, immune-mediated, neurogenic, toxicity
- Rebound vasodilation after ischemic crisis such as external constriction (rubber band, collar), embolic occlusion
- Altered perfusion states such as severe hypertension and hypotensive crises such as cardiac arrest
- Decreased venous return states: cardiac, hepatic, venous occlusion
- Episodic hyperemia: mast cell tumor, pheochromocytoma
- Acute contact dermatitis
- Congenital: telangiectasis
- Vasculitis
- Carbon monoxide intoxication
- Polycythemia
- Acute allergic reaction, drug reaction

INITIAL DATABASE

- Temperature, heart rate, respiration rate
    - Hyperthermia warrants consideration of true fever (infectious, inflammatory, neoplastic causes; see p. 589) versus environmental hyperthermia (hot weather, thick haircoat, anxiety, etc.).
- Diascopy: superficial lesions blanch with external pressure, such as with a glass slide.
    - This maneuver helps confirm whether hyperemia is present versus a normal coloration for the animal.

ADVANCED OR CONFIRMATORY TESTING

Use of these tests depends on determination of need. For example, in animals that are otherwise clinically normal (routine exam), behavioral agitation/anxiety, benign environmental hyperthermia, and exercise are common causes of hyperemia that generally do not warrant further evaluation.

- Blood pressure measurements
    - Systemic
    - Localized (if suspect embolic occlusion)
- CBC (infectious, inflammatory, neoplastic, polycythemia)
- Serum biochemistry panel (hepatic, renal elevations)
- Radiographs: organomegaly, neoplasia
- Neurologic evaluation (in cases of suspected intoxication or other systemic disorders with neurologic effects): see p. 1311
- Abdominal ultrasound (neoplasm, infection/abscess, chronic passive congestion)
- Echocardiogram (endocarditis, other)
- CT or MRI for embolism evaluation
- Aspirates and/or biopsies: masses/lesions
- Tickborne disease titers
- Blood gas analysis
- Cooximetry: carbon monoxide intoxication

TREATMENT

TREATMENT OVERVIEW

Goal of treatment is resolution of the underlying etiology, with special attention paid to ensuring adequate tissue perfusion.

ACUTE GENERAL TREATMENT

Supportive as needed: analgesia, oxygen, restoration of perfusion, cooling of affected region.

CHRONIC TREATMENT

Treatment as appropriate for underlying etiology

POSSIBLE COMPLICATIONS

- Reperfusion injury
- Tissue necrosis

PROGNOSIS AND OUTCOME

Highly variable depending on underlying etiology

PEARLS & CONSIDERATIONS

COMMENTS

- Presenting signs (true chief complaint, versus routine visit for preventive/annual exam) are extremely valuable in determining the importance of a patient's hyperemia.
- Intermittent/episodic hyperemia associated with behavioral changes, cardiac arrhythmias, or other systemic signs should arouse the suspicion of mast cell tumor or pheochromocytoma.

SUGGESTED READING

Lima I, et al: The peripheral perfusion index in reactive hyperemia in critically ill patients. Crit Care 8(Suppl 1):P53, 2004.

AUTHORS: LISA M. ABBOTT, ADAM J. REISS

EDITOR: ETIENNE CÔTÉ

Hypercalcemia

BASIC INFORMATION

DEFINITION

Elevation in serum calcium concentration

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Hypercalcemia can occur in dogs or cats of either gender and any age; depends on the underlying cause.
- Normal young dogs, cats <6 months old: commonly show mild, incidental hypercalcemia

GENETICS & BREED PREDISPOSITION

Depends on etiology, but there is a definite inherited predisposition for primary hyperparathyroidism in the keeshond.

RISK FACTORS

Depends on etiology

CONTAGION & ZOONOSIS

Rarely relevant. Common-source infections possible with systemic mycoses.

GEOGRAPHY AND SEASONALITY

Granulomatous diseases (systemic mycoses, schistosomiasis): specific geographic distributions

ASSOCIATED CONDITIONS & DISORDERS

Renal failure (potentially irreversible)

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Polyuria/polydipsia
- Malaise: lethargy, weakness, decrease in appetite. Each is mild in dogs and cats with hypercalcemia alone. Clinical signs are more worrisome if underlying cause is a condition other than primary hyperparathyroidism.
- Other signs depend on underlying problem.
- In reviewing the most common causes of hypercalcemia, the list includes: lymphosarcoma (15%-30% of lymphoma dogs), chronic renal failure (<5% of renal failure dogs), vitamin D toxicosis, hypoadrenocorticism, apocrine gland carcinoma of the anal sac, primary hyperparathyroidism, multiple myeloma, histoplasmosis (uncommon), blastomycosis (uncommon), various other malignancies (hypercalcemia uncommon in each). In general, all these conditions in dogs are associated with worrisome clinical signs, EXCEPT those dogs with primary hyperparathyroidism.

PHYSICAL EXAM FINDINGS

- Generally reflective of the underlying cause. For example, lymphadenopathy is possible with lymphoma, other malignancies, or granulomatous/fungal disease.
- No physical finding is pathognomonic for a specific cause of hypercalcemia.
- Rectal palpation: up to 30% of anal sac adenocarcinomas are found incidentally, emphasizing the importance of rectal palpation as a routine part of physical examination of dogs.

ETIOLOGY AND PATHOPHYSIOLOGY

- Normal range of serum total calcium concentration:
  - Dog: 9.5-11.5 mg/dL (2.32-3.06 mmol/L)
  - Cat: 9.0-11.5 mg/dL (2.20-3.04 mmol/L)
- Dystrophic, soft-tissue mineralization, specifically of nephrons) is more likely to occur if the product of calcium × phosphorus concentrations (in mg/dL) >60-80.
- Approximately 50% of circulating calcium is ionized, 40% is protein bound (mostly to albumin), and 10% is bound to other molecules (lactate, citrate, etc.).
- Mechanisms of causative disorders:
  - Primary hyperparathyroidism: elevated parathyroid hormone concentrations activate osteoclastic resorption of calcium from bone, renal conservation, and intestinal absorption
  - Hypercalcemia of malignancy: neoplastic cells elaborate parathyroid hormone-related protein (PTHrP: actions similar to parathyroid hormone [PTH]).
  - Granulomatous disease: elaboration of PTHrP-like substances
  - Idiopathic hypercalcemia of cats: this condition is poorly understood. Many hypercalcemic cats have underlying lymphoma. Some mildly hypercalcemic cats are predisposed to urolith formation. If uroliths are not present, there may be no reason to treat such cats.
  - Chronic renal failure: renal secondary hyperparathyroidism
  - Vitamin D toxicosis (rodenticide or human prescription medications, e. g., calcipotriene): heightened vitamin D-mediated intestinal calcium absorption, renal calcium conservation
  - Youth: normal bone growth

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Dogs: see Etiology and Pathophysiology and comments under Clinical Presentation, above.
- In hypercalcemic cats, malignancy (30%), renal failure (25%), and urolithiasis (15%) are recognized associations, in addition to idiopathic hypercalcemia and other less common disorders such as primary hyperparathyroidism.

INITIAL DATABASE

- CBC: changes depend on underlying cause
- Serum chemistry panel:
  - Blood urea nitrogen, creatinine, phosphorus: increases common; prerenal or renal
  - Potassium: increase suggests hypoadrenocorticism, acute renal failure, rupture in urinary tract, any illness associated with significant loss of appetite, vomiting, and diarrhea. Remember, in vitro hemolysis will result in dramatic increases in serum potassium, especially in the Akita and Japanese Tosa breeds. Other artifact hyperkalemia is rare.
  - Concomitant hypophosphatemia suggests primary hyperparathyroidism, hypercalcemia of malignancy.
  - Concomitant hyperphosphatemia suggests chronic renal failure, vitamin D toxicosis, hypoadrenocorticism.
- Urinalysis:
  - Hypercalcemia as the sole abnormality (as occurs with primary hyperparathyroidism) is associated with urine specific gravity <1.020 (mean -1.011), with values as low as 1.002. Dogs with this condition usually have low-normal or low BUN, creatinine, and phosphorus (increases in any of these parameters is rare).
  - Isosthenuria with concurrent azotemia and hypercalcemia suggests renal failure, hypoadrenocorticism, or blood and urine samples drawn at different times (no conclusions possible if blood and urine are not obtained simultaneously).
  - Dilute urine (specific gravity <1.020) is commonly associated with urinary tract infection.
  - Uroliths and calcium-containing crystalluria are common in hypercalcemia
- Thoracic radiographs:
  - Metastatic disease or sternal lymphadenopathy may suggest neoplasia (rule out fungal disease, if appropriate).
  - Cranial mediastinal mass (thymic?) is common in dogs that have hypercalcemia secondary to lymphosarcoma.
  - Radiographs should be assessed for any lytic bone lesion that might be suggestive of multiple myeloma (or other metastatic cancer), as well as for any pulmonary mass or masses consistent with neoplasia.
- Abdominal imaging (ultrasound ± radiographs):
  - Lesions suggesting malignancy (lymphadenopathy, hepatosplenomegaly, possible metastases)
  - Uroliths (calcium phosphate, calcium oxalate, or both) and bladder wall thickening due to chronic infection: common in canine hyperparathyroidism
  - Assess renal structure. Renal dystrophic mineralization due to chronic severe hypercalcemia usually is not apparent radiographically or ultraso-nographically.

ADVANCED OR CONFIRMATORY TESTING

- Ionized calcium: biologically active component of serum calcium. Elevated with primary hyperparathyroidism, hypercalcemia of

malignancy, and vitamin D toxicosis, but normal or low with chronic renal failure.
- Serum PTH and PTHrP concentrations: PTH should be undetectable in response to hypercalcemia of any cause. PTH values within reference range or higher (and ionized hypercalcemia) are consistent with primary hyperparathyroidism. Undetectable PTH and detectable PTHrP consistent with hypercalcemia of malignancy (lymphoma, apocrine gland carcinoma of the anal sac).
- Serum vitamin D concentrations: if suspect rodenticide intoxication
- Cervical ultrasound: ultrasound examination of the neck by a skilled ultrasonographer often allows visualization of a mass involving one or more parathyroid gland(s) (usually 4-8 mm in greatest diameter) in dogs with primary hyperparathyroidism. Dogs with renal secondary hyperparathyroidism have enlargement of 2, 3, or all 4 parathyroid glands.
- Confirmatory testing based on abnormalities identified (e.g., fine-needle aspiration of enlarged lymph node[s])

TREATMENT

THERAPEUTIC GOAL(S)

- Rapid lowering of serum calcium concentration is NOT necessary, even with extremely increased values (15-23 mg/dL) if the product of calcium × phosphorus (in mg/dL) is <60. This is often the case in dogs with primary hyperparathyroidism, whose product is usually <45. In contrast, dogs and cats with normal serum calcium and increased serum phosphorus, as with chronic renal failure, must have the phosphorus and calcium × phosphorus decreased to avoid nephron damage and worsening renal failure.
- Successful treatment of underlying cause will decrease the serum calcium.

ACUTE GENERAL TREATMENT

- *Primary:* most efficacious:
  - IV fluid therapy (calcium free; e.g., avoid lactated Ringer's solution).
    - Dilution of serum calcium and phosphorus concentrations, improvement in renal perfusion and glomerular filtration rate
    - Rate of 100-150 mL/kg/d (twice maintenance) plus any dehydration deficit (mL replacement = % dehydration [5 to 15] × body weight [kg] × 10) should be administered over the first 24 hours assuming no heart disease, oliguria, or other factor predisposing to intolerance of volume load: adjust according to clinical signs.
  - Furosemide: 2-3 mg/kg IV q 4-8 h. Calciuric diuretic (unlike thiazide diuretics or spironolactone, which do not promote calcium excretion). Prolonged use in hypercalcemic patients with renal insufficiency is not recommended, especially if the patient is anorexic and not receiving IV fluids.
  - Glucocorticoids: prednisone 1-2 mg/kg PO q 12 h or dexamethasone 0.1-0.2 mg/kg PO q 12 h. Decrease intestinal calcium absorption, increase renal calcium excretion. Since lymphoma is common cause of hypercalcemia, and glucocorticoids can interfere with a definitive diagnosis, diagnostic samples should be obtained before (e.g., lymph node aspirates) or within a maximum of 24 hours after the first dose of prednisone (e.g., for procedures requiring general anesthesia or refenal, such as bone marrow aspirate, liver or intestinal biopsy, etc.).
- *Secondary:* generally less efficacious:
  - Calcitonin: 4-6 IU/kg SQ q 8-12 h
  - Pamidronate: 1.3 mg/kg in 150 mL 0.9% NaCl, infused over 2 hours; may repeat in 1 week

CHRONIC TREATMENT

Treatment of the inciting cause

POSSIBLE COMPLICATIONS

- Renal failure is not caused by hypercalcemia. In a recent study, dogs with hypercalcemia secondary to primary hyperparathyroidism had a significantly lower incidence of renal failure than dogs that did not have primary hyperparathyroidism.
- Overcorrection (hypocalcemia)

RECOMMENDED MONITORING

- Serum total and ionized calcium
- Renal parameters
- Serum electrolytes

PROGNOSIS AND OUTCOME

- Variable; excellent with hyperparathyroidism if treated appropriately (secondary renal failure is rare) to poor with other disorders (e.g., end-stage chronic renal failure)
- Specific prognosis depends on ability to achieve normocalcemia rapidly and correct underlying cause.

PEARLS & CONSIDERATIONS

COMMENTS

- Correcting total calcium concentration for hypoalbuminemia or hyperalbuminemia is not reliable (measure serum ionized calcium instead).
- Oral consumption of calcium (e.g., calcium carbonate) alone can virtually never cause hypercalcemia.
- The more ill a dog with hypercalcemia, the more likely it has a condition other than primary hyperparathyroidism.

SUGGESTED READING

Feldman EC, Nelson RW: Hypercalcemia and primary hyperparathyroidism. In Feldman EC, Nelson RW, editors: Textbook of canine and feline endocrinology and reproduction, ed 3, St Louis, 2004, Elsevier Saunders, pp 660–715.

AUTHOR: EDWARD C. FELDMAN

EDITOR: ETIENNE CÔTÉ

Hyperaldosteronism, Primary

BASIC INFORMATION

DEFINITION

Autonomous secretion of aldosterone by abnormal zona glomerulosa tissue within the adrenal gland(s).

SYNONYM

Conn's syndrome

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Rare disease of dogs, with increasing recognition in cats
- Older animals (>8 years)
- No sex predilection

ASSOCIATED CONDITIONS & DISORDERS

Hypokalemia; occasionally systemic hyper-tension

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Adrenal tumor
- Bilateral adrenal hyperplasia

HISTORY, CHIEF COMPLAINT

Weakness (may be episodic), lethargy, polyuria/polydipsia, stiff gait, nocturia, loss of vision

PHYSICAL EXAM FINDINGS

Generalized muscular weakness, cervi-cal ventroflexion (cats), stiff gait,

muscle pain, retinal hemorrhages and/or detachment

ETIOLOGY AND PATHOPHYSIOLOGY

- Occurs as a result of an aldosterone-secreting adrenal tumor (adenoma or adenocarcinoma) or hyperplasia of the adrenal zona glomerulosa
- Circulating hyperaldosteronemia leads to increased renal potassium excretion (causing hypokalemia) and increased renal sodium and water resorption. Renin-angiotensin production is sup-pressed.
- Clinical signs result from serum hypokalemia and associated muscle weakness, and hypertension due to extracellular fluid volume expansion.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Hyperaldosteronism should be considered in all middle-aged to older dogs and cats with hypokalemic muscle weakness and/or systemic hypertension. Abdominal ultrasonography is indicated in all cases to rule out an adrenal mass, and diagnosis of hyperaldosteronism should be confirmed using plasma aldosterone and renin concentrations.

DIFFERENTIAL DIAGNOSIS

Adrenal enlargement or mass:

- Cortisol or sex hormone–secreting adrenal tumor
- Pheochromocytoma
- Nonsecretory adrenal mass (see p. 42)

For hyperaldosteronemia:

- Secondary to renal failure, heart failure, or severe hepatic dysfunction

For severe hypokalemia:

- Hypomagnesemia
- Polyuric renal failure
- Hyperthyroidism

INITIAL DATABASE

- CBC, serum biochemical profile, urinalysis, total thyroxine (T4): severe hypokalemia (often <3 mEq/L), normal or slightly increased sodium concentration, minimally concentrated urine, normal or low T4
- Abdominal ultrasound: possible unilateral adrenal mass ± intraabdominal metastasis. Cats with primary hyperaldosteronism secondary to micronodular adrenal hyperplasia may have grossly normal adrenal glands on abdominal imaging.
- Thoracic radiographs: possible metastasis from adrenal adenocarcinoma
- Systolic arterial blood pressure: usually increased >160-180 mm Hg
- Blood gas analysis: metabolic alkalosis

ADVANCED OR CONFIRMATORY TESTING

- Plasma aldosterone concentrations (PAC): usually markedly increased
- Plasma renin concentrations (PRC): may be decreased or within the normal reference range. In theory, an increased plasma renin concentration excludes a diagnosis of primary hyperaldosteronism.
- An increased PAC : PRC ratio may be useful in establishing the diagnosis in those animals without markedly elevated aldosterone concentrations.
- CT scan can be used for detecting subtle changes within the adrenal cortex and to better delineate in the preoperative phase the extent of the adrenal mass.

TREATMENT

TREATMENT OVERVIEW

Treatment is directed at resolving clinical signs associated with hypertension and hypokalemia by normalizing serum potassium and arterial blood pressure. Surgical excision is warranted if an adrenal tumor is identified.

ACUTE GENERAL TREATMENT

- Correct hypokalemia: oral supplementation of potassium (mild hypokalemia) or intravenous administration of potassium-supplemented fluids at a rate of potassium delivery not to exceed 0.5 mEq/L/h
- Manage hypertension (see p. 1068).
- Spironolactone, an aldosterone antagonist, may be effective alone for control of both hypokalemia and systemic hypertension at a dose of 1-2 mg/kg PO q 12 h.

CHRONIC TREATMENT

Surgical excision of the adrenal tumor is recommended if there is no evidence of abdominal or thoracic metastasis. Chronic medical management with spironolactone and oral potassium supplementation can be successful at managing clinical signs if surgery is not feasible.

DRUG INTERACTIONS

Hyperkalemia can occur if spironolactone is used concurrently with other potassium-sparing diuretics or with angiotensin-converting

enzyme inhibitors.

POSSIBLE COMPLICATIONS

- The major potential complication of unilateral adrenalectomy is perioperative hemorrhage.
- There are no reports of postoperative hypoaldosteronism occurring after excision of an aldosterone-secreting adrenal tumor.

RECOMMENDED MONITORING

- Successful surgical management of primary hyperaldosteronism should result in resolution of hypokalemia and hypertension and normalization of serum aldosterone concentrations.
- If chronic medical management is un-dertaken, serial electrolyte and blood pressure monitoring is recommended.

PROGNOSIS AND OUTCOME

- There are few reported cases of primary hyperaldosteronism in dogs, and two small case series in cats.
- Prognosis is fair to guarded in cases of adrenal adenocarcinoma, as metastasis can occur. Medical management of patients with inoperable disease may achieve good short-term control of hypokalemia and systemic hypertension.
- Animals with successfully removed adenomas or adrenal hyperplasia are likely to have a good outcome.
- Data concerning survival times are limited. Reported long-term survival times in cats and dogs with surgical management range from 1-5 years. There are reports of cats surviving from 1-2.7 years with medical management alone.

PEARLS & CONSIDERATIONS

COMMENTS

- In a series of cats with primary hyperaldosteronism secondary to adrenal micronodular hyperplasia, progressive renal insufficiency was observed despite medical management of the hyperaldosteronism and was thought to be a consequence of hyperaldosteronism. Serial monitoring of renal function in these cats is recom-mended.
- Hyperaldosteronism is an important differential diagnosis for highly refractory hypokalemia.

SUGGESTED READING

Ash RA, Harvey AM, Tasker S: Primary hyper-aldosteronism in the cat: a series of 13 cases. J Feline Med Surg 7:173–182, 2005.

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Javadi S, et al: Primary hyperaldosteronism, a mediator of progressive renal disease in cats. Domest Anim Endocrinol 28:85–104, 2005.

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EDITOR: SHERRI IHLE

Hyperadrenocorticism

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Syndrome caused by an excess of one or more adrenal steroids (i.e., cortisol, mineralocorticoids, adrenal androgens) but most commonly cortisol. Other causes of altered adrenal function are discussed in greater detail under their respective headings (see pp. 43, p. 6, and 551).

SYNONYMS

HAC; canine Cushing's syndrome: hypercortisolemia; Cushing's disease: hypercortisolemia secondary to excessive adrenocorticotropic hormone (ACTH) secretion from the pituitary gland

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Most common in dogs. Rare in cats.
- Dogs: middle-aged/old. Rare in dogs <6 years. Slight female predisposition.
- Cats: middle-aged/old (median 10.7 years); no sex predilection

GENETICS & BREED PREDISPOSITION

Dogs:

- Pituitary-dependent hyperadrenocorticism (PDH): small breeds predominate (75% weigh <20 kg). Beagles, boxers, dachshunds, German shepherds, poodles, and terriers are overrepresented.
- Adrenal tumor hyperadrenocorticism (ATH): medium to large breeds predominate (50% weigh >20 kg), dachshunds, German shepherds, Labrador retrievers, poodles, and terriers are overrepresented.

ASSOCIATED CONDITIONS & DISORDERS

- Urinary tract infections
- Urinary calculi
- Systemic hypertension
- Diabetes mellitus
- Sudden acquired retinal degeneration
- Glomerular disease
- Pancreatitis
- Neurologic signs with pituitary macroadenoma
- Thrombosis and pulmonary thromboembolism

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- PDH: 80%-85% of cases
- ATH: 15%-20% of cases
- Iatrogenic: due to glucocorticoid administration

HISTORY, CHIEF COMPLAINT

- Dogs: possibilities include varying combinations of polyuria, polydipsia, polyphagia, pendulous abdomen, excessive bruising, panting, alopecia, clitoral hypertrophy, testicular atrophy, anestrus, weakness/lethargy, exercise intolerance, muscle atrophy, obesity.
- Cats: polyuria, polydipsia, polyphagia, pendulous abdomen, unkempt haircoat, alopecia, fragile (easily torn) skin, lethargy, muscle wasting, obesity

PHYSICAL EXAM FINDINGS

- Dogs: thin skin, bilaterally symmetric alopecia, hepatomegaly, pyoderma, abdominal enlargement, clitoral hypertrophy, testicular atrophy, bruising, muscle wasting, seborrhea, calcinosis cutis, hyperpigmentation, comedones
- Cats: pendulous abdomen, unkempt haircoat, alopecia, fragile (easily torn) skin, muscle wasting, obesity

ETIOLOGY AND PATHOPHYSIOLOGY

- PDH:
  - 80%-90% caused by a pituitary microadenoma (<10 mm in diameter).
  - Pituitary carcinomas, macroadenomas, and corticotroph hyperplasia are rare.
  - Excessive ACTH secretion from the pituitary gland stimulates the adrenal glands (zonae fasciculata and reticularis of the adrenal cortex) to produce excessive amounts of cortisol, resulting in adrenal hypertrophy.
  - The abnormal pituitary cells become less sensitive to inhibition by cortisol, continuing to secrete ACTH despite hypercortisolemia.
- ATH: see p. 43
- Iatrogenic: Exogenous corticosteroids decrease pituitary ACTH secretion (with eventual adrenocortical atrophy), but clinical signs occur as a result of hypercortisolemia.
- Cortisol/glucocorticoids interfere with antidiuretic hormone release (causing polyuria with secondary polydipsia), stimulate protein catabolism (causing muscle loss, weakness, pendulous abdomen, polyphagia), cause hypertension (and secondary proteinuria, associated with low circulating levels of antithrombin III), and compromise normal processes of the skin (causing bilaterally symmetrical alopecia, pyoderma, and/or comedone formation).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

HAC is a clinical disease encompassing overt historical signs observed by the owner, physical examination findings, and biochemical abnormalities attributable to hypercortisolemia. To avoid misdiagnosis (common error), it is essential to interpret the hypothalamic/pituitary/adrenal function tests together with the physical and clinical signs.

DIFFERENTIAL DIAGNOSIS

- See Polyuria/Polydipsia,
- See Polyphagia,
- See Alopecia,

INITIAL DATABASE

- CBC: mature neutrophilia, monocytosis, lymphopenia, eosinopenia (“stress leukogram”), thrombocytosis
- Serum biochemical profile:
  - Dog: increased alkaline phosphatase (ALP), hypercholesterolemia, hyperglycemia (usually mild)
  - Cat: hyperglycemia (80% have concurrent diabetes mellitus), hypercholesterolemia, increased alanine aminotransferase (ALT), increased ALP (30% of cases)
- Urinalysis and bacterial culture: specific gravity <1.020; proteinuria common; infection in 40%-50% of cases regardless of urine sediment
- Abdominal radiographs: hepatomegaly, cystic calculi, mineralized adrenal gland, and/or osteopenia
- Thoracic radiographs (three views): possible metastasis (if adrenal tumor), hypovascular lungs and alveolar infiltrates (secondary thromboembolism), and airway mineralization
- Blood pressure: possible hypertension
- Fundic examination: possible retinal hemorrhage

ADVANCED OR CONFIRMATORY TESTING

- To identify HAC:
  - ACTH stimulation test:
    - Will not differentiate PDH from ATH
    - Sensitivity: dogs: PDH 87%, ATH 60%; cats: 81% for both PDH and ATH
    - Specificity: 85%-90% (dogs)
      - A 15% chance of false-positive exists with chronic nonadrenal illness, so adrenal testing should be postponed if other disease is present.
    - Only test that will identify iatrogenic HAC

        - Protocol: cortisol measured in blood collected before and 1 to 2 hours after administration of exogenous ACTH. Test times vary depending on the ACTH product used and laboratory (see p. 548 for general guidelines).
            - A poststimulation cortisol concentration greater than 25 mg/dL (690 mmol/L) is suspicious for HAC; >30 mg/dL (830 mmol/L) is usually diagnostic for HAC.
    - Low-dose dexamethasone suppression test (LDDS):
        - Can confirm HAC and in some cases discriminate between PDH and ATH
        - Sensitivity: dogs: 85%-95%; cats: 80%
        - Specificity 70%-75% (dogs)
        - A 50% chance of false-positive results with nonadrenal illness, so adrenal testing should be postponed if other disease is present.
        - Protocol:
            - Dogs: cortisol measured in blood collected before and 4 and 8 hours after administration of dexamethasone (0.01 mg/kg IV).
                - Normal: suppression of serum cortisol concentration (<1.4 mg/dL (40 mmol/L) at both 4 and 8 hours
                - Dogs with HAC: inadequate cortisol suppression (cortisol >1.4 mg/dL [40 mmol/L]) at 8 hours
                    - Dogs with ATH: inadequate cortisol suppression at either time point
                    - Dogs with PDH: 35% will not suppress at either time point; 65% will show one of three patterns of suppression:
                        - 8-hour cortisol concentration > reference range but <50% of basal value
                        - 4-hour cortisol concentration <50% of basal value or <reference range; 8-hour cortisol >1.4 mg/dL (40 mmol/L)
                        - 4-hour cortisol concentration <1.4 mg/dL, 8-hour cortisol >1.4 mg/dL (40 mmol/L)
            - Cats: protocol as for dogs except the dexamethasone dose is 0.1 mg/kg IV.
                - Between 65% and 90% of cats with PDH and 100% of ATH have inadequate cortisol suppression at this dose.
    - Low-dose dexamethasone test using oral dexamethasone:
        - Protocol, dog:
            - Owners collect urine from their dog on two consecutive mornings (8:00 am) for determination of baseline cortisol/creatinine ratios.
            - Immediately after collection of the second urine sample, owners administer dexamethasone (tablet form) 0.01 mg/kg PO.
            - Owners walk dog at 12:00 pm and 2:00 pm to ensure bladder emptying.
            - Owners collect a third urine sample for measurement of cortisol/creatinine ratio at 4:00 pm (8 hours after oral administration of dexamethasone).
            - Interpretation: a 50% suppression in the mean urinary cortisol/creatinine ratio is consistent with a normal response. Dogs with HAC would be expected to fail to show adequate suppression of the urine cortisol/creatinine 8 hours following oral dexamethasone administration.
    - Urine cortisol/creatinine ratio:
        - Between 90% and 100% sensitive for both dogs and cats; <10%-15% chance of dog having HAC if ratio is normal. False-positive results very common (75% of dogs with nonadrenal illness have ratio consistent with HAC).
        - Protocol: owner collects morning urine (at home), which is submitted for cortisol and creatinine measurement.
- To differentiate PDH from ATH once a diagnosis of HAC has been established:
    - In some cases, the LDDS results will identify PDH (see above).
        - High-dose dexamethasone suppression test (HDDS): often not performed if test results are consistent with HAC and an adrenal mass is present on ultrasound.
        - Protocol: cortisol measured in blood collected before and 4 and 8 hours after administration of dexamethasone (dogs: 0.1 mg/kg IV; cats: 1 mg/kg IV).
            - Dogs with PDH: suppression of cortisol concentrations (<50% of basal concentrations or <1.4 mg/dL [40 mmol/L]) at 4 or 8 hours. However, 24%-35% of dogs with PDH fail to suppress HDDS and need a further discriminating test.
            - Dogs with ATH: inadequate suppression, although random fluctuations in cortisol concentrations can be seen. Partial or unclear result warrants other test (e.g., ultrasonography).
    - Endogenous ACTH concentrations: (rarely assessed)
        - Low in dogs with ATH and high in dogs with PDH.
        - ACTH is very labile in plasma, and the hormone degrades rapidly if not handled correctly (risk of non-diagnostic result).
    - Abdominal ultrasonography: normal adrenal thickness: 3-7.5 mm
        - PDH: bilaterally symmetric enlargement of the adrenal glands; 5%-10% will have nodular hyperplasia.
        - ATH: unilateral adrenal enlargement with a small contralateral adrenal
    - CT or MRI: used for pituitary imaging (pituitary macroadenoma) or abdominal imaging (adrenal size, tumor invasion),

typically when central nervous system (CNS) deficits coexist with signs and test results indicating HAC.
    - Desmopressin stimulation test: preliminary results with this test are promising for the ability to differentiate PDH from ATH.

TREATMENT

TREATMENT OVERVIEW

- Resolution of clinical signs
- For medical therapy: cortisol concentrations within the basal reference range on both the pre- and post-ACTH stimulation samples

ACUTE GENERAL TREATMENT

By definition, hyperadrenocorticism is a chronic, slowly progressive disease. Therefore acute treatment is not indicated.

CHRONIC TREATMENT

- Medical therapy: mitotane, trilostane, ketoconazole, L-deprenyl:
    - Mitotane (o, p'-DDD, Lysodren):
        - Selectively destroys glucocorticoid-producing zones of the adrenal gland
        - Protocol:
            - PDH:
                - See treatment algorithm,
                - The owner should always have prednisone (0.2 mg/kg PO q 24 h) available for administration to the pet at home if needed.
            - ATH: see p. 43
        - Adverse effects: vomiting, hypocortisolism, complete hypoadrenocorticism (uncommon).
- Ketoconazole:
    - Inhibits adrenal synthesis of cortisol
    - Protocol: See treatment algorithm, .
    - Only effective in 50% of PDH and ATH cases
    - May be used short term to control signs of HAC before surgery for ATH
    - Adverse effects: anorexia, vomiting, diarrhea, lethargy, hepatopathy
- Trilostane (Vetoryl):
    - Inhibits cortisol synthesis
    - Dogs with PDH:
        - Protocol: See treatment algorithm, .
        - By the end of 6 months, doses can range from 4-16 mg/kg/d.
        - Some dogs require q 12 h therapy.
    - Adverse effects: hypocortisolism
- L-deprenyl (selegiline, Anipryl):
    - Decreases ACTH secretion by increasing dopaminergic tone to the hypothalamic-pituitary axis
    - Initial reports by Deprenyl Animal Health Inc. showed 75%-80% efficacy, but two independent studies showed poor efficacy.
    - Protocol: See treatment algorithm,
    - If no response is seen after 2-3 months, the diagnosis of hyperadrenocorticism should be reassessed; if confirmed, another treatment should be used.
- Medical treatment is inconsistent in cats. Mitotane, ketoconazole, and trilostane (30-60 mg/cat/d) are reported to have mixed results, but information is limited. Metyrapone (65 mg/kg PO q 12 h) and aminoglutethimide (6 mg/kg PO q 12 h) have also been tried.
- Surgical therapy:
    - Hypophysectomy has been described in both dogs and cats but is not widely available.
    - Bilateral adrenalectomy is the treatment of choice for PDH in cats.
    - Unilateral adrenalectomy is the treatment of choice for adrenal neoplasia in dogs and cats.
- Radiation therapy (cobalt teletherapy or linear accelerator) for pituitary macroadenomas

DRUG INTERACTIONS

- Mitotane: increases barbiturate and warfarin metabolism; additive depressive effects with CNS depressants; insulin requirements in diabetic dogs may decrease; spironolactone may block mitotane's actions.
- Ketoconazole: antacids and H2 bockers may decrease absorption; decreases theophylline and increases cyclosporine

concentrations; increases anticoagulant effects of warfarin.
- L-deprenyl: interacts with selective serotonin reuptake inhibitors, tricyclic antidepressants, meperidine.
- Trilostane: avoid concurrent use of other treatments for HAC.

POSSIBLE COMPLICATIONS

- Medical treatment: see adverse effects listed after each drug in Chronic Treatment above.
- Adrenalectomy: see p. 43

RECOMMENDED MONITORING

- See Chronic Treatment above and algorithm for treatment of hyperadrenocorticism, .
- At home: owner monitors clinical signs; treated patients may require short-term prednisone supplementation (0.2 mg/kg/d) during stressful situations.

PROGNOSIS AND OUTCOME

Dogs:

- PDH: mitotane therapy—median survival 23 months; average, 30 months,
- PDH: trilostane therapy—median survival 22 months
- PDH: ketoconazole therapy—median survival 25 months; range 2-61 months
- ATH: see p. 43

PEARLS & CONSIDERATIONS

COMMENTS

- For all endocrine tests, it is useful to consult the reference laboratory concerning specific test protocols and guidelines for interpretation.
- LDDS test requires very small volumes of dexamethasone; measure carefully and/or dilute for accurate dosing.
- Before medical therapy and during induction therapy, the owner must quantify water and food intake.
- No dog with a decreased appetite should receive mitotane.
- During induction therapy, have the owner feed one-third the normal food intake twice a day so that any reduction in appetite is obvious.
- Mitotane should be given after the dog's meal to enhance absorption and to confirm that all food is eaten.
- Never initiate antiadrenal therapy in hospital, as food and water intake is usually reduced.
- Daily phone contact with owners is recommended during induction therapy.

TECHNICIAN TIPS

- All dogs and cats having cortisol testing must be kept in a quiet, stress-free environment.
- Ensure samples for cortisol testing are not hemolyzed.

CLIENT EDUCATION

Clients must be educated as to the risks of medical therapy and be able to recognize clinical signs of hypoadrenocorticism.

SUGGESTED READING

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Brown CG, Graves TK: Hyperadrenocorticism: treating dogs. Compend Contin Educ Vet 29(3):132–138, 2007.

Feldman EC, Nelson RW: Hyperadrenocorti-cism. In Feldman EC, Nelson RW, editors: Canine and feline endocrinology and reproduction, ed 3, Philadelphia, 2004, WB Saun-ders, pp 252–357.

AUTHOR: KATE HILL

EDITOR: SHERRI IHLE

Hyperadrenocorticism Suspect/Conflicting Results

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Some of the clinical signs of hyperadrenocorticism (Cushing's disease) are present and/or biochemical test results are suggestive of hyperadrenocorticism, but there are conflicting results with other clinical features or with cortisol testing.

EPIDEMIOLOGY

SPECIES, AGE, SEX

Middle-aged or older dogs

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

One clinical sign (e.g., polyuria/polydipsia, endocrine alopecia, systemic hypertension), one biochemical abnormality (e.g., increased alkaline phosphatase concentration, proteinuria), or one other finding (e.g., vacuolar hepatopathy on biopsy) suggests hyperadrenocorticism, but other results are normal or contradictory.

HISTORY, CHIEF COMPLAINT

- The absence of any overt clinical signs of hyperadrenocorticism makes the diagnosis of hyperadrenocorticism extremely unlikely. Specifically, a dog showing no polyuria, no polydipsia, and no polyphagia almost certainly does not have hyperadrenocorticism.
    - Example: If hyperadrenocorticism is suspected only because of incidentally discovered elevated liver value(s) on a preanesthetic screen, a disease process other than hyperadrenocorticism is almost always the cause of the liver value elevation.
- If anorexia, vomiting, and/or diarrhea are present, a diagnosis other than hyperadrenocorticism is likely (exception: if undergoing treatment with o, p'-DDD).
- Polyphagia, one of the common signs of hyperadrenocorticism, also is very common in healthy, gluttonous dogs. The history therefore should assess whether appetite has increased in the preceding weeks to months despite no change in diet (more consistent with hyperadrenocorticism) or has always been voracious.
- Panting, which is noted in dogs with hyperadrenocorticism, is a common chief complaint in dogs with many disorders that occur more commonly than hyperadrenocorticism, including obesity, hyperthermia, anxiety, pain, and acid-base disorders.
- Seasonal, anxiety-related, or other environmental changes commonly increase water consumption in dogs, without producing true polydipsia. Normal daily water consumption: <70 mL/kg/d (dogs; higher in dogs <4 kg), <250 mL/d (average-size cat).
- Dogs first presented for evaluation of critical, severe clinical signs virtually never have hyperadrenocorticism (exception: severe complications of hyperadrenocorticism treatment or pulmonary thromboembolism).

PHYSICAL EXAM FINDINGS

- “Textbook” hyperadrenocorticism appearance (potbellied, thin-skinned, symmetrically alopecic dog with comedones) is not present in all patients with hyperadrenocorticism.
- Similarly, these typical features may be found in patients with diseases other than hyperadrenocorticism (see p. 6).
- Therefore, suggestive physical findings should be correlated to history, and if hyperadrenocorticism remains likely, testing to evaluate both hyperadrenocorticism and aberrant adrenocortical disease (see pp. 548 and p. 6) may be warranted.

ETIOLOGY AND PATHOPHYSIOLOGY

- Hyperadrenocorticism is a slowly progressive disease that produces clinical signs gradually and chronically.
- The prevalence of complications such as thromboembolic disease and systemic hypertension prior to the onset of overt clinical signs (polyuria/polydipsia, polyphagia) is not known.
- Other endocrine disorders, particularly aberrant adrenocortical disease may clinically mimic hyperadrenocorticism, so the diagnosis of hyperadrenocorticism and the decision to treat cannot be based on a single abnormality (be it historic, physical, or biochemical) alone.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Depends on the clinical signs and biochemical abnormalities seen:

- Polyuria/polydipsia (see p. 902)
- Polyphagia (see p. 899)
- Alopecia (see p. 58)
- Proteinuria (see pp. 926, p. 450, and p. 61) secondary to other systemic disease
- Hypertension (see p. 1068)
- Alkaline phosphatase elevation (see p. 1444)

INITIAL DATABASE

- Revisit a detailed history and physical examination to identify any previously missed signs or findings that would support hyperadrenocorticism or another disorder.
- CBC, serum biochemistry, urinalysis with urine culture, systemic blood pressure, fundic examination (see p. 548)

ADVANCED OR CONFIRMATORY TESTING

- Adrenocorticotropic hormone (ACTH) stimulation test with adrenal sex hormone panel (see p. 6)
  - ACTH stimulation test is abnormal in 60%-87% of dogs with hyperadrenocorticism.
- Low-dose dexamethasone suppression test (see p. 548).
  - Abnormal in 85%-95% of dogs with hyperadrenocorticism, provided dogs with signs of systemic illness such as anorexia or gastrointestinal signs are not tested (systemic illness falsifies results and precludes treatment for hyperadrenocorticism anyway).
- Urine cortisol/creatinine ratio (see p. 548)
  - Highly sensitive (90%-100% of dogs with hyperadrenocorticism have elevated result, and normal result means <15% likelihood of hyperadrenocorticism) but poorly specific (many other disorders elevate results).
- Abdominal ultrasound: see p. 548 for findings supportive of hyperadrenocorticism; with nonadrenal disease, findings will vary with the primary disease.
- Urine protein/creatinine ratio if proteinuria is present and urine culture is negative. Commonly elevated in hyperadrenocorticism.

TREATMENT

TREATMENT OVERVIEW

- Hyperadrenocorticism is a disease characterized by overt physical manifestations. Therefore:
  - Treatment for hyperadrenocorticism should ONLY be instituted when clinical signs consistent with the disease are present and should not be based solely on laboratory test results. None of the tests of the hypothalamic-pituitary-adrenal axis has 100% sensitivity or specificity, and all available information needs to be critically evaluated.
  - If cortisol testing is suggestive of hyperadrenocorticism but there are no clinical signs associated with the disease, either look for other underlying illnesses that could result in increased cortisol concentrations or have the owner monitor for signs of hyperadrenocorticism (e.g., increased water intake, polyphagia).
- Aberrant adrenocortical disease explains some cases of physically “typical” hyperadrenocorticism in which cortisol response is normal.
- If nonadrenal disease is identified, it should be treated and possible hyperadrenocorticism reassessed at a later time if clinical signs persist.

ACUTE GENERAL TREATMENT

- Virtually by definition, hyperadrenocorticism does not warrant acute treatment. Patients in whom the diagnosis is unclear may benefit from watchful waiting, given the potential negative effects of adrenal suppression (see p. 548).
- Proteinuria (see p. 926)
- Hypertension (see p. 1068)

CHRONIC TREATMENT

Treat for hyperadrenocorticism (see p. 548) if history, physical exam, and diagnostic testing together support the diagnosis

POSSIBLE COMPLICATIONS

Hypocortisolism, or full hypoadrenocorticism, if hyperadrenocorticism is mistakenly diagnosed and treated

RECOMMENDED MONITORING

- Home: owner to monitor clinical signs (e.g., polyuria/polydipsia, polyphagia)
- In-hospital:
  - Reevaluate a physical examination, history, and serum biochemical profile ± urinalysis and systolic blood pressure q 2-3 months to identify any new signs or abnormalities.
  - If proteinuria: assess UP: UC q 2-3 months.
- If/when clinical signs of hyperadrenocorticism develop, repeat a CBC, serum biochemical profile, urinalysis (±urine culture), and cortisol testing prior to instituting treatment.

PROGNOSIS AND OUTCOME

Dependent on the disease present

PEARLS & CONSIDERATIONS

COMMENTS

Because of the number of different combinations of signs and test results that can be seen, these can be challenging cases. Controversy exists even among specialists as to exactly which patients should be treated and when.

SUGGESTED READING

Feldman EC, Nelson RW: Hyperadrenocorti-cism. In Feldman EC, Nelson RW, editors: Canine and feline endocrinology and reproduction, ed 3, Philadelphia, 2004, WB Saun-ders, pp 252–357.

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Hydronephrosis

BASIC INFORMATION

DEFINITION

Dilation of the renal pelvis and calices (pyelectasia) in one or both kidneys, typically as a result of ureteral (or rarely urethral) obstruction, resulting in atrophy of the renal parenchyma.

EPIDEMIOLOGY

SPECIES, AGE, SEX

More common in dogs than cats; no age or sex predilection

RISK FACTORS

Any cause of ureteral (or urethral) obstruction, whether mechanical or functional:

- Bladder atonia/hypotonia
- Blood clots
- Celiotomy (inadvertent ligation or fibrotic entrapment of ureter)
- Congenital ureteral stenosis or stricture
- Ectopic ureter (common cause)
- Prostatic carcinoma
- Reflex dyssynergia
- Retroperitoneal mass/fibrosis/infarction
- Trauma
- Ureteral fibroepithelial polyps
- Urinary tract neoplasia
- Urolithiasis

ASSOCIATED CONDITIONS & DISORDERS

- Renal failure +/− uremia
- Hypertension
- Urinary tract infection

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Reversible or irreversible
- Unilateral or bilateral

HISTORY, CHIEF COMPLAINT

Often clinically normal. Signs can include:

- Vague abdominal pain associated with renomegaly
- Polydipsia/polyuria associated with chronic kidney disease
- Anorexia and vomiting associated with uremia
- Pollakiuria, stranguria, dysuria, hematuria possible
- Urinary incontinence (if hydronephrosis due to ectopic ureter)
- Oliguria or anuria (urethral obstruction or, rarely, bilateral ureteral obstruction)

PHYSICAL EXAM FINDINGS

Often normal. Abnormalities may include:

- Abdominal discomfort (severity related to rate of onset of obstruction rather than degree of obstruction)
- Renomegaly
- Distended bladder (if urethral obstruction)
- Abdominal mass (kidney, bladder, prostate, granuloma)
- Urethral mass (via rectal palpation)
- Prostatomegaly
- Dehydration
- Halitosis (due to uremia)
- Oral ulcerations (due to uremia)

ETIOLOGY AND PATHOPHYSIOLOGY

- Illness varies depending on whether obstruction is unilateral or bilateral, completeness and duration of obstruction, and preexisting renal function.
- Clinical signs can be absent, chronic, or acute; acute signs are more likely when obstruction is complete.
- Obstruction results in increased hydrostatic pressure in renal pelvis, collecting ducts, and distal tubules causing tubular dilatation with flattening of the tubular cells.
- Concurrently, renal vasculature and blood supply are compromised. Renal blood flow progressively decreases, arterioles constrict, capillary pressure decreases, and many arterioles collapse resulting in parenchymal atrophy.
- Changes may become irreversible after 14-45 days.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Hydronephrosis is usually diagnosed via renal imaging studies, including ultrasound or contrast studies, in conjunction with recognition of a functional or physical reason for urinary obstruction.

DIFFERENTIAL DIAGNOSIS

- Pyelectasia: pyelonephritis, iatrogenic fluid diuresis (mild)
- Renomegaly: renal cyst(s), perinephric pseudocyst, neoplasia (e.g., renal adenocarcinoma, lymphoma), amyloidosis, granuloma, perinephric abscess, feline infectious peritonitis, hematoma, compensatory hypertrophy (unilateral)

INITIAL DATABASE

- Digital rectal examination: lesions of the urethra and bladder trigone may cause hydronephrosis.
- Urethral catheterization: can rule out or confirm urethral obstruction from urolithiasis
- CBC: unremarkable; neutrophilia possible if concurrent pyelonephritis
- Serum biochemical profile: depending on degree of obstruction and/or nephron loss, azotemia, hyperphosphatemia, hyperkalemia, metabolic acidosis, increased anion gap
- Urinalysis: isosthenuria (e.g., if *>66%* nephron loss), sometimes hematuria, pyuria
- Urine culture and sensitivity (C&S) to rule out infection
- Blood pressure to rule out hypertension
- Abdominal radiographs: often renomegaly; additional findings may include
  - Urolithiasis
  - Urinary bladder distension
  - Prostatomegaly
  - Abdominal mass effect
  - Loss of contrast in retroperitoneal space
  - Loss of abdominal detail
- Abdominal ultrasound: pyelectasia; additional findings may include
  - Renomegaly
  - Loss of medullary parenchyma
  - Hydroureter
  - Uroliths
  - Masses in ureter, bladder, prostate, or urethra

ADVANCED OR CONFIRMATORY TESTING

- Additional testing is not always required or beneficial.
- Excretory urography (EU)/intravenous pyelography (IVP) (see p. 1265) to assess perfusion of each kidney; percutaneous

nephropyelography to assess structure of renal pelvis and ureter
  - Pyelectasia
  - Ureteral dilatation or lack of filling (EU only)
  - May identify ectopic ureter
- Renal scintigraphy or CT with contrast
  - Affected kidney contributes little to glomerular filtration rate.
- Other testing is aimed at characterizing underlying cause of hydronephrosis (e.g., quantitative analysis of uroliths, imaging studies to localize neurologic lesions contributing to reflex dyssynergia, cystoscopy for bladder abnormalities or ectopic ureter).

TREATMENT

TREATMENT OVERVIEW

Hydronephrosis has no specific treatment. Instead, obstruction of urine flow should be corrected when possible and complications of renal failure addressed.

ACUTE GENERAL TREATMENT

- Relieve urinary obstruction (see pp. 1131 and p. 1129)
- Crystalloid fluid therapy for azotemia (see pp. 31 and p. 207):
  - Initial rate of 120 mL/kg IV q 24 h if no concurrent heart disease, hypoalbuminemia, or vasculitis; adjust as needed based on degree of dehydration/hypovolemia
  - Postobstructive diuresis may require “ins-and-outs” method of fluid therapy (rate adjustments based on measured urine output)
- Analgesia for abdominal pain (e.g., buprenorphine, 0.01 mg/kg IM, IV, or SQ q 6-8 h)
- Address electrolyte disorders, acidosis
- Address uremia (see pp. 31 and p. 207)

CHRONIC TREATMENT

- Antibiotics if indicated by results of urine C&S:
  - If infection cannot be cured medically, nephrectomy may be indicated to remove infected, poorly functioning kidney if function of contralateral kidney is adequate.
- Address underlying cause of structural or functional urinary obstruction (e.g., therapeutic or prophylactic/dietary measures for urolithiasis, pharmacologic therapy of bladder atonia, reflex dyssynergia)

POSSIBLE COMPLICATIONS

- Renal failure
- Urinary tract infection
- Urinary rupture and uroabdomen (septic peritonitis if urinary tract is infected)

RECOMMENDED MONITORING

- Ultrasound is repeated several weeks after urinary obstruction relieved. If hydronephrosis persists after 6 weeks, changes are likely to be permanent.
- Animals with permanent hydronephrosis are monitored as for chronic kidney disease (see pp. 205 and p. 207) with periodic urinalysis and culture, assessment of azotemia, electrolytes, and packed cell volume. Azotemic animals are monitored more intensively than nonazotemic animals.

PROGNOSIS AND OUTCOME

- Dependent on extent of renal damage, underlying cause and resolution of cause, duration, and concurrent infection. Hydronephrosis can be associated with severe renal failure or may be an incidental finding.
- Structural kidney changes may be irreversible.

PEARLS & CONSIDERATIONS

COMMENTS

- Hydronephrosis is a consequence of obstructive urinary tract disease rather than a primary disease.
- Hydronephrosis can lead to renal failure or may be manifest only as subclinical pyelectasia.

PREVENTION

Strategies that limit the formation of uroliths are important for patients that have already demonstrated a predisposition to urolithiasis or those with known risk factors.

CLIENT EDUCATION

Urinary tract obstruction is life threatening. Stranguria or signs of systemic illness should prompt immediate veterinary attention.

SUGGESTED READING

Osborne CA, Finco DR: Canine and feline nephrology and urology. Baltimore, 1995, Williams & Wilkins, pp 474–482.

Steffey MA, et al: Congenital ectopic ureters in a continent male dog and cat. J Am Vet Med Assoc 224:1607, 2004.

AUTHORS: ADAM MORDECAI, RANCE K. SELLON

EDITOR: LEAH A. COHN

Hydrocephalus

BASIC INFORMATION

DEFINITION

An increase in volume of cerebrospinal fluid (CSF) within the ventricular system of the brain that causes signs of encephalopathy

EPIDEMIOLOGY

SPECIES, AGE, SEX

Congenital: dog, cat <6 months old. Acquired: any.

GENETICS & BREED PREDISPOSITION

- Toy breeds: Chihuahua, toy poodle, Pomeranian, Lhasa apso, pug, Pekingese, and Cairn, Yorkshire, Manchester, and Maltese terriers
- Brachycephalic breeds: Boston terrier, bulldog
- Autosomal-recessive inheritance in Siamese cats

RISK FACTORS

- Often represents a secondary manifestation of a developmental (Chiari malformation) or an acquired (neoplasia, inflammatory) disorder
- Vitamin A deficiency, toxicosis (cats: griseofulvin during pregnancy); infectious (cats: panleukopenia, feline infectious peritonitis; dogs: parainfluenza)

ASSOCIATED CONDITIONS & DISORDERS

Small birth size, short gestation periods, high stress at birth (dystocia)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Congenital: animal is born with clinical signs; usually associated with fusion of mesencephalic aqueduct.
- Acquired: caused by obstructive insults at any age (i.e., infection, trauma, neoplasia)

HISTORY, CHIEF COMPLAINT

- Changes in mentation: dullness, disorientation, stupor
- Behavioral abnormalities: inability to learn (e.g., litter box use), loss of housebreaking, compulsive activities, aggression
- Seizures

PHYSICAL EXAM FINDINGS

- Domed-shaped head and persistent fontanelle are possible
- Eye position typically will manifest ventrolateral deviation
- Neurologic examination: mentation changes; gait abnormalities may manifest as dysmetria, ataxia, circling, aimless wandering; central blindness; and seizure activity

ETIOLOGY AND PATHOPHYSIOLOGY

- Pathologic changes include focal destruction of the ependymal lining, compromise of cerebral vasculature, damage to periventricular white matter, and injury to neurons.
- Secondary calvarial abnormalities depend on the stage of ossification at onset of fluid accumulation.
- Ventriculomegaly results from obstruction within the ventricular system, overproduction of CSF, or insufficient absorption of CSF at the arachnoid villi.

- Congenital:
  - Fusion of the rostral colliculi, causing mesencephalic aqueductal stenosis. There is no other active disease process.
- Acquired:
  - Exposure to teratogenic drugs, chemicals, and viral diseases during gestation
  - Obstruction of ventricular system by neoplastic mass, hemorrhage, or inflammation
  - Hydrocephalus also may be a component of other anomalous disorders (i.e., Chiari malformation, Dandy-Walker syndrome, lissencephaly).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is suspected based on the physical examination and signalment. Confirmation comes from diagnostic imaging (beginning with ultrasound and proceeding to CT/MRI if needed) and procedures assisting with determining underlying causes.

DIFFERENTIAL DIAGNOSIS

- Hydrocephalus usually will manifest signs of forebrain dysfunction.
- Encephalopathies:
  - Degenerative disorders: storage diseases, leukodystrophies, multisystem atrophy
  - Anomalies (congenital): malformations (e.g. caudal occipital malformation syndrome, Dandy-Walker syndrome, hydranencephaly)
  - Metabolic: hepatic encephalopathy, organic acid disorders
  - Neoplasia: causes secondary obstructive hydrocephalus
  - Inflammatory: infectious (feline panleukopenia, feline infectious peritonitis, parainfluenza, canine distemper), noninfectious (breed specific, meningoencephalomyelitis of unknown etiology)
  - Idiopathic: arachnoidal cysts
  - Trauma: hydrocephalus ex vacuo occurs with destruction of brain tissue (e.g., cerebrovascular accidents)
  - Toxin exposure: griseofulvin

INITIAL DATABASE

- Signalment
- Neurologic examination (see p. 1311)
- CBC, serum biochemistry profile, urinalysis: generally unremarkable
- Serologic titers: to rule out infectious causes if appropriate
- Skull radiography: decreased prominence of normal calvarial convolutions

ADVANCED OR CONFIRMATORY TESTING

- Ultrasonography: through persistent fontanelles
- Advanced imaging: to confirm hydrocephalus but also rule out other contributing disorders and differentials that would mimic disease
  - CT: visualization of lateral ventricles
  - MRI: visualization of the ventricular system and the brain parenchyma
- CSF analysis: to rule out other disorders if appropriate
- Electroencephalography

TREATMENT

TREATMENT OVERVIEW

The treatment of hydrocephalus is guided by the underlying cause. Medical therapy offers temporary palliation of clinical signs. Surgical management using shunting procedures may offer a more permanent remedy.

ACUTE AND CHRONIC TREATMENT

- Medical:
  - Prednisone (↓ CSF production):
    - 0.25-0.5 mg/kg PO q 12-24 h, then tapered to lowest effective dose

- Furosemide (↓ CSF production; Na-K cotransport inhibition):
  - 0.5-2 mg/kg PO q 12-24 h
- Acetazolamide (↓ CSF production; carbonic anhydrase inhibition):
  - 10 mg/kg PO q 8 h
- Omeprazole (↓ CSF production; proton pump inhibition):
  - 0.7 mg/kg PO q 24 h
  - 10 mg q 24 h for dogs weighing <20 kg or 20 mg q 24 h for dogs weighing >20 kg
- Antiepileptic drug therapy for seizure control

- Surgical: advocated if clinical signs do not improve within 2-3 weeks:
  - Ventriculoperitoneal shunt
  - Ventriculoatrial shunt

DRUG INTERACTIONS

Prolonged use of glucocorticoids and acetazolamide may cause potassium depletion and other systemic disorders.

POSSIBLE COMPLICATIONS

- Generally, medical therapy may result in only transient improvement of clinical signs.
- Complications of shunt placement include mechanical and functional obstruction, infections, overshunting.

RECOMMENDED MONITORING

- Signs of acute decompensation: coma, seizures, behavior changes
- Seizure control

PROGNOSIS AND OUTCOME

- Congenital: guarded. Prognosis also is influenced by coexistence of other neural abnormalities.
- Acquired: prognosis depends on underlying cause.

PEARLS & CONSIDERATIONS

COMMENTS

- Every attempt is made to determine the underlying cause.
- Early shunt placement is advocated to lessen residual neurologic deficits and behavior abnormalities.

PREVENTION

Limit prenatal exposure to toxins, viral infections, and vaccines.

TECHNICIAN TIPS

- Avoid excessive holding and compression of the external jugular veins in these patients (can increase intracranial pressure).
- The owners need to be counseled on monitoring for gastrointestinal ulceration if the animal is being treated with glucocorticoids.
- After surgery for shunt placement, the skin over the shunt will need to be monitored for signs of pressure necrosis, especially in small-breed dogs with tendency for thin skin.

CLIENT EDUCATION

- Clinical signs of acute decompensation
- Guarded prognosis and likelihood of residual neurologic deficits with therapy
- Importance of maintaining the pet in a protective environment

SUGGESTED READING

Coates JR, Axlund TW, Dewey CW, et al: Hydrocephalus in dogs and cats. Compend Contin Educ Pract Vet 28(2):136, 2006.

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AUTHOR: JOAN R. COATES

EDITOR: CURTIS W. DEWEY

Horner's Syndrome

BASIC INFORMATION

DEFINITION

Manifestations of loss of sympathetic innervation to the eye. Signs are miosis (small pupil), ptosis (dropped upper eyelid, causing a smaller palpebral fissure), enophthalmos, and protrusion of the third eyelid.

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs and cats of any age and either sex

GENETICS & BREED PREDISPOSITION

Male golden retrievers may be overrepresented (of 155 dogs with Horner's syndrome in one study, 110 were golden retrievers; idiopathic Horner's syndrome was present in 100 of them, 95 were male).

HORNER'S SYNDROME Right-sided Horner's syndrome in a 9-year-old pointer-cross dog. Note right-sided ptosis, miosis, and protruding third eyelid caused by enophthalmos. The hematocrit was 75%, and pathologic proteinuria was present, leading to a suspicion of thromboembolic disease as the cause of the Horner's syndrome.

Modified from Collins BK, O'Brien D: Autonomic dysfunction of the eye. Semin Vet Med Surg Small Anim 5:24–36, 1990. Reprinted with permission.

FCE, Fibrocartilaginous emboli; *LMN,* lower motor neuron; *UMN,* upper motor neuron.*Most common.

Localizing Lesions in Horner's Syndrome

Location	Common Etiologies	Neuron Affected	Commonly Associated Signs
Brainstem	Neoplasia,* trauma, infection	UMN	Altered consciousness, thermoregulation, endocrine function, appetite, drinking, cranial nerve deficits, motor deficits, dyspnea

Location	Common Etiologies	Neuron Affected	Commonly Associated Signs
Cervical spinal cord	Trauma, neoplasia, FCE	UMN	Tetraparesis/plegia, hemiparesis/plegia, UMN signs in all four limbs if cranial lesion, LMN signs in thoracic limbs with UMN signs in pelvic limbs if caudal cervical lesion
T1-T3 spinal cord	Trauma,* neoplasia,* FCE	UMN	Thoracic limb paresis/paralysis with LMN thoracic limb signs, pelvic limb paresis/paralysis with UMN thoracic limb signs
T1-T3 ventral nerve roots	Brachial plexus avulsion,* neurofibroma	Preganglionic	Brachial plexus paresis/paralysis of ipsilateral limb
Cranial thoracic sympathetic trunk	Lymphoma, neurofibroma, thoracic disease	Preganglionic	Respiratory distress; no other signs if confined to trunk
Cervical sympathetic trunk	Trauma, iatrogenic, neoplasia	Preganglionic	May be none if unilateral; may interfere with laryngeal or esophageal function from vagal involvement
Middle ear	Otitis media,* neoplasia	Postganglionic	Head tilt, nystagmus, and/or facial paralysis
Cavernous sinus	Neoplasia, vascular disease	Postganglionic	Internal, external, or complete ophthalmoplegia (may produce mydriasis rather than miosis)
Orbital disease	Abscess, neoplasia, contusion, pseudotumor	Postganglionic	Exophthalmos, discomfort, optic nerve or oculomotor deficits

RISK FACTORS

Blunt trauma (e.g., hit by car), other cervical/thoracic spinal cord damage (fibrocartilaginous embolization, intervertebral disk disease) or infiltration (lymphoma), surgical trauma or neoplastic infiltration of the neck (affecting the sympathetic trunk), intracranial neoplasia, otitis media or other middle ear lesions, retrobulbar inflammation or mass

ASSOCIATED CONDITIONS & DISORDERS

Exposure keratitis. The inability to blink normally is mostly compensated for by the third eyelid, but a band of desiccated cornea may occur across the central cornea (lagophthalmos). Keratoconjunctivitis sicca and facial neuropathies have also been associated with Horner's syndrome.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Signs referable to the underlying cause
- Trauma (e.g., hit by car) to the head, neck, chest or brachial plexus is the most common historically identifiable cause in dogs and cats, followed by history of a recent or current ear infection.
- Ocular signs observed by the owner

PHYSICAL EXAM FINDINGS

- Enophthalmos (retracted/sunken globe)
- Ptosis
- Miosis
- Third eyelid protrusion
- Other associated signs may be present, depending on the location of the inciting lesion (see table).

ETIOLOGY AND PATHOPHYSIOLOGY

- Interference with the sympathetic innervation to the eye: brainstem. → cervical spinal cord → T1-T3 spinal cord segments → thoracic sympathetic truck → vagosympathetic trunk → cranial cervical ganglion (synapse; lesion preceding this point is preganglionic or UMN/central, and lesion after this point is postganglionic) → middle ear → ophthalmic branch of the trigeminal nerve → orbit → orbitalis muscle, ciliaris muscle, and smooth muscle of the pupil (see table)
- An immune-mediated mechanism has been speculated as a possible cause for idiopathic Horner's syndrome.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

History and physical/neurologic examination are generally sufficient for differentiation.

DIFFERENTIAL DIAGNOSIS

Ocular trauma causing miosis (uveitis)

- Phthisis bulbi causing protrusion of the third eyelid and a small palpebral fissure
- Hypothyroidism

INITIAL DATABASE

- Minimum database
- Otoscopic examination
- Thoracic and cervical radiographs

ADVANCED OR CONFIRMATORY TESTING

- Thyroid testing
- MRI of brain and cervical spine
- Pharmacologic testing. Suggested protocol:
    - Topical 10% phenylephrine solution: 1 drop applied to affected eye
    - Mydriasis occurs in <20 minutes when lesion is postganglionic.
    - Mydriasis occurs in 20-45 minutes when lesion is preganglionic.
    - Mydriasis occurs in >45 minutes when lesion is central/UMN.
    - Results have been inconsistent; reliability of test is controversial.

TREATMENT

TREATMENT OVERVIEW

Horner's syndrome is not treated; it is a sign that may indicate an underlying lesion that may require treatment.

ACUTE GENERAL TREATMENT

Treat underlying cause, if any. Prevent/treat corneal ulcerations secondary to exposure keratitis.

PROGNOSIS AND OUTCOME

- The prognosis depends on resolution of the underlying cause. Patients with traumatic causes have quicker resolution (days/weeks) than patients with idiopathic or iatrogenic causes.
- In idiopathic Horner's syndrome, essentially all patients have resolution of the signs of Horner' syndrome within 6 months after diagnosis.

PEARLS & CONSIDERATIONS

COMMENTS

- Approximately 50% of cases of Horner's syndrome in dogs are idiopathic, and the syndrome generally resolves without treatment in <6 months.
- In cats, a cause is virtually always found: idiopathic Horner's syndrome is very rare.
- Strictly speaking, Horner's syndrome also affects the surface of the face and neck (causing erythema/flushing of the skin) and the nasal mucosa (causing congestion), but these manifestations usually have no clinical significance.
- Pharmacologic testing to determine the site of the lesion has produced inconsistent results.

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Hookworm Infection

BASIC INFORMATION

DEFINITION

Infection with nematode parasites of dogs and cats that colonize the gastrointestinal tract and cause blood loss anemia

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Cats: *Ancylostoma tubaeforme, Ancylostoma braziliense, Uncinaria stenocephala* (rare)
- Dogs: *Ancylostoma caninum;* less commonly *Uncinaria stenocephala, Ancylostoma braziliense*
- Young animals of both species are primarily affected.

RISK FACTORS

Small body size (smaller blood volumes such as in puppies, kittens) increases risk for disproportionately greater anemia with high worm burdens. Puppies born to bitches with poor husbandry are at increased risk, especially from 2-8 weeks old.

CONTAGION & ZOONOSIS

- Contagion: arrested larvae in the female dog become reactivated during pregnancy and migrate to the placenta and mammary glands, where they are transmitted to pups. No similar transplacental or transmammary transmission of *A. tubaeforme* in the cat.
- Zoonosis: *A. braziliense* and less commonly *A. caninum* can cause cutaneous larval migrans (CLM) in humans. Infective larvae penetrate and migrate through the skin, causing intensely pruritic elevated winding tracts. Adult *A. caninum* can parasitize the human intestine human.

GEOGRAPHY AND SEASONALITY

- *A. tubaeforme:* worldwide. *A. caninum:* worldwide subtropical and temperate regions. *A. braziliense:* tropical and subtropical climates in North and South America, Africa; near coastlines. *U. stenocephala:* temperate to cooler climates, North and Central America, Europe, Asia.
- Eggs only develop into infective third-stage larvae above 15°C, so infection occurs primarily in warmer months in temperate regions.

ASSOCIATED CONDITIONS & DISORDERS

Coinfection with other nematodes (particularly *Toxocara canis* and *Toxocara cati)* is common in young animals.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Weight loss
- Lethargy
- Polydipsia
- Poor growth and unthriftiness (puppies/kittens)
- Melena
- Diarrhea
- Ova may be found incidentally on fecal examination.

PHYSICAL EXAM FINDINGS

- Pale mucous membranes are the hallmark, owing to the bloodsucking activity of adult hookworms.
- Poor body condition and haircoat
- Melena on rectal examination

- Heart murmur due to anemia (systolic, left-sided, soft)
- Tachycardia, tachypnea, weakness or obtundation if in hemorrhagic shock
- Clinical signs vary based on degree of blood loss and chronicity of parasitism.
- Physical examination may be normal if worm burden is low.

ETIOLOGY AND PATHOPHYSIOLOGY

- Hookworms attach to the small-intestinal mucosa. Host blood travels through hookworm gut, providing oxygen and nutrients to the worm. Attached worms essentially mimic open blood vessels, causing persistent gastrointestinal hemorrhage. Hookworms are also known to change their attachment sites, moving from one site to another within the small intestine. The buccal cavity of hookworms naturally secretes a potent anticoagulant, so the former attachment sites continue to bleed after the detachment/reattachment.
- *A. caninum* consumes more of the host's blood than the other hookworms. *U. stenocephala* rarely causes clinical disease or significant anemia.
- Life cycles among species are similar. Prepatent periods (incubation period, from the time of ingestion to the appearance of ova in feces) vary from 12-28 days depending on species.
    - Inoculation occurs via oral ingestion or skin penetration from infective third-stage larvae in the environment. Puppies are infected via transmammary or transplacental transmission.
        - Oral: swallowed infective third-stage larvae penetrate stomach and intestinal wall, where they become arrested in submucosa or other tissues, are reactivated, and return to intestine to attach to mucosa.
        - Skin: third-stage larvae penetrate skin, migrate through lungs and up trachea, are swallowed, and ultimately attach to intestinal wall.

DIAGNOSIS

DIAGNOSIS OVERVIEW

A small, young animal with evidence of internal blood loss should trigger the consideration of hookworm infection, particularly in warm climates. Basic fecal flotation is the preferred diagnostic test, though empirical treatment without testing (subclinical infection) is also reasonable.

DIFFERENTIAL DIAGNOSIS

- Foreign body ingestion
- Canine parvovirus (puppies)
- Feline leukemia virus infection (kittens)
- Gastrointestinal ulceration
- Gastrointestinal neoplasia (older animals)
- Anemia due to hemolysis
- Anemia due to ectoparasites (e.g., fleas, ticks)

INITIAL DATABASE

- Fecal flotation: diagnostic test of choice:
    - Eggs of *Ancylostoma* species and *U. stenocephala* appear similar: characteristic ova are ellipsoidal and contain an 8-cell morula.

ADVANCED OR CONFIRMATORY TESTING

- CBC:
    - Regenerative anemia (most cases)
    - Nonregenerative anemia with microcytic hypochromic red cells may occur secondary to chronic gastrointestinal blood loss and subsequent iron deficiency.
    - Eosinophilia
- Serum biochemistry profile:
    - Hypoproteinemia/hypoalbuminemia
    - Hyponatremia/hypochloremia in polydipsic animals
- Urinalysis: generally unremarkable

TREATMENT

TREATMENT OVERVIEW

Rapid eradication is important in affected puppies and kittens (anthelmintics). Severe cases may require transfusion.

ACUTE GENERAL TREATMENT

- Transfuse severely anemic or compromised patients with blood products or oxygen-carrying fluids (20 mL/kg whole blood or polymerized bovine hemoglobin [Oxyglobin]). See p. 1347.
- Iron supplementation may be required in patients with prolonged or profound gastrointestinal blood loss (dam's/queen's milk is a poor source of iron).
    - For severe iron-deficiency anemia: iron dextran, 10-20 mg/kg IM once (dogs), 50 mg/animal IM once (cats), followed by oral supplementation.
    - Ferrous sulfate, 100-300 mg/animal PO once daily (dogs), 50-100 mg/animal PO once daily (cats). May cause gastric irritation; should be given with food.
- Anthelmintics should be administered once every 2 weeks to puppies and kittens until adolescence (6 months of age); 1-2 treatments usually adequate:
    - Pyrantel pamoate, 5-10 mg/kg PO; *or*
    - Febantel, 10-15 mg/kg PO (higher dose in younger animals); *or*
    - Fenbendazole, 50 mg/kg PO q 24 h for 3 days; *or*
    - Ivermectin, 0.2 mg/kg PO or SQ (beware risks; see p. 625)

CHRONIC TREATMENT

- Repeat dewormings necessary to prevent reinfection. Resistance to infection increases with age and exposure.
- Deworm every 2-3 weeks.
- To prevent passage of infective larvae from lactating bitches to puppies, treat with of fenbendazole 50 mg/kg PO q 24 h from day 40 of gestation to day 14 of lactation.

RECOMMENDED MONITORING

- Acute anemia: monitor hematocrit, reticulocyte counts
- Repeat fecal flotations

PROGNOSIS AND OUTCOME

Prognosis is excellent with removal of parasites in compensated infection but guarded in cases of acute severe anemia.

PEARLS & CONSIDERATIONS

COMMENTS

Peak blood loss from hookworm infestation occurs before eggs are shed in feces. Therefore, a negative fecal examination does not rule out hookworm disease, especially in very young puppies or kittens that present with evidence of anemia and shock.

PREVENTION

- Sodium borate applied to gravel or concrete will control hookworm larvae in the environment.
- Best prevention is regular administration of anthelmintics. Commercial heartworm preventives containing ivermectin/pyrantel pamoate, milbemycin, and selamectin have simultaneous anthelmintic properties for monthly control of hookworms in adult dogs and cats. Note that selamectin does not control hookworms in dogs but is efficacious in cats at heartworm preventive doses.

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Hit by Car

BASIC INFORMATION

DEFINITION

Trauma sustained as a result of direct impact from a car, truck, or other motorized vehicle

SYNONYMS

HBC, vehicular trauma, motor vehicle accident

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs and cats of any age, breed, or sex can be affected.

RISK FACTORS

Young, male dogs and cats may be at increased risk.

ASSOCIATED CONDITIONS & DISORDERS

Hypovolemic shock, hemorrhage, fractures, neurologic deficits, ocular lesions, skin abrasions/lacerations

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- The accident may be witnessed or not (e.g., the animal may be found near the side of the road).
- Primary complaints include acute collapse, difficulty breathing, lacerations, lameness, and suspected fractures.
- If the accident is witnessed, it is important to determine:
  - Primary location of impact on the animal's body
  - Whether the animal was seen walking after the accident
  - Other signs the owner has noticed since the accident

PHYSICAL EXAM FINDINGS

Dependent on site and extent of injuries:

- Altered mentation (dull, depressed, comatose), ocular injuries, and/or skull fractures with head trauma
- Tachycardia (usually sinus) reflecting pain, hypovolemia, hypotension, or combinations thereof:
  - Sinus tachycardia is essentially never treated with antitachycardic drugs (β-blockers, calcium channel blockers, etc.), because it almost always represents a physiologic response. Rather, the underlying cause needs to be identified and treated.
- Increased respiratory rate and effort (pulmonary contusions, pneumothorax, pain)
- Skin lacerations:
  - Often associated with incrusted debris or road/tire marking, increasing the suspicion of hit by car in an animal with an uncertain history
- Fractures
- Other specific injuries reflective of the site of the impact

ETIOLOGY AND PATHOPHYSIOLOGY

- Physiologic response to trauma is complex, involving catecholamine and hormone release.
- Goal of physiologic response is to maintain oxygen delivery to the heart and brain at expense of other tissues (e.g., skeletal muscle, abdominal viscera).
- Initial response results in clinical signs of early/compensatory shock:

    - Tachycardia
    - Tachypnea
    - Increased capillary refill time
    - Bounding femoral pulses
- Compensatory phase of shock has high energy demands and if untreated can rapidly progress to decompensatory (terminal) phase of shock.
- Continued reduction in oxygen delivery to tissues results in clinical signs of decompensatory (terminal) shock:
    - Bradycardia (less of a severe indicator in cats, who may have heart rates <150 beats/min without being in advanced shock states)
    - Pale mucous membranes
    - Weak femoral pulses
    - Hypotension
    - Cardiopulmonary arrest

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

The history is conclusive if the event was witnessed; otherwise, a presumptive diagnosis can be made from cutaneous wounds and internal injuries. Diagnostic evaluation centers around assessing all body systems for traumatic injury.

DIFFERENTIAL DIAGNOSIS

- Metabolic causes of shock (e.g., sepsis, endocrine, heat stroke)
- Other causes of trauma (e.g., kicks, fall from height, bite wounds)

INITIAL DATABASE

- Triage: a wide spectrum of patient states can result when an animal is hit by a vehicle.
    - Rapid assessment of neurologic (mentation, ability to ambulate), cardiorespiratory (dyspnea, respiratory arrest, palpable heartbeat and pulse), skeletal (fractures), and pain parameters determines the immediate extent of diagnostic and treatment efforts.
    - An interim prognosis based on a brief but thorough physical examination may often dictate the extent to which an owner wishes to support the patient's diagnostic testing and treatment.
- Packed cell volume/total solids (PCV/TS):
    - Can be normal in a hit-by-car patient even with acute hemorrhage
    - Decrease may take hours but is more rapid if intravenous fluids are administered (dilution).
    - Serial monitoring of PCV/TS 1-2 hours after admission and every 4-6 hours is recommended to detect changes associated with hemorrhage.
- Blood glucose, electrolytes, venous or arterial blood gas, lactate measurement if available, CBC, serum chemistry profile, urinalysis
- Electrocardiogram:
    - Monitor arrhythmias (especially ventricular [see p. 1165]; occasionally premature atrial complexes, atrial fibrillation, or others).
    - Monitor heart rate during fluid resuscitation. Heart rate in dogs will often decrease with successful correction of hypovolemia through fluid resuscitation (e.g., initial heart rate 180-200 beats/min decreasing to 100-130 in a medium- to large-breed dog).
- Blood pressure
- Blood lactate concentration
    - Can determine if lactic acidosis is present (e.g., from prolonged hypo-perfusion associated with shock)
    - Blood lactate level should return to normal once adequate perfusion is restored with intravascular volume replacement.
- Survey radiographs of chest, abdomen, ± axial or appendicular skeletal system structures as dictated by physical findings
- Pulse oximetry:
    - Assess oxygenation (possibility of pulmonary contusions or pneumothorax if desaturation [i.e., if <90%-93% O2 saturation]).

ADVANCED OR CONFIRMATORY TESTING

- Radiographic contrast studies to assess integrity of urinary tract if indicated
- Ultrasound to assess abdominal structures
- Advanced neuroimaging modalities such as CT or MRI to better define skull and brain injuries

TREATMENT

TREATMENT OVERVIEW

- Rapid restoration of effective circulating volume with bolus intravenous fluid administration
- Stabilization of life-threatening respiratory compromise
- Identification of ongoing blood loss that may require surgical intervention
- Identification of internal injuries (e.g., organ rupture, diaphragmatic hernia)
- Pain management of musculoskeletal injuries, including appropriate bandaging of fractures

ACUTE GENERAL TREATMENT

- Bolus intravenous crystalloid fluid administration up to 90 mL/kg/h in dogs and up to 45 mL/kg/h in cats; may start with 25 mL/kg bolus over 5 minutes and repeat as necessary.
- Bolus intravenous colloid administration (dosages vary with different colloids) if crystalloids do not restore cardiovascular function
- Consider hypertonic fluid therapy (e.g., hypertonic saline [7% NaCl 2-6 mL/kg slow IV; acceptable to inject into peripheral or central IV catheter; follow with isotonic crystalloids such as lactated Ringer's]) in cases of head trauma and/or hemorrhagic shock.
- Packed red blood cells or fresh whole blood transfusion in cases of severe hemorrhagic shock (see p. 1347)
- Supplemental oxygen administration in cases of respiratory compromise or head trauma (see p. 1318)
- Use of sterile bandages to cover wounds, including appropriate bandaging of fractures (definitive wound and fracture repair often not possible until cardiovascular and respiratory systems are stabilized).
- Pain management with systemic narcotics when cardiovascular stability achieved
    - Options include:
        - Hydromorphone, 0.05-0.1 mg/kg IM, IV q 4-6 h; *or*
        - Morphine (dogs), 0.5-1 mg/kg SQ, IM q 4-6 h; *or*
        - Fentanyl, constant rate IV infusion 0.002-0.006 mg/kg/h; *or*
        - Morphine-ketamine combination, constant rate infusion; can mix together in syringe or bag diluted in 0.9% saline or lactated Ringer's solution:
            - Morphine, 0.5 mg/kg IM initial loading dose then 0.12-0.36 mg/kg/h IV
            - Ketamine, 0.25-0.5 mg/kg IV initial loading dose then 0.12-1.2 mg/kg/h IV
- Antibiotics (topical or systemic for superficial or deep wounds, respectively) as needed

POSSIBLE COMPLICATIONS

- Thoracic injuries including rib fractures, pneumothorax, hemothorax, pulmonary contusions, and diaphragmatic hernias
- Abdominal injuries including body wall hernias and hollow and solid organ rupture
- Musculoskeletal injuries (fractures, luxations, ligament injuries)
- Integument injuries (lacerations, degloving wounds, others)
- Traumatic brain or spinal cord injury
- Peripheral nerve damage (sciatic nerve injury, brachial plexus avulsion, others)

RECOMMENDED MONITORING

- Physical parameters including heart rate, respiratory rate/effort, mucous membrane color, body temperature, and blood pressure
- Oxygenation assessment using pulse oximetry and or arterial blood gas measurement as needed
- PCV/TS to assess for blood loss, recheck of other blood work indicated by baseline values and clinical course
- Urination:
    - Frequency, estimated amount and character
    - May need to place urinary catheter if concerned about urine output or integrity of urinary tract
    - Note that patients with ruptured urinary bladder may still pass urine and may also have a palpable bladder; suspect bladder rupture if ascites, abdominal distention, hematuria, pelvic fractures, or lethargy with hyperkalemia are present.

PROGNOSIS AND OUTCOME

- Reported survival rate in dogs is 82%-87%; reported survival rate in cats is 84%.
- In one study:
    - Death most commonly resulted from intrathoracic and intraabdominal injuries.

- Most of the dogs that were euthanized had central nervous system injury.

PEARLS & CONSIDERATIONS

COMMENTS

- Tachycardia, tachypnea, hyperemia/injected mucous membranes, and bounding femoral pulses are signs of early compensatory shock and require immediate treatment.
- Acute blood loss causes a decrease in the plasma TS before a drop in the PCV, because splenic and hepatic contraction replace lost red cells; if blood loss continues, the PCV will decrease rapidly.
- Thoracic radiographs are recommended in all cases, especially dogs requiring general anesthesia and surgical repair of fractures; prevalence of thoracic wall and pulmonary trauma was reported as 39% in one study.
- Uroabdomen may be predicted with an abnormal abdominal fluid creatinine concentration to peripheral blood creatinine ratio of >2:f or an abnormal potassium concentration to peripheral blood potassium concentration of >1.4:1.
- In rare cases, injuries to gastrointestinal tract or biliary tract are undetectable for several days.

PREVENTION

- Keep cats housed indoors.
- Walk dogs on a leash at all times.
- Frequently check fences and other enclosure systems for damage.
- Do not allow dogs to sleep or lie in driveways.

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Histoplasmosis

BASIC INFORMATION

DEFINITION

A systemic fungal disease caused by the soil-dwelling dimorphic fungus, *Histoplasma capsulatum;* affects both companion animals and humans.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs and cats are equally likely to develop histoplasmosis once exposed.
- Young adult (<4 years) large-breed dogs; no apparent sex predilection
- Most cats with histoplasmosis are young (<4 years). Females may be more commonly affected.

GENETICS & BREED PREDISPOSITION

- Sporting (hunting) breeds may be overrepresented, likely due to greater environmental exposure.

RISK FACTORS

- Outdoor activities in endemic areas
- Contact with nitrogen-rich organic material such as moist soil containing bird (classically, starling, but many bird species are implicated) or bat excrement

CONTAGION & ZOONOSIS

Common-source exposure possible, but true zoonosis does not occur (exception: accidental laboratory inoculation/inhalation).

GEOGRAPHY AND SEASONALITY

H. capsulatum is endemic to many temperate and subtropical regions of the world. In the United States, histoplasmosis occurs most commonly in the Missouri, Mississippi, and Ohio River valleys. *H. capsulatum* may thrive in nonendemic regions, however, if soil conditions change to favor fungal growth.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Disease may remain confined to the lungs or gastrointestinal (GI) tract or may become disseminated (commonly with **GI** involvement).

HISTOPLASMOSIS Geographic area in which histoplasmosis is endemic. Areas of highest prevalence are cross-hatched.

(From Rippon JW: Medical mycology, ed 3, Philadelphia, 1988, Saunders. Reprinted with permission.)

HISTORY, CHIEF COMPLAINT

- Clinical signs are determined by the major organ system(s) affected. Clients should be carefully questioned about recent travel with their pets to endemic areas in the preceding 1-2 months.
- Nonspecific signs of disease are common (especially in cats), typically including depression, anorexia, and weight loss. Clients may notice labored breathing in dogs and cats with pulmonary histoplasmosis. Dogs with GI involvement may exhibit signs consistent with small- and/or large-bowel diarrhea, melena/hematochezia, tenesmus, and recent weight loss. Signs of GI involvement in cats are less readily identifiable versus those in dogs and may manifest merely as weight loss and anorexia.

PHYSICAL EXAM FINDINGS

- Dyspnea, tachypnea, coughing, abnormal lung sounds, pale mucous membranes
- Lymphadenopathy
- Poor body condition/emaciation
- Fever
- Hepatomegaly, splenomegaly (or both if disseminated disease)
- Ocular and dermal lesions (rare)

ETIOLOGY AND PATHOPHYSIOLOGY

- The mycelial stage (in soil; releases spores [microconidia and macroconidia]) of *H. capsulatum* is responsible for mammalian infections. Exposure probably most commonly occurs by inhaling microconidia, which are small enough to reach the lower airways. Oral exposure may result in disease, as evidenced by some animals developing only GI signs.
- After inhalation, microconidia convert to the yeast form in the small airways of the lower respiratory tract, where they reproduce by budding.
- The organisms are phagocytosed by host mononuclear cells, in which they undergo further replication. Disease at this point may remain limited to the respiratory system or become generalized via lymphatic and/or hematogenous dissemination.
- Dissemination to the GI tract, lymph nodes, spleen, liver, and bone marrow is common. The organism load in infected tissues is generally high, and affected tissues respond with granulomatous inflammation.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is suspected based on the presence of a miliary or nodular pattern on thoracic radiographs in a dog with exposure to an endemic region; lymphadenopathy and hepatomegaly further support the diagnosis. Confirmation requires cytologic or histologic analysis.

DIFFERENTIAL DIAGNOSIS

- Other systemic mycoses (e.g., blastomycosis, cryptococcosis, coccidioido-mycosis)
- Neoplasia

INITIAL DATABASE

- CBC:
  - Nonregenerative anemia (the most consistent, albeit nonspecific, finding with histoplasmosis). Likely secondary to chronic disease, bone marrow infiltration, and/or GI blood loss.
  - Leukocyte parameters are variably affected, and thrombocytopenia may be present.
  - Intracellular organisms may be (very rarely) observed on blood smears.
- Serum chemistry profile: variable abnormalities; commonly hypoalbuminemia, elevated liver enzyme activity, and/or hypercalcemia
- Radiography:
  - Dogs and cats with active pulmonary histoplasmosis often exhibit a diffuse miliary interstitial or nodular pattern on thoracic radiographs consistent with mycotic pneumonia.
  - Tracheobronchial lymphadenopathy is commonly observed.
  - Pleural effusion may occasionally be present and obscure the aforementioned radiographic findings.
  - Osseous lesions are rarely observed, but when present, they consist of a mixed pattern of osteolysis and osteoproliferation.

ADVANCED OR CONFIRMATORY TESTING

- Fine-needle aspiration and cytologic evaluation:
  - Usually provides a definitive ante-mortem diagnosis
  - The organisms are usually observed within phagocytic cells and appear as single to multiple round bodies with a basophilic center and clear, thin outer rim.
  - Tissues most rewarding for obtaining a diagnostic sample in the dog include rectal scrapings (see p. 1334), colonic biopsy imprints, and aspirates of bone marrow (see p. 1212), liver, spleen (see p. 1275), and lung (see p. 1277), depending on the extent of disease. Organ enlargement and ease of access determine which organs are sampled.
  - In cats, tissues that may successfully be sampled include bone marrow, lung, and lymph nodes.
- Histologic analysis of biopsy specimens may be necessary if cytologic testing results are inconclusive.
- Serologic testing is not recommended owing to the unreliability of current immunodiagnostic tests.

TREATMENT

TREATMENT OVERVIEW

- Treatment has focused on clearing *H. capsulatum* infection with oral azole antifungal agents and in some cases controlling inflammation with antiinflammatory medication. Duration of treatment depends on severity of disease and the patient's response to therapy. Typically, animals are treated with oral antifungals for at least 4-6 months.
- Itraconazole is the treatment of choice for mild histoplasmosis infections. Fluconazole is not effective in treating histoplasmosis.
- Ketoconazole has lower potency and increased toxicity compared to itraconazole and is not generally recommended for treatment of histoplasmosis.

ACUTE GENERAL TREATMENT

- Azole drugs (mild cases):
  - For mild cases (local involvement only, no overt respiratory signs, patient is eating and is not debilitated).
  - Itraconazole capsules 10 mg/kg PO q 24 h (dogs), 10 mg/kg PO q 12 h (cats); *or*
  - Itraconazole oral solution (5 mg/kg PO q 24 h [cats, dogs])
  - Treatment should be initiated as early as possible in the disease process to improve the probability of preventing dissemination.
- Itraconazole + amphotericin B:
  - For severe disseminated histoplasmosis or fulrninant pulmonary or GI disease, combination therapy of an oral azole with parenteral amphotericin B should be considered (various protocols).
  - The drugs are started concomitantly, with the azole continued past cessation of amphotericin B therapy.
  - Sample protocol for amphotericin B: Dog, 0.5 mg/kg IV q 48-72 h up to 60 days or until signs of toxicosis, usually renal. Cat, 0.25 mg/kg IV q 48-72 h or until signs of toxicosis, usually renal.
  - Sample protocol for lipid-soluble amphotericin B (lower risk of nephrotoxicosis) for dogs and cats: 1 mg/kg IV q 48-72

h × 60 days or until signs of toxicosis.
- Amphotericin B is fungicidal (versus azoles, which are fungistatic) but is limited by its high risk of progressive nephrotoxicosis (ensure patient is well hydrated and undergoing diuresis during treatment; monitor daily blood urea nitrogen and creatinine during treatment, and stop treatment if >50% increase in either parameter), the potentially severe perivascular reaction or sloughing elicited by extravasation, and the possibility of anaphylaxis.
- Prednisone, 2 mg/kg PO q 24 h hastens resolution of dyspnea in dogs with histoplasmosis-induced tracheobronchial lymphadenomegaly (in the absence of systemic histoplasmosis). When used alone or with antifungals, clinical signs resolve faster (<2.6 weeks) compared to dogs treated with antifungals alone (8.8 weeks).
- Voriconazole: treatment of choice in human histoplasmosis; very costly

CHRONIC TREATMENT

Itraconazole or voriconazole PO for at least 4-6 months. The most difficult to treat tissues include ocular, central nervous system, bone, and epididymis. Orchiectomy is advised for epididymal histoplasmosis.

POSSIBLE COMPLICATIONS

Renal failure with amphotericin B

RECOMMENDED MONITORING

Response to treatment is monitored by periodically assessing CBC and serum chemistry values, observing for improvement in body condition, and monitoring for resolution of radiographic lesions.

PROGNOSIS AND OUTCOME

- Prognosis may vary from guarded to good depending on the extent of disease.
- Disease limited to the lungs typically carries a better prognosis compared to GI or disseminated histoplasmosis.
- Prognosis is guarded for return of vision with ocular involvement, depending on severity of retinal damage prior to treatment.

PEARLS & CONSIDERATIONS

COMMENTS

- Depending on the degree of *H. capsulatum* infection, some patients may be successfully treated with oral antifungals alone. Alternatively, some patients may be critically ill and require more intense combination therapy and supportive care. The need for fluid and nutritional support should not be overlooked in these patients.
- Itraconazole capsules should always be administered with food; bioavailability is optimized in the presence of ingesta. Itraconazole liquid solution should be given on an empty stomach and has a greater bioavailability than capsules.
- Therapeutic drug monitoring (serum level measurement) is available for itraconazole.

PREVENTION

There is no effective vaccine against *H. capsulatum.* Disease is best prevented by avoiding contact with contaminated soil in endemic areas.

SUGGESTED READING

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Histiocytic Diseases

BASIC INFORMATION

DEFINITION

A complex group of syndromes resulting from an accumulation of histiocytes, which are cells of macrophage or dendritic origin. These disease syndromes share many common features, though clinical and histologic aspects help differentiate each one. Most are shown to arise from dendritic cell (DC) origin, specifically interstitial DCs, and less commonly Langerhans DCs. Histiocytic diseases occur in both dogs and cats, though reports in cats are sparse. Syndromes overlap, diverge, and converge but can be simplified into the following groups:

- Benign tumors:
  - Histiocytoma: spontaneously regressing skin tumor common in young animals
  - Idiopathic periadnexal multinodular granulomatous dermatitis
- Reactive histiocytic disorders:
  - Cutaneous histiocytosis: a benign accumulation of histiocytes in the skin, with predilection for the nasal planum, head, and neck
  - Systemic histiocytosis: similar to cutaneous histiocytosis but characterized by lymph node and organ involvement
- Malignant histiocytic neoplasia:
  - Histiocytic sarcoma: focal or disseminated, the latter is commonly considered synonymous with malignant histiocytosis.
  - Malignant fibrous histiocytoma: despite its name, this focal lesion is a unique soft tissue sarcoma with three histologic subtypes: storiform-pleomorphic (mesenchymal tissue with histiocytic infiltrate, the most common form in dogs), inflammatory (most common in the spleen of dogs), and giant cell (the most common type in cats). The histiocytic infiltrate is not neoplastic and is of questionable importance (see p. 684).
  - Malignant fibrous histiocytoma: despite its name, this focal lesion is a unique soft tissue sarcoma with three histologic subtypes: storiform-pleomorphic (mesenchymal tissue with histiocytic infiltrate, the most common form in dogs), inflammatory (most common in the spleen of dogs), and giant cell (the most common type in cats). The histiocytic infiltrate is not neoplastic and is of questionable importance (see p. 684).

SYNONYM

Histiocytic sarcoma (disseminated): malignant histiocytosis (though some texts describe disseminated histiocytic sarcoma as having features of both malignant histiocytosis and malignant fibrous histiocytoma).

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Histiocytic diseases have predominantly been reported in dogs, but reports exist in cats (malignant histiocytosis), cattle (malignant histiocytosis), and people.
- Cutaneous histiocytosis can occur in younger dogs, with systemic histiocytosis and malignant histiocytosis in middle-aged dogs (median age 6 years).
- Equal prevalence in males and females

GENETICS & BREED PREDISPOSITION

Bernese mountain dogs (BMD) are predisposed to many types of histiocytic disease, though as a breed they are not as commonly affected with malignant fibrous histiocytoma. In BMD, heritability is oligogenic and almost certainly *not* autosomal or sex linked. Other breeds overrepresented in histiocytic diseases include golden retrievers, flat-coated retrievers (44% of all tumors), rottweilers, and Doberman pinschers. Flat-coated retrievers are predisposed to malignant fibrous histiocytoma. No breed predisposition has been reported in cats.

RISK FACTORS

For cats, vaccination may predispose to malignant fibrous histiocytoma.

GEOGRAPHY AND SEASONALITY

Initially, histiocytosis in BMD primarily affected dogs from Switzerland, where the breed originated. Many cases have now been reported in dogs born in the United States and the United Kingdom. There is no reported seasonality.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- As detailed above, histiocytic diseases can be divided in different ways but ultimately are either local or diffuse, reactive, benign, or malignant.
- A hemophagocytic variant occurs in both dogs and cats and leads to anemia and thrombocytopenia. This variant is very aggressive.

HISTORY, CHIEF COMPLAINT

- Most dogs are presented for signs referable to the primary tumor.
- Dogs with cutaneous histiocytosis and systemic histiocytosis are typically presented for evaluation of skin lesions.
- Systemic histiocytosis can have orbital involvement, and patients may be presented for evaluation of ocular signs.
- Dogs with malignant fibrous histiocytoma are usually presented for evaluation of a soft-tissue mass or lameness (if the joint tissues or bones are involved).
- Disseminated HS (MH) is a much more insidious disease, since masses are primarily visceral (spleen, liver, bone marrow, lymph nodes, lungs). Cutaneous and subcutaneous masses are uncommon with malignant histiocytosis. These dogs and cats are often presented for evaluation of nonspecific systemic signs such as lethargy and anorexia/weight loss. Skeletal tumors can also be of histiocytic origin, cause lameness, are usually associated with a soft-tissue mass, and usually associated with the disseminated form of the disease.

PHYSICAL EXAM FINDINGS

- Focal lesions typically involve a palpable mass, often on the extremities. If the mass is subarticular, lameness may be prominent, especially with bone involvement.
- A prominent spleen may be palpated with splenic malignant fibrous histiocytoma or with splenic involvement of malignant histiocytosis and can correlate with worse prognosis.
- Dogs with malignant histiocytosis often have significant pulmonary involvement and may be dyspneic with advanced disease. Cough is a common presenting complaint.
- With systemic histiocytosis, skin lesions may be seen on the nasal planum, muzzle, flank, and scrotum as well as the periocular tissues. Skin lesions in cutaneous histiocytosis and systemic histiocytosis are typically nodular to plaquelike.
- Generalized lymphadenopathy may be appreciated with systemic histiocytosis and malignant histiocytosis, and enlargement of the draining lymph node may be found with malignant fibrous histiocytoma.

ETIOLOGY AND PATHOPHYSIOLOGY

- Largely unknown in dogs, although oligogenic inheritance has been shown in BMD, and 25% of BMD are affected by clinical HS.
- Hemophagocytic HS is of macrophage origin and originates in the splenic red pulp or bone marrow.
- Malignant fibrous histiocytoma in cats possibly resulting from vaccination is covered elsewhere under injection-site sarcomas (see p. 610).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Histiocytic diseases occur in dogs and cats and have many forms which can be distinguished from each other based on clinical presentation, including site(s) of involvement, and immunohistochemistry.

DIFFERENTIAL DIAGNOSIS

- Granulomatous disease
- Lymphoma
- Poorly differentiated mast cell tumor
- Anaplastic sarcoma or carcinoma
- Synovial sarcoma (joint tumors)
- Other soft-tissue or bone sarcomas (for local disease)

INITIAL DATABASE

- CBC, serum chemistry profile, and urinalysis. No characteristic or specific findings with histiocytic diseases, except hemophagocytic syndrome results in Coombs-negative anemia and thrombocytopenia. Hypoalbuminemia may be present.
- Fine-needle aspiration of accessible masses and lymph nodes for cytologic examination (look for multinucleated giant cells and erythrophagocytosis by macrophages).
- Biopsy of affected tissue
- Radiography of affected area if bony involvement is suspected typically reveals a lesion that is permeative, punctate, or moth-eaten.
- Thoracic radiography to evaluate pulmonary parenchyma for nodules (often large)
- Abdominal ultrasound to screen for visceral involvement
- Bone marrow aspiration and cytology if suspect systemic disease

ADVANCED OR CONFIRMATORY TESTING

- CT scan of affected area if focal and considering resection
- Immunohistochemistry on biopsy tissue (see Pearls & Considerations below)

TREATMENT

TREATMENT OVERVIEW

For benign/reactive disease, immunosuppression may suppress disease, but lesions are often resistant to treatment. For malignant disease, if only local involvement is present, surgical removal should be followed by adjuvant CCNU. If disseminated disease is present, CCNU and palliative care may extend survival time, but long-term prognosis is poor.

ACUTE GENERAL TREATMENT

- Patients with malignant histiocytosis having significant erythrophagocytosis may require red blood cell transfusion, ideally in conjunction with initiation of therapy to abort red cell loss.
- Dyspneic patients with malignant histiocytosis may benefit temporarily from oxygen therapy, but the prognosis is grave when the disease has reached the point of producing respiratory compromise.

CHRONIC TREATMENT

- Reactive histiocytoses are typically treated with immunosuppressive therapy. Initially prednisone is used (2 mg/kg PO q 24 h until clinical response is noted, then a slow taper of 1 mg/kg PO q 24 h for 1 month, 0.5 mg/kg PO q 24 h for 1 month, 0.5 mg/kg PO q 48 h for 3 months, then stop or maintain at lowest effective dose). If no response is noted within 1 month of prednisone therapy, or if lesions relapse and no longer respond to prednisone, then azathioprine (at 2 mg/kg PO q 24 h, with the same taper schedule as prednisone) or cyclosporine may be added. Recent anecdotal evidence suggests efficacy of tetracycline and niacinamide (dogs under 10 kg: 250 mg of each drug q 8 h, and dogs over 10 kg: 500 mg of each drug q 8 h). All treatments can be used with or without antibiotics depending on appearance of skin lesions and at the discretion of the treating clinician.
- Systemic malignant histiocytic diseases are poorly responsive to therapy and remissions, if achieved, are typically short lived.
    - Therapies attempted include: chemotherapy (29%-46% response of macroscopic disease to 60-90 mg/m^2 CCNU, doxorubicin 30 mg/m^2 also suggested) and TALL104 therapy (cytotoxic T-lymphocytes; not commercially available)
- Focal malignant histiocytic diseases respond well to surgical resection (amputation if joint or bone affected or if complete resection with limb salvage impossible) ± irradiation.

RECOMMENDED MONITORING

- The involved site(s) should be monitored closely via regular observation and diagnostic imaging as appropriate.
- Three-view thoracic radiographs and physical examination including lymph node palpation and examination of the site should be performed every 3 months for the first year after diagnosis for malignant fibrous histiocytoma and every 4-6 months thereafter.

PROGNOSIS AND OUTCOME

- Cutaneous histiocytosis: good; may regress spontaneously or respond to immunosuppressive doses of prednisone.
- Systemic histiocytosis and disseminated HS (malignant histiocytosis): poor. For both dogs and cats, systemic histiocytosis

may wax and wane but is ultimately progressive, whereas malignant histiocytosis is rapidly progressive, with both leading to euthanasia. Disseminated HS (malignant histiocytosis) is considered uniformly fatal. Survival of dogs with systemic histiocytosis ranges from months to years. Survival for dogs with disseminated HS/malignant histiocytosis averages around 4 months, though chemotherapy in the adjuvant setting with CCNU may prolong survival to greater than f year in some dogs. Prognosis to date for cats with malignant histiocytosis is similarly grave, and response to therapy has been poor.

- Malignant fibrous histiocytoma or focal histiocytic sarcoma: good if low-grade and local control is achieved with surgery ± radiation.

PEARLS & CONSIDERATIONS 

COMMENTS

The following clinical and pathologic differences can help differentiate histiocytic syndromes:

- Clinical findings/behavior:
  - Disseminated HS (malignant histiocytosis) is a multiorgan disease typically arising from internal sites including viscera, whereas systemic histiocytosis involves skin and lymph nodes with occasional internal sites.
  - Systemic histiocytosis may wax and wane but ultimately progresses, whereas malignant histiocytosis is rapidly progressive.
  - Cutaneous histiocytosis is limited to the skin and does not lead to malignant histiocytosis.
  - When malignant fibrous histiocytoma occurs in the viscera, the spleen is the most common location.
  - Malignant fibrous histiocytoma can metastasize to the lymph nodes, especially the giant cell variant, which is unusual for sarcomas.
- Histopathology:
  - Malignant histiocytosis exhibits a greater degree of cellular atypia than systemic histiocytosis.
  - Malignant histiocytosis often exhibits erythrocytophagy and sometimes leukocytophagy.
  - Multinucleated giant cells can be seen in malignant histiocytosis and in MFH, but the neoplastic population in MFH is spindyloid.
- Immunohistochemistry for both dogs and cats:
  - CD 18+ (leukocyte marker), CD 3–, and CD 79a– are the three immunohistochemical stains and the pattern most useful for diagnosing dendritic cell origin and ruling out lymphoma. CD f8 positivity combined with stains negative for other lineages may confirm HS at other sites such as ocular HS.
  - Dendritic cells should be CD 1a or c+, CD 11c+, and MHC ll+ (Langerhans DCs are associated with E-cadherin positivity) and macrophages should be CD 1-, CD 11c- and CD 11d+ as well as lysozyme positive.
  - Malignant histiocytic diseases should be CD 4- and reactive syndromes, CD 4+.
  - Macrophage origin HS is associated with hemophagocytic syndrome.

PREVENTION

Because histiocytic diseases are often inherited, careful documentation of pedigrees for affected animals is crucial to the eventual control by selective breeding. Inheritance of histiocytosis in Bernese mountain dogs has been calculated at a moderate 0.298, suggesting that careful breeding could be effective at eliminating this disease. This means that 29.8% of the risk of developing histiocytosis in the population of Bernese mountain dogs is attributable to genetic differences among individuals. The remainder of the risk is environmental, though specific factors have not been identified.

CLIENT EDUCATION

- Owners should contact the breeder or source of affected animals.
- An overtly (phenotypically) normal breeding pair of Bernese mountain dogs with one affected offspring will produce on average one in seven puppies that will ultimately succumb to histiocytosis.

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Hip Luxation

BASIC INFORMATION

DEFINITION

- Dislocation of the femoral head relative to the acetabulum, most frequently in a craniodorsal direction
- Luxation: complete displacement of the femoral head relative to the acetabulum
- Subluxation: partial or incomplete dislocation of the femoral head relative to the acetabulum (i.e., joint incongruity exists)

SYNONYMS

Coxofemoral luxation, dislocated hip

EPIDEMIOLOGY

RISK FACTORS

Dogs with hip dysplasia are at risk for luxation with even minor trauma.

ASSOCIATED CONDITIONS & DISORDERS

Pelvic and proximal femoral fractures

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Craniodorsal luxation most common; caudoventral is uncommon.

HISTORY, CHIEF COMPLAINT

- Trauma (falls, vehicular) causing acute non-weight-bearing lameness
- Intermittent lameness in chronic cases with unrecognized trauma

PHYSICAL EXAM FINDINGS

- Variable lameness
- With craniodorsal luxation, leg appears shortened, stifle rotated externally, and tarsus internally.
- Palpation of hip reveals swelling, pain, crepitus, and abnormal position of greater trochanter.

ETIOLOGY AND PATHOPHYSIOLOGY

Traumatic coxofemoral luxations comprise 90% of all luxations in small animals.

- With craniodorsal luxation, femoral head is driven dorsally over the acetabular rim:
  - Both femoral head ligament and joint capsule are torn.
  - Avulsion fracture associated with ligament can occur.
  - Gluteal muscle contractions exacerbate craniodorsal displacement of proximal femur.
- With ventral luxation, transverse acetabular ligament is ruptured.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Orthogonal view radiography is critical in establishing a diagnosis and delineating concomitant regional osseous injuries.

DIFFERENTIAL DIAGNOSIS

Subluxation due to hip dysplasia, femoral capital physeal fracture, femoral neck fracture, acetabular fracture

INITIAL DATABASE

- Physical examination: findings as described previously (see Physical Exam Findings above)
- CBC/serum chemistry panel/urinalysis and thoracic/abdominal radiographs based on patient stability and the American Society of Anesthesiologists' classification (see p. 1372)
- Limb and pelvis examinations plus orthogonal view radiography to confirm the diagnosis and determine concomitant or inciting disorders

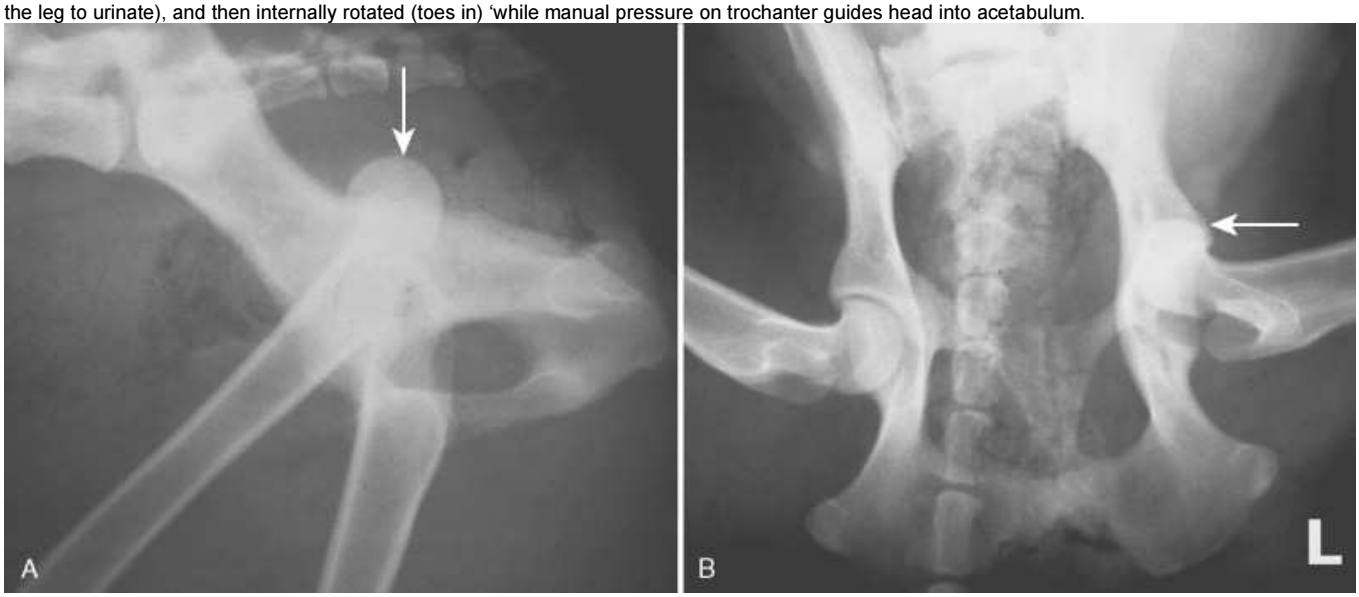
TREATMENT

TREATMENT OVERVIEW

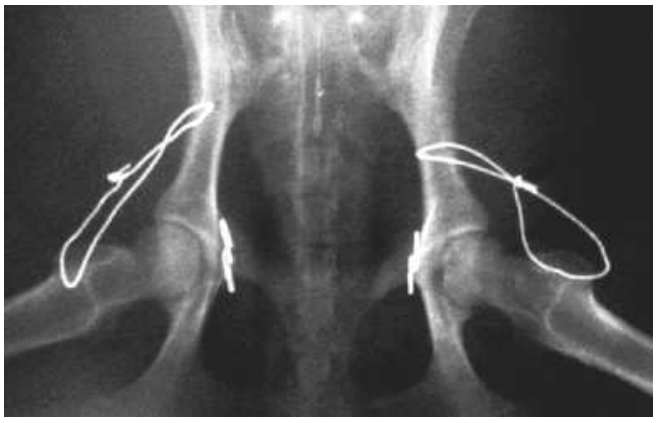
- With acute injury of a normal hip joint, the goal is closed or open anatomic joint reduction/stabilization.
- With an abnormal or chronically luxated normal joint, goal is to save limb and treat joint by femoral head osteotomy (FHO), total hip replacement (THR), or triple pelvic osteotomy (TPO).

ACUTE GENERAL TREATMENT

- Closed reduction and Ehmer sling application if:
  - Duration of injury is <48 hours, *and*
  - Hip is otherwise structurally normal, *and*
  - Patient is sufficiently stable to undergo general anesthesia.
- With patient in lateral recumbency (unaffected side down), the upper (affected) limb is externally rotated (toes out), abducted (lifted, as a male dog lifts the leg to urinate), and then internally rotated (toes in) 'while manual pressure on trochanter guides head into acetabulum.



HIP LUXATION Lateral **(A)** and ventrodorsal **(B)** projections of a craniodorsal luxation of left hip joint. Note dorsal and cranial displacement of femoral head relative to acetabulum *(arrows).*



HIP LUXATION Postoperative ventrodorsal projection of hip joints of an obese 45-kg dog treated for traumatic bilateral hip luxation. Bilateral toggle pins and greater trochanter-to-ilium wires were used for stabilizing injuries.

- After reduction, extensive range-of-motion maneuvers are performed to force soft tissue out of acetabulum and test joint stability.
- Open reduction is performed in failed or unstable closed reductions in a patient 'with normal coxofemoral joint.
- Extraarticular techniques include suture between origin of greater trochanter and rectus femoris muscle, iliofemoral suture, synthetic sutures to replace capsule, capsulorrhaphy, or De Vita pinning (controversial).
- Intraarticular techniques: toggle pinning, fascia lata loop or sacrotuberal ligament transposition
- Triple pelvic osteotomy can be performed for mildly dysplastic immature dogs 'with no degenerative joint changes.
- For chronic injuries, open reduction is difficult owing to muscular contraction and tissue fibrosis; cartilage degeneration exists. FHO or THR may be required in place of primary repairs.

CHRONIC TREATMENT

- Physical rehabilitation to maintain muscle tone, joint health, and overall limb functions

- Controlled activity to avoid relaxation, implant failures
- Nonsteroidal antiinflammatory drugs (NSAIDs) as needed to reduce pain and inflammation:
  - Aspirin, 10-25 mg/kg PO q 8-24 h *or*
  - Carprofen, 2 mg/kg PO q 12 h; *or*
  - Etodolac, 10-15 mg/kg PO q 24 h *or*
  - Deracoxib, 1-2 mg/kg PO q 24 h (may use 3-4 mg/kg PO q 24 h for first 7 days only); *or*
  - Meloxicam, 0.1 mg/kg PO q 24 h; *or*
  - Firocoxib, 5 mg/kg PO q 24 h; *or*
  - Tepoxalin, 10 mg/kg PO q 24 h (new product, objective data pending); *or*
  - Others

POSSIBLE COMPLICATIONS

- Reluxation
- Implant failure
- Degenerative joint disease
- Infection

RECOMMENDED MONITORING

- For closed reduction:
  - Frequent sling evaluations and removal 7-10 days post application
  - Limited activity for 1 month
  - Radiography after sling application and if lameness recurs
- For open repairs:
  - Restricted ambulation 1-2 months
  - Radiography if lameness recurs and based on fixation method

PROGNOSIS AND OUTCOME

- Variable ‘with closed reduction: 50% fail due to technical error or unrecognized joint disease.
- Good to excellent ‘with most operative procedures of acute injuries (i.e., previously normal joint)
- Guarded for dysplastic hips unless TPO, FHO, THR performed

PEARLS & CONSIDERATIONS

COMMENTS

- With normal hips, reduction/stabilization is preferred over FHO for all patient sizes.
- Extensive joint capsule and ligament damage impede successful closed reduction.
- Femoral head ligament avulsion fractures are often not recognized radiographically.

SUGGESTED READING

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AUTHOR: JONATHAN SHANI

AUTHOR & EDITOR: JOSEPH HARARI

Hip Dysplasia

Video Available on Website

BASIC INFORMATION

DEFINITION

A condition caused by abnormal development of the coxofemoral joint, characterized by joint laxity in young patients and degenerative joint disease (DJD) of variable severity in both young and adult patients

EPIDEMIOLOGY

SPECIES, AGE, SEX

- The condition is a developmental disease and occurs in young dogs. Clinical signs may be recognized in the immature or mature patient, or the condition may remain occult throughout life.
- Less frequent in cats

GENETICS & BREED PREDISPOSITION

- Most common in large and giant breeds (Labrador retriever, golden retriever, German shepherd dog, rottweiler, Newfoundland)
- May be more common in the Maine coon than other cat breeds

RISK FACTORS

- Rapid weight gain and growth associated with excessive caloric intake
- Factors causing synovial inflammation of the coxofemoral joint

ASSOCIATED CONDITIONS & DISORDERS

Affected animals may have other genetically predisposed or developmental conditions concurrently. These include:

- Elbow dysplasia
- Osteochondrosis
- Stifle disease
- Panosteitis
- Hypertrophic osteodystrophy

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Hip laxity is the main cause of juvenile and mature manifestations.
- Juvenile:
  - Hip laxity characterized by subluxation or luxation of the coxofemoral joint
    - Acetabular dysplasia
    - Femoral head/neck malformations
- Mature:
  - Degenerative joint disease

HISTORY, CHIEF COMPLAINT

- Juvenile patients typically have hindlimb lameness characterized by:
  - “Bunny-hopping” gait
  - Unilateral or bilateral pelvic limb lameness
  - Difficulty rising
  - Exercise intolerance
  - Description of an audible “clicking” when rising or walking
  - Shifting of weight to the thoracic limbs and extension of the hocks

- Mature patients have progressively worsening hindlimb lameness characterized by:
  - Weight-bearing lameness
  - Lameness following exercise
  - Pelvic musculature disuse atrophy

PHYSICAL EXAM FINDINGS

- Juvenile patient:
  - Pain during caudal extension, external rotation, and abduction of the coxofemoral joint
  - Hip joint laxity (positive Ortolani sign) characterized by dorsal subluxation of the femoral head with the limb adducted, followed by a palpable click with reduction of the femoral head when the limb is abducted
    - Angle of reduction is the measured point at which the femoral head slips back into the acetabulum as the limb is abducted.
    - Angle of subluxation is the measured point at which the femoral head slips out of the acetabulum as the limb is then adducted.
  - Poor pelvic limb musculature
  - Abnormal pelvic limb conformation (tarsal hyperextension)
  - Patient may appear to have an arched spine as weight is shifted forward to the forelimbs.
  - Narrow pelvic limb stance
- Mature patient:
  - Pain during extension, external rotation, and abduction of the hip
  - Decreased joint range of motion
  - Coxofemoral joint crepitus
  - Ortolani sign is lost as periarticular fibrosis limits femoral head movements
  - Hind limb muscle atrophy
  - Exaggerated hip movement at a walk (see online video clip)

ETIOLOGY AND PATHOPHYSIOLOGY

- A combination of genetic and environmental factors lead to hip joint laxity, resulting in joint instability and abnormal progression of endochondral ossification.
- Puppies with a genetic predisposition to canine hip dysplasia are born with hips that are grossly normal. Changes in the hip joint begin within the first few weeks after birth.
- Lameness and gait abnormalities appear during growth between 3 and 8 months old.
- Lameness may resolve over time as joint stability is gained through periarticular fibrosis (this process recently has been called into question). As degenerative changes accumulate, clinical signs of mature hip dysplasia will develop.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is based on clinical signs of lameness, hip joint laxity or degeneration, and radiographs delineating a malformed and/or arthritic joint

DIFFERENTIAL DIAGNOSIS

Any cause of hind limb lameness in the juvenile or adult dog, including:

- In the immature patient:
  - Panosteitis
  - Osteochondrosis
  - Physeal fractures of the femoral head
  - Hypertrophic osteodystrophy
  - Muscle injury (iliopsoas, gracilis, adductor, pectineus, and sartorius muscles)
  - Patella luxation
- In the mature patient:
  - Cranial cruciate ligament injury
  - Patella luxation
  - Lumbosacral disease
  - Polyarthritis
  - Bone neoplasia
  - Rickettsial and fungal disease (geographic)
  - Muscle injury

INITIAL DATABASE

In the young patient:

- Palpation of hip joints for Ortolani sign, in addition to calculation of angles of subluxation and reduction (may require sedation/anesthesia)
- Lateral and ventrodorsal pelvic radiographs

ADVANCED OR CONFIRMATORY TESTING

- Orthopedic Foundation for Animals (OFA) for radiographic protocol subjective evaluation
- PennHIP radiographic protocol or dorsolateral subluxation radiographic views for objective evaluation of joint laxity to aid in individual and familial prognostication
- Coxofemoral arthroscopy to identify ligament and cartilage damage

TREATMENT

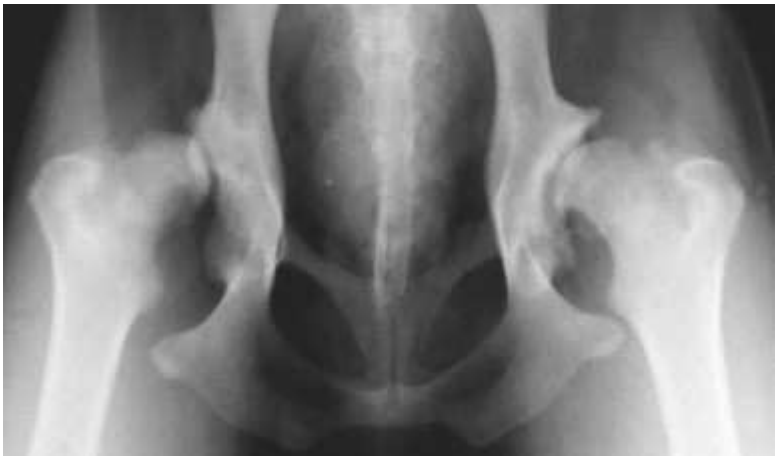
TREATMENT OVERVIEW

In cases without complete luxation of the coxofemoral joint, medical therapy is typically the initial recommended treatment. In general, medical management and progression of DJD will not encumber future surgical intervention with THR or FHO, as these surgical treatments are considered salvage procedures. Therapeutic goals are to:

- Reduce pain through decreasing inflammation and surgical improvement of malarticulation.
- Improve function through biomechanical stabilization of the hip joint or joint replacement.

ACUTE GENERAL TREATMENT

- Medical management (see p. 1565):
  - Nonsteroidal antiinflammatory drugs (NSAIDs):
    - Carprofen, 2 mg/kg PO q 12 h;*or*
    - Etodolac, 10-15 mg/kg PO q 24 h;*or*
    - Deracoxib, 1-2 mg/kg PO q 24 h;*or*
    - Meloxicam, 0.1 mg/kg PO q 24 h;*or*
    - Tepoxalin, 10 mg/kg PO q 24 h;*or*
    - Firocoxib, 5 mg/kg PO q 24 h
- Surgical management:
  - Juvenile pubic symphysiodesis (JPS):
    - In immature patients with joint laxity and without DJD (14-20 weeks of age)
    - To increase acetabular coverage of the femoral head; prevents osteoarthritis
    - Not recommended in cases with severe subluxation or luxation
  - Triple pelvic osteotomy (TPO):
    - In young dogs with joint laxity and ‘without DJD
    - To increase acetabular coverage of the femoral head and prevent osteoarthritis
    - Not recommended in cases with severe subluxation or luxation
  - Total hip replacement (THR): gold standard for restoration of normal joint function
    - In mature dogs
    - To replace degenerative joint structures with synthetic components
  - Femoral head and neck ostectomy (FHO):
    - Young to mature dogs
    - To reduce degenerative bone contact and form a pseudoarthrosis



HIP DYSPLASIA Ventrodorsal projection of severely dysplastic hips in a 16-month-old retriever cross dog. Radiographic abnormalities include subluxation of the femoral heads and remodeling of the shallow acetabula and femoral necks. This dog would be a candidate for total hip replacement or femoral head/neck ostectomies, based on clinical parameters described in the text.

        - Some surgeons do not recommend this procedure in giant-breed dogs.
        - Requires immediate and aggressive postoperative physical therapy to improve long-term outcome
        - Once a patient has undergone this procedure, future THR becomes exceptionally difficult and is typically accompanied by an unacceptable complication rate.
    - Acetabular denervation
        - Neurotomy of nerve fibers in the periarticular region to partially desensitize the hip joint
        - Only a palliative procedure
        - Objective (force plate) evaluations question efficacy of the procedure.

CHRONIC TREATMENT

- Medical management:
    - Prevention or elimination of overweight/obesity is the most important factor for long-term successful medical management (see p. 773).
    - PRN or daily NSAID administration as listed under Acute General Treatment above
    - Analgesia
        - Amantadine, 2-4 mg/kg PO q 24 h; *and/or*
        - Gabapentin, 3 mg/kg PO q 24 h; *and/or*
        - Tramadol, 2-4 mg/kg PO q 8-12 h; *or*
        - Codeine, 0.5-2 mg/kg PO q 8-12 h; *or*
        - Buprenorphine (cats), 0.01-0.03 mg/kg PO q 6 h
    - Joint fluid modifiers may be beneficial:
        - Polysulfated glycosaminoglycan 5 mg/kg IM twice weekly × 4-6 weeks; *or*
        - Pentosan polysulfate (from beech-wood hemicellulose) 3 mg/kg SQ once weekly; *or*
        - Oral formulations (glucosamine, chondroitin sulfate, hyaluronan): according to formulation/labeled instructions
    - Nutrition (energy restricted diet, as appropriate)
        - High omega-3 fatty acid diet
- Surgical management:
    - JPS or TPO are performed in some young animals with hip laxity.
    - FHO or THR are performed in mature animals with chronic disease (joint degeneration) unresponsive to medical therapies.

BEHAVIOR/EXERCISE

- Exercise moderation; limit high impact activities such as jogging and rough play
- Physical rehabilitation (see p. 1329); increase low impact activities to encourage muscular development-underwater treadmill, swimming and walking

POSSIBLE COMPLICATIONS

- Medical management:
    - Adverse reaction to NSAID
    - Continued progression of DJD necessitating surgical intervention

- Failure of medical management to control pain
- Surgical management:
  - Nerve and/or urinary tract damage from TPO or JPS surgery
  - Implant failure/pelvic canal narrowing with TPO
  - Osteomyelitis
  - Hip luxation or femoral fracture with THR
  - Poor limb usage after FHO due to patient obesity, muscular atony, or poor postoperative rehabilitation

RECOMMENDED MONITORING

- Basic laboratory monitoring of patients on NSAID therapy
- Weight, exercise level, clinical signs
- Radiographic monitoring if clinical signs progress and surgical intervention is warranted

PROGNOSIS AND OUTCOME

- The majority of patients will function at an improved level of activity with appropriate medical and surgical intervention.
- Postoperative rehabilitation (see p. 1329) is critical for good clinical recovery.

PEARLS & CONSIDERATIONS

COMMENTS

- Bilateral lameness may be difficult to recognize; musculature asymmetry between pelvic and thoracic limbs is suggestive of bilateral disease.
- Animals with a history of hip dysplasia that are acutely “down in the hind end” likely have concurrent bilateral cranial cruciate ligament rupture. A full orthopedic evaluation should be performed in these dogs prior to referral for surgical management of hip dysplasia.
- A total of 60%-75% of juvenile patients who are lame due to hip joint laxity and are treated with medical management may return to acceptable clinical function with maturity.
- Radiographic signs do not always correlate with clinical signs.
- FHO significantly complicates further surgical procedures such as THR. If THR is an option, then FHO should not be the first surgical intervention attempted.
- Routine radiographic monitoring of the clinically stable patient is generally not necessary, because further intervention is dictated by failure of medical management/progression of clinical signs.
- Editor's Note: Practitioners should consider consultation and referral with an orthopedic surgeon for management of this condition.

PREVENTION

- Screening and control of breeding animals for hip dysplasia:
  - Avoid breeding animals that have not been evaluated for hip conformation or hip laxity using either the OFA or the PennHIP methods.
  - Controversy exists regarding which of the two systems is “best;” OFA evaluation has been the traditional and simpler methodology, but evaluation is subjective and is performed on animals >2 years old. Only dogs receiving “excellent” or “good” evaluations should be bred. The PennHIP method is an objective measure of hip laxity performed as early as 16 weeks of age. Breeding just dogs that are in the top 50% (dogs with less joint laxity) of the breed will help to decrease laxity within the breed and decrease the incidence of hip dysplasia for that breed.
- Avoid high-energy diets in young, rapidly growing large-dog breeds.
- Based on equivalent human medical approaches, low-impact activities such as walking, swimming, and underwater treadmill therapy under the guidance of a trained canine rehabilitation specialist may provide benefit to affected individuals by increasing muscle mass and subsequently coxofemoral joint congruity (see p. 1329).

CLIENT EDUCATION

- Knowledge and careful screening of genetic history of the siblings and parents of potential pets
- Early sterilization of affected dogs and dogs treated with TPO or JPS
- Minimize the phenotypic expression of the disease in affected dogs through diet, low-impact exercise (see Prevention), and medical management.

SUGGESTED READING

Schulz: Hip dysplasia. In Fossum TW, editor: Small animal surgery, ed 3, St Louis, 2007, Mosby, pp 1233–1246.

AUTHORS: MATHIEU M. GLASSMAN, SPENCER A. JOHNSTON

EDITOR: JOSEPH HARARI

1ST EDITION AUTHORS: JAMES BOULAY, BARBARA GORES

High-Rise Syndrome

BASIC INFORMATION

DEFINITION

A collection of traumatic injuries sustained by an animal that falls from a substantial height. The term was originally coined in reference to cats, associated with a triad of injuries (epistaxis, hard palate fracture and pneumothorax) sustained by falls from a height of two or more stories. The orofacial aspects of high-rise syndrome are discussed in detail separately (see online chapter: High-Rise Syndrome, Craniofacial).

SYNONYMS

High-flyer syndrome, jumper's syndrome (both in humans)

EPIDEMIOLOGY

SPECIES, AGE, SEX

Predominantly young animals; cats less than 3 years old (reported age range 2.5 months to 20 years) and dogs less than 5 years old (range 2.5 months to 13 years 8 months).

RISK FACTORS

- Urban areas
- Tall buildings, particularly high-rise apartment buildings
- Open windows and balcony doors; access to roof tops

GEOGRAPHY AND SEASONALITY

Falls occur more frequently in summer, followed by autumn, when windows and balcony doors are open, and outdoor play is a factor.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

A witnessed (most commonly in dogs) or suspected (more common in cats) fall from a height such as a window sill, balcony, or roof

PHYSICAL EXAM FINDINGS

- A substantial number of animals present in a life-threatening condition requiring emergency treatment (7.8%-57.6% of cats and 44% of dogs)
- Clinical signs consistent with shock/cardiovascular instability (seen in 10%-24% of cats; exact incidence not known in dogs) including:
    - Tachycardia or bradycardia
    - Poor pulse quality and/or low blood pressure
    - Pale mucous membranes
    - Prolonged capillary refill time
    - Decreased core body temperature
- Respiratory distress (e.g. dyspnea, tachypnea, paradoxical respiration, cyanosis, and open-mouth breathing) due to pulmonary contusion, pneumothorax, rib fractures, diaphragmatic hernia and/or pain
- Facial injuries (see p. 531)
- Orthopedic injuries:
- Limb fractures (39%-61% of cats; 80% of dogs)
- Femoral and tibial fractures most common in cats
- Dogs that jump tend to land on their thoracic limbs, resulting in a higher percentage of forelimb injuries, whereas dogs that fall accidentally are reported to land predominantly on their pelvic limbs, resulting in a higher percentage of hindlimb injuries.
- Open fractures occur commonly.
- Pelvic fractures

- Luxations (e.g. coxofemoral, elbow and tibiotarsal)
- Ligamentous injuries:
  - Rupture (e.g., cruciate ligament, Achilles tendon)
  - Carpal hyperextension (more prevalent in dogs than cats)
- Evidence of visceral injury due to blunt abdominal trauma:
  - Uroabdomen secondary to urinary tract rupture (most commonly bladder)
  - Hematuria secondary to urinary bladder contusion
  - Hemoabdomen (may be mild and self-limiting or require surgical intervention [e.g., secondary to splenic rupture])
  - Abdominal wall rupture/herniation
  - Prepubic tendon rupture
- Spinal injuries (e.g., fracture, luxation or traumatic intervertebral disk herniation resulting in caudal paresis/plegia, tetraparesis or brachial palsy (due to brachial plexus avulsion)
- Penetrating abdominal or thoracic wounds secondary to impalement. May be accompanied by subcutaneous emphysema, abdominal wall herniation, or flail chest. Reported predominantly in cats falling onto spiked wrought iron fences.
- Evidence of head trauma/traumatic brain injury including:
  - Cranial neurologic abnormalities (such as anisocoria, Horner's syndrome)
  - Depressed level of consciousness
- Soft-tissue abrasions

ETIOLOGY AND PATHOPHYSIOLOGY

- Jumping during play or while chasing a squirrel, bird, insect, other animal (e.g., dogs chasing cats or other dogs), intruders, owners driving away in the street below or objects thrown while playing. Most common in dogs.
- Slipping while walking on the edge of a balcony railing or window, including icy ledges; suspected to be most common in cats.
- Thunderstorms or fireworks may incite a dog to jump if phobic.
- Range of documented heights fallen by cats (1-32 stories) and humans (1-20 stories) is high compared to that by dogs (1-6 stories)
- Injuries result from extreme vertical deceleration trauma.
- Impact surface is usually concrete; less commonly grass, rocks, snow, rubble, or dirt. Rarely impalement on metal railings. Objects encountered during the fall (e.g., potted plants on balcony railings, metal structures for hanging laundry, fire escapes, awnings, and trees) may result in additional injury or could help reduce injury by breaking the fall.
- Height of the fall is thought to have the greatest effect on injury pattern. In cats, severity of injury has been reported to increase up to seven stories (each story is 12-15 feet), after which further increases in height do not exacerbate injury severity; however, not all case series are consistent with this theory.
- Cats are better able to withstand free falls than dogs or humans due to their:
  - Highly developed vestibular system and righting reflex resulting in a unique ability to fall in a feet-first position from heights up to −100 feet, thereby minimizing postural torque, tumbling and rotation
  - Rapid achievement of terminal velocity (60 mph after −5 stories) such that their vestibular system is no longer stimulated by acceleration, reflex limb extension resolves, and the cat adopts a horizontal position, favoring a wider distribution of energy on impact
- Dogs experience a higher proportion of limb injuries, suggested to be associated with the greater size and strength of their limbs absorbing more of the impact before their trunk. Spinal injuries increase with increasing height of fall, as dogs have a tendency to tumble, landing on their back or in a vertical position.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

High-rise syndrome is usually diagnosed via history and physical examination. Following stabilization, thorough orthopedic and neurologic examination is vital. Diagnostic imaging (radiography, ultrasonography and/or CT) is then used to further characterize injury.

DIFFERENTIAL DIAGNOSIS

- Hit-by-car trauma
- Hit by a blunt object
- Kicked by an ungulate animal
- Fights with other animals
- Foreign body penetration
- Gunshot trauma
- Malicious injury

INITIAL DATABASE

- Orthopedic and neurologic examination (following stabilization if necessary)
- CBC, serum biochemistry panel, urinalysis
- Abdominal and thoracic ultrasound (abdominal and thoracic focused assessment sonography for trauma [AFAST and TFAST, respectively]; description of the procedures has been published for dogs but can be applied in cats if tolerated).
- Radiographs of thorax, abdomen, spine, and limbs
- Abdominocentesis and fluid analysis
- Full mouth (intraoral) dental radiographs
- Radiographs of the head, temporomandibular joints, and bullae

ADVANCED OR CONFIRMATORY TESTING

CT of head and spine

TREATMENT

TREATMENT OVERVIEW

- Stabilize animal; priorities are to resolve/improve dyspnea and shock and minimize stress (especially in cats).
- Orthopedic manipulations, radiography, or surgical procedures may initially need to be delayed, with adjunctive pain control, if the patient is systemically unstable at the time of presentation.

ACUTE GENERAL TREATMENT

- Management of respiratory distress:
  - Oxygen supplementation
  - Thoracocentesis if respiratory pattern suggestive of pneumothorax
- Fluid resuscitation from shock:
  - Obtain IV access in an uninjured limb.
  - Administer isotonic crystalloid ± colloid fluids to effect.
  - Start with 20 mL/kg crystalloid bolus in dogs or 10 mL/kg in cats, and titrate to effect up to 80-90 mL/kg/h in dogs and 50-60 mL/kg/h in cats. Consider judicious fluid use, particularly in animals with evidence of pulmonary contusions.
  - Consider addition of colloids if cardiovascular instability persists; start with a 5 mL/kg bolus in dogs and 1-2 mL/kg in cats, and titrate to effect up to 20 mL/kg in dogs and 10 mL/kg in cats.
  - Consider hypertonic saline (3-5 mL/kg once) ± hetastarch if evidence of traumatic brain injury.
- Blood product transfusion (whole blood or packed red blood cells) may be necessary if severe hemorrhage has occurred.
- Provision of appropriate analgesia (opioid analgesia is recommended initially; nonsteroidal antiinflammatory drugs may be added following patient stabilization and assessment of suitability).
- Broad-spectrum antibiotic coverage in animals with penetrating body cavity wounds prior to exploratory surgery
- Further treatment, if sedation or general anesthesia is required, depends on the successful outcome of this initial stabilization.
- Surgical treatment of skeletal injuries
- Exploratory thoracotomy or celiotomy in patients with penetrating thoracic or abdominal wounds, respectively
- Oral/dental treatment (see p. 531)

CHRONIC TREATMENT

- If response to emergency treatment is poor, visceral injury (abdominal and thoracic) with possible hemorrhage should be considered and pursued diagnostically, even in the absence of penetrating body cavity wounds as blunt trauma can occur.
- Chronic oronasal communication: medially positioned double flaps with releasing incisions along dental arch or overlapping double flaps.
- Temporomandibular joint injury (chronic luxation or ankylosis): unilateral or bilateral condylectomy.
- Extraction or endodontic therapy of teeth with pulp exposure.

NUTRITION/DIET

- With dental injuries, soft food is usually adequate; esophagostomy tubes are rarely necessary.

POSSIBLE COMPLICATIONS

- Chronic oronasal communication

- Temporomandibular joint ankylosis in very young animals with difficulty or inability to open the mouth
- Chylothorax

RECOMMENDED MONITORING

- In-patient monitoring until discharge
- Reexamination and removal of skin sutures in 2 weeks
- Removal of cerclage wire around mandibles in 4-5 weeks
- Routine follow-up and radiography to ensure fracture healing following orthopedic surgery

PROGNOSIS AND OUTCOME 

- Good prognosis for survival for ~90% of cats and dogs
- Euthanasia due to client financial constraints is reported, given the high percentage of animals requiring surgery.
- Death, excluding euthanasia, is generally due to shock, stress, and respiratory distress due to thoracic trauma.
- Most deaths occur within 24-36 hours of admission or in the immediate postoperative period
- It is suspected that most dogs falling >6 stories do not survive and hence are not brought to the hospital and assessed in case series

PEARLS & CONSIDERATIONS 

COMMENTS

Number and severity of injuries increase with increasing height of fall; it has been reported that the association between injuries and height of fall follows a curvilinear pattern.

CLIENT EDUCATION

Close windows and balcony doors in the presence of animals

SUGGESTED READING

Gordon LE, et al: High-rise syndrome in dogs: 81 cases (1985-1991). J Am Vet Med Assoc 202:118, 1993.

Papazoglou LG, et al: High-rise syndrome in cats: 207 cases (1988-1998). Aust Vet Pract 31:98, 2001.

AUTHOR: CLAIRE R. SHARP

EDITOR: ELIZABETH ROZANSKI

High-Rise Syndrome, Craniofacial

BASIC INFORMATION

DEFINITION

Triad of craniofacial, thoracic, and limb injuries sustained by an animal that falls from a height of one or more stories. The term was originally coined in reference to cats, associated primarily with falls from a height of two or more stories. For systemic effects of high-rise syndrome, see 529.

SYNONYMS

High-flyer syndrome (in humans), jumper's syndrome, extreme deceleration trauma

EPIDEMIOLOGY

SPECIES, AGE, SEX

Predominantly affects cats <3 years old and dogs <5 years old. There is no sex predilection in either species.

RISK FACTORS

- Urban areas
- Tall buildings
- Open windows and balcony doors; roofs

GEOGRAPHY AND SEASONALITY

Falls occur more frequently in summer, followed by autumn, when windows and balcony doors are open and outdoor play is a factor.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Triad of craniofacial, thorax and limb injuries; focus in this chapter is on craniofacial injury.

HISTORY, CHIEF COMPLAINT

Observed fall from window sills, narrow ledges, balconies, and roofs. Encounter of animal with typical injuries in location consistent with prior fall.

PHYSICAL EXAM FINDINGS

Typical craniofacial findings include:

- Mandibular symphysis separation and perisymphyseal fracture (malalignment in the mandibular incisor area)
- Split hard palate (with or without extension into soft palate and malalignment in the maxillary incisor area)
- Epistaxis
- Fractured maxillary canines (with or without pulp exposure), maxillary fourth premolars (traumatic hemisection between mesiobuccal and mesiopalatal crown-root segments), and mandibular first molars
- Temporomandibular joint luxation or fracture
- Zygomatic arch fracture
- Facial wounds
- Orofacial abrasion and hematoma

ETIOLOGY AND PATHOPHYSIOLOGY

- Jumping during play or while chasing a squirrel, bird, insect, or other animal
- Slipping while walking on the edge of a balcony railing or window

- Range of heights fallen by surviving cats (2-32 stories) is high compared to those fallen by dogs (1-6 stories), probably because most dogs do not survive falls from distances higher than 6 stories and thus are not brought to the veterinarian.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The combination of history and characteristic lesions on physical exam is diagnostic. The extent of diagnostic imaging performed on a case depends on the distribution and severity of lesions; most cases require a thoracic radiograph to assess for pneumothorax, pulmonary contusions, and chest wall injuries.

DIFFERENTIAL DIAGNOSIS

- Hit-by-car trauma
- Hit by a blunt object
- Kicked by an ungulate animal
- Fights with other animals
- Foreign-body penetration
- Gunshot trauma
- Animal abuse

INITIAL DATABASE

- Orthopedic and neurologic examination
- CBC, serum biochemistry panel, urinalysis
- Full mouth (intraoral) dental radiographs
- Radiographs of the head, temporomandibular joints, and tympanic bullae
- Radiographs of thorax, abdomen, spine, pelvis, and limbs

ADVANCED OR CONFIRMATORY TESTING

CT of head and spine

TREATMENT

TREATMENT OVERVIEW

- Stabilize animal, especially upper and lower airways and cardiovascular system (hypotension/blood loss).
- Preserve normal anatomic structure and function. Orthopedic manipulations or surgical procedures may initially need to be delayed, with adjunctive pain control, if the patient is unstable at the time of presentation.

ACUTE GENERAL TREATMENT

- Initial treatment for shock (fluid therapy) and thoracic injury (thoracocentesis if pneumothorax) followed by orthopedic/neurologic examination. Further treatment, if sedation or general anesthesia is required, depends on the successful outcome of this initial stabilization.
- Surgical treatment of skeletal injuries
- Cerclage wiring for perisymphyseal fracture/symphyseal separation
- Extraction of teeth with pulp exposure or displacement injury
- Fresh midline clefts of the hard palate: elevation of medially positioned flaps with full-thickness releasing incisions made into palatal mucoperiosteum 1 mm away from the teeth along the dental arches, followed by approximation of the displaced bony structures with digital pressure and suturing of the torn palatal soft tissues in a simple interrupted or mattress pattern. If the separation is extensive, interarcade fixation may be required. Very narrow and short clefts may sometimes heal spontaneously in 2-4 weeks with conservative management, but the benefit of initial surgical management outweighs the risk of developing a persistent oronasal communication.
- Temporomandibular joint luxation: conservative reduction with a wooden dowel (pencil in a cat; see p. 1078)

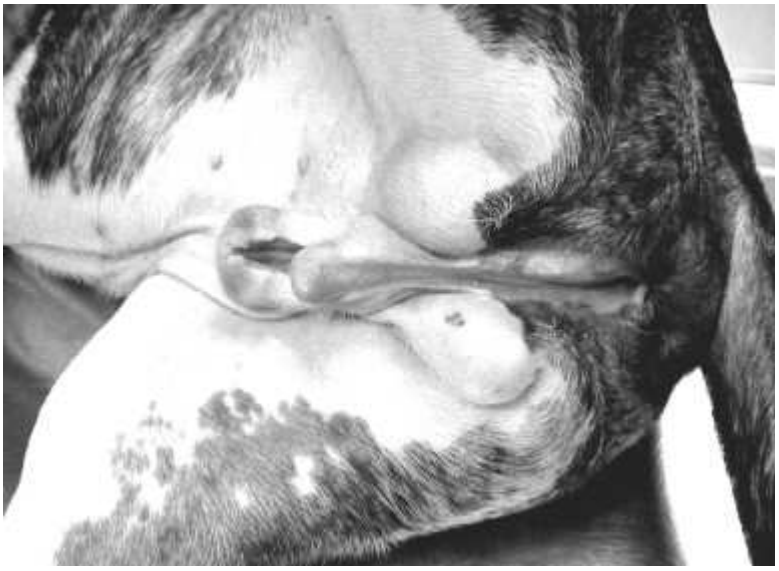
CHRONIC TREATMENT

- If response to emergency treatment is poor, visceral injury (abdominal and thoracic) with possible hemorrhage should be considered and pursued diagnostically.

- Chronic oronasal communication: medially positioned double flaps with releasing incisions along dental arch or overlapping double flaps
- Temporomandibular joint injury (chronic luxation or ankylosis): unilateral or bilateral condylectomy
- Extraction or endodontic therapy of teeth with pulp exposure

NUTRITION/DIET

Nutritional support: soft food is appropriate. An esophagostomy tube is rarely necessary (see p. 1267).



HIGH-RISE SYNDROME, CRANIOFACIAL A, Open-mouth clinical image of the dorsal aspect of the oral cavity; rostral is toward the bottom of the image. Traumatic cleft palate in a cat after falling from a height. Note separation of left and right incisive bones *(arrow)*, fractured left maxillary canine tooth *(asterisk)*, and midline defect in hard and soft palates. **B,** Postoperative image of the same patient. Repair of traumatic cleft palate was accomplished by means of approximation and suturing of medially positioned flaps after creation of bilateral releasing incisions *(arrows)* into palatal mucoperiosteum along dental arches. Note interarcade fixation (twisted wire reinforced with composite resin) between maxillary canine teeth. (Copyright Dr. Alexander M. Reiter, with permission.)

POSSIBLE COMPLICATIONS

- Chronic oronasal communication
- Malocclusion
- Temporomandibular joint ankylosis in very young animals with difficulty or inability to open the mouth
- Chylothorax

RECOMMENDED MONITORING

- In-patient monitoring until discharge
- Reexamination and removal of skin sutures in 2 weeks
- Removal of cerclage wire around mandibles in 4-5 weeks

PROGNOSIS AND OUTCOME

Good prognosis for survival and return to normal function for ~90% of cats

PEARLS & CONSIDERATIONS

COMMENTS

Number and severity of injuries increase with increasing height of fall; others reported that the association between injuries and height of fall follows a curvilinear pattern.

TECHNICIAN TIPS

Gently offering soft food during the healing period can be the cornerstone of nutritional support.

CLIENT EDUCATION

Close windows and balcony doors in the presence of animals.

SUGGESTED READING

Gordon LE, et al: High-rise syndrome in dogs: 81 cases (1985-1991). J Am Vet Med Assoc 202:118, 1993.

Papazoglou LG, et al: High-rise syndrome in cats: 207 cases (1988-1998). Aust Vet Pract 31:98, 2001.

Vnuk D, et al: Feline high-rise syndrome: 119 cases (1998-2001). J Feline Med Surg 6:305, 2004.

Whitney WO, Mehlhaff CJ: High-rise syndrome in cats. J Am Vet Med Assoc 191:1399, 1987.

AUTHOR & EDITOR: ALEXANDER M. REITER

Hiatal Hernia/Gastroesophageal Intussusception

BASIC INFORMATION

Hiatal hernia (HH) and gastroesophageal intussusception (GEI) are problems associated with the esophageal hiatus of the diaphragm. They represent very different conditions, in that HH is often subclinical and GEI is often an acute clinical and potentially fatal problem. This indicates the need for accurate diagnosis of caudal esophageal mass lesions.

DEFINITION

- Hiatal hernia:
  - An uncommon condition in dogs, rare in cats, representing protrusion of the abdominal esophagus, gastroesophageal junction, cardia, or gastric fundus through the esophageal hiatus of the diaphragm into the caudal mediastinum
- Gastroesophageal intussusception:
  - An extremely rare condition, seen more often in dogs than in cats
  - An imagination of the cardia into the terminal esophagus through the esophageal hiatus

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Congenital hiatal hernia: primarily dogs <1 year of age
- Acquired hiatal hernia: dogs or cats of any age

GENETICS & BREED PREDISPOSITION

Shar-pei and brachycephalic breeds (e.g., bulldog) may be predisposed to hiatal hernia.

German shepherd dogs may be overrepresented for gastroesophageal intussusception.

RISK FACTORS

Trauma (both)

ASSOCIATED CONDITIONS & DISORDERS

- Esophageal hypomotility or megaesophagus
- Gastroesophageal reflux/esophagitis

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Sliding or axial hiatal hernia:
  - Longitudinal displacement of the abdominal esophagus, gastroesophageal junction, or stomach into the caudal mediastinum
- Paraesophageal hernia:
  - Gastroesophageal junction remains caudal to the hiatus, and the fundus of the stomach protrudes adjacent to and parallel to the gastroesophageal junction through the hiatus.
- Gastroesophageal intussusception (rare):
  - Cardia invaginates into the terminal esophagus and through the hiatus.
  - Associated with acute obstruction and severe clinical signs in dogs

HISTORY, CHIEF COMPLAINT

- Absence of clinical signs:
  - Incidental finding on thoracic radiograph (50% of hiatal hernia cases; smaller proportion of gastroesophageal intussusception cases)
- Intermittent signs with sliding HH; typically:

- Regurgitation, dysphagia, ptyalism, and weight loss or slow growth
- GEI
  - Acute vomiting or regurgitation, dyspnea, hematemesis, abdominal pain, and collapse
  - Chronic intermittent vomiting and regurgitation are far less common.

PHYSICAL EXAM FINDINGS

- May be unremarkable
- If clinical signs are present, they may include:
  - Thin body condition
  - Dehydration
- Ptyalism
- Fever, harsh lung sounds, cough, dyspnea
- Possible aspiration pneumonia

ETIOLOGY AND PATHOPHYSIOLOGY

Etiology:

- Congenital hiatal hernia:
  - Abnormal diaphragmatic esophageal hiatus (abnormally large or abnormal laxity of phrenicoesophageal ligament)
- Trauma:
  - Esophageal hiatal enlargement and/or stretching of phrenicoesophageal ligament
- Severe respiratory disease:
  - Intense negative intrapleural pressure required for ventilation may be associated with hiatal hernia in dogs and cats.

Mechanism:

- Loss of normal anatomic relationship:
  - Adversely affects the normal high-pressure zone at the gastroesophageal junction, causing reflux esophagitis
- Primary or secondary esophageal motility disorders and megaesophagus can exacerbate signs.
- Upper airway obstruction (e.g. brachycephalic syndrome):
  - May result in significant negative intrapleural pressure required for inspiration, causing hiatal herniation/gastroesophageal reflux
- Large hernias may allow other abdominal organs to enter the caudal mediastinum.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is suspected based on patient signalment, presenting history, physical examination findings, and above all, demonstration of a mass effect in the area of the terminal esophagus on thoracic radiographs. Elucidation of the diagnosis requires radiographic contrast studies and endoscopy.

DIFFERENTIAL DIAGNOSIS

- Megaesophagus
- Esophageal foreign body, stricture, or mass
- Mediastinal or pulmonary mass

INITIAL DATABASE

- CBC:
  - Neutrophilia with toxic changes and/or left shift, associated with inflammation/infection: suspect aspiration pneumonia
- Serum biochemistry profile:
  - Hypoproteinemia possible (malnutrition)
- Diagnostic imaging:
  - Survey thoracic radiographs
    - Increased density/mass lesion in the caudodorsal mediastinum. Highly characteristic of these disorders. Disappearance/reappearance on repeated radiographs is characteristic but not essential.
    - Can be within normal limits if sliding hernia

ADVANCED OR CONFIRMATORY TESTING

- Fluoroscopy with a positive contrast esophagram:
  - Evaluate esophageal size and motility.
  - Identify sliding hernia. Application of external abdominal pressure during fluoroscopy may aid in diagnosis of sliding hernia.
- Esophagoscopy:
  - Assess presence/severity of esophagitis.
  - Gastroesophageal intussusception: confirm diagnosis.

TREATMENT

TREATMENT OVERVIEW

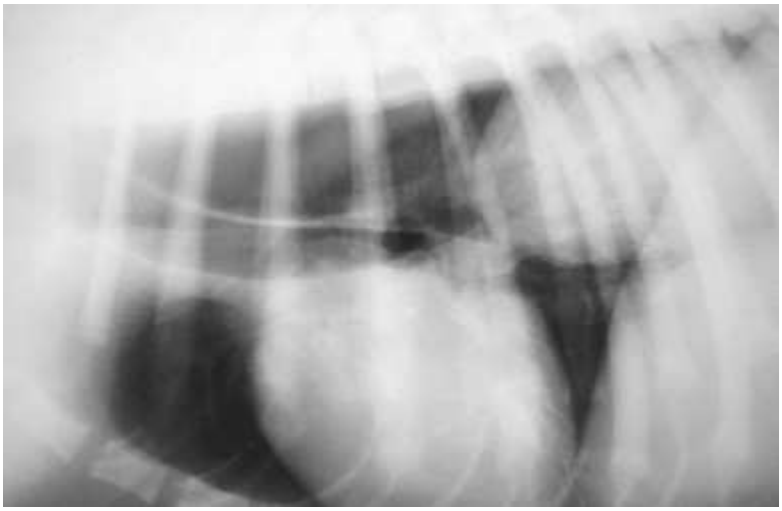
Treatment of hiatal hernia is aimed at diminishing gastroesophageal reflux, providing nutritional support, and managing aspiration pneumonia if present. Surgery is performed on cases that fail to respond to medical therapy. Treatment of paraesophageal hernia and GEI requires surgery to address the anatomic malpositioning of organs through the esophageal hiatus.

ACUTE GENERAL TREATMENT

- Medical management:
  - Correction of fluid and electrolyte deficits if present
  - Aggressive treatment of aspiration pneumonia (see p. 885)
  - Treatment of gastroesophageal reflux/esophagitis (see p. 367)
- Surgical management: patients showing clinical signs referable to hernia/intussusception:
  - Reduction of hiatal hernia/gastroesophageal intussusception
  - Closure of esophageal hiatus to a normal size
  - Left-fundic gastropexy to prevent recurrence

CHRONIC TREATMENT

- Continuation of treatment of gastroesophageal reflux/esophagitis
- Surgical correction of hiatal hernia in patients that do not respond to medical management within 30 days



HIATAL HERNIA/GASTROESOPHAGEAL INTUSSUSCEPTION Lateral thoracic radiograph of a dog, demonstrating a large soft-tissue mass due to gastroesophageal intussusception, located characteristically in the caudodorsal thorax. The dog suffered strangulation injury when it became caught in a snare. Also visible is an air-filled esophagus which demonstrates both sides of the dorsal tracheal membrane ("tracheal stripe sign"). A differential diagnosis for the radiographic appearance of the mass lesion is primary lung tumor.

(Courtesy Dr. Richard Walshaw.)

NUTRITION/DIET

Acute:

- Upright feeding of small, frequent meals to promote normal function of the esophagus/gastroesophageal junction
- Feeding (percutaneous endogastric) tube if oral intake inadequate (see p. 1270)

Chronic:

- Continuation of feeding regimen
- Upright feeding in cases of megaesophagus associated with GEI

POSSIBLE COMPLICATIONS

- Failure of medical management to adequately resolve problem
- Recurrence of hiatal hernia after surgical correction
- Development of esophageal stricture secondary to gastroesophageal reflux/esophagitis

RECOMMENDED MONITORING

Follow-up positive contrast esophagram (4-6 weeks):

- Demonstrate resolution of
  - Hiatal hernia/gastroesophageal intussusception
  - Gastroesophageal reflux
- Assess esophageal motility
- Determine whether continuation of feeding regimen and treatment of gastroesophageal reflux/esophagitis still necessary.

PROGNOSIS AND OUTCOME

- Good prognosis:
  - If the patient has no or mild clinical signs
  - With surgical intervention in the absence of aspiration pneumonia
- Poor prognosis associated with:
  - Resistant aspiration pneumonia
  - Severe esophagitis/stricture
  - Persistent megaesophagus

PEARLS & CONSIDERATIONS

COMMENTS

- Treatment for esophagitis should be continued postoperatively in any patient undergoing surgical correction of hiatal hernia.
- Aspiration pneumonia requires intensive treatment prior to considering surgical intervention.

SUGGESTED READING

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Tams TR: Diseases of the esophagus. In Tams TR, editor: Handbook of small animal gas-troenterology, St Louis, 2003, WB Saunders, pp 118–157.

AUTHOR: MARYANN G. RADLINSKY

EDITOR: RICHARD WALSHAW

Heterobilharzia americana Infection

BASIC INFORMATION

DEFINITION

Infection with trematodes (flukes) of the blood vasculature of the small intestine, primarily the mesenteric veins, of mammals

SYNONYMS

These parasites may be referred to as blood flukes or schistosomes. The syndrome may be referred to as canine heterobilharziasis, canine bilharziasis, or canine schistosomiasis.

EPIDEMIOLOGY

SPECIES, AGE, SEX

Rare in dogs and very rare in cats. Definitive hosts include members of the Canidae and Felidae families. Raccoons may serve as reservoir hosts.

GENETICS & BREED PREDISPOSITION

Sporting/hunting breeds of dogs (environmental exposure)

RISK FACTORS

Hunting and exposure to/contact with large stationary or slow-moving bodies of water inhabited by molluscan (snail) intermediate hosts of the genera *Lymnaea*, *Pseudosuccinea*, and *Fossaria.*

CONTAGION & ZOONOSIS

Cercarial stages of the parasite emerge from aquatic snails, swim in the water, and directly penetrate the skin of the definitive host. Cercarial dermatitis, schistosome dermatitis, “swimmer's itch,” or “water dermatitis” due to *Heterobilharzia americana* has been reported in humans in Louisiana. This is due to the cercarial stages of the parasite repeatedly penetrating human skin following human contact with “infected water.”

GEOGRAPHY AND SEASONALITY

These blood flukes are found in definitive hosts in North America, particularly the states bordering the Gulf of Mexico (range extends from Texas to North Carolina).

ASSOCIATED CONDITIONS & DISORDERS

Granulomatous inflammation, hypercalcemia, rectal strictures, and bloody diarrhea have been reported.

CLINICAL PRESENTATION

Clinical signs of heterobilharziasis in dogs are poorly described but may include weight loss, hematochezia, melena, borborygmus, flatulence, and diarrhea. Severe cases may exhibit hepatomegaly and ascites. Cutaneous erythema and dermatitis may be seen, especially on the extremities.

HISTORY, CHIEF COMPLAINT

The dog or cat typically will have had a history of roaming freely and having had contact with fresh water. Infected dogs may demonstrate weight loss, diarrhea, hematochezia, and other clinical signs related to the gastrointestinal (GI) tract.

PHYSICAL EXAM FINDINGS

- Loss of weight

- Abdominal pain
- Dermatitis, redness, urticaria
- Afebrile
- Rectal examination may reveal melena, mucoid or hemorrhagic stool.

ETIOLOGY AND PATHOPHYSIOLOGY

- The parasites are also referred to as schistosomes or blood flukes (they are closely related to *Schistosoma* species, the number-one helminth parasite of humans throughout the world).
- The adult stages of this parasite (both male and female blood flukes) are found within the blood vasculature in copula; the female fluke resides within the gynecophoric (female-carrying) canal of the male fluke.
- The life cycle involves intermediate hosts, aquatic snails of the genera *Lymnaea*, *Pseudosuccinea*, and *Fossaria.*
- Fluke ova (eggs) exit the definitive (mammal) host in the feces. Eggs must make contact with fresh water inhabited by certain species of snails.
- Each ovum will hatch, releasing a motile larval stage, the miracidium. The miracidium actively penetrates the epithelium of an aquatic snail. Within the snail, the miracidium undergoes asexual (multiplicative) development, ultimately producing a larval stage known as a cercaria. Hundreds of cercariae may be produced from a single miracidium.
- The cercarial stage emerges from the aquatic snail and swims about in the water, ready to actively penetrate the skin of the definitive host.
- The cercariae transform into schistosomula which are transported to the host's lungs hematogenously.
- The schistosomula are then carried to the liver via the blood stream and are found in the portal vessels of the liver. The male and female flukes pair up in the portal veins before they leave the liver, reaching maturity in the mesenteric veins.
- Within the veins, the male and female worms are permanently in copula.
- The egg-laying female penetrates deeply into the small vessels of the mucosa or submucosa of the intestine, laying her eggs in the capillaries.
- From the capillaries, the eggs pass through the host intestinal wall into the small-intestinal lumen and pass out in the host feces.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected in endemic areas when outdoor dogs show gastrointestinal signs and is most easily confirmed via fecal flotation. Cases that are more challenging require advanced diagnostic testing if other more likely causes have been ruled out.

DIFFERENTIAL DIAGNOSIS

Hemorrhagic gastroenteritis, clostridial diarrhea, hypoadrenocorticism, GI histoplasmosis, lymphosarcoma, apocrine gland adenocarcinoma

INITIAL DATABASE

- CBC and serum chemistry profile (often normal but may reveal anemia, eosinophilia, increased liver enzyme levels, hypercalcemia, hypoalbuminemia, hyperglobulinemia, and azotemia)
- Fecal smear to check for the characteristic ovum containing the miracidium. Should be preformed on multiple occasions because of intermittent shedding of ova in host feces.
    - Eggs can sometimes be seen on a direct fecal smear. They are thin walled with a single operculum.
    - An alternate method of diagnosis is to place a large amount of stool in water and obtain a sample from the top layer in 2 hours. Miracidia that hatch can be seen “swimming” under the microscope.
- Since eggs are difficult to observe on fecal flotation or sedimentation, the practitioner may have to resort to more invasive forms of diagnostics (liver or intestinal biopsies) or submission of feces to an outside diagnostic service for a PCR-based assay (www.cvm.tamu.edu/gilab)
    - Liver and/or intestinal biopsies with histopathologic examination revealing granulomatous lesions with helminth ova or trematode nidi

ADVANCED OR CONFIRMATORY TESTING

- A PCR-based assay for the detection of DNA from the ova in host feces
- Indirect hemagglutination may be useful.

TREATMENT

TREATMENT OVERVIEW

Eliminate adult male and female schistosomes within blood vasculature.

ACUTE AND CHRONIC TREATMENT

- Praziquantel (25 mg/kg PO q 8 h for 2 days); nausea and vomiting may be side effects.
- Fenbendazole (40 mg/kg PO q 24 h) SID for 10 days, repeat in 3 weeks.

NUTRITION/DIET

Bland, high-carbohydrate, low-fat diets that are easily digested are recommended until GI signs abate.

POSSIBLE COMPLICATIONS

Adult blood flukes may be killed en masse then embolize the portal system (large infections).

RECOMMENDED MONITORING

- Serum liver values +/- liver function tests
- May repeat PCR on feces to ensure that it is negative following treatment

PROGNOSIS AND OUTCOME

Generally good, barring complications of massive parasite kill

PEARLS & CONSIDERATIONS

COMMENTS

Since this larval cestode is rare, diagnosis can be challenging. A pathologist or parasitologist at a veterinary diagnostic laboratory may be called on to assist in the definitive diagnosis of the parasite.

PREVENTION

Prevent dogs and cats from roaming and coming into contact with freshwater aquatic environments (large stationary or slow-moving bodies of water) inhabited by the snail intermediate host.

TECHNICIAN TIPS

- Fecal smears should be performed on multiple occasions because of intermittent shedding of ova in host feces.
- Fecal flotation and sedimentation techniques may offer low/no yield because the thin-walled eggs burst.

CLIENT EDUCATION

To avoid infection in endemic areas, dogs should not be allowed to roam freely, thus avoiding contact with infested waters.

SUGGESTED READING

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Rohrer CR, Phillips LA, Ford SL, et al: Hyper-calcemia in a dog: a challenging case. J Am Anim Hosp Assoc 36(1):20–25, 2000.

Ronald NC, Craig TM: Fenbendazole for the treatment of *Heterobilharzia americana* infection in dogs. J Am Vet Med Assoc

182(2):172, 1983.

AUTHOR: CHARLES HENDRIX

EDITOR: DOUGLASS K. MACINTIRE

Herpesvirus, Dog

BASIC INFORMATION

DEFINITION

Viral infection of canids that can present one of four possible clinical scenarios: respiratory distress from upper airway infection; abortion; vaginitis; and neonatal puppy mortality up to 3 weeks of age.

SYNONYMS

Canine herpesvirus type 1 (CHV-1), CHV, dog herpes, neonatal herpes, fading puppy syndrome

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Domestic dogs; wild canids (coyotes, wolves, etc.)
- Immunologically naive pregnant dams are most susceptible to the reproductive effects of CHV-1, and their offspring are most susceptible to systemic disease, with high puppy mortality.

RISK FACTORS

There are nine major risk factors: immunologic status of dams (pups), age, mating experience, reproductive cycle, breeding kennel, kennel size, breeding management (use of nonresident males), kennel cough, and kennel hygiene.

CONTAGION & ZOONOSIS

- Highly contagious among canids only via saliva and vaginal secretions
- Fomites may contribute to spread.
- Direct contact (saliva, urogenital secretions) is the most efficient mode of transmission, especially from dogs with clinical signs but possibly from latent carriers also.
- The virus is readily inactivated outside the body by heat, drying, or disinfectants (diluted bleach 1:30).
- Not zoonotic

GEOGRAPHY AND SEASONALITY

The virus persists in carrier dogs worldwide as a latent infection and may be exacerbated with stress-induced or physiologic/hormone-related immune suppression.

ASSOCIATED CONDITIONS & DISORDERS

Surviving puppies may have deafness, neurologic dysfunction or renal damage.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Dogs, usually <2 years old; acute to chronic upper airway signs
- Dam aborts litter, usually with 100% puppy mortality if infection of dam occurs during last trimester.
- Dam infects her litter during whelping, usually 80%-100% puppy mortality if infection is a reexacerbation of latent infection.
- Naïve dam gives birth to naïve litter, and secondary contact with CHV-shed-ding dog carries virus back to litter. Mortality rate varies from 25%-80% depending on virus challenge dose, age of puppies, and body temperature of puppies.
- Dam or sire presented for evaluation of papulovesicular lesions of the external genital organs.

HISTORY, CHIEF COMPLAINT

As described above

PHYSICAL EXAM FINDINGS

Puppies appear lethargic, fail to nurse; decreased body weight; soft, yellow-green feces; no fever; rhinitis possible, with serous/mucopurulent/hemorrhagic nasal discharge; mucosal petechiae common. Puppies lose consciousness and may have opisthotonos and seizures before death.

ETIOLOGY AND PATHOPHYSIOLOGY

- CHV has a predilection for lymphoid and neural cells, both of which may become latently infected (no mature viral production), but a dog remains a potential shedder if the virus is reexacerbated due to stress (e.g., pregnancy, corticosteroids, irradiation).
- The optimal temperature for CHV replication is 33°C-35°C (i.e., the temperature of the outer genital and upper respiratory tracts).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Although a presumptive diagnosis of CHV-induced disease can be achieved by the observation of ill pups <3 weeks of age, confirmation of CHV can be obtained histopathologically on fixed liver and kidney tissue of affected pups, virus isolation from fresh/frozen tissues, and/or PCR on whole blood from pups. Carrier dogs can be identified by PCR on whole blood from adult dogs.

DIFFERENTIAL DIAGNOSIS

- Acute-onset respiratory signs/respiratory distress of upper airway origin: canine adenovirus type 2; canine parainfluenza; *Bordetella bronchiseptica;* upper airway foreign body
- Reproductive disease: *Brucella canis, Streptococcus* spp.; canine distemper virus; neosporosis; toxoplasmosis

INITIAL DATABASE

CBC, serum biochemistry profile, urinalysis: hematologic and biochemical values are usually nonspecific, but a marked thrombocytopenia may be observed. A marked increase in the alanine aminotransferase activity may be found in affected neonatal puppies.

ADVANCED OR CONFIRMATORY TESTING

- Antemortem testing:
  - Serologic titers from affected adult dogs (titers equal to or greater than 1:2 indicate exposure/infection). Antibody titers do not correlate with active viral shedding but are good indicators of prior infection and latency status.
  - Virus isolation from nasal/urogenital swabs indicates infection and active shedding.
  - PCR on whole blood indicates infection and either active viremia or latency.
- Postmortem testing (aborted/neonatal dead puppies):
  - Virus isolation from lung, bronchiolar lymph nodes, liver, kidney, and spleen
  - Histopathologic evaluation of lung, liver, kidney, spleen, small intestine, and brain. Depending on the stage of cellular infection and method of fixation, basophilic or acidophilic intranuclear inclusions may be noted. These intranuclear inclusion bodies are considered pathognomonic for CHV.
  - No CHV immunohistochemical test is commercially available.
  - PCR can also be done on the aforementioned selected tissues but is usually reserved for determining latency.

TREATMENT

TREATMENT OVERVIEW

Treatment of CHV-induced neonatal disease requires rapid response on the part of owner and veterinarian. Usually by the time clinical signs occur, individually affected pups have a poor prognosis. Unaffected litter mates may be treated with antiviral drugs and/or CHV-hyper-immune serum. The temperature of the puppy environment should be raised without the dam and surviving pups becoming dehydrated.

ACUTE GENERAL TREATMENT

- Treatment of neonatal puppies with CHV-induced disease is usually not recommended because of rapid progression, poor prognosis, and the potential for cerebellar and retinal dysplasias in surviving puppies.
- If only a portion of the litter demonstrates overt signs, the remaining littermates can be treated with immune serum (2 mL of serum from a dog with known anti-CHV titer, given intraperitoneally).
- Neonates can also be maintained in an environment with high humidity (up to 55%) and elevated ambient temperatures of 26.6°C-37.7°C (98°F-100&°F). Because CHV is naturally temperature sensitive, raising the pup's body temperature by artificial heating early in the course of the infection may have therapeutic value; caution and constant body temperature monitoring are essential to avoid iatrogenic hyperthermia.

CHRONIC TREATMENT

Owing to high incidence of life-threatening sequelae, treatment is not recommended if pup is presented already showing clinical signs.

BEHAVIOR/EXCERCISE

Puppies will be in pain and crying. Keep as comfortable as possible with warm cloths.

POSSIBLE COMPLICATIONS

Treatment of clinically ill puppies may result in associated conditions and disorders (see above).

RECOMMENDED MONITORING

Puppies presented while showing clinical signs should be monitored every few hours, as prognosis is poor. Dam can be monitored by checking CHV antibody titers and by PCR on urogenital secretions (swabs).

PROGNOSIS AND OUTCOME

- Unaffected neonatal puppies from an affected litter have a good prognosis.
- Dams that abort or have a naive litter that subsequently becomes infected by a secondary source of CHV commonly seroconvert and will subsequently have normal litter. CHV immunity will be passed onto litters via colostrum. Colostral immunity, which persists to 8 weeks, will prevent clinical signs in the puppies but will not prevent against primary infection and subsequent latency.

PEARLS & CONSIDERATIONS

COMMENTS

CHV is a manageable infection and a preventable disease (see Prevention and Client Education below).

PREVENTION

- Good hygiene: cleanliness of dam, rigorous handwashing or use of gloves by handlers, together with a warm and clean puppy environment
- No vaccine available in the United States. A European product has been licensed, with good results reported when used prebreeding.

TECHNICIAN TIPS

- Emphasize good prenatal and postnatal hygiene with clients.
- Incorporate kennel surveillance program for *Brucella cants* and CHV testing prebreeding.
- Identify first-time pregnant dogs as high risk, and quarantine from outside dogs/humans as much as possible.

CLIENT EDUCATION

- Planned exposure of young (>6 months) puppies to older dogs to “naturally immunize” them before breeding and whelping. This induced infection rarely becomes clinically overt, and if it does as a respiratory disease, a 2-week quarantine is advised.
- Maintenance of a strict quarantine period to work within the “6-week danger period” (3 weeks before and 3 weeks after whelping)

- Maintaining ambient body temperature to minimize risk of hypothermia. CHV is very heat sensitive.

SUGGESTED READING

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Morresey PR: Reproductive effects of canine herpesvirus. Compend Contin Educ Pract Vet 26:804–811, 2004.

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EDITOR: MICHELLE A. KUTZLER

Herpesviral Keratitis, Cats

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

- Corneal inflammation associated with feline herpesvirus type 1 (FHV-1) infection
- Sometimes divided into ulcerative and nonulcerative (or stromal) keratitis or into an overlapping pair of epidemiologically relevant categories: primary and recrudescent herpesviral keratitis

SYNONYMS

Herpetic keratitis

Feline viral rhinotracheitis: FHV-1, FVR

EPIDEMIOLOGY

SPECIES, AGE, SEX

- FHV-1 is highly species specific. Domestic and wild cats of any age may be affected (see p. 1127).
- Young kittens undergoing primary exposure usually display ulcerative disease, and older cats undergoing viral reactivation may experience ulcerative or nonulcerative recrudescent disease.

GENETICS & BREED PREDISPOSITION

- No breed predilection has been proven (prevalence in breeding catteries may give false impression of susceptibility).
- Individual variation in susceptibility to recrudescent herpetic keratitis suggests immunologic predisposition.

RISK FACTORS

- Stresses such as rehousing, intercurrent disease, or pregnancy/parturition/lactation; corticosteroid administration; multicat households or shelters; inadequate vaccination

CONTAGION & ZOONOSIS

- Highly contagious among cats
- Not zoonotic

GEOGRAPHY AND SEASONALITY

- Worldwide viral distribution without seasonality
- Because of susceptibility of kittens, trends in disease prevalence may be noted in association with feline breeding seasons.

ASSOCIATED CONDITIONS & DISORDERS

- FHV-1 also causes conjunctivitis, dermatitis, and may cause anterior uveitis.
- FHV-1 is associated with corneal sequestra and eosinophilic/proliferative keratitis.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Ulcerative keratitis (seen most often upon initial exposure but also in recurrent forms)
- Nonulcerative keratitis (seen most often in chronic primary or recurrent forms)

HISTORY, CHIEF COMPLAINT

- Ocular discharge

- Blepharospasm (squinting)
- Corneal opacification
- Upper respiratory signs may be seen, including nasal congestion, sneezing, and serous or mucopurulent nasal discharge
- Ocular signs are typically bilateral in primary disease but often unilateral during recrudescences.

PHYSICAL EXAM FINDINGS

- Ocular discharge (serous, mucoid, purulent, sanguineous, or dry and crusty; sometimes dark red or black-stained)
- Blepharospasm
- Deep or superficial corneal vascularization, ulceration (dendritic early; usually geographic by time of presentation; often chronic nonhealing and sometimes with a lip of redundant epithelium)
- Corneal opacification due to white blood cell infiltration and/or corneal edema and/or scarring
- Conjunctival or episcleral injection
- Chemosis (conjunctival edema), blepharoedema
- Reflex uveitis (e.g., miotic pupil; aqueous flare and/or inflammatory cells in the anterior chamber); see p. 1151
- Eosinophilic/proliferative keratitis appears as raised pink, sometimes chalky plaques extending from the limbus often with a leading zone of ulceration.
- Corneal sequestration appears as a planar to sometimes raised amber to dark black region of axial to paraxial cornea often surrounded by corneal vascularization and sometimes stromal inflammatory cell infiltration.

ETIOLOGY AND PATHOPHYSIOLOGY

- FHV-1 is a ubiquitous virus.
- Infection causes usually self-limiting primary disease in essentially all cats infected with the virus.
- Approximately 80% of affected cats become latently infected for life.
- Periodic reactivation occurs in about half of these.
- Periodic recrudescent disease occurs in a minority of cats.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The frequency with which cats are vaccinated and the number of normal cats that shed virus at ocular sites make serologic and viral detection methods unhelpful. Inclusion bodies are rarely seen on cytologic specimens. Diagnosis is made based on visualization of dendritic ulcers, presence of supportive signs, and/or response to therapy.

DIFFERENTIAL DIAGNOSIS

- There are no other recognized primary feline corneal pathogens.
- *Chlamydophila felis* (formerly *Chlamydia psittaci)* causes conjunctivitis but is not known to cause keratitis.
- Feline calicivirus is not a primary corneoconjunctival pathogen but rather causes lesions of the oral and pharyngeal mucosa.
- Noninfectious corneal disease (immune-mediated, neoplastic, KCS, foreign body, traumatic) is uncommon in cats compared to dogs but should be considered.

INITIAL DATABASE

- Thorough ophthalmic examination (see p. 1313) including application of fluorescein and sometimes rose bengal stains
- Corneal or conjunctival cytologic evaluation will eliminate the possibility of eosinophilic/proliferative keratocon-junctivitis; however, herpesviral inclusions are seen extremely rarely.

ADVANCED OR CONFIRMATORY TESTING

- Serologic titers are not useful because of vaccination and widespread (97%) seroprevalence.
- Detection of virus (isolation) or its proteins (immunofluorescent antibody testing) or DNA (PCR) is of limited value because of the number of normal animals that may shed these.

TREATMENT

TREATMENT OVERVIEW

Cats with primary and many mild recrudescent forms of herpetic disease improve with supportive care only. Cats with severe or frequently recurrent keratitis require specific antiviral therapy. Due to toxicity and efficacy profiles, such treatment is largely limited to topical therapy (many systemic antiviral agents are of low efficacy and/or high toxicity). Lysine may limit recurrences in some cats.

ACUTE GENERAL TREATMENT

- Cats with respiratory signs may need supportive care.
- Cats with ulcerative keratitis require a topical broad-spectrum antibiotic.
- Consider a topical antiviral for chronic or severe signs. Topical antiviral agents (e.g., idoxuridine, trifluridine, vidarabine) are virostatic and must be administered at least 4-6 times daily. The exception is cidofovir, which because of tissue accumulation may be administered twice daily.
- Use systemic antiviral agents (e.g., acyclovir) with extreme care if at all, owing to toxicity.
- Consider mucinomimetic tear-replacement products (hyaluronic acid).
- Avoid topical or systemic corticosteroid administration.

CHRONIC TREATMENT

- Consider oral administration of lysine (500 mg/cat PO q 12 h: lifelong treatment) to reduce viral replication in cats with frequent recurrences.
- Avoid prolonged topical antiviral administration if possible.
- Avoid topical or systemic corticosteroid administration.

BEHAVIOR/EXERCISE

- Reduce known stresses.
- Reduce overcrowding in multicat situations.

POSSIBLE COMPLICATIONS

- Topical antiviral agents are epitheliotoxic.
- Valacyclovir is toxic to cats.

RECOMMENDED MONITORING

- Frequent ophthalmic examinations, especially of ulcerative keratitis
- Monitor CBC and serum biochemistry panels if systemic antiviral agents are used.

PROGNOSIS AND OUTCOME

- Primary disease is self-limiting in most cats.
- A minority experience chronic and/or recrudescent disease.
- Treat recurrences early and aggressively.
- Secondary bacterial invasion of corneal ulcers can cause globe perforation.
- Chronic stromal herpetic keratitis is painful and can be blinding secondary to corneal scarring.

PEARLS & CONSIDERATIONS

COMMENTS

- FHV-1 is the most common cause of ulcerative and nonulcerative keratitis in cats.
- Diagnostic testing is confounded by viral shedding in normal cats.
- Topical antiviral agents must be administered frequently to be effective.

PREVENTION

- Vaccination lessens signs but may not reduce recurrences or establishment of latency.

TECHNICIAN TIPS

- Minimize transfer of FHV-1 between cats by handwashing.
- Clean contaminated equipment with standard disinfectants.

CLIENT EDUCATION

- Minimize known stresses.
- Early recognition and therapy of recrudescent disease are important.

SUGGESTED READING

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Stiles J, et al: Effect of oral administration of L-lysine on conjunctivitis caused by feline herpesvirus in cats. Am J Vet Res 63:99, 2002.

AUTHOR: DAVID J. MAGGS

EDITOR: CHERYL L. CULLEN

Herbicide (Phenoxy, Others) Toxicosis

BASIC INFORMATION

DEFINITION

- Phenoxy-type herbicides include: *2, 4-D* (2, 4-dichlorophenoxyacetic acid), *MCPA* (2-methy1-4-chlorophenoxyacetic acid), *MCPP* (2-[4-chloro-2-methoxy] propionic acid), and *dicamba* (3,6-dichloro-2-methoxybenzoic acid).
- Commonly used in a residential setting (lawns, along fences) and available through lawn care professionals or local retail outlets
- Available as concentrates or ready-to-use products. Most exposures in animals occur from walking through a recently treated yard (dermal and oral exposure) or chewing and puncturing the container to produce a **spill** situation.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs most commonly involved; outdoor cats on occasion
- Younger, inquisitive or active dogs more likely to be exposed. Dogs lick or sometimes “graze” an herbicide-treated area.
- Cats exposed by running through a freshly treated area then ingesting the product through grooming

GENETICS & BREED PREDISPOSITION

Dogs eliminate chlorophenoxy compounds (e.g., 2,4-D, MCPA) slowly owing to saturation of the renal organic anion system, which can prolong urinary excretion and extend recovery times.

RISK FACTORS

- Preexisting debilitation or chronic kidney disease
- Exposures to concentrated products are typically of greater concern.

GEOGRAPHY AND SEASONALITY

Spring and summer provide greater opportunity for accidental exposure.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Most cases involve ready-to-use products, are acute in nature (onset of signs <1-4 hours after exposure), and are restricted to mild, self-limiting hypersalivation, excessive licking, hacking, retching, vomiting, diarrhea, anorexia within 4 hours of exposure. Systemic effects are not expected in these cases.
- Much less commonly, exposure to concentrated products in substantial amounts can cause systemic absorption and subsequent gastritis, myotonia, paresis, generalized muscle weakness, ataxia, and seizures.

HISTORY, CHIEF COMPLAINT

- Most common: patient was on a treated lawn; signs as listed above.
- Licking furniture or other inanimate objects (contact irritant nature of the product)

PHYSICAL EXAM FINDINGS

- Routine presentation: as above plus increased cough/gag reflex, soft abdomen; vital signs typically within normal limits
- With substantial ingestion of concentrate (rare): as described above

ETIOLOGY AND PATHOPHYSIOLOGY

- Local contact: physical irritant effect in most cases (due to normally low-end-use concentrations of active ingredients and

surfactants)
- Consumption of concentrates may lead to systemic absorption and in very large doses may uncouple oxidative phosphorylation, induce systemic metabolic acidosis, cause hepatic and renal toxicosis, and cause gastrointestinal ulceration and bleeding. Death is rarely encountered.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is based entirely on history of exposure (walking through a treated lawn) and clinical signs (vomiting, gagging, muscle weakness), as timely clinical testing is not available.

DIFFERENTIAL DIAGNOSIS

- Lawn grass or nontoxic outdoor plant ingestion
- Mild oral mucosal or dental trauma
- Bufo toad ingestion (acute transient hypersalivation effect)
- Exposure to cleaning agents, petroleum distillates, and the like
- Marijuana, macadamia nuts toxicosis

INITIAL DATABASE

- No significant serum biochemical changes expected with exposure to routine ready-to-use products
- With systemic effects (paresis, ataxia, myotonia), serum biochemical changes may include:
  - ± Azotemiaa
  - ± Increased liver enzymes
  - ± Increased creatine kinase
  - ± Myoglobinuria
  - ± Metabolic acidosis

ADVANCED OR CONFIRMATORY TESTING

- Rarely needed or done. Identification of source container (contents list on label) can confirm herbicide.
- Antemortem: chilled vomitus, serum, urine, for toxicology herbicide screen within 48-72 hours post exposure
- Postmortem: liver, kidney, muscle, and brain, chilled or frozen for toxicology herbicide screen

TREATMENT

TREATMENT OVERVIEW

Most cases are treated empirically by diluting the orally ingested product with milk or water and by keeping the animal off food and water to control vomiting. Induction of emesis and administration of activated charcoal with supportive care may be needed first if concentrated products have been ingested.

ACUTE GENERAL TREATMENT

- Decontamination of patient:
  - Oral rinsing with water or milk to dilute, flush, and dampen the contact irritant effect to the oral mucosa
  - Administration of milk or water (2-6 mL/kg PO or via stomach tube [see p. 454]) to dilute ingested product 0-6 hours after ingestion.
  - Bathe with water and mild liquid detergent solution for dermal exposure (acutely; <30 minutes postingestion).
  - Inducing emesis and/or activated charcoal procedures are generally not beneficial or indicated because of rapid absorption; may be considered if concentrated products are involved.
  - Control vomiting (if severe).
    - Withhold food and water for 2 hours after the start of vomiting.
    - Maropitant, 1 mg/kg SQ (or 2 mg/kg PO q 24 h) for up to 5 days, *or*
    - Metoclopramide, 0.2-0.5 mg/kg PO or SQ q 6-12 h
- Supportive care:
  - Intravenous fluids
  - Urine trapping (alkaline diuresis) to enhance chlorophenoxy excretion and decrease risk of renal failure due to

rhabdomyolysis; beneficial if systemic involvement. Consider 1-2 mEq/kg of sodium bicarbonate added to fluids; maintain a urine pH of ≥7.5. Monitor acid-base status closely.
- Forced saline diuresis alone is not likely to enhance clearance of the chemical.
- Gastrointestinal protectants if needed (see p. 440).

POSSIBLE COMPLICATIONS

- Metabolic acidosis (rare)
- Renal and hepatic complications (rare)
- A controversial literature report (Hayes, et al., 1991) suggesting a modest increase in the incidence of lymphoma in dogs exposed to 2,4-D-treated lawns is considered suspect in terms of accuracy by many toxicology experts.

RECOMMENDED MONITORING

Only in patients with systemic effects:

- Serum renal and hepatic values
- Acid-base status

PROGNOSIS AND OUTCOME

- Excellent; self-limiting signs usually resolve in 12-24 hours.
- Good with systemic effects; signs resolve within 24-96 hours; long-term adverse health effects are rare.

PEARLS & CONSIDERATIONS

COMMENTS

- Other common herbicides to which dogs and cats are exposed include *glyphosate* (Roundup) (see p. 1281) and *pendimethalin.* These herbicides also have low order of toxicity, and most exposures result in mild self-limiting gastrointestinal signs.
- Most exposures to phenoxy-type herbicides involve exposure to very low concentrations (<1% active ingredient) on treated lawns and therefore are of low-risk concern.
- “Weed-and-feed” lawn care products contain herbicide (weed) and fertilizer (feed) components. Typically, low risk is expected from accidental exposures to these products unless an insecticide component has been added.
- No significant exposure or risk of acute toxicosis if animal eats treated grass or goes in the treated yard after the spray has already dried (within a few hours).

PREVENTION

Keep product containers locked and away from animals.

CLIENT EDUCATION

- Always read the label and follow label directions before applying any herbicide.
- Allow adequate drying time before allowing pets to reenter.

SUGGESTED READING

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Herbal Drugs/Natural Supplements Toxicosis

BASIC INFORMATION

DEFINITION

- Herbal preparations are obtained from plants. The use of medicinal plants and herbal medications in humans is a multibillion dollar industry around the world.
- Herbal medications are available in the form of nutritional or dietary supplements, extracts, teas, tablets, powders, creams, ointments, beverages, or tinctures either as a single ingredient or multiple ingredients.
- Toxicosis occurs when pets ingest large amounts of owners' medication (e.g., ma huang, guarana, 5-hydroxytryptophan [5HTP]) or when animal owners use concentrated herbal products (e.g., melaleuca oil) on the animal, assuming all natural products are safe. Adverse effects can also occur secondary to drug interactions with the herbal drugs (e.g., concurrent use of St. John's wort and antidepressants).
- Acute toxicosis is reported commonly in dogs, owing to their indiscrete eating habits. Cats mostly eat a single tablet/capsule. Dogs and cats of all breeds, ages, and both sexes are susceptible.

PEARLS & CONSIDERATIONS

- Safety and efficacy of herbal drugs in pets are not evaluated and labeled as for approved prescription drugs.
- Concentration of active ingredients in the herbal supplement can vary between brands and from plant to plant because of several environmental factors (growth stage, soil conditions, weather, etc.) or manufacturing processes.
- Many pet owners use herbal supplements as alternative/complementary/integrative therapy with or without discussing it with their veterinarian. Since there is usually no warning on the label, many pet owners do not consider herbal drugs/nutritional supplements hazardous and do not keep them out of reach of pets.
- Most herbal supplements contain multiple ingredients, and if their mechanisms of action are similar, one supplement may cause additive or synergistic toxic effects (uncharacteristically severe signs). For example, presence of guarana and green tea or presence of ma huang and guarana together may lead to additive or synergistic toxic effects.
- Below, the most commonly involved ingredients, their actions, and treatments are listed. For more detail, readers are encouraged to read supplemental information or other chapters listed in this book.

HERBAL DRUGS/NATURAL SUPPLEMENTS TOXICOSIS Toxicology of Commonly Used Herbal Ingredients Present in Various Formulations

Common Name(s)	Genus, Species	Toxic Principle if Known	Popular Usage	Toxicity Signs/Major Effect/Actions	Treatment Overview/Comments
Ma huang, Indian common mallow, bitter orange	*Ephedra sinica, Sida cordifolia, Citrus aurantium*	Ephedrine, pseudoephedrine, synephrine	Weight loss, weight lifting, "herbal ecstasy," decongestants	Sympathomimetic effects; hyperthermia, hypertension, tachycardia, tremors, seizures, hallucinations, agitation	See Decongestant Toxicosis, p. 284
ECGC (green tea), guarana, cocoa, cola, kola nut, chocolate	*Camellia sinensis, Paullinia cupana, Cola acuninata, Theobroma cacao*	Caffeine, theobromine (methylxanthines)	Weight loss, "herbal No Doz"	Agitation, hyperactivity, polyuria, polydipsia, cardiac arrhythmias, seizures	See Chocolate Toxicosis, p. 194
Thioctic acid, cinnamon	Alpha lipoic acid (ALA), *Cinnamomum cassia*	Alpha lipoic acid, cinnamon	Diabetic treatment, *Amanita* mushroom poisoning (ALA)	Hypoglycemic effects; hypersalivation, vomiting, hypoglycemia, increased serum liver or renal values, death (ALA)	See Hypoglycemia (), Xylitol Toxicosis, p. 1184
5-HTP	*Griffonia simplicifolia*	5-hydroxytryptophan (5-HTP)	Depression, headaches, insomnia, obesity, over-the-counter antidepressant	Serotonin syndrome; sedation, vomiting, diarrhea, tremors, seizures, ataxia, hyperesthesia, hyperthermia	See Tricyclic Antidepressant Toxicosis,p. 85 and Serotonin Syndrome p. 1427
Purple coneflower	*Echinacea purpurea*	Arabinogalactan	Cold and flu support, immune stimulant, wound healing	Signs due to allergenic effects; vomiting, diarrhea	Low toxicity; no systemic effects likely from acute exposure
Chamomile	*Matricaria recutita, Chamaemelum nobile*	Hydroxycoumarin, bisabolol, chamazulene	Sedative, gastrointestinal ulcers, wound healing, antibacterial, antiinflammatory	Vomiting, diarrhea, lethargy; rarely, anticoagulant effects; epistaxis, hematoma (cats)	Low toxicity; no systemic effects likely; mild GI signs expected with acute ingestion
St. John's wort	*Hypericum perforatum*	Hypericin	Antidepressant, insomnia, anxiety, wound healing, skin conditions	Monoamine oxidase (MAO) inhibitor, depression, vomiting, diarrhea; rarely, tremors, seizures	• See Antidepressant Toxicosis, p. 85. • Decontamination, supportive care
Valerian	*Valeriana officinalis*	Valpotriates, mono- and sesquiterpenes	Sedative, sleep aid, antianxiety	Affects the GABA receptor; lethargy, sedation, muscle	Decontamination, supportive care

Common Name(s)	Genus, Species	Toxic Principle if Known	Popular Usage	Toxicity Signs/Major Effect/Actions	Treatment Overview/Comments
Tea tree oil, pennyroyal oil	*Melaleuca alternifolia, Mentha pulegium*	Melaleuca oil, pulegone, menthofuran	Germicidal, fungal infections, antiseptic, flea control, dermatitis	• Terpenes; essential oils; Orally: vomiting, diarrhea, CNS depression, hepatotoxicity, aspiration pneumonia. • Dermally: transient paresis, ataxia, weakness hypothermia	Cats more sensitive; bathing, fluids, thermoregulation; may need few days of supportive treatment
Grapefruit seed extract	*Citrus X paradise Pausinystalia yohimbine*	Quaternary ammonium compounds, cationic detergents	Disinfectant, antifungal, antimicrobial	Oral ulcers; hypersalivation, vomiting +/− blood, weakness, anorexia, hyperthermia, dermal erythema, pain, ulceration	• Cats more sensitive; see Cleaning Products Toxicosis, p. 217 • Dilution, bathing, GI protectants, pain control, supportive care
Yohimbine		Alpha2-adrenergic blocking agent	Stimulant; hypertension, angina, “herbal Viagra”	• Signs due to alpha2-adrenergic blocking activity; • Hyperactivity, agitation, tremors, seizures, vomiting, diarrhea, hypotension	Decontamination, diazepam, fluids, stabilize heart rate, blood pressure, thermoregulation
Wintergreen extract/oil	*Gaultheria procumbens*	Oil can contain 98% methyl salicylate; essential oils	Topical pain control; oral digestive	Signs similar to aspirin toxicosis; vomiting, diarrhea, gastric ulceration, hyperthermia, sedation, coma, acute hepatic injury	• See Nonsteroidal Antiinflammatory Drugs Toxicosis, p. 768. • Cats more sensitive; GI protectants, fluids, management of acidosis or alkalosis
Evening primrose	*Oenothera biennis*	Oil can contain 50%–70% *cis*-linoleic acid & other fatty acids	Supports cardiovascular function; used for rheumatoid arthritis, multiple sclerosis	Self-limiting stomach upset	Low toxicity; systemic effects not expected; mild vomiting or diarrhea possible

Common Name(s)	Genus, Species	Toxic Principle if Known	Popular Usage	Toxicity Signs/Major Effect/Actions	Treatment Overview/Comments
Kava, yangona, kawa	*Piper methysticum*	Kawain and several other lactones	Beverages prepared from roots used as a relaxant; euphoric effect; sedative	Expected clinical signs similar to benzodiazepines; sedation, ataxia, lethargy, visual disturbances	Decontamination of patient, supportive care
Khat, kat, gat, Kus	*Catha edulis*	Alkaloid katin (amphetamine-like)	Used in East African countries; stimulant, mood elevator; leaves and stems chewed	Amphetamine-like effects; hyperactivity, agitation, seizures, tachycardia, hypertension	See Amphetamine Toxicosis, p. 59
Neem, nim, nimbi	*Azadirachta indica*	Azadiracthin as insecticide; neem oil	Insecticidal properties, birth control agent, hypoglycemic properties	Hypothermia, ataxia, lethargy, coma, in cats	Used for controlling fleas in dips/shampoos on cats; bathing, thermoregulation, supportive care
Ginkgo, ginkyo	*Ginkgo biloba*	Several flavonoids; terpenoids, alkaloid ginkgo toxin in the seed	Leaf extract used for antioxidant properties, dementia treatment, circulatory disorders, neuroprotection	• From leaf extract: vomiting, diarrhea, lethargy. • From seeds: seizures, shaking, tremors possible	• Mild effects from leaf extract • Patient decontamination, diazepam, fluids if seeds involved (treat based on clinical signs).
Ginseng	*Panax quinquefolium; panax ginseng*	Steroid-like compounds, ginsenosides, and panaxosides, saponins,	Roots, teas, cosmetics used for general well-being, aging, diabetes, neurosis, cancer	Vomiting, diarrhea, nervousness, excitation, lethargy, hypoglycemia possible	• Good safety index in humans • Decontamination of patient, fluids, and supportive care (treat based on clinical signs).

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Hepatozoonosis

BASIC INFORMATION

DEFINITION

Emerging tickborne protozoal disease of dogs that has a gametocyte stage in white blood cells and a cystic stage in host tissues; common in the southeastern United States.

SYNONYMS

Hepatozoon canis and *Hepatozoon americanum* are the two species known to infect dogs.

EPIDEMIOLOGY

SPECIES, AGE, SEX

Usually outdoor dogs; also reported in foxes, coyotes, jackals, hyenas, bobcats, ocelots.

RISK FACTORS

Areas with large coyote populations. History of tick exposure. Ingestion of deer carcass or other mammal with ticks.

CONTAGION & ZOONOSIS

No reported human cases

GEOGRAPHY AND SEASONALITY

- *H. canis* is endemic in southern Europe, the Middle East, Africa, and South America. Reported in dogs in the Gulf Coast area of the United States in 2008.
- *H. americanum* is endemic in the Gulf Coast area of the United States and now ranges from Oklahoma to Florida.
- Most cases present in the summer and fall.

ASSOCIATED CONDITIONS & DISORDERS

- *H. canis:* usually subclinical unless there is other disease or immunosuppression
- *H. americanum:* pyogranulomatous myositis, marked leukocytosis, fever of unknown origin

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- *H. canis:* usually no overt clinical signs
- *H. americanum:* chronic wasting disease characterized by waxing and waning muscle pain and fever

HISTORY, CHIEF COMPLAINT

- *H. canis:* incidental finding of gametocytes on blood smear. Dogs usually show no clinical signs.
- *H. americanum:* depression, reluctance to move, stiff gait, mucopurulent ocular discharge, weight loss. Dogs may have history of ingesting a deer carcass 3-4 weeks earlier. Some dogs develop transient bloody diarrhea before signs of muscle pain and fever.

PHYSICAL EXAM FINDINGS

Fever, mucopurulent ocular discharge, hyperesthesia, neck guarding, stiffness, ataxia, unwillingness to rise, cachexia, muscle wasting *(H. americanum).*

ETIOLOGY AND PATHOPHYSIOLOGY

- The parasite has a complex life cycle. The definitive host of *H. canis* is the brown dog tick, *Rhipicephalus sanguineus,* and for *H. americanum* it is the Gulf Coast tick, *Amblyomma maculatum.* The dog must ingest the infected tick. Recent information reveals that dogs can also be infected by ingesting small mammals such as cotton rats that live in endemic areas and harbor the disease.
- Sporozoites are released and penetrate the wall of the dog's gastrointestinal tract. These are phagocytized by macrophages and distributed throughout the body to form meronts, or “cysts.”
- The organisms replicate inside the cyst until it ruptures, and merozoites are released. *H. canis* cysts are primarily in the lymph nodes and spleen. *H. americanum* cysts are primarily in skeletal muscle.
- When the merozoites are released, an intense inflammatory reaction occurs, resulting in painful myositis and fever *(H. americanum).*
- Merozoites can either enter leukocytes and become circulating gametocytes infectious to ticks that feed on the dog, or they may enter a macrophage and undergo secondary merogony and continue the cycle of releasing merozoites to cause repeated episodes of pyogranulomatous myositis.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis of *H. canis* is usually made by finding gametocytes on a blood smear. *H. americanum* should be suspected in dogs with fever, cachexia, ocular discharge, leukocytes, and periosteal proliferation on long bones. Diagnosis can be confirmed with PCR testing or muscle biopsy.

DIFFERENTIAL DIAGNOSIS

- Meningitis
- Diskospondylitis
- Polyarthritis
- Pyometra
- Other tickborne diseases

INITIAL DATABASE

- CBC may reveal extreme leukocytosis (20,000-200,000 cells/mcL; typically mature neutrophilia with left shift possible) and mild nonregenerative anemia. Platelet count is usually normal; thrombocytopenia may indicate coinfection with other tickborne disease.
- Serum chemistry profile: hypoalbuminemia, hyperglobulinemia, elevated serum alkaline phosphatase, low glucose, low blood urea nitrogen are commonly seen.
- Long-bone radiographs: periosteal proliferation secondary to adjacent muscle inflammation is possible.
- Dogs with chronic disease may develop glomerulonephritis with an increased urine protein/creatinine ratio.
- Blood smear or buffy coat smear may reveal gametocytes in circulating white blood cells.

ADVANCED OR CONFIRMATORY TESTING

- Immunofluorescent antibody and PCR tests available for *H. canis* (in Israel)
- PCR test for *H. americanum* and *H. canis is* available through Auburn University Molecular Diagnostics Lab (http://www.vetmed.auburn.edu/index.pl/molecular_diagnostics).
- Definitive diagnosis usually made by finding organisms in muscle biopsy (see p. 1305). Any muscle can be sampled, but hindlimb muscles are most commonly used.

TREATMENT

TREATMENT OVERVIEW

Acute antiprotozoal therapy eradicates circulating organisms. Chronic therapy is necessary to prevent relapses from continued release of merozoites from tissue cysts.

ACUTE GENERAL TREATMENT

- For *H. americanum,* combination therapy for 2 weeks: trimethoprim-sulfadiazine (15 mg/kg PO q 12 h), clindamycin (10 mg/kg PO q 8 h), and pyrimethamine (0.25 mg/kg PO q 24 h). If clinical signs are still evident at 14 days, continue 2 more weeks.
- For *H. canis:* imidocarb (5 mg/kg SQ repeated every 14 days until parasitemia has resolved)
- Nonsteroidal antiinflammatory drugs at standard doses for muscle pain
- Doxycycline (5-10 mg/kg PO q 12-24 h). May be required if there is coinfection with other tickborne diseases.
- IV fluids may be needed for hypoglycemia and dehydration.

CHRONIC TREATMENT

Decoquinate (Deccox 22.7 g/lb Premix [Alphama, Fort Lee, NJ]) at a dosage of 20 mg/kg or 1 tsp/10 kg mixed in food q 12 h for 2 years or until PCR testing is negative will inhibit development of merozoites released from tissue cysts, thereby preventing reinfection of the dog and cyclic bouts of illness. This drug is very safe for long-term use and has not been associated with any known side effects.

NUTRITION/DIET

Dogs with hepatozoonosis usually retain their appetite but often are too painful to move. They should be hand fed and offered water until they become ambulatory. High-calorie diets, such as growth or puppy diets, can help reverse the cachexia and hypoalbuminemia.

BEHAVIOR/EXERCISE

Clients should not allow dogs to eat dead animals that may harbor ticks (e.g., deer carcasses) or consume prey in endemic areas.

POSSIBLE COMPLICATIONS

Dogs may require repeated administration of combination therapy if relapses occur with severe clinical signs.

RECOMMENDED MONITORING

Repeat CBC and physical examination in 2 weeks. If fever, muscle pain, or marked leukocytosis is present, continue combination therapy for 2 more weeks. PCR should be checked every 6 months. Decoquinate can be discontinued when PCR is negative. Some dogs remain infected for >5 years but continue to be free of clinical signs while receiving decoquinate.

PROGNOSIS AND OUTCOME

- Without treatment, American hepatozoonosis is usually fatal within several months.
- With antiprotozoal combination therapy alone, relapses occur requiring repeated therapy. Relapses become more frequent and refractory to treatment. Death usually occurs within 1 year of the initial diagnosis.
- Long-term cure (>5 years) has been achieved with combination therapy followed by long-term decoquinate therapy.

PEARLS & CONSIDERATIONS

PREVENTION

- Effective tick control with a topical acaricide and a repellent collar is recommended.

TECHNICIAN TIPS

- Making a buffy coat smear may enhance the possibility of finding gametocytes.
- Gametocytes appear as oblong intracellular single inclusions in leukocytes (rare).
- Spurious hypoglycemia can occur if the blood sample is not run immediately, because WBCs can metabolize glucose in the tube.

CLIENT EDUCATION

- Clean matted eyes with a warm, moist towel as needed.
- Provide soft bedding.
- Bring food and water to dogs that are nonambulatory.
- Continue all medications for recommended duration. Stopping decoquinate too early can result in reinfestation of the dog and

exacerbation of the disease.

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Hepatopathy, Copper-Associated

BASIC INFORMATION

DEFINITION

Accumulation of copper within hepatocytes, leading to hepatotoxicosis

EPIDEMIOLOGY

SPECIES, AGE, SEX

Primarily in dogs; rare in cats. Copper accumulates slowly, so clinical signs are typically not present until middle age.

GENETICS & BREED PREDISPOSITION

- Autosomal recessive in Bedlington terriers
- Predisposition in dalmatians, West Highland white terriers, and Skye terriers
- Possible association in Doberman pinschers and Labrador retrievers
- Reported in other canine breeds, but it is unknown if copper accumulation is the cause or effect of hepatopathy.

CLINICAL PRESENTATION

DISEASE FORM/SUBTYPES

- Subclinical
- Chronic inflammatory liver disease/cirrhosis
- Acute hepatic failure with hemolytic anemia (rare)

HISTORY, CHIEF COMPLAINT, AND PHYSICAL EXAM FINDINGS: Patients usually present with features of chronic hepatic disease such as lethargy, vomiting, abdominal distention, or encephalopathy (see p. 212) or less commonly with acute hepatic failure (see p. 503) and hemolytic anemia (see p. 71).

ETIOLOGY AND PATHOPHYSIOLOGY

- Copper homeostasis is maintained by biliary excretion of excess copper.
- Copper is absorbed from ingesta in the small intestine and extracted by hepatocytes.
- Chaperoned around the hepatocyte by a number of proteins before being either released into the serum or excreted in bile. A small amount is stored in lysosomes.
- Abnormal hepatic copper accumulation occurs because of primary inborn error of metabolism or secondary to acquired cholestatic liver disease.
    - In Bedlingtons, copper accumulation in lysosomes is due to a genetic defect in the COMMD1 gene, leading to excessive copper binding by an abnormal metallothionein (a protein required for the final stages of copper excretion into the bile). When the storage capacity of the lysosomes is exceeded, copper breaks out into the cytoplasm, where it is toxic.
    - Genetic basis for copper accumulation in other breeds is unknown.
- Excess copper damages hepatocytes by inducing the formation of free radicals.
- Secondary copper accumulation is due to a generalized impairment in biliary excretion (i.e., cholestasis).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The disorder may be suspected in two contexts: either as part of any cholestatic liver disease (detected as part of evaluation of liver biopsy specimens) or in cases where copper accumulation is the dominant feature of hepatopathy in a dog (e.g., Bedlington terrier) with or without overt clinical signs. Definitive quantification of hepatic copper content, which carries important treatment implications, requires a liver biopsy.

DIFFERENTIAL DIAGNOSIS

- Chronic:
  - Infectious, immune, or toxic causes of inflammatory hepatic disease
  - Hepatic neoplasia
  - Congenital portosystemic shunts
- Acute:
  - Infectious, immune, drug, or toxin-induced (zinc) hemolytic anemia
  - Exposure to hepatotoxic drugs or environmental toxins
  - Infectious canine hepatitis, leptospirosis

INITIAL DATABASE

See pp. 503, 513, , and .

ADVANCED OR CONFIRMATORY TESTING

- Determination of hepatic copper concentration:
  - Quantitative analysis on hepatic wedge or needle biopsies
  - Qualitative analysis by rhodanine or rubeanic acid staining of histopathology specimen. Permits determination of copper distribution within the hepatic lobule.
    - Normal hepatic copper levels from 200-400 mcg/g dry weight (DW)
    - Secondary copper accumulation levels <1000-2000 mcg/g DW
    - Copper >2000 mcg/g dry weight suggests a primary copper abnormality.
    - In Bedlingtons, copper levels gradually increase with age, with levels reported from 850-12,000 mcg/g DW.
    - In West Highland white terriers, copper accumulation does not correlate as well with age (levels up to 3500 mcg/g DW reported).
    - Lower copper levels (1000-2000 mcg/g dry weight) associated with toxicity in some Labradors and Dobermans.
- Histopathologic findings:
  - In Bedlingtons, copper initially accumulates centrilobularly.
    - Initial finding is centrilobular hepatocellular vacuolation followed by degeneration/necrosis and finally inflammation and fibrosis. Progresses to become more panlobular eventually with periportal orientation. Findings can mimic idiopathic chronic hepatitis.
  - In secondary copper accumulation, copper staining located primarily in areas of inflammation or degeneration.
- Genetic test, microsatellite marker (C04107) available to screen Bedlingtons, but may miss disease in some pedigrees (5%-10% false negatives). No test for COMMD1 mutation available.

TREATMENT

TREATMENT OVERVIEW

Decrease hepatic copper concentration, decrease copper absorption.

ACUTE GENERAL TREATMENT

Manage the complications of acute or chronic hepatic disease (see pp. 503, p. 212, and 501).

CHRONIC TREATMENT

- Copper chelators for initial decoppering of liver and maintenance therapy:
  - Penicillamine (10-15 mg/kg PO q 12 h). Increases urinary copper excretion. Works slowly (removes ~900 mcg/g per year), so copper levels take several months to years to decrease. Vomiting is a common side effect; begin at low end of dosage range and titrate upward.
  - Trientine (10-15 mg/kg PO q 12 h). Increases urinary copper excretion and may also block intestinal uptake. Fewer side effects than penicillamine but more expensive.
  - Give all medications on an empty stomach, and follow with a water bolus.
- Inhibit intestinal copper absorption, maintenance therapy.
  - Zinc (100 mg elemental zinc PO q 12 h). Induces intestinal metallothionein, a protein that binds copper, keeping it sequestered within the enterocyte and thus preventing copper absorption. May be combined with chelators (separate administration by 2 hours). Side effects include gastritis, hemolytic anemia, and iron deficiency. Keep serum zinc levels <600 mcg/dL to avoid hemolysis. Effective zinc levels are >200 mcg/dL.

- Reduce dietary intake of copper.
  - Avoid shellfish, nuts, chocolate, mushrooms, and organ meats. Check water supply if not public. Copper restricted prescription diets are available.
- Antioxidants
  - Induction of oxidant stress is central to copper-induced hepatic damage.
  - Vitamin E supplementation (200-400 IU PO q 24 h)
  - *S*-adenosylmethionine (20 mg/kg PO q 24 h).

RECOMMENDED MONITORING

Serum liver enzymes every 4-6 months

PROGNOSIS AND OUTCOME

- Subclinical disease: excellent with therapy
- Chronic: depends on stage. Mild to moderate inflammatory disease: good. Severe inflammatory disease/cirrhosis: guarded.
- Acute: grave

PEARLS & CONSIDERATIONS

COMMENTS

- All Bedlington terriers should be tested at 1 year of age by determination of hepatic copper concentration and/or genetic testing. Affected dogs should not be bred.
- All dogs with chronic inflammatory hepatitis, particularly West Highland white terriers, Doberman pinschers, Skye terriers, Labrador retrievers and dalmatians, should have hepatic copper analysis. If concentrations are > 1000-2000 mcg/g DW, they should be treated to decrease hepatic copper.

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Hepatomegaly

BASIC INFORMATION

DEFINITION

Liver enlargement

EPIDEMIOLOGY

SPECIES, AGE, SEX

Observed in both dogs and cats, more frequently in middle-aged to older animals owing to age-related prevalence of associated diseases. However, younger animals can also present with hepatomegaly (e.g., with feline infectious peritonitis [FIP], congenital veno-occlusive disease, infectious disease, lymphoma).

GENETICS & BREED PREDISPOSITION

- Dogs: Doberman pinschers (inflammatory liver disease), cocker spaniels, Labrador retrievers, Skye terriers; Labrador retrievers (tricuspid dysplasia causing right-sided heart failure)
- Cats: Abyssinians (amyloidosis), Asian breeds (FIP)

CLINICAL PRESENTATION

HISTORY/CHIEF COMPLAINT

Depends on etiology:

- Can be an incidental finding
- Abdominal distention
- Polyuria, polydipsia
- Anorexia, lethargy/weight loss
- Exercise intolerance
- Vomiting/diarrhea
- Pale mucous membranes
- Hepatic encephalopathy
- Coagulopathy
- Cutaneous disease/hair loss/poor haircoat

PHYSICAL EXAM FINDINGS

- Abdominal distention
- Palpable cranial organomegaly
- Ascites
- Icterus
- Concurrent hepatosplenomegaly suggests a multicentric neoplastic, passive congestive, systemic inflammatory/infectious, or anemia-inducing process, or unrelated disorders.

ETIOLOGY AND PATHOPHYSIOLOGY

Hepatomegaly is caused by inflammation, infiltration, congestion/obstruction, infection, or hyperplasia of the liver.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The presence of an enlarged liver is noted on physical examination, radiographs, or abdominal ultrasound. The first diagnostic step

consists of reviewing the history and physical examination for evidence of liver dysfunction. Benign causes of hepatomegaly are common, but hepatomegaly may be the first clue that nonspecific clinical signs are caused by liver disease. Routine blood and urine tests and abdominal ultrasonography, postprandial serum bile acid levels, and diagnostic sampling of the liver help identify cases that require treatment and follow-up.

DIFFERENTIAL DIAGNOSIS

- Inflammatory diseases of the liver:
  - Cholangitis/cholangiohepatitis complex (cats)
  - Cirrhosis (end stage usually produces microhepatica, not hepatomegaly)
  - Abscess
  - Neoplasia
  - Chronic active hepatitis (idiopathic chronic hepatitis) (dogs)
  - Canine breed-specific hepatopathies
- Neoplastic/cystic diseases:
  - Lymphoma, biliary cystadenoma, bile duct carcinoma, hemangiosarcoma, metastatic neoplasia
  - Hepatocellular carcinoma, hepatoma (enlargement of a single lobe)
  - Malignant histiocytosis
  - Diffuse mast cell tumor
  - Parenchymal/biliary cysts
- Extrahepatic obstruction:
  - Pancreatitis
  - Cholelithiasis (rare in dogs and cats)
  - Bile duct neoplasia
  - Biliary mucocele
  - Inspissated bile syndrome of cats
- Metabolic disease:
  - Diabetes mellitus (lipid accumulation)
  - Hepatic lipidosis (cats)
  - Amyloidosis (Abyssinian/Chinese shar-pei)
  - Storage disease (rare in cats and dogs)
  - Hyperadrenocorticism (dogs/glycogen accumulation)
- Drugs:
  - Glucocorticoids
  - Phenobarbital
- Infectious disease (many cause hepatosplenomegaly due to systemic immune stimulation):
  - Bacterial, rickettsial, protozoal, fungal
  - Liver abscess (enlargement localized to a single lobe)
  - FIP
  - Erythrocyte parasitism *(Mycoplasma baemofelts/*hemobartonellosis, *Babesia* spp.)
- Immune-mediated disease (hepatosplenomegaly common secondary to systemic immune stimulation):
  - Immune-mediated hemolytic anemia (IMHA)
  - Immune-mediated thrombocytopenia (ITP)
  - Systemic lupus erythematosus
  - Vasculitis
  - Any systemic immune-mediated disease
- Congestion (often associated with ascites):
  - Right-sided heart failure
  - Budd-Chiari syndrome/venoocclusive disease (rare)
  - Liver lobe torsion (rare)
- Intoxications
- Benign conditions:
  - Nodular hyperplasia (older dogs)
  - Nodular regeneration (associated with severe liver disease)
  - Extramedullary hematopoiesis
  - Individual variation (pseudohepatomegaly)
- Radiographic differential diagnosis for hepatomegaly:
  - Cranial abdominal mass, marked splenomegaly, ascites, dyspnea (caudal displacement of liver), youth (nonmineralized distal ribs gives false impression of liver protruding beyond costal arch)

INITIAL DATABASE

- CBC, chemistry profile, urinalysis, and urine culture
- Abdominal radiographs (most accurate assessment of liver size)

- Abdominal ultrasound
- Thoracic radiographs (cardiac structures, metastatic disease)

ADVANCED OR CONFIRMATORY TESTING

- Coagulation profile (prothrombin time/activated partial thromboplastin time/platelet count), buccal mucosal bleeding time
- Preprandial and postprandial serum bile acids
- Urine bile acids
- Serum ammonia (poor specificity/sensitivity)
- Liver aspirate or biopsy for histopathologic evaluation and culture (aerobic/anaerobic). See p. 1298.
- Copper quantification of biopsy specimen
- Amylase/lipase/pancreatic lipase immunoreactivity
- Adrenocorticotropic hormone (ACTH) stimulation, ACTH level, low-dose dexamethasone suppression test
- Antinuclear antibody test
- Infectious disease titers/PCR
- FIP serology
- Echocardiography/central venous pressure
- Abdominocentesis (if ascites)
- Abdominal CT
- Venography (Budd-Chiari, veno-occlusive disease)
- D-dimer (thromboembolic disease)
- Bone marrow aspirate (immune-mediated hemolytic anemia/immune-mediated thrombocytopenia, lymphoma staging)

TREATMENT

TREATMENT OVERVIEW

Treat specifically on the basis of an established diagnosis. Hepatomegaly is a sign, not an etiology. Suppress the disease process/manage the metabolic condition/treat any infectious or immune-mediated disease with appropriate medication or surgical intervention.

GENERAL TREATMENT

- Inflammatory diseases:
  - Immunosuppressant therapy (i.e., glucocorticoids, azathioprine, cyclosporine)
  - Antioxidant therapy (S-adenosylmethionine, silymarin, zinc, vitamin E)
  - Immune-modulatory medications; ursodeoxycholate, metronidazole
  - Antifibrotics: colchicine, D-penicillamine, methotrexate
  - Antibiotics: metronidazole, amoxicillin, cephalexin, enrofloxacin
  - Gastric protectants
  - Vitamins: carnitine (lipidosis), vitamin C, vitamin E, zinc, vitamin K (if coagulopathy)
  - Dietary therapy
  - Treatment for hepatic encephalopathy: lactulose, neomycin, metronidazole
  - Management for ascites (abdominocentesis/abdominal drainage; diuretics: spironolactone)
  - Fluid therapy
- Neoplastic diseases: surgery/chemotherapy
- Extrahepatic obstruction: supportive care, surgery
- Metabolic diseases:
  - Insulin therapy
  - Colchicine/dimethylsulfoxide for amyloidosis
  - Aggressive feeding (hepatic lipidosis)
  - Lysodren/trilostane/ketoconazole for hyperadrenocorticism
- Infectious diseases:
  - Treatment depends on the organism
- Immune-mediated diseases:
  - Immunosuppressant therapy/depends on the disorder
- Congestion:
  - Treatment depends on the cause

RECOMMENDED MONITORING

Dictated by the disease process. Examples include liver enzyme profile 1-2 weeks post diagnosis, then monthly for 3 months, then

every 3-4 months. Repeat serum or urine bile acids/liver aspirate or biopsy at 6- to 12-month intervals; ACTH-stimulation every 3-6 months; convalescent infectious disease titers/PCR at 4-week to 6-month intervals.

PROGNOSIS AND OUTCOME

Varies with the cause of each disease

PEARLS & CONSIDERATIONS

COMMENTS

- Bile acids are an unnecessary test in an icteric patient (rare exception: icteric patient suspected of having both hemolysis and hepatobiliary disease concurrently, where bile acids can help differentiate).
- Fine-needle aspiration and cytologic evaluation of the liver does not reliably assess hepatic structure or function, even with diffuse hepatopathies.
- Normal serum bile acid levels in a patient with progressively increasing liver enzymes does not preclude the need for liver biopsy.
- Cats with hepatic lipidosis tend to have greater bleeding after liver biopsy than those with other diseases.
- Abnormal urine bile acids test result should be confirmed with serum bile acids measurement before liver biopsy.
- In cats, most diseases of the liver (including cirrhosis) result in hepatomegaly, whereas in dogs this is not necessarily the case.
- Ursodeoxycholate (e.g., Actigall) therapy can interfere with the interpretation of the urine bile acids test.

SUGGESTED READING

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Hepatitis, Canine Infectious

BASIC INFORMATION

DEFINITION

A specific form of liver disease caused by canine adenovirus-1 (CAV-1) that can cause acute death or chronic hepatitis. Infectious canine hepatitis (ICH) is uncommon in well-vaccinated dog populations. Antigenically and genetically distinct from CAV-2 which causes infectious tracheobronchitis.

SYNONYMS

CIH (canine infectious hepatitis); ICH; "blue eye"

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs, coyotes, foxes, wolves, and bears can be infected. Usually the disease is seen in dogs <1 year old, but unvaccinated dogs of any age can be affected.

RISK FACTORS

Nonvaccinated dogs. Resistant to environmental inactivation and survives for days at room temperature on soiled fomites; can remain viable for months at temperatures below 4°C.

CONTAGION & ZOONOSIS

- Dog-to-dog transmission occurs directly or indirectly (oronasal infection from secretions of infected animals—saliva, urine, feces, respiratory secretions)
- Not zoonotic
- The virus is resistant to environmental inactivation and survives for days at room temperature on soiled fomites; can remain viable for months at temperatures below 4°C.

ASSOCIATED CONDITIONS & DISORDERS

Chronic hepatitis may occur if the patient survives the initial viremia.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Animals usually have a poor vaccination history on presentation.
- During the acute viremic stage, animals can become moribund and die within a few hours.
- After the acute viremic stage, animals typically present with vomiting, diarrhea, and/or abdominal pain.

PHYSICAL EXAM FINDINGS

- Fever (can be biphasic), tonsillar enlargement, cervical lymphadenopathy, tachycardia, tachypnea, abdominal tenderness, hepatomegaly
- Icterus uncommon in the acute phase. Icterus and abdominal distention may be seen in advanced cases that survive acute viremic stage.
- Anterior uveitis and corneal edema ("blue eye") are hallmarks. They develop 7-21 days post infection.
- Signs of coagulopathy: petechial and ecchymotic hemorrhages, epistaxis, excessive bleeding from venipuncture sites
- Central nervous system signs consistent with hepatic encephalopathy or viral encephalitis (rare), including depression, seizures, disorientation, coma

ETIOLOGY AND PATHOPHYSIOLOGY

- Adenovirus-1 is transmitted by oronasal exposure to secretions of infected animals, notably urine. It can also be transmitted by fomites, and ectoparasites can harbor CAV-1.
- The virus initially localizes in the tonsils after exposure. From the tonsils, it disseminates to regional lymph nodes and then through the thoracic duct to the systemic circulation.
- Virus is found in body tissues and secretions, including urine, feces, and saliva, 4-8 days post infection.
- The virus is found in many tissues, including the kidneys 10-14 days post infection; secreted in urine for 6-9 months post infection.
- Predilection for hepatic parenchymal cells (causing acute hepatic injury/necrosis) and vascular endothelial cells (multiple organ injury)
- Cytotoxic effects of the virus cause initial cellular injury to the eye, liver, and kidney.
- Subclinical infections are widespread, predominantly in dogs with circulating antibody at the time of infection.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is made based on signalment (young unvaccinated dog) with clinical signs consistent with acute hepatic failure. Confirmation requires ruling out other differentials and serologic testing, virus isolation, or PCR.

DIFFERENTIAL DIAGNOSIS

- Liver disease:
  - Portosystemic shunts
  - Leptospirosis
  - Toxins
  - Copper hepatopathy
  - Cholelithiasis/cholangitis
  - Gallbladder rupture
- Pancreatitis
- Canine distemper

INITIAL DATABASE

- CBC/serum biochemistry profile
  - Neutropenia and lymphopenia initially, then rebound neutrophilia and lymphocytosis.
  - Alanine aminotransferase (ALT) and alkaline phosphatase elevation for 14 days post infection, then decline unless chronic hepatitis occurs. With chronic hepatitis, signs of hepatic synthetic failure (hypoglycemia hypoalbuminemia, low blood urea nitrogen) may be present. Hyperbilirubinemia is uncommon in the acute phase.
- Urinalysis: proteinuria, bilirubinuria (note: mild bilirubinuria is normal in healthy dogs)
- Coagulation panel: changes are most often seen in the viremic stage and include thrombocytopenia, prolongation of prothrombin time, activated partial thromboplastin time, and thrombin time (TT).
- Serum bile acids (postprandial): often elevated with hepatic encephalopathy

ADVANCED OR CONFIRMATORY TESTING

- Cytologic (aspirates, impression smears) or histologic examination of liver: characteristic inclusion bodies (Cowdry type A). Widespread centrilobular to panlobular necrosis.
- Cerebrospinal fluid: usually normal
- Bone marrow aspirate: decreased megakaryocytes during viremic stage
- Serologic testing (complement fixation, immunodiffusion, ELISA), virus isolation, and immunofluorescent testing are available, but an accurate clinical diagnosis is generally possible without these tests.
- PCR techniques can distinguish CAV-1 from CAV-2 infection.
- Similarly, the virus can be cultured from any body tissue 5 days post infection; the kidney is the most persistent site.

TREATMENT

TREATMENT OVERVIEW

Treatment is supportive and nonspecific in nature. Uncomplicated cases may not show improvement in clinical signs for up to 5-7 days.

ACUTE GENERAL TREATMENT

- Fluid therapy
- Correction of coagulation disturbances with fresh frozen plasma or whole blood transfusion (see p. 1347). Supplement with vitamin K, 0.625-1.25 mg/kg PO or SQ q 12 h for up to 36 h.
- *N*-acetylcysteine (50 mg/kg diluted 1 part acetylcysteine to 4 parts 0.9% NaCl, given IV through micropore filter over 1 hour, q 6 h)
- Management of hypoglycemia: intravenous glucose 0.5 g/kg IV bolus (= 1 mL 50% dextrose/kg body weight; before administration, must be diluted with sterile water by at least 50% to avoid phlebitis/perivascular irritation) followed by 2.5%-5% dextrose infused in balanced electrolyte solution
- Lactulose for animals exhibiting neurologic signs (0.5 mL/kg PO q 8 h)

CHRONIC TREATMENT

If chronic hepatitis results (see pp. 212 and 501), the following therapy may be considered:

- Diet: protein-restricted diet in animals with hepatic encephalopathy. All other animals should be given a high-carbohydrate, moderate-fat diet. Dietary fiber has been shown to bind bile acids and aid in their removal; psyllium 1-3 tsp/d can be added to the diet.
- Prednisone or prednisolone: 1-2 mg/ kg PO q 24 h. After clinical improvement, taper the dose to 0.5 mg/kg q 24 h, then q 48 h.
- Colchicine 0.03 mg/kg PO q 24 h may help decrease formation of hepatic fibrosis.
- Vitamin E: 50-400 IU PO q 24 h
- *S*-adenosylmethionine (SAMe): 20 mg/kg PO q 24 h
- Milk thistle: 50-250 mg/kg PO q 12 h

DRUG INTERACTIONS

May need to decrease dosages for drugs metabolized by the liver in acute hepatic failure phase

POSSIBLE COMPLICATIONS

Pyelonephritis, disseminated intravascular coagulation, glaucoma

RECOMMENDED MONITORING

For the acute phase:

- Coagulation times, blood glucose, albumin, blood ammonia levels

For chronic hepatitis:

- Serum bile acids
- Repeat liver biopsy 6 months after starting treatment

PROGNOSIS AND OUTCOME

- Prognosis for acute, fulminant infection is grave: animals often die within hours.
- Long-term prognosis for chronic hepatitis secondary to adenovirus-1 is guarded.
    - Animals with hypoalbuminemia, hypoglycemia, and coagulopathies usually die within 1 week of diagnosis.

PEARLS & CONSIDERATIONS

TECHNICIAN TIP

Puppies with acute fulminant ICH require intensive nursing care, and even with the best treatment, mortality rates are high.

PREVENTION

- Routine vaccination (D***H***LPP or D***H***PP) provides protection against infectious canine hepatitis.

- Modified live vaccine using CAV-2 isolates is used for preventing infectious canine hepatitis. The CAV-2 MLV vaccine confers cross-protection and has fewer side effects (corneal edema, fever) compared to the CAV-1 vaccine.
- A routine initial series followed by a booster at 1 year and then every 3-5 years is recommended.

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Hepatitis (Chronic, Idiopathic) of Dogs

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Chronic progressive hepatic disorder of unknown etiology, characterized by parenchymal inflammation, hepatocyte necrosis, and variable fibrosis that can ultimately progress to cirrhosis

SYNONYMS

Chronic active hepatitis, chronic hepatitis/hepatopathy

EPIDEMIOLOGY

SPECIES, AGE, SEX

Middle-aged dogs 3-10 years of age (mean: 7 years). Females tend to be overrepresented.

GENETICS & BREED PREDISPOSITION

Breed predispositions occur in the Labrador retriever, standard poodle, cocker spaniel (see online chapter: Hepatitis (Chronic) of Cocker Spaniel Dogs), and Scottish terrier. There is also chronic hepatitis-associated genetic-based copper accumulation (see p. 517) observed in the Bedlington terrier, West Highland white terrier, Doberman pinscher (see online chapter: Hepatitis (Chronic) of Doberman Pinscher Dogs), Labrador retriever, dalmatian, and Skye terrier.

RISK FACTORS

Drug therapy (including phenobarbital, nonsteroidal antiinflammatory, or potentially any other drug), infectious agents such as leptospirosis, and post toxin-induced hepatic damage may result in hepatitis, which eventually may progress to chronic hepatitis.

CONTAGION & ZOONOSIS

Leptospirosis, canine adenovirus type 1, and canine acidophil cell hepatitis (suspected but poorly documented) are associated with chronic hepatitis and potentially are contagious (all three) and zoonotic (leptospirosis).

ASSOCIATED CONDITIONS & DISORDERS

Hepatic inflammation can occur secondary to disorders such as pancreatitis, peritonitis, or inflammatory bowel disease. The type and character of inflammation in the liver is different from typical progressive idiopathic chronic hepatitis: in these disorders, the inflammation is usually mild, confined to the portal triads, and there is an absence of fibrosis. This is commonly referred to as a *reactive hepatopathy*.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Chronic hepatitis is a progressive disease associated with several clinical stages:

- Subclinical hepatitis associated only with abnormal serum liver enzyme activites
- Clinical hepatitis
- Cirrhosis and hepatic failure

HISTORY, CHIEF COMPLAINT

Historic signs for clinical disease will vary based on the extent of liver damage and include:

- Subclinical:
  - None

- Clinical hepatitis:
  - Vomiting
  - Anorexia
  - Weight loss
  - Lethargy
  - Polyuria or polydipsia
- Cirrhosis/hepatic failure:
  - Abdominal distention from ascites
  - Signs of neurologic dysfunction associated with hepatic encephalopathy (HE)
  - Bleeding due to coagulopathy
  - Anorexia, vomiting, and other signs of gastrointestinal ulceration

PHYSICAL EXAM FINDINGS

Physical findings will vary with severity of disease:

- Subclinical dogs appear normal.
- Abnormal findings in clinically ill dogs include (see also History, above):
  - Icterus
  - Poor body condition
  - Hepatic encephalopathy (see p. 501)
  - Ascites (mainly in cirrhosis/hepatic failure; see pp. 93)

ETIOLOGY AND PATHOPHYSIOLOGY

- In most all cases the etiology is unknown.
- Infectious causes including leptospirosis, canine adenovirus 1 (infectious canine hepatitis) infection and possibly *Helicobacter* spp., *Bartonella* spp., or other infectious agents
- Immune-mediated mechanisms may be responsible, but this has been poorly documented in the dog. Studies measuring liver-associated antibodies or cell-mediated responses in affected cases fail to determine if the response is primary or a secondary phenomenon.
- Drug-associated chronic hepatitis from anticonvulsants, nonsteroidal antiinflammatory drugs (NSAIDs) or trime-thoprim-sulfa antibiotics. It is possible that any drug has potential to cause liver disease.
- Copper-associated liver disease due to defective copper metabolism
- Other conditions such as aflatoxins, chemicals, or other environmental factors may be responsible.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected in any dog with historical, physical, biochemical, or imaging-identified signs of hepatobiliary disease; confirmation is achieved via histologic analysis of a liver biopsy specimen.

DIFFERENTIAL DIAGNOSIS

- Acute hepatitis
- Hepatic neoplasia
- Pancreatitis
- Reactive hepatopathies secondary to systemic or metabolic disease and gastrointestinal (GI) disease
- Congenital portosystemic shunts
- Extrahepatic bile duct obstruction

INITIAL DATABASE

- CBC: nonregenerative anemia, variable white blood cell count
- Serum biochemistry profile: increased liver enzyme activities, including alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and γ-glutamyl transferase (GGT). In advanced disease, increased total bilirubin concentration and decreased albumin, glucose, blood urea nitrogen, and/or cholesterol concentrations may occur. Hyperglobulinemia is often observed.
- Urinalysis: bilirubinuria, variable specific gravity, and sometimes ammonium biurate crystalluria associated with hyperammonemia
- Abdominal radiographs: small liver and possibly signs of ascites in advanced disease (cirrhosis/hepatic failure)

ADVANCED OR CONFIRMATORY TESTING

- Elevated serum bile acid concentrations suggesting altered hepatic function or portal shunting
- Elevated plasma ammonia concentrations or ammonia tolerance test (variable results)
- Coagulation tests: prothrombin time (PT), activated partial thromboplastin time (APTT), and proteins inducted by vitamin K antagonism (PIVKA). With advanced disease, these become abnormal and reflect severe liver dysfunction.
- Abdominal ultrasonography: variable hepatic parenchymal changes. Micro-hepatica, nodular liver, and ascites (normal-diameter caudal vena cava and hepatic veins help rule out right-sided heart failure as cause of ascites) in late-stage disease (cirrhosis/hepatic failure).
- Serologic testing for antinuclear antibody (ANA) titer and infectious agents such as *Leptospira interrogans, Bartonella* spp., or other specific tests where indicated
- Abdominocentesis in patients with ascites may reveal either a pure transudate or modified transudate.
- Surgery or laparoscopy: liver may appear normal in subclinical disease or may be small, nodular, and bibrotic/firm in advanced clinical disease.
- Liver biopsy and histopathologic evaluation:
  - Large biopsies (obtained via laparoscopy or laparotomy) are preferred over needle core biopsies or fine-needle aspirates, owing to superior diagnostic accuracy.
  - Liver samples for metal analysis and culture and sensitivity should be obtained.
  - Subclinical disease is associated with infiltration of mononuclear inflammatory cells into portal and parenchymal areas.
  - Clinical disease is associated with evidence of active hepatitis, with areas of piecemeal and bridging necrosis.
  - In cirrhosis, extensive fibrosis and nodular regeneration are present.
  - Histochemical staining for copper and iron are often positive.
- Hepatic metal quantitative analysis: hepatic copper can accumulate secondary to the liver disease; concentrations often range from 600-1500 g/g dry weight liver (normal <400 g/g). Values >1500 g/g could be associated with a primary copper-associated hepatopathy (see p. 517). Hepatic iron is often elevated, and zinc concentrations are frequently subnormal.

TREATMENT

TREATMENT OVERVIEW

- Remove the inciting etiology if identified.
- Provide optimal nutrition.
- Stop the progression of ongoing inflammation.
- Provide for optimal hepatic support.
- Treat specific complications of liver disease as they occur.

ACUTE GENERAL TREATMENT

Acute complications of chronic hepatitis should be treated as they occur. Commonly used treatments during acute management of idiopathic chronic hepatitis include:

- Fluid therapy to correct deficits and electrolyte losses. Supplemental dextrose (2.5%-5%) is recommended; limit sodium with ascites (e.g., switch to low-sodium, isotonic maintenance fluid when patient is hydrated [e.g., Plasmalyte 56 + 5% dextrose, with potassium supplementation]).
- Dextrans, Hetastarch, plasma, or albumin infusions may be used for improving oncotic pressure.
  - Plasma advantages include presence of albumin (contributes positively to protein balance), presence of coagulation factors, and persistence in the circulation (versus protein-losing enteropathy or nephropathy, where the transfused proteins may be lost quickly); drawbacks include cost and short shelf life (fresh) or need to freeze (fresh frozen).
  - Gastric ulceration managed using sucralfate (0.5-1 g PO q 8 h) and famotidine (0.5 mg/kg PO q 12 h) or omeprazole (0.5-1 mg/kg PO q 24 h).
- Avoid cimetidine because of hepatic metabolism.
- HE treatment using cleansing enemas or retention enemas (Betadine diluted 1:10 or lactulose diluted 1:3). If encephalopathy is severe enough to warrant this, the prognosis is poor. Chronic management involves low-protein diets, lactulose, and neomycin or ampicillin (see p. 501).
- Coagulopathies are treated with fresh frozen plasma or fresh whole blood if there is clinical evidence of overt bleeding and anemia. Stored blood should be avoided owing to high ammonia concentrations.
- Ascites treated with abdominocentesis if abdomen is tense and the animal is uncomfortable (see pp. 1192 and p. 1194). Diuretics are less effective and possibly associated with greater side effects in the acute stages of mobilizing ascitic fluid (see below).
- Sepsis is treated with appropriate antibiotics (see p. 1014).

CHRONIC TREATMENT

All therapy discussed below lacks critical scientific review in dogs but reflects the current consensus of a majority of veterinary gastroenterologists:

- Antiinflammatory therapy using prednisolone or prednisone (2.2 mg/kg PO q 24 h; maximum dose 80 mg/d). Dosage is often tapered to an alternate-day therapy once there is clinical improvement. Corticosteroids cause a secondary steroid hepatopathy; monitoring liver enzymes is generally not helpful, but there should be a decline in serum bilirubin concentration and an increase in serum albumin concentration as the patient improves. With ascites, dexamethasone (0.2 mg/kg PO q 24-48 h) should be used instead to avoid mineralocorticoid effect. For corticosteroid-intolerant animals or when additional immunomodulation is desired, azathioprine (2 mg/kg q 24 h for 1 week, then q 48 h) can be given alone or in combination with glucocorticoids. Cyclosporine (5 mg/kg BID tapering to 5 mg/kg PO q 24 hours) can be given for immunosuppression without the need for glucocorticoids, with potentially less side effects than azathioprine.
- Copper chelation is indicated if hepatic copper concentrations are >1000 mcg/g dry liver weight. d-penicillamine or trientine (10-15 mg/kg PO q 12 h) is administered to remove copper. Following chelation, chronic zinc supplementation is used for blocking GI absorption of copper.
- Zinc has antioxidant and antifibrotic effects. Hepatic zinc deficiency occurs in advanced liver disease, and supplementation is indicated with zinc gluconate at 2-3 mg/kg PO q 24 h with deficiency. Higher doses of zinc will block intestinal copper absorption (see p. 517).
- Ursodeoxycholic acid (10-15 mg PO q 24 h) is a hydrophilic bile acid that has immunomodulatory, antioxidant, hepatoprotective, and choleretic effects.
- Antifibrotic drug colchicine (0.03 mg/kg PO q 24 h) inhibits collagen formation. However, few studies report its use in dogs, and human studies fail to show prolonged survival. Side effects are often GI. The angiotensin receptor antagonist, losartan (0.5 mg/kg PO q 12-24 h), recently has shown promise in inhibiting fibrosis in humans.
- Antioxidant therapy is used as adjunct liver support. Selection of one or several antioxidants is suggested, including vitamin E (10 IU/kg PO q 24 h), *S*-adenosylmethionine (20 mg/kg PO q 24 h or q 48 h), milk thistle (silybin complexed with phosphatidylcholine 24-70 mg/day), or others could be used for oxidative damage shown to occur in many dogs having hepatic disease.
- Antibiotics are used to modify GI bacterial flora in HE (see p. 501), to treat or reduce the incidence of secondary infection, or to treat a primary pathogen (leptospirosis or other pathogen).
- Ascites:
    - Medical treatment involves diuretics for long-term chronic management. Spironolactone (0.5-1 mg/kg PO q 12 h) is suggested as the initial diuretic. If failure of ascites control, furosemide (0.5-2 mg/kg PO q 12 h) or combination of both drugs should be considered.
    - Centesis/drainage may be performed intermittently as needed for comfort when patients develop tense ascites (very large volumes of abdominal fluid). Caution is advised because abdominocentesis will result in protein loss to the patient.

NUTRITION/DIET

- Diet is important to supply adequate calories. Palatability is important in advanced cases.
- Dietary protein is restricted only with protein intolerance (HE). Dietary protein content should represent 18%-22% of digestible kcal/day. Feed a high-quality moderate-protein diet given in small multiple feedings. Milk and vegetable protein sources are more beneficial in HE than meat protein-based diets.
- Fermentable fiber may also be beneficial in controlling HE.

DRUG INTERACTIONS

- Avoid drugs that require hepatic metabolism or alter hepatic biotransformation (e.g., cimetidine). Glucocorticoids may cause sodium retention, promote GI ulceration, or precipitate hepatic failure with advanced disease. Glucocorticoids also result in a steroid hepatopathy, making laboratory evaluation of treatment response difficult.
- Penicillamine and zinc should not be given together; penicillamine may chelate zinc.
- Animals with hepatic failure are anesthetic risks. Barbiturates should be avoided, and benzodiazepines should be used with care. Isoflurane or sevoflurane are the gas anesthetics of choice. Propofol, although hepatically metabolized, may be administered to effect (usually requiring a small fraction of normal doses) for anesthetic induction or for controlling seizures due to HE.
- Lidocaine, theophylline, propranolol, captopril, and tetracyclines should be avoided if possible.
- Diuretics may worsen HE, promote dehydration or metabolic alkalosis, and should be used only in otherwise stable patients for the long-term delay of return of ascites or for concurrent conditions (e.g., congestive heart failure).
- NSAIDs may exacerbate GI ulceration.

POSSIBLE COMPLICATIONS

Ascites, HE, GI ulceration, sepsis, disseminated intravascular coagulation, hepatic failure, and death

RECOMMENDED MONITORING

- Monitor general condition, body weight, and behavior.
- Periodic evaluation of laboratory tests (CBC and serum biochemical profile)
- Follow-up liver biopsy provides the best means of evaluating treatment response.

PROGNOSIS AND OUTCOME

- Guarded to fair based on clinical signs at the time of diagnosis and extent of liver damage as determined grossly and histopathologically.
- Most dogs are diagnosed when clinical signs occur, which is usually associated with advanced hepatitis and a guarded prognosis.
- When severe signs of liver failure occur, such as ascites, HE, and hypoalbuminemia, the prognosis is grave.
- Early diagnosis and therapy will prolong survival, but limited studies are available on survival times (cirrhosis 1-2 months; chronic hepatitis I month to 5 years).

PEARLS & CONSIDERATIONS

COMMENTS

- The first clue to chronic hepatitis is unexplained abnormal serum liver enzyme activities.
- Because of the great reserve capacity of the liver, signs of liver failure do not occur until the disease is advanced.
- Therapy in early stages of hepatitis may prolong survival.

CLIENT EDUCATION

- A complete cure is unlikely.
- Medication is generally lifelong but may prolong quality of life and survival times.
- There are few studies evaluating therapy for chronic hepatitis in the dog; repeat liver biopsies are recommended to monitor response to therapy.

SUGGESTED READING

Watson PJ: Chronic hepatitis in dogs: a review of current understanding of the aetiology, progression and treatment. Vet J 167(3):228– 241, 2004.

Favier RP: Idiopathic hepatitis and cirrhosis in dogs. Vet Clin North Am Small Anim Pract 39(3):481–488, 2009.

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Hepatitis (Chronic) of Doberman Pinscher Dogs

BASIC INFORMATION

DEFINITION

A progressive chronic inflammatory liver disease associated with hepatic copper accumulation distinct to Doberman pinschers

SYNONYMS

Chronic active hepatitis in Doberman pinschers, copper-associated chronic hepatitis, Doberman hepatitis

EPIDEMIOLOGY

SPECIES, AGE, SEX

Doberman pinschers. Most are diagnosed between the ages of 2 and 7 years. Most are females.

GENETICS & BREED PREDISPOSITION

- The high incidence in this breed suggests a genetic predisposition.
- Occurrence in this breed may have a prevalence of 2%-20% depending on clinical reports.
- Mode of genetic transmission is unknown.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Subclinical hepatitis
- Clinical hepatitis/cirrhosis

HISTORY, CHIEF COMPLAINT

- Dogs with subclinical hepatitis show no clinical signs; the disease is usually discovered incidentally (e.g., diagnostic workup triggered by elevated serum liver enzyme activities on serum biochemistry panel or microhepatica on abdominal imaging).
- Historic signs of early clinical hepatitis are often vague and may be associated with intermittent gastrointestinal signs and weight loss.
- When clinical hepatitis progresses, some or all of the following historic signs may occur:
    - Polydipsia, polyuria
    - Weight loss
    - Abdominal distension
    - Altered mental status associated with hepatic encephalopathy
- In advanced disease liver failure ensues, and the patient may have a rapid deterioration.

PHYSICAL EXAM FINDINGS

With clinical hepatitis some or all of the following may be found:

- Weight loss
- Icterus
- Ascites
- Signs of hepatic encephalopathy (depression/drowsiness, propulsive pacing, seizures; see p. 501)
- Evidence of hemorrhage (gastrointestinal, overt)

ETIOLOGY AND PATHOPHYSIOLOGY

- The etiology and mode of genetic transmission are unknown.
- Two theories suggested include either primary copper hepatotoxicity autoimmune mechanisms:
    - Primary copper hepatotoxicosis is supported by the fact that hepatic copper accumulation occurs in affected dogs

prior to hepatitis, and studies demonstrating affected dogs have a defect in biliary copper excretion, and copper chelation therapy improves pathology. Oxidative damage was also shown to occur in the liver from copper accumulation.
- Inappropriate major histocompatibility complex (MHC) class II antigen expression in affected dogs suggests the disease could be an autoimmune disorder, but presence of MHC class II can also occur as a secondary phenomenon.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The combination of signalment (breed) and physical and/or biochemical signs of hepatobiliary disease are strongly suggestive of the diagnosis; confirmation is obtained with liver biopsy.

DIFFERENTIAL DIAGNOSIS

- Hepatic disease from other causes
- Nonhepatic conditions associated with abnormal liver enzymes

INITIAL DATABASE

- Subclinical disease:
  - Elevation in serum alanine aminotransferase (ALT) activity first, followed by increases in other liver enzymes
- Clinical disease:
  - Elevation in serum ALT, aspartate aminotransferase, g-glutamyl transferase (GGT), and alkaline phosphatase (ALP) activities
  - Abnormal serum bile acid concentrations
- Advanced disease with loss of liver function: some or all of the following abnormalities may result:
  - Elevation in serum total bilirubin concentration
  - Low serum albumin, blood urea nitrogen, and glucose concentrations
  - Abnormal clotting times

ADVANCED OR CONFIRMATORY TESTING

- Abdominal radiographs show a small liver ± evidence of ascites (loss of serosal detail, abdominal distention).
- Abdominal ultrasound may demonstrate:
  - A small liver with altered parenchymal echogenicity. Findings vary from normal appearance (in early disease) to heterogeneous mottling, microhepatica with nodular changes, and an irregular surface.
  - Ascites which, on centesis, may be a pure transudate or a modified transudate; the cellular composition is not usually helpful diagnostically.
  - Vascular changes (e.g., multiple extrahepatic portosystemic shunts) associated with portal hypertension
- Surgery or laparoscopy: liver may appear normal in subclinical disease or may be small, micronodular, macronodular, and/or fibrotic in clinical disease.
- Liver biopsy and histopathology:
  - Large biopsies (obtained via laparoscopy or laparotomy) are preferred over small-diameter needle core biopsies or fine-needle aspirates, owing to superior diagnostic accuracy and ability to adequately measure hepatic copper concentrations.
  - Subclinical disease is associated with copper accumulation and infiltration of mononuclear inflammatory cells in centrilobular areas.
  - Clinical disease can progress to a micronodular cirrhosis with bridging fibrosis, piecemeal necrosis, progressive inflammatory infiltrates in the portal triads, and eventually macronodular cirrhosis with regenerative nodules.
  - Histochemical staining for copper is generally positive when copper concentrations are above 1000 mg/g dry weight liver.
- Hepatic metal quantitative analysis: Hepatic copper concentrations often range from 1000 to 2000 mg/g dry weight liver (normal <400 mg/g). Hepatic iron accumulation also occurs, thought to be secondary to chronic inflammation and not diagnostic of this disease specifically, with ranges from 1500 to 7000 mg/g dry weight liver.

TREATMENT

TREATMENT OVERVIEW

Goals of treatment are to slow progression of liver disease in subclinical cases, provide specific therapy for chronic hepatitis and

copper accumulation, and provide supportive treatment specifically aimed at controlling or avoiding complications of liver disease, including hepatic encephalopathy, ascites, gastrointestinal ulceration, and nutritional imbalance.

ACUTE GENERAL TREATMENT

- Subclinical and early clinical hepatitis with high copper concentrations (>600 mg/g liver).
  - D-penicillamine or trientine (15 mg/kg PO q 12 h) for 2-4 months or longer after measuring hepatic copper concentrations. Liver lesions improve as a result of lowering copper concentrations. Chelator therapy use should be based on identifying the characteristic histopathologic lesions and hepatic copper concentrations.
  - Glucocorticoid therapy (prednisone or prednisolone, 2-4 mg/kg PO q 24-48 h; maximum dose 80 mg/d) may be beneficial in slowing inflammatory component of liver disease.
  - Ensure adequate nutrient intake.
- Advanced clinical hepatitis (see 513):
  - Treatment for hepatic encephalopathy (see 501): high-quality low-protein diet, lactulose (0.1-0.5 mL/kg PO q 12 h, adjusted to achieve loose fecal consistency) and/or intestinal antibiotics (e.g., neomycin, 20 mg/kg PO q 8 h; ampicillin, 22 mg/kg PO q 8 h; metronidazole, 7.5 mg/kg PO q 12 h; or amoxicillin-clavulanate, 15 mg/kg PO q 12 h). If encephalopathy is severe enough to warrant these efforts, the prognosis is poor.
  - Treatment for ascites: see pp. 93, 501, and .
  - Treatment for gastric ulceration: famotidine (0.5 mg/kg PO q 12 h) or omeprazole (0.5-1 mg/kg PO q 24 h)

CHRONIC TREATMENT

- Copper chelation to maintain hepatic concentrations near normal
- Affected dogs should be placed on a low copper-containing diet (most therapeutic liver diets are low in copper).
  - After adequate chelation, zinc acetate or gluconate may be used for blocking enteric copper uptake. Adequate chelation is most accurately determined by rebiopsy; if rebiopsy is not possible, the change from chelation therapy to zinc therapy is generally warranted after 6-12 months of treatment if the dog is doing well clinically, with improving biochemical parameters.
  - Zinc acetate: 100 mg elemental zinc PO q 12 h as loading dose for 2 months, then 50 mg PO q 12 h. Zinc gluconate: 2-3 mg/kg PO q 12 h.
  - Zinc dose should be adjusted to keep serum zinc concentrations between 200 and 800 mcg/dL. NOTE: blood samples for zinc levels must be drawn into specific tubes (navy top), because standard rubber tops contain zinc.
- Antiinflammatory therapy using prednisolone or prednisone (2 mg/kg PO q 24 h; maximum dose 80 mg/d).
  - Dosage is often tapered to an alternate-day therapy once there is clinical improvement.
  - Glucocorticoids cause a secondary steroid hepatopathy, and monitoring liver enzymes is generally not helpful. However, there should be a decline in serum bilirubin concentration and an increase in serum albumin concentration as the patient improves.
  - With ascites, dexamethasone (0.2 mg/kg PO q 24 h) should be used instead to avoid mineralocorticoid effect.
  - For glucocorticoid-intolerant animals or when additional immunomodulation is desired, azathioprine or cyclosporine can be given alone or in combination with glucocorticoids (see 513).
- Ascites long-term management:
  - In the hydrated patient, diuretics (see previous) also may be used long term, either alone or as an adjunct to abdominal drainage, to delay the recurrence of ascites.
  - Repeated abdominocentesis or drainage (when ascites becomes large-volume/tense, and causes lethargy/inappetence) is also possible for long-term management of ascites (see ,pp. 1192).
- Diet is important to supply adequate calories. Palatability is important in advanced cases. Diets low in copper content should be fed. Dietary protein restriction is necessary only as protein intolerance occurs (i.e., hepatic encephalopathy). Feed a high-quality moderate-protein diet given in small multiple feedings. Milk and vegetable protein sources are better for avoiding hepatic encephalopathy than meat protein–based diets. Fermentable fiber may also be beneficial in controlling hepatic encephalopathy.
- General liver support may include ursodeoxycholic acid (15 mg/kg PO q 24 h), antioxidants (vitamin E, 10-15 IU/kg PO q 24 h); *S*-adenosylmethionine, 20 mg/kg PO q 24 h, or milk thistle [silybin complexed with phosphatidylcholine] 24-70 mg/d and antifibrotics (colchicine, 0.03 mg/kg PO q 24 h; or losartan, 0.5 mg/kg PO q 12-24 h).

DRUG INTERACTIONS

- Penicillamine and zinc should not be given together, as penicillamine may chelate zinc.
- Animals with hepatic failure are anesthetic risks. Barbiturates should be avoided, and benzodiazepines should be used with care, if at all. Isoflurane or sevoflurane are the gas anesthetics of choice. Propofol, although hepatically metabolized, may be administered to effect (usually requiring a small fraction of normal doses) for anesthetic induction and for controlling seizures due to hepatic encephalopathy.
- Lidocaine, theophylline, propranolol, captopril, and tetracyclines should be avoided.
- Diuretics may worsen hepatic encephalopathy, promote dehydration or metabolic alkalosis, and should be used only in otherwise stable patients for the long-term delay of return of ascites or for concurrent conditions (e.g., congestive heart

failure).
- Nonsteroidal antiinflammatory drugs may exacerbate gastrointestinal ulceration.
- Avoid drugs that require hepatic metabolism or alter hepatic biotransformation (e.g., cimetidine). Glucocorticoids may cause sodium retention, promote gastrointestinal ulceration, or precipitate hepatic failure in advanced disease.

POSSIBLE COMPLICATIONS

- Glucocorticoids may precipitate ascites, hepatic encephalopathy, and early death in advanced cases. Therefore, if ascites develops shortly after starting prednisone, consider switching to dexamethasone. If gastrointestinal ulceration develops, it should be addressed as discussed previously.
- Penicillamine and zinc should be given on an empty stomach but may cause vomiting. The risk of vomiting may be reduced by beginning penicillamine at the low end of the dosage range and titrating up. Zinc overdose may cause hemolysis, although the doses required to reach toxic levels are extremely high (many times higher than the therapeutic dose).
- Because von Willebrand disease (see p. 1176) is common in the breed, von Willebrand factor, buccal mucosal bleeding time (see p. 1222), or both should be evaluated prior to biopsy procedures.

RECOMMENDED MONITORING

- CBC, serum biochemistry profile, and urinalysis for disease progression, remission, or complications
- Periodic liver biopsies are the best means of evaluating the stage and progression of the disease during therapy.

PROGNOSIS AND OUTCOME

- Diagnosis and appropriate therapy in subclinical cases may delay or lessen the disease for years.
- Overt clinical manifestations of hepatitis denote advanced disease, and the long-term prognosis is guarded.

PEARLS & CONSIDERATIONS

COMMENTS

- The first abnormality observed in young, subclinically affected dogs is an increase in serum ALT activity, and therefore unexplained ALT activities should be investigated.
- Copper reduction appears to be helpful, but clinical studies evaluating therapy are limited to a small population of affected dogs.
- Diagnosis is confirmed with a liver biopsy; treatment and prognosis depend mainly on whether disease is subclinical (incidental finding, no clinical signs) or clinically overt (presence of advanced signs of liver disease, including encephalopathy and portal hypertension).

CLIENT EDUCATION

- The incidence and genetic mode of inheritance are unknown. Affected dogs or related dogs should not be used for breeding.
- Screening serum levels of liver enzymes in young dogs will lead to an early diagnosis and improved prognosis with therapy. Since the disease is common in the Doberman breed, all dogs should undergo yearly or biannual blood biochemical screening after 2 years of age.

SUGGESTED READING

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Speeti M, et al: Subclinical versus clinical hepatitis in the Doberman: evaluation of changes in blood parameters. J Small Anim Pract 37:465–470, 1996.

Mandigers PJJ, et al: Chronic hepatitis in Doberman pinschers. A review. Vet Quarterly 26(3):98–106, 2004.

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Hepatitis (Chronic) of Cocker Spaniel Dogs

BASIC INFORMATION

DEFINITION

A progressive chronic inflammatory liver disease distinct to cocker spaniels

SYNONYMS

Cocker spaniel hepatitis, chronic hepatitis, chronic idiopathic hepatitis

EPIDEMIOLOGY

SPECIES, AGE, SEX

English and American cocker spaniels are affected. Most are diagnosed between the ages of 2 and 6 years. Both sexes appear to be affected; male predominance.

GENETICS & BREED PREDISPOSITION

The high incidence in this breed suggests a genetic predisposition, but the mode of genetic transmission is unknown. Certain lines of dogs seem to be more affected.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Subclinical hepatitis
- Clinical hepatitis

HISTORY, CHIEF COMPLAINT

- Dogs with subclinical hepatitis show no overt signs.
- Historic signs of early clinical hepatitis are often vague and may be associated with intermittent gastrointestinal signs and weight loss.
- When clinical hepatitis progresses to liver failure, some or all of the following historic signs may occur:
    - Polydipsia, polyuria
    - Weight loss
    - Abdominal distension
    - Anorexia and vomiting
    - Altered mental status associated with hepatic encephalopathy

PHYSICAL EXAM FINDINGS

With clinical hepatitis some or all of the following may be found:

- Weight loss
- Icterus
- Ascites
- Signs of hepatic encephalopathy
- Hemorrhage

ETIOLOGY AND PATHOPHYSIOLOGY

- Etiology is unknown, but α-1 antitrypsin (AAT) may be involved.
- Hepatitis is not associated with AAT (also called α-*1 protease inhibitor*) deficiency, but rather cocker spaniels were found to be prone to abnormal accumulation of AAT (type I) in hepatocytes compared to other breeds. Researchers speculate AAT accumulation may contribute to progression of chronic hepatitis but may not be the causative agent.

- Immune mechanisms have not yet been documented in cocker spaniel hepatitis.
- Hepatic copper accumulation is not a consistent feature.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The combination of signalment (breed) and physical and/or biochemical signs of hepatobiliary disease are strongly suggestive of the diagnosis; confirmation is obtained with a liver biopsy.

DIFFERENTIAL DIAGNOSIS

- Hepatic disease from other causes
- Nonhepatic conditions associated with abnormal liver enzyme activities

INITIAL DATABASE

- Subclinical disease:
  - Elevation in serum alanine aminotransferase (ALT) activity
- Clinical disease:
  - Elevation in serum ALT, aspartate aminotransferase (AST), g-glutamyl transferase, and alkaline phosphatase activities
  - Elevated serum bile acid concentrations
- Advanced disease:
  - Elevation in serum total bilirubin concentration
  - Low serum albumin, blood urea nitrogen, and glucose concentrations
  - Abnormal clotting times

ADVANCED OR CONFIRMATORY TESTING

- Abdominal radiographs: microhepatica ± signs of ascites (loss of serosal detail)
- Ultrasound: microhepatica with altered parenchymal echogenicity, ± ascites, ± vascular changes associated with portal hypertension
- Surgery or laparoscopy: small liver; micronodular or macronodular, and fibrotic in advanced clinical disease
- Liver histopathology: subclinical disease is associated with infiltration of mononuclear inflammatory cells into portal and parenchymal areas; clinical disease has evidence of active hepatitis with areas of piecemeal and bridging necrosis. Cirrhosis develops as the disease advances.
- Histochemical staining for AAT may show globoid accumulations within hepatocytes.
- Hepatic metal quantitative analysis: hepatic copper usually normal, but secondary increases in copper may occur. Hepatic iron is increased, thought to be secondary to chronic inflammation; zinc concentrations may be reduced.

TREATMENT

TREATMENT OVERVIEW

Goals of treatment are to slow progression of liver disease in subclinical cases, provide specific therapy for chronic hepatitis, and provide general supportive care, treating complications of liver disease such as hepatic encephalopathy, ascites, gastrointestinal ulceration, and nutritional imbalance.

ACUTE GENERAL TREATMENT

- Fluid support
- Treatment of hepatic encephalopathy (see 501)
- Coagulopathies or sepsis are treated as they occur (see 513)

CHRONIC TREATMENT

- Subclinical and early clinical hepatitis (see 513):
  - Glucocorticoid therapy (prednisone or prednisolone, 2 mg/kg PO q 24-48 h; maximum of 80 mg/d) may be beneficial in slowing inflammatory component of the liver disease. Anecdotal reports suggest improved survival following therapy.

Other immunosuppressive therapy such as azathioprine or cyclosporine may be used in addition to or in place of glucocorticoid therapy.
    - Ensure adequate nutrient intake.
    - Provide liver support with antioxidants (vitamin E, 10 IU/kg PO q 24 h; *S*-adenosylmethionine, 20 mg/ kg PO q 24 h; and/or milk thistle [silybin complexed with phosphatidylcholine], 24-70 mg PO q 24 h).
    - Antifibrotics (see) such as colchicine can be used (0.03 mg/kg PO q 24 h), but few studies report its use in dogs, and human studies fail to show prolonged survival. Gastrointestinal side effects are well-recognized. The angiotensin II receptor antagonist, losartan (0.5 mg/kg PO q 12-24 h), recently has shown promise in inhibiting fibrosis in humans.
    - Ursodeoxycholic acid (15 mg/kg PO q 24 h) is given for hepatic support and choleresis.
    - If secondary copper accumulation occurs, chelator or zinc therapy should be used (see 517).
- Advanced clinical hepatitis (see 517):
    - Treatment for hepatic encephalopathy (see 501): high-quality, low-protein diet, lactulose (0.1-0.5 mL/kg PO q 12 h, titrated to achieve loose fecal consistency) and/or intestinal antibiotics (metronidazole, 7.5-10 mg/kg PO q 12 h; or amoxicillin-clavulanate, 15 mg/kg PO q 12 h)
    - Ascites therapy: spironolactone (1 mg/kg PO q 12 h) or furosemide (0.5-2 mg/kg PO q 12 h)
    - Gastric ulceration: famotidine (0.5 mg/kg PO q 12 h) or omeprazole (0.5-1 mg/kg PO q 24 h)

DRUG INTERACTIONS

Avoid drugs that require hepatic metabolism.

POSSIBLE COMPLICATIONS

Glucocorticoids may precipitate ascites, hepatic encephalopathy, and result in an early death in advanced cases.

RECOMMENDED MONITORING

- Young dogs should have periodic liver enzymes measured as screening test to help identify affected dogs.
- Routine CBC, serum biochemistry profile, and urinalysis to monitor disease progression, remission, or complications
- Periodic liver biopsies (yearly) are the best means of evaluating the stage and progression of the disease during therapy.

PROGNOSIS AND OUTCOME

- Diagnosis and appropriate therapy in subclinical cases may slow progression of disease.
- Clinical hepatitis denotes advanced disease and the long-term prognosis is guarded.

PEARLS & CONSIDERATIONS

COMMENTS

- The first abnormality observed in young subclinical dogs is an increase in serum ALT activity. Unexplained elevated serum ALT activities in this breed should be investigated.
- The disease continues to be explored; there is little objective information on chronic hepatitis in cocker spaniels.
- Many dogs are presented when the disease is advanced. The prognosis is poor at this stage.

CLIENT EDUCATION

- The incidence and genetic mode of inheritance are unknown. Affected dogs or related dogs should not be used for breeding.
- Screening laboratory enzymes in young dogs will lead to an early diagnosis and may improve prognosis with therapy.

SUGGESTED READING

Anderson M, et al: Breed, sex, and age distribution in dogs with chronic liver disease: a demographic study. J Small Anim Pract 32:1–5, 1991.

Watson PJ: Chronic hepatitis in dogs: a review of current understanding, aetiology, progression and treatment. Vet J 167(3):228–241, 2004.

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Hepatic Nodules, Benign

BASIC INFORMATION

DEFINITION

- Hepatic adenoma: benign neoplasia of hepatocytes
- Nodular hyperplasia: discrete accumulation of hyperplastic hepatocytes surrounded by normal hepatocytes
- Nodular regeneration: discrete accumulation of hyperplastic hepatocytes surrounded by abnormal hepatocellular parenchyma, particularly fibrotic changes

SYNONYMS

Nodular hyperplasia: hyperplastic nodules; nodular regeneration: regenerative nodules

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Hepatic adenomas: rare tumors in dogs and cats; patients usually >10 years old
- Nodular hyperplasia: common lesion in old dogs. Incidence in dogs >14 years old: 70%-100%
- Nodular regeneration: seen in dogs with acquired parenchymal hepatic disease. Middle-aged to older dogs

GENETICS & BREED PREDISPOSITION

Nodular regeneration: seen in breeds predisposed to chronic hepatitis (Doberman pinscher, cocker spaniel, Labrador retriever) and copper-storage hepatopathy (Bedlington terrier, West Highland white terrier, Skye terrier)

RISK FACTORS

Nodular regeneration: chronic hepatic disease, cirrhotic/fibrosing liver disease

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Nodular hyperplasia: incidental finding, no clinical signs, rare hepatic failure
- Adenoma: incidental finding, no clinical signs; rarely, abdominal discomfort or rupture with hemoperitoneum or abscessation with signs of chronic infection
- Nodular regeneration: see sections on chronic hepatic diseases (, 512, and 513).

PHYSICAL EXAM FINDINGS

- Hepatic adenoma: rarely abdominal pain, inappetence, ascites and pallor (if ruptured)
- Nodular hyperplasia: normal exam
- Nodular regeneration: see sections on chronic hepatic disease noted above.

ETIOLOGY AND PATHOPHYSIOLOGY

- Nodular hyperplasia: unknown; may be associated with nutritional factors or a result of focal areas of ischemia; not preneoplastic
- Adenoma: unknown; may be associated with chronic inflammation or hepatotoxicity
- Nodular regeneration: compensatory response of the liver to chronic injury

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Their benign nature makes these lesions almost always incidentally encountered during abdominal ultrasound exams or abdominal surgery, or occasionally on abdominal palpation if very large.

DIFFERENTIAL DIAGNOSIS

- Nodular hyperplasia:
  - Primary or metastatic hepatic neoplasia
  - Cirrhosis with nodular regeneration
  - Vacuolar hepatopathy
- Adenoma:
  - Nodular hyperplasia
  - Primary or metastatic hepatic neoplasia
  - Hepatic abscess
- Nodular regeneration:
  - Nodular hyperplasia
  - Metastatic hepatic neoplasia
  - Vacuolar hepatopathy

INITIAL DATABASE

Nodular Hyperplasia:

- Commonly associated with mild to moderate increases in serum alkaline phosphatase (ALP) activity, less commonly with mild increases in serum alanine transaminase (ALT) and aspartate aminotransferase (AST) activities
- Serum bile acids concentration usually normal
- Abdominal ultrasonography reveals single to multiple lesions with highly variable appearance. Easily mistaken for primary or metastatic neoplasia or nodular regeneration.

Hepatic Adenoma:

- Variable increases in ALP, ALT, and AST activities
- Serum bile acids concentration usually normal
  - Leukocytosis ± monocytosis if necrotic regions within adenomas
  - Anemia if adenoma ruptures and hemoperitoneum
- Radiographs may identify a mass in the cranial abdomen or rarely a gas pocket in a necrotic region.
- Abdominal ultrasonography demonstrates a solitary mass with variable echogenicity that may contain cystic cavities and/or blood-or gas-filled spaces. Ascites seen with rupture and hemoperitoneum.

Nodular Regeneration:

- Serum bile acids concentration usually abnormal
- See sections on chronic hepatic disease (pp. 212 and 513).

ADVANCED OR CONFIRMATORY TESTS

General:

- Hepatic histopathology differentiates the three conditions but often requires wedge biopsy, as adjacent hepatic tissue is necessary to make a definitive diagnosis.
- Fine-needle aspiration or single needle biopsies of these focal lesions may result in misdiagnosis of hepatic vacuolar hepatopathy.
- MRI of focal hepatic masses may provide better discrimination of these lesions (future direction).
- Preliminary studies with contrast enhanced ultrasonography have shown some ability to discriminate benign nodules from malignant ones.

Specific:

- Nodular hyperplasia:
  - Well-circumscribed expansive nodule usually <3 cm, containing hyperplastic hepatocytes that often contain cytoplasmic vacuoles and are loosely organized into hepatic cords with discernable portal tracts
  - Nodules surrounded by normal hepatic parenchyma
  - Lipogranulomas are a common associated finding.
- Adenoma:

- Well-circumscribed expansive nodule of variable size containing hyperplastic but well-differentiated hepatocytes arranged in cords that are 1-2 cells thick with a conspicuous absence of portal tracts.
- Adenomas are surrounded by normal hepatic parenchyma.

- Nodular regeneration:
  - Similar histologic appearance as nodular hyperplasia, but surrounding hepatic parenchyma is abnormal, most often with mixed inflammation and fibrosis.

TREATMENT

TREATMENT OVERVIEW

Determine if the focal lesions present on abdominal ultrasound, which may or may not be accompanied by increases in serum hepatic enzyme activities, require any therapeutic intervention.

ACUTE GENERAL TREATMENT

- Nodular hyperplasia:
  - No treatment necessary
- Adenoma:
  - No treatment necessary for small masses not associated with clinical signs
  - Surgical excision for large masses causing abdominal discomfort or for those associated with abscessation or hemorrhage
- Nodular regeneration:
  - Treatment of the underlying disorder (see sections on chronic hepatic disease noted earlier)

RECOMMENDED MONITORING

Sequential monitoring of serum hepatic enzyme activity and abdominal ultrasonography q 4-6 months

PROGNOSIS AND OUTCOME

- Nodular hyperplasia or adenoma: excellent long-term prognosis
- Nodular regeneration: see p. 212

PEARLS & CONSIDERATIONS

COMMENTS

- Nodular hyperplasia is primarily of clinical concern for two reasons:
  - It is a common cause of increased serum ALP activity in older dogs.
  - The ultrasonographic appearance may mimic primary or metastatic hepatic neoplasia.
- Differentiation of the three conditions usually requires hepatic wedge biopsy (obtained via laparoscopy or surgery).

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Hepatic Neoplasia, Malignant

BASIC INFORMATION

DEFINITION

- Primary malignant neoplasm of the liver or biliary tract
- Epithelial origin: hepatocellular carcinoma (most common), hepatocellular adenoma/hepatoma, biliary carcinoma, biliary adenoma, hepatic carcinoid
- Mesenchymal origin: hemangiosarcoma and leiomyosarcoma are the most common.
- Hemolymphatic tumors: lymphoma (dogs, cats) and myeloproliferative disorders (cats). Hepatic lymphoma may be part of multicentric disease or the primary site.
- Metastatic hepatic neoplasia (hemangiosarcoma, histiocytic sarcoma, islet cell carcinoma, pancreatic adenocarcinoma, intestinal adenocarcinoma, leiomyosarcoma, mammary carcinoma, transitional cell carcinoma, renal carcinoma, pheochromocytoma, and others)

SYNONYMS

- Biliary adenoma: biliary cystadenoma in cats
- Biliary carcinoma: cholangiocarcinoma, biliary cystadenocarcinoma

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Primary hepatobiliary tumors are uncommon, accounting for less than 1.5% of all canine neoplasms and 1%-2.9% of all feline neoplasms.
- Hepatocellular carcinoma is the most common primary liver tumor in dogs, accounting for more than half of all hepatobiliary tumors.
- Biliary carcinomas and adenomas are the most common primary hepatic tumors in cats. Biliary tumors are uncommon in dogs.
- Occur primarily in older animals (average age 10-12 years)

GENETICS & BREED PREDISPOSITION

Domestic shorthair cats may have a higher rate of development of hepatic neoplasia than purebred cats.

RISK FACTORS

- Potential causes include aflatoxins, diethylnitrosamine, dichlorobenzidine, aramite, liver flukes *(Clonorchis* spp., *Platynosomum concinnum)*, and radioactive compounds such as strontium 90 and cesium 144.
- Biliary carcinoma can occur in juvenile cats with feline leukemia virus infection.
- In humans, hepatitis B and C and cirrhosis are common risk factors for hepatocellular carcinoma. A similar association with viruses is not known to occur in dogs. Cirrhosis was only found in 7% of dogs with hepatocellular carcinoma.

CONTAGION & ZOONOSIS

As opposed to humans, no association with viral infection has been found.

ASSOCIATED CONDITIONS & DISORDERS

- Paraneoplastic hypoglycemia is occasionally noted in dogs with hepatocellular carcinoma (up to 38% of cases) and less frequently in dogs with hepatocellular adenoma, leiomyosarcoma, and hemangiosarcoma. Serum insulin concentrations are normal to decreased. Potential mechanisms of hypoglycemia include excess use of glucose by the tumor, release of insulin-like factors from the tumor, release of other substances such as somatostatin from the tumor, and secondary hepatic parenchymal destruction with impaired glycogenolysis or gluconeogenesis.
- Paraneoplastic alopecia (see p. 834) has been reported in cats with biliary carcinoma and hepatocellular carcinoma.
- Bile duct obstruction, coagulopathies, and hepatic encephalopathy are uncommon.
- Myasthenia gravis was associated with biliary carcinoma in one report.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Hepatocellular carcinoma—three gross morphologic subtypes: massive, nodular, and diffuse.
    - Massive hepatocellular carcinoma, defined as a large tumor affecting a single liver lobe, represents 53%-84% of cases. The nodular form occurs in 16%-25% and the diffuse form in 0%-19% of cases.
- Biliary carcinoma; also occurs as massive, nodular, or diffuse forms in dogs: massive form occurs in 37%-46%, nodular in 0%-21%, and diffuse in 17%-54% of cases. Biliary carcinomas can also be extrahepatic within bile ducts or gallbladder.
- Hepatic carcinoid: a primary neuroendocrine tumor that is uncommon, typified by aggressive biological behavior, and most commonly diffuse with early metastasis.

HISTORY, CHIEF COMPLAINT

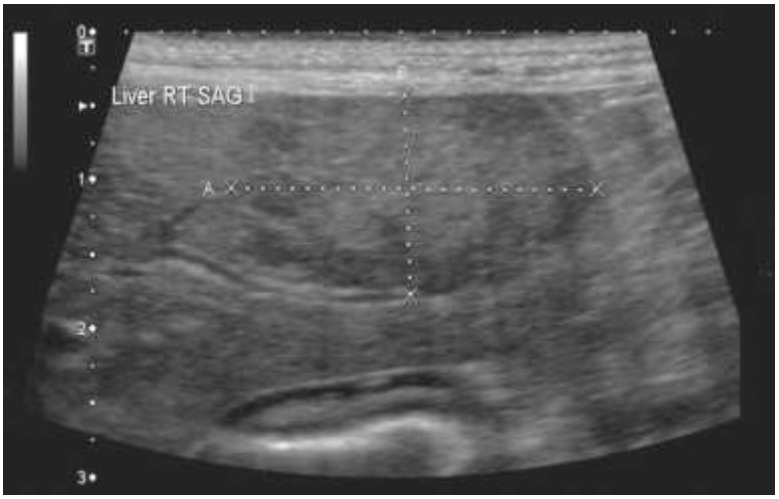
Clinical signs are usually vague and nonspecific. Anorexia, lethargy, weight loss, polydipsia, polyuria, vomiting, and abdominal distention are the most common presenting complaints. Less frequent presenting problems are jaundice, diarrhea, excessive bleeding, and signs of central nervous system dysfunction due to hepatic encephalopathy, hypoglycemia, or central nervous system metastases.

PHYSICAL EXAM FINDINGS

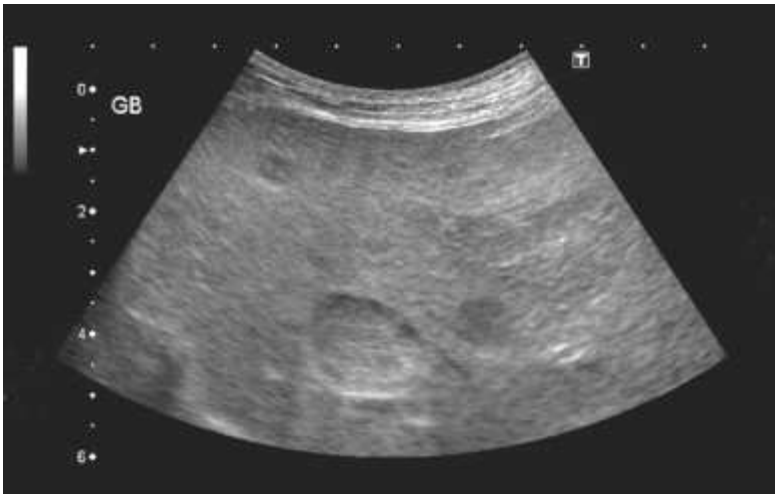
- The most common finding in dogs and cats with primary hepatic tumors is a palpable cranial abdominal mass or marked hepatomegaly.
- Ascites or hemoabdomen may also contribute to abdominal distention.
- Pale mucous membranes due to anemia, jaundice, cachexia, and weakness are other potential findings.

ETIOLOGY AND PATHOPHYSIOLOGY

- Etiology unknown
- The more common massive hepatocellular carcinomas generally have a low potential for metastasis, with rates varying from 0%-37%. The less common nodular and diffuse hepatocellular carcinomas have metastatic rates as high as 100% reported.
    - Extrahepatic metastases occur more commonly with biliary carcinoma, with metastasis occurring in 56%-88% of cases.
    - Hepatic carcinoids and sarcomas have the highest metastatic rates, with metastasis occurring in 86%-93% of cases. Metastasis is most commonly to hepatic lymph nodes, peritoneal cavity, and lungs, although widespread metastases can occur.
- Less is known about the metastatic rate of feline malignant hepatobiliary tumors, with estimates of metastasis in 56%-67% of cases; diffuse intraperitoneal involvement is the most common manifestation.



HEPATIC NEOPLASIA, MALIGNANT Abdominal ultrasound: hepatocellular carcinoma. Solitary well-circumscribed complex echogenic liver mass.



HEPATIC NEOPLASIA, MALIGNANT Abdominal ultrasound: metastatic carcinoma. Multiple hypoechoic liver lesions. The larger structure at the bottom of the image is the gallbladder, containing inspissated bile.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Vague nonspecific clinical signs, elevated liver enzymes, and a palpable cranial abdominal mass or hepatomegaly are commonly present. The diagnosis is typically based on the presence of a liver mass or masses which are palpated and/or seen on abdominal ultrasound; conformation is via cytologic or histopathologic examination of smears or biopsy specimens, respectively.

DIFFERENTIAL DIAGNOSIS

- Metastatic hepatic neoplasia (liver metastasis from nonhepatic neoplasia occurs 2.5 times more frequently than primary liver neoplasia in dogs, particularly from primary neoplasia of the spleen, pancreas, and gastrointestinal tract, whereas in cats primary hepatobiliary tumors are more common than metastatic disease).
- Hepatic nodular hyperplasia
- Diffuse hepatomegaly (e.g., vacuolar hepatopathy, hepatic congestion, lipidosis
- Hepatic regenerative hyperplasia, cirrhosis (presence of nodular regeneration)
- Hepatobiliary cysts
- Hepatic abscess

INITIAL DATABASE

- CBC: variable anemia and leukocytosis, pancytopenia may be seen with hematopoietic or lymphoid malignancies that involve bone marrow and only secondarily involve the liver.
- Coagulation profile: prolonged prothrombin times and activated partial thromboplastin times are not common (when coagulopathies occur, they are most common with hepatic hemangiosarcoma).
- Serum chemistry profile: mild to marked increases in liver enzyme activities: alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP). Hyperbilirubinemia (uncommon in dogs with primary hepatic neoplasia, more common in dogs with metastatic liver disease, occurs in one-third of cats with primary liver tumors). Other quite variable biochemical abnormalities include hypoalbuminemia, hyperglobulinemia, and hypoglycemia.
- Serum bile acids concentration: elevated in 50%-75% of cases, with magnitude of elevation often mild
- Abdominal radiographs: symmetric or asymmetric hepatomegaly, ascites, and caudolateral gastric displacement
- Three-view thoracic radiographs: evaluate for pulmonary metastasis.
- Abdominal ultrasound: very useful for evaluation of the liver when primary or metastatic hepatic neoplasia is suspected:
    - Hepatocellular carcinoma usually appears as a focal hyperechoic or mixed echogenic mass.
    - Primary or metastatic neoplasia often appears as focal or multifocal hypoechoic or mixed echogenic lesions.
    - “Target” lesions, nodules or masses with a hypoechoic rim and a hyperechoic or isoechoic center, are often neoplastic, with a positive predictive value for malignancy of 74% for solitary lesions and 81% for multiple lesions in one report.
    - Hyperplastic nodules are usually multifocal hyperechoic lesions, although hypoechoic or mixed echogenic lesions can occur.
    - The ultrasonographic appearance of hepatic lymphoma is quite variable, ranging from normal to mild diffuse hyperechogenicity or hypoechogenicity, multifocal hypoechoic lesions, or mixed echogenic target lesions.

- Contrast harmonic ultrasound has recently been reported as a method for discriminating between benign and malignant nodules in the liver of dogs. This method requires ultrasound contrast medium and contrast harmonic software.

ADVANCED OR CONFIRMATORY TESTING

- Ultrasound-guided percutaneous fine-needle aspirate for cytology. Cytologic evaluation can correctly diagnose neoplasia in up to 62% of patients with liver tumors, although it is often unreliable. Cytologic evaluation is most useful for the diagnosis of diffuse hemolymphatic tumors such as lymphoma, myeloproliferative disease, and mast cell tumors. There is low risk to the patient with fine-needle aspiration.
- Ultrasound-guided percutaneous core needle biopsy versus laparoscopic biopsy for histopathologic evaluation of liver tissue (confirmatory). Needle biopsies are generally accurate, but because of the small size of biopsy samples, differentiation of nodular hyperplasia from primary hepatic neoplasia may be difficult. Sometimes a larger biopsy specimen obtained via laparoscopy or laparotomy is necessary. Laparoscopy allows for larger biopsy samples and is also useful for staging (observe peritoneal surface and lymph nodes for infiltration or other abnormalities). See p. 1298.
- Peritoneal fluid cytology in animals that have ascites may reveal neoplastic cells, especially in advanced cases, although often ascites is a modified transudate without exfoliation of neoplastic cells.
- Abdominal CT scan or MRI could be considered for lesion characterization and staging. MRI has been shown to be useful for differentiating benign from malignant focal hepatic lesions in dogs.
- α-fetoprotein is an oncofetal glycoprotein that is a useful serum tumor marker for human hepatocellular carcinoma. It was shown to be elevated significantly in 55% of dogs with biliary carcinoma and 75% of dogs with hepatocellular carcinoma, but not in dogs with other primary or metastatic hepatic tumors or other types of liver disease. This assay is not readily available in most veterinary laboratories at this time.

TREATMENT

TREATMENT OVERVIEW

- Surgical removal of the tumor for primary hepatic neoplasia such as hepatocellular carcinoma, hepatoma, and biliary carcinoma
- Chemotherapy for hepatic lymphoma and hepatic mast cell tumor
- Palliative therapy for metastatic hepatic cancer

ACUTE GENERAL TREATMENT

- Supportive therapy for paraneoplastic hypoglycemia, coagulopathies, or hepatic encephalopathy
- Liver lobectomy for primary hepatic tumors involving a single lobe. Fewer biliary carcinomas can be resected, owing to the higher percentage that are multifocal or metastatic at presentation.
- Treatment options are very limited for nodular, diffuse, and metastatic liver cancer.

CHRONIC TREATMENT

- Chemotherapy for hepatic lymphoma, mast cell tumor, myeloproliferative disease, and possibly for hemangiosarcoma
- No effective chemotherapy or radiation therapy protocols have been reported for primary hepatic tumors.
- Several chemotherapy drugs have been used anecdotally (carboplatin, gemcitabine, mitoxantrone, doxorubicin, 5-fluorouracil), although efficacy has not been proven. Given the poor response in humans with hepatobiliary cancer, it is unlikely that systemic chemotherapy with the currently available agents will play a major role in the treatment of hepatobiliary cancer in dogs and or cats.
  - Chemoresistance may be due to expression of P-glycoprotein, which is associated with multidrug resistance, and/or the presence of detoxification enzymes contained in hepatocytes.
- Newer treatment modalities such as intraarterial chemotherapy, transarterial chemoembolization, percutaneous ethanol injection, microwave coagulation, and immunotherapeutic strategies may be applicable in veterinary patients. A novel treatment method for hepatocellular carcinoma in dogs using fractional excision with a Cavitron ultrasonic surgical aspirator has recently been described.

POSSIBLE COMPLICATIONS

- Hemorrhage is the most common surgical complication. Blood products should be available in the event a transfusion is necessary.
- Although not common, hypoglycemia is a potential transient complication of extensive partial hepatectomy.

RECOMMENDED MONITORING

After removal of primary liver tumors, follow-up abdominal ultrasound and three-view thoracic radiographs are recommended every 3-6 months for 1-2 years.

PROGNOSIS AND OUTCOME

- For massive hepatocellular carcinoma treated by liver lobectomy, the prognosis is good with a complete excision, with average survival times of more than a year and many patients being cured.
- The median survival time for massive hepatocellular carcinoma treated with liver lobectomy is >1460 days, with high serum ALT and AST activity and right-sided tumors conveying a worse prognosis.
- The prognosis for nodular or diffuse hepatocellular carcinoma is poor.
- Biliary carcinoma, hepatic carcinoids, and hepatic sarcomas have a worse prognosis, as they are commonly nodular or diffuse, resistant to chemotherapy, and have high metastatic rates.
- Hepatic lymphoma has a variable prognosis depending on the grade and response to chemotherapy.
- The liver is a common site of metastasis for a variety of cancers, and metastatic liver disease has a poor prognosis.

PEARLS & CONSIDERATIONS

COMMENTS

- The most common primary hepatobiliary tumor in dogs is a massive hepatocellular carcinoma. With liver lobectomy providing a complete excision of massive hepatocellular carcinoma, long-term survival or cure is common.
- The most common feline hepatobiliary tumors are bile duct carcinoma and biliary cystadenoma. Bile duct carcinoma has a high metastatic rate and a poor prognosis, whereas biliary cystadenoma is benign and generally has a good prognosis.

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Hepatic Lipidosis

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

A well-recognized syndrome in cats, characterized by excessive accumulation of fat (triglyceride) in the liver; associated with severe intrahepatic cholestasis and hepatic dysfunction

SYNONYMS

Fatty liver syndrome, feline hepatic lipidosis (FHL), idiopathic hepatic lipidosis

EPIDEMIOLOGY

SPECIES, AGE, SEX

Cats; middle-aged or older

RISK FACTORS

Obesity before onset of anorexia; prior stressful event (boarding, surgery, change in living arrangements, diet change) preceding anorexia; systemic diseases associated with anorexia and a catabolic state. May be associated with pancreatitis.

ASSOCIATED CONDITIONS & DISORDERS

Cholangitis, pancreatitis, inflammatory bowel disease, systemic neoplasia, diabetes mellitus, toxin-or drug-induced injury (stanozolol, tetracyclines), and many other systemic disorders associated with anorexia and weight loss

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Idiopathic hepatic lipidosis: primary disorder of unknown cause
- Secondary hepatic lipidosis: associated with inciting cause (see Associated Conditions and Disorders above)

HISTORY, CHIEF COMPLAINT

Prolonged anorexia, often several weeks in duration; rapid weight loss (often >25% of body weight). History of stressful event (see Risk Factors above), or nonhepatic diseases associated with anorexia. Other signs: lethargy, depression, sporadic vomiting, constipation, or diarrhea.

PHYSICAL EXAM FINDINGS

Icterus, hepatomegaly, dehydration, muscle wasting, seborrhea, pale mucous membranes, weight loss. Overt findings of hepatic encephalopathy (ptyalism, severe depression, stupor) or bleeding are uncommon and indicate severe liver failure. Head or neck ventroflexion may occur with severe electrolyte imbalances (hypokalemia, hypophosphatemia) or thiamine deficiency.

ETIOLOGY AND PATHOPHYSIOLOGY

- Cats have higher nutritional requirements for protein, essential amino acids, and essential fatty acids than dogs.
- Systemically ill cats have a propensity for accumulating fat in their hepatocytes.
- Profound anorexia and stress may be associated with hormonal (catecholamines, other) alterations that influence fat metabolism and predispose to peripheral fat mobilization and hepatic fat uptake.
- Obese cats appear unable to adapt to metabolism of fat for energy during starvation. The exact metabolic or biochemical aberrations in cats with hepatic lipidosis are unknown, but there appears to be an imbalance between mobilization of peripheral fat, hepatic use of fatty acids for energy, and hepatic dispersal of triglycerides.
- Lipid accumulation is not directly toxic to liver but is a marker for an underlying metabolic disorder.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on the findings of icterus in an afebrile obese cat with a history of anorexia and weight loss and laboratory features of hyperbilirubinemia, increased serum alkaline phosphatase (ALP) activity with normal to mildly increased serum gamma-glutamyltransferase (GGT) activity and a non-inflammatory CBC. Definitive diagnosis requires liver biopsy, but cytology often suffices for a presumptive diagnosis (though cytology can yield false-positive results).

DIFFERENTIAL DIAGNOSIS

- Cholangitis/cholangiohepatitis
- Pancreatitis
- Hepatic manifestations of feline infectious peritonitis
- Hepatic neoplasia
- Drug-or toxin-induced hepatic injury
- Extrahepatic bile duct obstruction

INITIAL DATABASE

- CBC:
  - Normocytic, normochromic anemia
  - Poikilocytosis (acanthocytes and elliptocytes)
  - Hemolysis (secondary to hypophosphatemia or Heinz bodies)
  - Mature neutrophilia and lymphopenia (stress response)
- Serum biochemistry profile:
  - ALP: moderate to marked increases. Earliest biochemical change; precedes hyperbilirubinemia.
  - Alanine aminotransferase (ALT): mild to moderate increases
  - GGT: normal to mild increase (as opposed to increased serum GGT activity seen with other feline cholestatic disorders). The finding of a greater magnitude of elevation of ALP compared with GGT is highly suggestive of feline hepatic lipidosis (seen in virtually 100% of cases).
  - Hyperbilirubinemia
  - Hyperammonemia, hypoalbuminemia, hypoglycemia (severe hepatic dysfunction)
- Urinalysis: may show bilirubinuria (always abnormal in the cat)
- Coagulation abnormalities (prothrombin time and proteins induced by vitamin K antagonism increased; hypofibrinogenemia)
- Abdominal radiographs: normal to increased liver size
- Abdominal ultrasound: normal to increased liver size; diffusely hyperechoic parenchyma (seen in virtually 100% of cases), far field beam attenuation, vessels difficult to recognize. Ascites rare. Evaluate for concurrent pancreatitis or other disorders causing secondary hepatic lipidosis.
- Bile acids: usually elevated (not necessary to measure if hyperbilirubinemia is present)

ADVANCED OR CONFIRMATORY TESTING

- Fine-needle aspiration and cytologic evaluation of the liver are preferred over liver biopsy (less invasive, allows presumptive diagnosis of hepatic lipidosis). However, cytologic evaluation is not accurate in diagnosing other hepatopathies, and therefore these may be missed. False-positive results also commonly occur. In hepatic lipidosis, cytologic evaluation reveals vacuolated hepatocytes without inflammation. Correction of any coagulopathy with vitamin K1 prior to performing liver aspirate or biopsy is warranted. However, coagulation studies do not necessarily predict bleeding tendency after liver aspirate or biopsy.
- Liver biopsy provides definitive diagnosis. Not routinely performed when supporting lab work (in particular the elevated serum ALP activity relative to serum GGT activity) and fine-needle aspirate and cytologic study suggest the diagnosis, unless there is failure to respond to therapy for hepatic lipidosis or a high level of suspicion of other primary hepatic disorder(s) exists. With hepatic lipidosis, the biopsy sample typically is a pale tan/yellow color and floats in formalin. Biopsy results show severe vacuolization of hepatocytes (>50% of acinar unit involved). Inflammation and necrosis absent. Vacuoles stain positive for fat with oil red O.
- Consider serum feline pancreatic lipase immunoreactivity to evaluate for concurrent feline pancreatitis (see p. 817). Consider serum cobalamin (vitamin B12) levels if underlying primary intestinal disorder suspected.
- Evaluate for underlying systemic disorder as necessary.

TREATMENT

TREATMENT OVERVIEW

- Correct fluid and electrolyte abnormalities.
- Control complications of liver failure.
- Give nutritional support to provide adequate calorie and protein intake.
- Treat underlying systemic disorder if identified.

ACUTE GENERAL TREATMENT

- Initial fluid therapy: intravenous balanced electrolyte solution supplemented with KCl using conventional sliding scale (20-40 mEq/L). Monitor serum potassium twice daily initially and readjust as needed; avoid lactated Ringer's solution (impaired lactate metabolism in severe hepatic lipidosis); avoid dextrose supplementation unless hypoglycemic (promotes hepatic lipid deposition).
- Vitamin K1 (0.5-1.5 mg/kg SQ q 12 h for three injections) for coagulopathy
- Water-soluble vitamin supplementation:
  - B-complex vitamins (added to fluids: 1-2 ml/L).
  - Cobalamin (vitamin B12): 250 mcg SQ initially while awaiting serum cobalamin levels. If decreased serum cobalamin is documented (primary intestinal disease), continue with 250 mcg SQ once weekly.
  - Thiamine supplementation (if severe ventroflexion of neck): 50-100 mg PO/cat/d for 1 week. Use with caution: potential anaphylactic reactions.
- Blood transfusion as needed for anemia (preferably fresh; stored blood can exacerbate encephalopathy due to high ammonia concentration).

NUTRITION/DIET

- Nasogastric tube feeding of CliniCare (Abbott Veterinary Diets) for initial 24-48 hours (see p. 1269). This will allow initial stabilization prior to general anesthesia for long-term feeding tube placement.
- Place gastrostomy or esophagostomy tube (by least invasive method possible; see pp. 1267 and p. 1273).
  - Feed Maximum Calorie (The Iams Co.), Prescription Diet a/d (Hill's Pet Nutrition), or other complete and balanced feline diet. Do not restrict dietary protein unless overt signs of hepatic encephalopathy are present.
  - Provide 40-60 kcal/kg/d. Start with ¼ to ½ of daily requirements given through tube and divided into 4-6 feedings. Gradually increase to daily requirements over 3-4 days.
  - If vomiting occurs, consider metoclopramide (0.4 mg/kg q 8 h SQ or through the tube 30 minutes before feeding), cisapride (1 mg/kg q 8 h through the tube), prochlorperazine (0.1-0.3 mg/kg q 8-12 h SQ or IV) or maropitant (1 mg/kg IV, SQ, PO), or tube feedings by slow constant rate infusion. Be sure that any tablet-formulated medications are ground to a fine powder before being administered through the tube; otherwise, there is a risk of tube occlusion.
  - Tube feeding usually required for 3-6 weeks (or longer in some cases) pending clinical and biochemical improvement.
  - Do not remove tube until cat eating on its own for at least a week.
- Other dietary supplements used empirically:
  - l-carnitine 250-500 mg PO q 24 h (essential cofactor for fatty acid oxidation; relative carnitine deficiency in hepatic lipidosis)
  - Taurine 250-500 mg PO q 24 h for initial 7-10 days (plasma levels have been found to be decreased in many cats with hepatic lipidosis; required for bile acid conjugation)
  - Vitamin E (water soluble form) 50-100 units/cat PO q 24 h (antioxidant)
  - s-adenosylmethionine (SAMe; Denosyl SD4 [Nutramax Labs]) 20 mg/kg PO q 24 h (glutathione source). Do not give through the tube (would disrupt enteric coating).

POSSIBLE COMPLICATIONS

- Hepatic encephalopathy (see p. 501):
- Hypophosphatemia (see p. 969)
- Heinz body hemolysis:
  - Cats with hepatic lipidosis have decreased hepatic glutathione and are at risk for red blood cell oxidant injury/Heinz body hemolysis. For critical Heinz body hemolytic anemia, provide glutathione source as *N*-acetylcysteine 140 mg/kg (20% solution diluted at least 1:2 with saline) IV over 20 to 30 minutes through 0.25-mm nonpyrogenic filter; then 70 mg/kg IV q 8-12 h depending on clinical signs. When enteral feeding is established, switch to SAMe 20 mg/kg PO q 24 h (do not give through the tube so the enteric coating is not disrupted) as a glutathione source. Propofol does not appear to be a risk factor for Heinz body hemolytic anemia in cats with hepatic lipidosis.
- Hypomagnesemia:
  - Monitor serum magnesium. Supplement if mg < 1.2 mg/dL. Magnesium sulfate (8.13 mEq/g) and magnesium chloride (9.25 mEq/g) salts available in 50% solution; dilute to a concentration of 20% or less in 5% dextrose in water. Give 0.75-1 mEq/kg/d constant rate infusion.

RECOMMENDED MONITORING

Biochemical improvement (decreases in bilirubin, ALP, ALT) usually seen within 1-2 weeks of initiating tube feeding. Normalization

may take several weeks.

PROGNOSIS AND OUTCOME

- Early diagnosis is key to successful management.
- Recovery in approximately 60%-85% of cases. If the cat survives the initial few days, the prognosis for complete recovery is excellent.
- Poorer prognosis with concurrent pancreatitis

PEARLS & CONSIDERATIONS

COMMENTS

- Oral appetite stimulants usually are inadequate for aggressive nutritional support required for feline hepatic lipidosis therapy. Oral diazepam is associated with idiosyncratic hepatic necrosis in cats.
- Correct fluid and electrolyte imbalances before anesthesia for tube placement.
- In critically ill cats with hepatic lipidosis, the stress of general anesthesia may be fatal. Therefore initial feeding through a nasogastric tube (placed in awake state) before anesthesia for long-term feeding tube placement is recommended. Once the patient is more stable, anesthesia for long-tereeding tube placement can be more safely accomplished.
- Establishing the diagnosis, identifying any underlying causes (which may require long-term treatment), and initial management (often requires several days of hospitalization, including anesthesia and feeding tube placement) can be costly, time consuming, but ultimately rewarding.
- Evaluate for underlying systemic disorder (feline hepatic lipidosis may be secondary).
- Strategies to control vomiting are important for a successful outcome.

PREVENTION

- Do not switch obese cats to unpalatable diet for weight loss. Consider smaller amounts of favorite food given in parallel (not mixed in) with a weight-loss diet to avoid reducing appetite while allowing the cat to become accustomed to the new food.
- l-carnitine (250 mg/cat PO q 24 h) may improve fatty acid oxidation in obese cats undergoing weight loss but won't prevent hepatic lipidosis.

CLIENT EDUCATION

- Tube feeding for 3-6 weeks (or longer) at home will be required for recovery.
- Recurrence is unlikely unless an underlying chronic cause is present; the owner should take care to not allow cat to become anorexic again.

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Hepatic Injury, Acute

BASIC INFORMATION

DEFINITION

Sudden insult to the liver, which if severe enough to compromise at least 70%-80% of functional hepatic tissue, results in acute hepatic failure

SYNONYM

Acute or fulminant hepatic failure

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs and cats; no age or sex predilection

RISK FACTORS

Drug administration; free-roaming animals with access to potential hepatotoxins (chemicals and pesticides, pond water [blue-green algae], poisonous mushrooms, cycad palms)

CONTAGION & ZOONOSIS

Infectious diseases (see Etiology and Pathophysiology below) for dog-to-dog or cat-to-cat transmission; leptospirosis (dog-to-human)

GEOGRAPHY AND SEASONALITY

Cycad palm toxicosis (dogs): southern United States and Hawaii; fungal: Mississippi and Ohio River Valley (dogs: histoplasmosis), southwestern United States (dogs: coccidioidomycosis). Blue-green algae hepatotoxicity (dogs): late summer or early fall.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Unexpected finding of increased serum liver enzyme activities and bilirubin concentration detected on routine biochemistries (mild hepatic injury or reactive hepatopathy secondary to systemic disorder) in patient who is asymptomatic or has only minimal clinical signs
- Clinical and biochemical evidence of acute hepatic failure (liver dysfunction occurring in the absence of known preexisting liver disease, accompanied by hepatic encephalopathy and coagulopathy). Findings reflect general hepatic dysfunction rather than specific underlying cause

HISTORY, CHIEF COMPLAINT

- History of recent drug administration (prescription, over-the-counter, herbals, or dietary supplements may be implicated) or exposure to other potential hepatotoxins (e.g., aflatoxin-contaminated pet food: feeding from a new bag of food, or multiple affected dogs in a household)
- Acute onset of anorexia, lethargy, vomiting, and diarrhea in previously healthy animal
- Other signs: polyuria/polydipsia, hepatic encephalopathy, signs of extrahepatic or multisystemic disease, dependent on underlying cause

PHYSICAL EXAM FINDINGS

- Dehydration, icterus (+/−), excessive bleeding (hematemesis, melena, hemorrhages of skin or mucous membranes) and hepatic encephalopathy indicate severe hepatic failure.
- Other findings dependent on specific cause (e.g., fever: consider infectious causes or secondary to acute pancreatitis; signs of abdominal pain: acute pancreatitis, cholangitis, liver abscess, acute swelling and stretching of liver capsule [nonspecific])

ETIOLOGY AND PATHOPHYSIOLOGY

- Drugs and anesthetics:
  - Hepatic drug reactions may be classified as predictable (e.g., acetaminophen) or idiosyncratic (most drugs). Usually acute but may be chronic (phenobarbital, primidone, lomustine).
  - Acetaminophen (dogs and cats), amiodarone (dogs), azathioprine (dogs), carprofen and other nonsteroidal antiinflammatory drugs (NSAIDs) (dogs), clonazepam (cats), danazol (dogs), diazepam (cats), doxycycline (dogs), glipizide (cats), griseofulvin (cats), halothane (dogs), itraconazole (dogs and cats), ketoconazole (dogs and cats), lomustine (dogs), methimazole (cats), methoxyflurane (dogs), mitotane (dogs), nitrofurantoin (dogs), oxibendazole (dogs), phenobarbital (dogs), primidone (dogs), potentiated sulfonamides (dogs), stanozolol (cats), tetracycline (dogs and cats), thiacetarsemide (dogs)
  - Idiosyncratic reaction can occur with *any* drug. Diagnosis is presumptive; cannot be proven. Do not rechallenge with suspect drug. Withdrawal of hepatotoxic drug can result in improvement or resolution of hepatic injury (within days to weeks), depending on severity of lesion.
- Biological substances:
  - Aflatoxin (contaminated dog food)
  - *Amanita* mushrooms
  - Blue-green *algae*
  - Sago palms
  - Hornet stings
  - Herbal derivatives (pennyroyal oil, chaparral leaf, comfrey, jin bu huan, kava kava)
  - Xylitol (5-carbon sugar alcohol used as a sugar substitute and is anticariogenic)
- Chemicals and toxins:
  - Carbon tetrachloride
  - Dimethylnitrosamine
  - Metals (e.g., copper, lead, iron, zinc)
  - Organochloride pesticides
  - Many others
- Infectious agents:
  - Viral: infectious canine hepatitis, canine herpesvirus, feline infectious peritonitis, virulent feline calicivirus
  - Bacterial: leptospirosis, liver abscess, cholangitis/cholangiohepatitis, *Bartonella* spp.
  - Fungal: histoplasmosis, coccidioidomycosis, others
  - Protozoal: *Toxoplasma gondii, Babesia* spp., *Cytauxzoon felis*
  - Rickettsial: *Ehrlichia* spp., *Rickettsia rickettsiae*
- Systemic or metabolic disorders:
  - Acute pancreatitis
  - Extrahepatic infection, septicemia, endotoxemia
  - Hemolytic anemia and DIC
  - Inflammatory bowel disease
  - Feline hepatic lipidosis
  - Copper storage hepatopathy
- Miscellaneous causes of liver injury:
  - Trauma
  - Heat stroke
  - Liver lobe torsion
  - Thromboembolic disease
  - Shock
  - Surgical hypotension and hypoxia

DIAGNOSIS

DIAGNOSTIC OVERVIEW

When acute hepatic injury or overt hepatic failure is detected, obtain a thorough history for potential hepatotoxin exposure, and evaluate for systemic disorders that could secondarily affect the liver. Evaluate for primary hepatobiliary disease with biochemical and imaging studies. If a cause of liver injury/failure is not apparent, consider liver biopsy to further characterize the type of injury and look for an underlying cause.

DIFFERENTIAL DIAGNOSIS

- For acute hepatic injury accompanied by icterus/hyperbilirubinemia:
  - Prehepatic causes (hemolytic anemia)

- Posthepatic causes (biliary obstruction)
- Sepsis

- Chronic hepatic disease; recent decompensation of chronic hepatic disease may mimic acute hepatic injury:
  - Determine if subtle signs of chronic illness (weight loss, poor body condition) are present.
  - Findings of ascites, small liver, and hypoalbuminemia suggest chronic rather than acute disease.
  - Chronic liver disease in the final phases of decompensation may not warrant the same aggressive therapeutic approach as acute hepatic failure, because the long-term prognosis is poor.

INITIAL DATABASE

- Routine hematologic and biochemical evaluation:
  - Inflammatory CBC (infectious diseases, acute pancreatitis, extrahepatic infections with secondary reactive hepatopathy); also for ruling out hemolytic anemia as cause of icterus.
  - Serum biochemistry profile: increased serum alanine aminotransferase activity, especially with hepatic necrosis; increased alkaline phosphatase activity; hyperbilirubinemia; hypoglycemia (like hyperammonemia and coagulopathy) suggests severe hepatic dysfunction; xylitol toxicosis also associated with hypoglycemia due to excess insulin release; hypoalbuminemia suggests chronic rather than acute disease; azotemia: consider dehydration or concurrent renal damage (leptospirosis, NSAIDs)
  - Increased serum bile acids
  - Coagulopathy: prolonged PT and APTT, low fibrinogen, low plasma protein C, thrombocytopenia
  - Other findings depend on underlying systemic disorder.
  - Urinalysis: hyperbilirubinuria (small degrees of bilirubinuria may be normal in dogs, because dogs can conjugate bilirubin renally). In cats, all bilirubinuria is considered pathologic.
- Imaging:
  - Abdominal radiographs: liver normal or increased in size
  - Abdominal ultrasound: liver normal or increased in size; variable changes in echogenicity; hypoechoic mass or fluid collection possible (abscess). Evaluate gallbladder and bile ducts to rule out disorders other than acute hepatic injury as a cause of jaundice/icterus, such as posthepatic disorders including extrahepatic biliary tract disease (gallbladder mucocele, cholecystitis, cholelithiasis) or obstruction (distended gallbladder and bile ducts). Evaluate pancreas for acute pancreatitis; other findings dependent on underlying multisystemic or extrahepatic disorder.

ADVANCED OR CONFIRMATORY TESTING

- Liver biopsy:
  - Characterize hepatic lesion histologically; hepatic necrosis most common lesion associated with acute hepatic failure; differentiate acute from chronic (fibrosis, nodular regeneration). May provide specific diagnosis (infectious diseases).
- Fine-needle aspiration and cytologic evaluation of the liver: rapid screening for mycoses, neoplasia, feline hepatic lipidosis, abscess (ultrasound-guided); accuracy is poor for many hepatic diseases.
- Bacterial cultures: aerobic and anaerobic of liver and bile (cholangitis, abscess)
- Serum antibody titers for infectious diseases (leptospirosis, mycoses, toxoplasmosis, others)
- Tests to evaluate for systemic or extrahepatic disorders (pancreatic lipase immunoreactivity for acute pancreatitis; thoracic radiographs for systemic fungal infection, toxoplasmosis, metastatic neoplasia)
- If aflatoxin contamination of pet food is suspected, save a sample of suspect food in an airtight bag, with packaging information including product and date code. Submit food for aflatoxin level determination. Because of the rapid metabolism and excretion of aflatoxin, detection of aflatoxin in serum and liver tissue is less reliable.

TREATMENT

TREATMENT OVERVIEW

For patients with mild hepatic injury (not in acute hepatic failure) showing few or no clinical signs, treat underlying systemic disorder, discontinue any potentially hepatotoxic medications, provide supportive care including oral hepatoprotective agents such as *S*-adenosylmethionine (SAMe) and silybin, and monitor liver biochemistries to assess response. For patients with acute hepatic failure, intensive supportive therapy is warranted as described below. The goal of treatment is to allow adequate time for hepatic regeneration and repair, prevent or control complications of liver failure, and treat the underlying cause when possible.

ACUTE GENERAL TREATMENT

- IV fluid therapy with balanced electrolyte solution; supplement with KCl using conventional sliding scale(20-40 mEq/L to start); maintain normoglycemia by adding 2.5%-5% dextrose to fluids. Avoid alkalosis in hepatic encephalopathy (give 0.9% saline rather than lactated Ringer's solution).
- Treat underlying cause when possible; discontinue any suspect drug; start amoxicillin or penicillin for empirical treatment of

suspected leptospirosis (dogs), or broad-spectrum systemic antibiotics for sepsis.

- Give *N*-acetylcysteine as a glutathione source/antioxidant for treatment of acetaminophen toxicity at 140 mg/kg (10% or 20% solution diluted at least 1:2 with saline) IV over 20-30 minutes through 0.25-m nonpyrogenic filter; then 70 mg/kg IV or PO q 6 h for 7 treatments. May also be beneficial for treatment of other drug-induced injuries (carprofen, potentiated sulfonamides, diazepam, methimazole, others), aflatoxin-induced hepatic injury, or organic solvents and heavy metal toxicity.
- Other hepatoprotective therapy (empirical therapy):
  - SAMe, 20 mg/kg PO q 24 h, as a glutathione source (given as follow-up to IV *N*-acetylcysteine when oral therapy is tolerated)
  - Silybin (milk thistle) protective against *Amanita* mushroom toxicity in an experimental study in dogs at 50 mg/kg IV. Oral dose for dogs and cats is 20-50 mg/kg q 24 h of 60%-80% silybin but poor absorption. Veterinary product, Marin (Nuramax Laboratories Inc.), 5-10 mg/kg q 24 h, contains silybin bound to phosphatidylcholine to improve gastrointestinal absorption.
  - Vitamin E (15 IU/kg PO q 24 h) as an antioxidant
- For nonspecific control of vomiting use antiemetics such as maropitant (1 mg/kg SQ q 24 h or 2 mg/kg PO q 24 h), metoclopramide (0.2-0.4 mg/kg IV, IM, SQ, PO q 6-8 h or 1-2 mg/kg/24 h IV constant rate infusion), or ondansetron (0.1-0.2 mg/kg SQ or slow IV q 8 h).
- Treat or prevent gastric ulceration with famotidine (0.5-1 mg/kg IV or PO q 12-24 h), omeprazole (0.7-1 mg/kg PO q 12-24 h) or pantoprazole (0.7-1 mg/kg IV q 12-24 h).
- For treatment of coagulopathy, give fresh-frozen plasma and parenteral vitamin K1 (0.5-1 mg/kg q 12-24 h SQ for two or three doses or until PT normalizes).
- Treat for hepatic encephalopathy (if present; see p. 501) using a high-quality low-protein diet, lactulose (0.1-0.5 mL/kg PO q 12 h, adjusted to achieve soft fecal consistency), and/or intestinal antibiotics such as metronidazole (7.5-10 mg/kg PO q 12 h) or amoxicillin-clavulanate (15 mg/kg PO q 12 h).

CHRONIC TREATMENT

- Consider empirical oral hepatoprotective therapy (SAMe, silybin, or vitamin E) until evidence of hepatic injury resolves.
- Glucocorticoids are generally not warranted.

NUTRITION/DIET

Provide adequate dietary protein and calories. Do not restrict dietary protein unless hepatic encephalopathy is present (see p. 501); choose nonmeat protein sources such as dairy (e.g., cottage cheese) and eggs.

DRUG INTERACTIONS

Avoid drugs that require hepatic metabolism

POSSIBLE COMPLICATIONS

- Hepatic encephalopathy
- Hypoglycemia
- Coagulopathy and anemia
- Gastrointestinal ulceration
- Septicemia

RECOMMENDED MONITORING

- Serum biochemistry profiles
- Blood glucose
- Serum bile acids (anicteric patients)
- Packed cell volume/total protein (anemia/bleeding)

PROGNOSIS AND OUTCOME

- If patient presents with signs of advanced liver failure (e.g., hepatic encephalopathy, coagulopathy, hypoglycemia), the prognosis is guarded.
- For milder hepatic injury, complete recovery is possible, especially when underlying cause is detected and treated.

PEARLS & CONSIDERATIONS

COMMENTS

- Clinical and laboratory features reflect general hepatic failure; they are not specific for underlying cause of hepatic injury.
- Always consider an adverse drug reaction as the cause of acute hepatic injury or failure, as discontinuing suspect drug can result in improved hepatic function.

PREVENTION

- Vaccinate for infectious diseases (e.g., infectious canine hepatitis, leptospirosis).
- Monitor liver enzymes when prescribing a drug with potential to cause hepatotoxicity; promptly discontinue if enzyme elevations arise.
- Avoid reexposure of patient to drug suspected to have caused hepatic reaction.

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Hepatic Encephalopathy

BASIC INFORMATION

DEFINITION

A reversible metabolic central nervous system (CNS) disturbance secondary to hepatic disease

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs and cats
- Congenital hepatic vascular disease: young
- Acquired hepatic disease: middle-aged to older

GENETICS & BREED PREDISPOSITION

- Hepatic vascular disease: several breed predispositions (see p. 905)
- Acquired liver disease: see pp. 1054, and 513.

RISK FACTORS

- Acute hepatic disease
- Hepatotoxic drugs and toxins
- Congenital hepatic vascular disease:
    - Single portosystemic vascular anomalies
    - Primary hypoplasia of the portal veins (microvascular dysplasia)
    - Hepatic arteriovenous fistula or malformation
- Multiple acquired portosystemic shunts secondary to portal hypertension from chronic hepatic disease

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Historic signs of chronic liver disease typically are episodic, involving three systems:

- Neurologic: diffuse cerebral disturbance: lethargy, poor appetite, aimless wandering, head pressing, disorientation, seizures, blindness, depression, stupor, coma, behavioral changes. Poor anesthesia tolerance/prolonged recovery.
- Gastrointestinal (GI): vomiting, diarrhea, poor weight gain, ptyalism (cats)
- Urinary: polyuria and polydipsia, stranguria, pollakiuria, dysuria, and/or hematuria associated with ammonia biurate uroliths

PHYSICAL EXAMINATION

- Signs of diffuse cerebral disease but may be subclinical at the time of examination owing to the episodic nature of hepatic encephalopathy. Rarely, multifocal and lateralizing neurologic signs are present.
- Congenital patients: stunted growth possible
- Cats with congenital portosystemic shunts often have copper-colored irises.
- Acquired hepatic disease: ascites, icterus
- Acute hepatic failure: initial neuroexcitatory behavior (restlessness, agitation, seizure) progressing to more neuroinhibitory states (depression, coma)
- Hepatic arteriovenous fistula: a continuous murmur may be ausculted on the cranioventral abdomen.

ETIOLOGY AND PATHOPHYSIOLOGY

Complex multifactorial etiology:

- Associated with the accumulation of neurologic toxins, most likely of gut origin, that escape hepatic detoxification as a result of shunting of blood away from the portal vasculature into the systemic vasculature.
- GI toxins derived primarily from bacterial metabolism of proteinaceous waste
    - Ammonia generation in the colon

- Endogenous benzodiazepine-like substances
- Alterations in inhibitory (γ-aminobutyric acid) and excitatory (glutamate) neurotransmitter balance playing a secondary role
- Low-grade cerebral edema due to astrocyte detoxification of ammonia to glutamine may also play a role in the development of chronic hepatic encephalopathy associated with portosystemic shunting.
- Pathophysiology of encephalopathy associated with acute hepatic failure is distinct from chronic hepatic en cephalopathy and is complicated by development of overt intracranial hypertension with cerebral edema secondary to alterations in the blood-brain barrier, disturbances in cerebral blood flow, and release of neurotoxic substances by the necrotic liver; frequently is complicated by neuroglycopenia.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A tentative diagnosis is made when a patient with liver disease shows signs of neurologic dysfunction.

DIFFERENTIAL DIAGNOSIS

- Neurologic signs: hypoglycemia, lead toxicity, congenital CNS malformation such as hydrocephalus or storage disease, infectious encephalitis/meningitis (e.g., feline infectious peritonitis infection, toxoplasmosis, neosporosis, canine distemper encephalitis), granulomatous meningoencephalitis, CNS neoplasia, thiamine deficiency (cats).
- Chronic GI or urinary signs may mimic primary GI disease or suggest primary genitourinary or endocrine disorders.

INITIAL DATABASE

- CBC: microcytosis, poikilocytosis (cats)
- Serum biochemistry profile:
  - Hepatic vascular disease: profile results may be normal or show mild hypoalbuminemia, low blood urea nitrogen, mild increases in serum alanine aminotransferase and serum alkaline phosphatase (ALP) activities (some elevation of ALP activity in young animals may be normal bone isoenzyme), hypocholesterolemia, hypoglycemia (especially in young toy breeds)
  - Acquired hepatic disease: hypoalbuminemia, moderate to severe increases in all serum hepatic enzyme activities, ± hyperbilirubinemia, hypercholesterolemia or hypocholesterolemia, hypoglycemia (with acute hepatic failure)
- Urinalysis: isosthenuria common; ammonia biurate crystalluria, hematuria, pyuria, bacteruria possible

ADVANCED OR CONFIRMATORY TESTING

Clinical Pathology:

- Total serum bile acids: sensitive for the detection of congenital or acquired portosystemic shunting (2-hour postprandial sample more sensitive)
- Blood ammonia: specific indicator of hepatic encephalopathy but can be normal even during overt hepatic encephalopathy. Ammonia tolerance test more sensitive to detect hepatic encephalopathy but may induce severe neurologic signs.
- Urinary bile acids: less sensitive than serum bile acids in the dog (but may be more convenient)
- Abdominal effusion: pure or modified transudate

Imaging:

- Abdominal ultrasound:
  - Portosystemic vascular anomaly: identification of a vascular communication between the intrahepatic or extrahepatic portal circulation and the systemic vasculature (see p. 905), microhepatica, renomegaly, urolithiasis
  - Primary hypoplasia of the portal veins (see p. 723): ± microhepatica, ± abdominal effusion, may be unremarkable
  - Hepatoarteriovenous fistula or malformation: identification of fistula, abdominal effusion
  - Chronic hepatitis/hepatopathies, cirrhotic/fibrosing liver disease: microhepatica, possible nodular liver with cirrhosis, abdominal effusion; visualization of multiple portosystemic shunts may be difficult.
- Rectal or splenic technetium scans (see p. 1259):
  - Abnormal with single or multiple portosystemic shunts and normal with primary hypoplasia of the portal veins without portal hypertension (microvascular dysplasia)

Histopathology:

- Hepatic histopathology:
  - Same pattern of changes (arteriolar proliferation, hepatic atrophy, attenuation of portal vasculature, lobular collapse)

seen with all forms of hepatic vascular disease

TREATMENT

TREATMENT OVERVIEW

Goals of treatment are to lower levels of circulating neurotoxins by modulating GI protein metabolism, maintain optimum nutritional plane, and control precipitating factors.

ACUTE AND CHRONIC TREATMENT

- Nothing per os if stupor or coma is present
- Address fluid and electrolyte imbalances, avoid lactated solutions with acute hepatic failure, sodium restrict fluids with ascites, potassium and glucose supplementation as needed, B vitamins (especially thiamine and cobalamin in cats).
- Medications that increase GI protein tolerance
    - Lactulose: drug of choice. Nonabsorbable disaccharide broken down by colonic bacteria into short-chain fatty acids. Traps soluble NH3 as $NH4^+$, which is nonabsorbable and thus excreted in the feces. Alters bacterial metabolism so that less ammonia is generated.
        - Titrated from an initial dose of 0.5 to 1 mL/kg PO q 8-12 h to dose that produces 3-4 soft stools per day. If stupor or coma is present, may be given rectally in a retention enema (see p. 1258).
    - Antibiotics:
        - Alter bacterial metabolism, synergistic with lactulose
        - Metronidazole (7.5 mg/kg PO q 8-12 h, low dose to avoid neurotoxicity secondary to decreased hepatic metabolism of the antibiotic); *or*
        - Neomycin (10-22 mg/kg PO q 12 h) (may be difficult to obtain; can be given orally or as a retention enema) or ampicillin (22 mg/kg PO q 12 h)
- Seizures: control seizure activity:
    - Barbiturates (e.g., phenobarbital 6-10 mg/kg slowly IV to effect); the patient should be monitored closely for respiratory depression.
    - Propofol is useful for controlling hepatic encephalopathy–induced status epilepticus. Because it is metabolized by the liver, small doses may be used and may have a longer duration of action. Maintain an anesthetized state for several hours before tapering and observing for recurrence. Monitor for apnea during use.
- If patient is seizuring due to hepatic encephalopathy from acute liver injury: cerebral edema is likely, and the prognosis is grave (seizures often refractory to treatment).
    - Mannitol (0.5 g/kg given IV over 10-15 minutes).
    - Infusion of *N*-acetylcysteine (140 mg/kg IV initially followed by 70 mg/kg as needed) may correct disturbances in microcirculation.
    - Corticosteroids of no benefit and may be detrimental.
    - Monitor closely (q 4 h) for hypoglycemia; may require infusion of high concentrations of dextrose-containing solutions.
- Control precipitating factors:
    - Oral protein loading: gastrointestinal hemorrhage, high protein meals
    - Catabolic conditions such as infections, dehydration, azotemia
    - Alkalosis with hypokalemia: increases renal ammonia production
    - Synergistic neural inhibition with sedatives, tranquilizers, or anesthetic agents; use these with caution if at all (e.g., diazepam).
    - Constipation
    - Transfusion with stored blood products containing high ammonia concentrations
- Medications to increase GI protein tolerance are first-line therapy (see Acute General Treatment above).

NUTRITION/DIET

- Adequate calories to avoid catabolism of muscle, which is highly ammongenic and may make control of hepatic encephalopathy difficult.
- Modulation of protein content: high-quality protein derived preferably from plant and dairy products. Start with diet containing minimum daily protein requirements (cat: 6.5 g/100 kcal; dog: 5.1 g/100 kcal) in combination with medications to increase protein tolerance and decrease protein only if necessary.
- Increase fiber content (e.g., by adding bran or canned/cooked pumpkin).
- Vitamin supplementation: thiamine in cats (50-100 mg PO daily), vitamin K (if associated coagulopathy) initially parenterally (0.5 mg/kg SQ q 12 h) for 5-7 days then once weekly.
- Sodium restriction necessary only with ascites: 0.04-0.05 g/100 kcal.

DRUG INTERACTIONS

- Neuroinhibitory drugs (e.g., sedatives, anesthetics, and tranquilizers) should be used cautiously, as they may potentiate the neuroinhibition of hepatic encephalopathy.
- Avoid drugs that depend heavily on hepatic metabolism and/or excretion if possible.

RECOMMENDED MONITORING

- Blood ammonia concentration
- Mentation and appetite at home
- Body weight and body condition score
- Serum albumin

PROGNOSIS AND OUTCOME

Depends on nature of underlying liver disease causing encephalopathy:

- Hepatic vascular disease (portosystemic shunt, microvascular dysplasia, arteriovenous fistula or malformation): in general, clinical signs of hepatic encephalopathy due to congenital hepatic vascular disease respond quickly and fully to appropriate drug and dietary intervention. Long-term prognosis depends on whether the congenital intrahepatic or extrahepatic shunt can be fully attenuated or the arteriovenous fistula can be resected (in which case signs of hepatic encephalopathy typically abate) and whether these conditions are complicated by primary hypoplasia of the portal veins (microvascular dysplasia), which causes continued shunting of blood from the portal circulation.
- Acquired chronic hepatic disease: clinical signs of hepatic encephalopathy generally abate with proper intervention, but long-term prognosis depends on severity of the underlying hepatic disorder. Generally, patients with signs of severe hepatic encephalopathy due to acquired hepatic diseases have a very poor prognosis unless the underlying disease can be reversed.
- Acute liver failure: encephalopathy generally is more refractory to therapy, probably reflecting a more complex underlying cerebral lesion or process. Encephalopathy progressing to coma or stupor (grade 3-4) is considered a grave prognostic sign and is one of the criteria used for determining the need for transplantation in human patients.

PEARLS & CONSIDERATIONS

COMMENTS

- Normal blood ammonia concentration does not rule out the presence of hepatic encephalopathy.
- Initial treatment of hepatic encephalopathy involves steps to increase dietary protein tolerance (nonabsorbable disaccharides and antibiotics) in combination with dietary protein modulation, but not excessive restriction.
- Be aware of common comorbid conditions that can complicate control of hepatic encephalopathy, such as GI bleeding, dehydration, hypokalemia, azotemia, constipation, and alkalosis.
- Encephalopathy accompanying acute hepatic failure differs from that accompanying congenital vascular disorders or chronic hepatic failure in that it involves the development of overt cerebral edema and an initial neuro-excitatory state often refractory to therapeutic intervention. In addition, patients with signs of severe hepatic encephalopathy due to acquired hepatic diseases have a very poor prognosis.

CLIENT EDUCATION

Hepatic encephalopathy is an episodic chronic condition that cannot be cured but can be controlled with strict adherence to dietary modulation and drug therapy.

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Hemotropic Mycoplasmosis, Cat

BASIC INFORMATION

DEFINITION

An infection of feline red blood cells (RBCs) with the bacterial organisms *Mycoplasma haemofelis*, "*Candidatus* Mycoplasma turicensis" or "*Candidatus* Mycoplasma haemominutum." *Mycoplasma haemofelis* is the most pathogenic species and it causes hemolytic anemia, which is usually extravascular.

SYNONYM

Haemobartonella felis (outdated); feline hemotropic (or hemotrophic) mycoplasmosis; feline infectious anemia

EPIDEMIOLOGY

SPECIES, AGE, SEX

Domestic and wild felines of all ages. Young cats may be more likely to present with hemolytic anemia secondary to *Mycoplasma haemofelis* infection. Male cats are more likely to be infected than females, possibly due to roaming and fighting behavior.

RISK FACTORS

- Access to outdoors
- Bloodsucking arthropods, including fleas, ticks, and mosquitoes, have been suggested to play a role in transmission.
- Underlying retrovirus infection, in particular with feline immunodeficiency virus
- A history of cat bite abscess often precedes hemoplasmosis by a few weeks, and hemoplasmas have been detected in saliva, suggesting a possible mode of transmission.

CONTAGION AND ZOONOSIS

- Transplacental spread has been hypothesized.
- Transmission via blood transfusion is possible.
- The DNA of *Mycoplasma haemofelis* has been detected in a person coinfected with HIV and *Bartonella henselae* from Brazil, so these organisms may have zoonotic potential.

GEOGRAPHY AND SEASONALITY

Worldwide

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Acute, chronic, or subclinical
- Clinical signs depend on anemia (severity and rate of development)

HISTORY, CHIEF COMPLAINT

- Acute: sudden death, weakness, depression, collapse, pale mucous membranes, tachypnea, anorexia, ± vomiting, neurologic signs
- Chronic: lethargy, anorexia, weight loss
- Subclinical: no abnormalities reported; more likely with *"Candidatus* M. turicensis" and *"Candidatus* M. haemominutum" infections

PHYSICAL EXAM FINDINGS

- Acute: pale mucous membranes, fever, tachypnea, tachycardia, mental depression, weakness, splenomegaly, systolic cardiac murmur due to amnesia, rarely icterus

- Chronic: pale mucous membranes, poor body condition, weakness, splenomegaly

ETIOLOGY AND PATHOPHYSIOLOGY

- Three species of feline hemotropic mycoplasmas have been identified in cats:
  - *Mycoplasma haemofelis:* this is the most pathogenic species, causing hemolytic anemia in immunocompetent cats.
  - *"Candidatus* Mycoplasma haemominutum": this is detected in as many as one in five cats visiting veterinary hospitals and is usually not associated with hemolytic anemia.
  - *"Candidatus* Mycoplasma turicensis": this is the most recently recognized species, and its pathogenicity may lie between that of *M. haemofelis* and "*Candidatus* M. haemominutum."
- Coinfection may occur with two or more hemoplasma species.
- Organisms reside on the surface of—and possibly replicate within—RBCs, causing RBC destruction, which is predominantly extravascular, and ultimately a regenerative anemia, possibly via increased RBC fragility, erythrophagocytosis, and/or immune-mediated destruction.
- Appearance of large numbers of organisms on blood smears is associated with precipitous declines in the hematocrit, after which organisms may disappear for several days. Eventually cats recover from this phase of infection, after which the hematocrit increases, and organisms disappear from blood smears. A carrier state may develop in some cats, especially those infected with *"Candidatus* M. haemominutum."

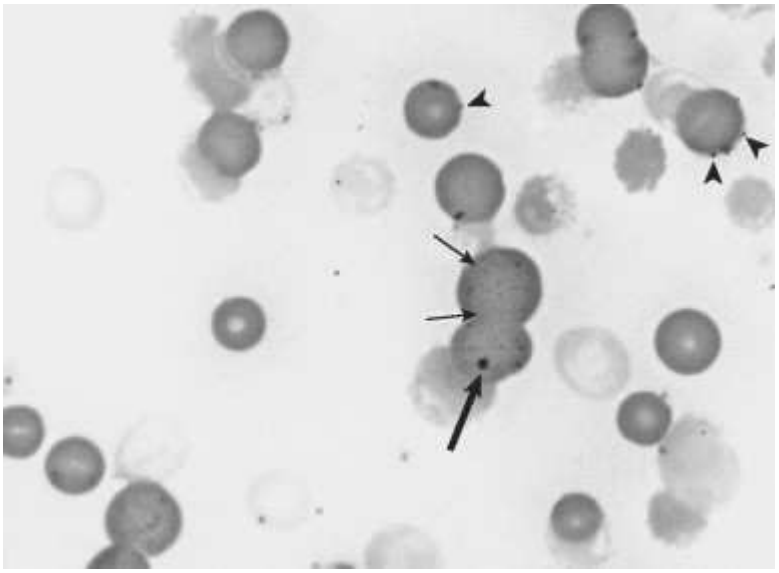
DIAGNOSIS

DIAGNOSTIC OVERVIEW

This diagnosis becomes suspected either when a cat is anemic or when a blood smear appears to be consistent with RBC infection by these organisms. Hemoplasmas are unculturable mycoplasmas, so diagnosis relies on organism identification on blood smears (which has low sensitivity and specificity) or molecular diagnosis using PCR. PCR assays are considered the gold standard for diagnosis, but results must be interpreted differently depending on the hemoplasma species detected.

DIFFERENTIAL DIAGNOSIS

- Primary immune-mediated hemolytic anemia
- Heinz body anemia (acetaminophen toxicity, zinc toxicity, diabetic ketoacidosis, ingestion of onions or baby food containing onion powder)
- Cytauxzoonosis
- Hereditary erythrocyte disorders such as those of Abyssinian and Somali cats
- External or internal blood loss
- Feline leukemia virus (FeLV) infection



HEMOTROPIC MYCOPLASMOSIS, CAT Hematologic differential diagnosis. The larger Howell-Jolly body *(large arrow)* or multiple punctate appearance of basophilic stippling (seen throughout the two red cells in the center of the image *[small arrows]*) should not be mistaken for *M. haemofelis (many arrowheads)*.

(Courtesy of Department of Clinical Pathology, Atlantic Veterinary College; reproduced with permission.)

INITIAL DATABASE

- Blood smear: visual identification of organism:
  - Nonrefractile basophilic cocci, rods, or ring-forms on the surface of RBCs
  - Such cytologic detection of organisms is <50% sensitive. In addition, *"Candidatus* M. turicensis" has never been seen on blood smears.
  - For optimal recognition, a thin fresh blood smear should be made immediately after blood collection (prior to adding EDTA) and stained with Romanowsky stains.
  - False-positive results are common owing to confusion with Howell-Jolly bodies, Heinz bodies, stain precipitates, or refractile artifacts (see figure).
- CBC: regenerative anemia, macrocytosis, normoblastosis, ± mild to moderate neutrophilia and monocytosis are typical. Thrombocytopenia may also be noted. Anemia may be nonregenerative if disease is very acute.
- Serum biochemistry profile: typically unremarkable; hyperbilirubinemia uncommon despite hemolysis, occasional elevations in alanine aminotransferase, alkaline phosphatase.
- Urinalysis: unremarkable
- Abdominal imaging: changes are minimal. Diffuse, mild to marked splenomegaly possible.
- Retrovirus testing: to rule out coinfection

ADVANCED OR CONFIRMATORY TESTING

- Hemoplasmas cannot be cultured in the laboratory.
- If doubt persists, blood can be submitted for PCR testing, which is more sensitive and specific than blood smear detection. Consult the laboratory to determine which hemoplasma species its PCR assays detects. Cats testing positive for "*Candidatus* M. turicensis" or *"Candidatus* M. haemominutum," should still undergo a thorough investigation to rule out alternative causes of anemia, because they have not been definitely associated with disease.

TREATMENT

TREATMENT OVERVIEW

The antimicrobial of choice for treatment is doxycycline, although enrofloxacin may also be effective. Treatment leads to resolution of anemia for cats infected with *M. haemofelis* but may not completely eliminate the infection as determined using PCR. Therapeutic goals are resolution of acute clinical bacteremia and restoration of red cell volume.

ACUTE GENERAL TREATMENT

- Supportive care:
  - Blood transfusion (see p. 1347) or oxygen-carrying compounds for severe anemia
  - IV crystalloid fluid replacement as needed
- Doxycycline is the drug of choice for reduction of bacteremia: 10 mg/kg PO q 24 h for a minimum of 14 days.
- Fluoroquinolones may also be effective: enrofloxacin, 5 mg/kg PO q 24 h for a minimum of 14 days.
- Cats may remain PCR-positive after treatment; no antimicrobial therapy has been shown to completely eliminate infection. Treatment of cats that are not anemic and showing no clinical signs is therefore not recommended.
- Use of glucocorticoids should be restricted to cats not responding to antimicrobial therapy alone, or when the diagnosis is uncertain and primary immune-mediated hemolytic anemia is possible.

DRUG INTERACTIONS

- Fluoroquinolones given at high doses may cause blindness in cats; do not exceed 5 mg/kg q 24 h.
- Doxycycline: esophagitis/esophageal strictures in cats. Follow oral doxycycline administration with a bolus of water or food to ensure passage into the stomach.

RECOMMENDED MONITORING

Packed cell volume or CBC

PROGNOSIS AND OUTCOME

Severity of infection varies from subclinical to life threatening. Prognosis is generally good with intensive supportive care when needed and appropriate antibiotic treatment. Infections may recrudesce with stress or other disease.

PEARLS & CONSIDERATIONS

PREVENTION

- To decrease risk of exposure, confine cats indoors or reduce contact with other felines, especially feral populations.
- Neuter to decrease roaming and fighting in outside cats.
- Practice effective flea and tick control.

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Hemothorax

BASIC INFORMATION

DEFINITION

Accumulation of blood within the pleural space; a relatively infrequent cause of respiratory disease but somewhat common cause of pleural space disease, especially in dogs

SYNONYM

Pleural hemorrhage

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Both dogs and cats can be affected.
- Any age, breed, or sex of cat and dog is susceptible, but traumatic hemothorax may be more common in dogs.

GENETICS & BREED PREDISPOSITION

Dogs or cats with congenital coagulopathies are predisposed.

RISK FACTORS

Common:

- Trauma
- Coagulopathy
    - Anticoagulant rodenticide ingestion
- Intrathoracic neoplasia

Uncommon/rare:

- *Spirocerca lupi* (esophageal worm)
- *Angiostrongylus vasorum*
- Pneumonia *(S. equi* subsp. *zooepidemicus)*
- Esophageal or migrating intrathoracic foreign body
- Fat embolism
- Thymic hemorrhage
- Congenital coagulation disorder

GEOGRAPHY AND SEASONALITY

S. lupi is more prevalent in warmer climates (southern United States); most cases of *A. vasorum* infections have been reported from Europe and Canada.

ASSOCIATED CONDITIONS & DISORDERS

- Pleuritis
- Pyothorax
- Intrathoracic neoplasia
- Reexpansion pulmonary edema
- Pulmonary contusions
- Lung lobe torsion
- Fibrosing pleuritis
- Hypovolemic shock

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Increased respiratory effort or respiratory distress
  - Open-mouth breathing
  - Restrictive breathing pattern
  - Tachypnea
- Lethargy
- Exercise intolerance
- Weakness or collapse
- History of trauma or anticoagulant rodenticide ingestion

PHYSICAL EXAM FINDINGS

- Dyspnea and/or tachypnea
- Decreased heart and lung sounds ventrally on thoracic auscultation; may detect a fluid line
  - Increased bronchovesicular lung sounds dorsally
  - Cats may not have any appreciable change in thoracic auscultation.
- Pain when breathing (associated with trauma)
- Peritoneal effusion or other evidence of hemorrhage
- Signs consistent with hypovolemic shock (tachycardia, pale mucous membranes, weak pulses, prolonged capillary refill time)

ETIOLOGY AND PATHOPHYSIOLOGY

- Local factors that disrupt the integrity of vascular structures within the thoracic cavity:
  - Trauma to the lung, heart, mediastinum, or thoracic great vessels
  - Primary or metastatic neoplasia (hemangiosarcoma, mesothelioma, osteosarcoma, and pulmonary carcinoma) involving intrathoracic structures (including ribs, vertebral bodies)
  - Lung lobe torsion
  - Herniated abdominal viscera
  - Thymic hemorrhage (young animals)
  - Hemorrhagic pneumonia (*S. equi* subsp. *zooepidemicus)*
  - Pulmonary infarction (rare)
  - Migrating foreign body (uncommon)
  - Fat embolism (rare)
- Increased spontaneous bleeding tendencies, more often secondary to clotting-factor deficiencies/defects than to platelet disorders
  - Most commonly anticoagulant rodenticide ingestion
  - Congenital disorders of coagulation possible
  - Vitamin K deficiency secondary to poor intestinal lipid absorption is a very rare cause of vitamin K–responsive coagulopathy to consider in animals with a concurrent history compatible with chronic small-intestinal enteropathies.

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on a known history of trauma or anticoagulant rodenticide ingestion and appropriate clinical signs. Confirmation requires assessment of packed cell volume (PCV) and total protein (TP) of the effusion. The proportion of blood needed to classify an effusion as hemorrhagic is variable, but generally an effusion with Hct > 3% should be viewed as having a hemorrhagic contribution.

DIFFERENTIAL DIAGNOSIS

- Other pleural space disease
  - Hydrothorax (see p. 882), pyothorax, chylothorax, pneumothorax
- Diaphragmatic hernia
- Pulmonary parenchymal disease
- Intrathoracic neoplasia
- Pericardial effusion

INITIAL DATABASE

- CBC:
  - Can be normal if hemorrhage is acute; may reveal mild anemia if hemorrhage is chronic and slow
  - Increased numbers of nucleated red cells, thrombocytopenia, acanthocytes, and schistocytes are suggestive of hemangiosarcoma.
  - Inflammatory and/or stress leukogram
- Serum biochemistry profile:
  - Hypoalbuminemia (if enough time has passed for fluid shifts)
  - Hypoalbuminemia, hypocholesterolemia, hypoglycemia, and low BUN in patients with coagulopathy secondary to hepatic failure.
- Thoracic radiographs:
  - Radiographic appearance depends on fluid volume:
    - Small volumes may result in only the presence of interlobar fissure lines.
    - Larger volumes may reveal scalloping or retraction of lung lobes from the thoracic wall, blunting of the lung lobes, impaired visualization of the cardiac silhouette (especially on dorsoventral views), or the presence of a soft tissue opacity ventrally on lateral views.
  - May help with visualization of primary or metastatic neoplasms
    - The presence of pleural effusion can obscure parenchymal lesions, so if neoplasia is a concern, repeat thoracic radiographs after thoracocentesis.
  - May reveal evidence of trauma (rib fractures and pulmonary contusions)
  - Assess integrity of the diaphragm
  - Thoracocentesis prior to radiography increases ability to visualize underlying cause such as neoplasia or diaphragmatic hernia, or concurrent disease such as pulmonary contusions.
- Thoracocentesis (see p. 1338):
  - Fluid obtained should be collected in EDTA (purple-top) and plain (red-top) tubes for evaluation.
  - PCV and TP will be similar to that of peripheral blood in acute cases.
- Prothrombin time (OSPT) and activated partial thromboplastin time (APTT) if anticoagulant rodenticide intoxication or congenital coagulopathy is suspected.
  - Prolonged OSPT and APTT are expected in patients with vitamin K rodenticide intoxication.
  - Abnormalities of coagulation times seen with congenital coagulopathy will reflect the specific defect; prolongation of only the OSPT, only the APTT, or both are possible.
  - Can also be supportive of disseminated intravascular coagulation (DIC).

ADVANCED OR CONFIRMATORY TESTING

- Pleural effusion cytologic examination:
  - Useful for neoplasia (lymphoma) and infectious cases, although an absence of either does not preclude them as causes of hemothorax.
  - Erythrophagocytosis or hemosiderin in macrophages is indicative of chronicity.
- Thoracic ultrasonography:
  - Should be performed prior to thoracocentesis to improve visualization of intrathoracic structures unless the patient is in respiratory distress
  - Confirms pleural effusion
  - Can guide thoracocentesis
  - Investigation for tumors (pulmonary, mediastinal, heart base, or right auricular masses), lung lobe torsion, abdominal organs within the thoracic cavity, pulmonary thromboembolism
- Thoracic CT:
  - Similar to thoracic ultrasonography, but thoracocentesis should be performed prior to imaging to improve visualization of parenchyma and vasculature.
- Proteins induced by vitamin K antagonism (PIVKA):
  - Abnormality is suggestive of rodenticide ingestion.
  - More sensitive than OSPT and APTT
- D-Dimers:
  - Elevations are supportive of DIC and thromboembolism.
- Exploratory thoracotomy (usually median sternotomy):
  - Diagnostic test of choice when the cause of hemothorax is not explained by history, physical examination, and results of other diagnostic tests.

TREATMENT

TREATMENT OVERVIEW

- Stabilization of patient and treatment for shock if hemothorax is secondary to trauma
- Improve respiratory function with supplemental oxygen and/or removal of hemorrhage in patients that are in distress.

- Because autotransfusion occurs rapidly, resulting in resolution of hemothorax within days, complete removal of blood is typically unnecessary unless large volumes of hemorrhage are present. Consequently, thoracocentesis should be performed primarily to alleviate respiratory distress.
- Identification and treatment of underlying cause when possible

ACUTE GENERAL TREATMENT

- Improve oxygenation via an intranasal cannula, face mask, or oxygen cage (see p. 1318).
- Thoracocentesis if in respiratory distress
  - Complete drainage is generally not necessary.
- Transfusion with whole blood, packed red blood cells, and/or plasma (coagulation disorders) if severe anemia.
- Vitamin K1 1-2.5 mg/kg PO q 12 h for 14-30 days depending on the anticoagulant rodenticide ingested
  - Can administer subcutaneously initially at same dose
  - Anaphylactic reactions have been reported following intravenous administration.
- Stabilization of respiratory and circulatory function if secondary to trauma or diaphragmatic hernia
  - Mechanical ventilatory support may be necessary if pulmonary contusions are present.

CHRONIC TREATMENT

- Repeated thoracocentesis or thoracostomy tube placement
  - Relieves respiratory distress
  - Prevents atelectasis
  - Can quantify hemorrhage
  - Removal of blood can reduce the risk of development of pleuritis, empyema (pyothorax), and pleural fibrosis.
- Management of pneumonia or systemic disease if present
- Exploratory thoracoscopy or thoracotomy to surgically excise tumors or locate and ligate bleeding vessels if hemothorax is unexplained or persists despite conservative interventions
- For some patients, chemotherapy may be indicated following cytologic or histologic confirmation of tumor type.

BEHAVIOR/EXERCISE

Activity should be limited until hemorrhage, anemia, or traumatic injuries have resolved.

POSSIBLE COMPLICATIONS

- Recurrent effusion
- Dyspnea from large-volume pleural effusion
- Related to thoracocentesis or thoracostomy tube placement
  - Pneumothorax
  - Parenchymal injury and further hemorrhage
- Pleuritis, empyema, or fibrosis
- Rapid reexpansion of lungs can result in reexpansion pulmonary edema.
  - More common with chronic effusions
  - Risk can be minimized by removing large-volume effusions gradually over several hours.

RECOMMENDED MONITORING

- Respiratory rate and effort
- Thoracic radiographs or ultrasound
  - Assess need for repeated thoracocentesis.

PROGNOSIS AND OUTCOME

- Dependent on underlying cause
  - Variable with trauma
  - Good with appropriate treatment of anticoagulant rodenticide intoxication
  - Poor to guarded with most neoplasms and congenital coagulation disorders

PEARLS & CONSIDERATIONS

COMMENTS

- Hemorrhagic pleural effusion fluid should not clot after removal from the pleural space unless there is continuous bleeding.
- Trauma significant enough to cause hemothorax will likely result in pulmonary contusions.
- Cats may require thoracocentesis prior to other diagnostics, as they are easily stressed and can decompensate quickly.
- In patients with no history of trauma and no evidence of a coagulation defect, neoplasia is a common cause of hemothorax.

PREVENTION

- Minimize risk of blunt trauma (automobile accident) by using leashes or keeping in enclosed areas.
- Limit access to anticoagulant rodenticides.

TECHNICIAN TIPS

- When obtaining blood from patients with known or suspected hemothorax, ideally draw as much blood as needed to accomplish all laboratory diagnostics (CBC, biochemical profile, coagulation tests) at the first draw to minimize venipunctures in case other bleeding tendencies are present.
- Maintain pressure on venipuncture sites a bit longer than for normal dogs in case there is a more widespread bleeding disorder present.
- Avoid cystocentesis urine collection until cause of hemothorax has been identified.
- Collect effusion as aseptically as possible; in occasional cases, especially traumatic hemothorax, hemorrhagic effusion may be autotransfused.

CLIENT EDUCATION

Most cases of hemothorax can be avoided by minimizing risk of trauma and access to anticoagulant rodenticides.

SUGGESTED READING

Nakamura R, Rozanski E, Rush J: Non-coagu-lopathic spontaneous hemothorax in dogs. J Vet Emerg Crit Care 18(3):292–297, 2008.

Prittie J, Barton L: Hemothorax and sanguineous effusions. In King LG, editor: Textbook of respiratory disease in dogs and cats, St Louis, 2004, Saunders, p 610.

AUTHOR: ERICK SPENCER

EDITOR: RANCE K. SELLON

Hemorrhagic Gastroenteritis

BASIC INFORMATION

DEFINITION

Acute and profuse hematemesis and hemorrhagic diarrhea accompanied by hypovolemia; may progress to circulatory collapse, multiple organ dysfunction and death

SYNONYMS

Acute hemorrhagic enteritis, acute hemorrhagic enteropathy, HGE

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs, usually young (mean of 5 years)

GENETICS & BREED PREDISPOSITION: Hemorrhagic gastroenteritis (HGE) can occur in any breed; toy and small breed dogs may be predisposed.

RISK FACTORS: None known; most dogs are otherwise healthy.

CONTAGION & ZOONOSIS: Does not appear to be contagious or zoonotic

GEOGRAPHY AND SEASONALITY: More prevalent in urban dogs

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Anorexia and lethargy may be noted initially.
- Acute onset of vomiting; this may be profuse and often contains fresh blood.
- Acute onset of diarrhea; this may be brown initially but soon becomes grossly bloody; consistency varies from watery to jamlike.

PHYSICAL EXAM FINDINGS

- Depressed but afebrile
- Markers of perfusion: heart rate, pulse quality, gum color, capillary refill time (CRT) are all normal in the early stages of the disease. As fluid is lost into the gastrointestinal tract, signs of hypovolemia quickly develop, characterized by pallor, slow CRT, and tachycardia.
- Skin turgor may not reflect the full extent of fluid losses. Patients may be moribund at presentation if veterinary attention is delayed.
- Abdominal palpation reveals fluid-filled bowel loops with nonlocalized discomfort.
- Rectal examination: fresh dark blood or strawberry jam–like feces.

ETIOLOGY AND PATHOPHYSIOLOGY

- Cause unknown, but an anaphylactic reaction to unidentified bacterial antigens has been implicated.
- *Clostridium perfringens* enterotoxins and enteropathogenic/enterotoxigenic *E. coli* have been associated with HGE, but causal relationships have not been demonstrated.
- Peracute, massive increase in intestinal permeability results in extravasation of fluid, proteins, and red blood cells into the intestinal lumen.
- Loss of plasma water, electrolytes, and protein can be extreme. Packed cell volume will rise rapidly and often exceeds 65%.
- If untreated, disease can progress to hypovolemic shock and death.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A presumptive diagnosis (sufficient to start treatment) is made based on acute gastroenteritis associated with erythrocytosis (hematocrit often >65%). Dogs with HGE can die unless the disorder is recognized quickly and treated aggressively. It is important to rule out other possible causes of bloody vomiting and diarrhea, but treatment should not be delayed while diagnostic tests are performed.

DIFFERENTIAL DIAGNOSIS

- Infectious: viral (parvovirus) or bacterial *(Salmonella, Campylobacter enteritidis)*
- Dietary indiscretion, toxicity
- Hypoadrenocorticism
- Intestinal volvulus, partial obstruction or intussusception
- Other causes of hypovolemic or endotoxic shock, such as intestinal perforation, peritonitis
- Necrotizing pancreatitis
- Coagulopathy

INITIAL DATABASE

- Hematocrit is classically elevated, often >65%; total solids are low or borderline normal.
- CBC: expect to see hemoconcentration with a stress leukogram; immature neutrophils or mild toxicity may be noted; modest thrombocytopenia is common.
- Serum biochemistry profile: increased blood urea nitrogen and alanine aminotransferase activity are expected; hypokalemia and panhypoproteinemia are also common; metabolic acidosis may be severe.
- Urinalysis: unremarkable; high specific gravity expected in response to hypovolemia
- Coagulation profile: usually normal early on; may show abnormalities if condition progresses to disseminated intravascular coagulation (DIC)
- Fecal evaluation (centrifuged flotation and saline preparation): no pathogens noted
- Fecal stained microscopic exam: increased numbers of red cells, some white cells; organisms consistent with clostridial spores (“safety pins”) may be present.
- Fecal ELISA for parvovirus (if neonate or unvaccinated): negative
- Abdominal radiographs: fluid and gas-filled small-intestinal loops; colon may be empty.
- Colloid oncotic pressure (COP): usually normal at presentation but then declines
- +/− Cortisol (if breed type or other clinical findings suggest hypoadrenocorticism): baseline cortisol should be >2 µg/dL/55 nmol/L.

TREATMENT

TREATMENT OVERVIEW

- Quickly restore and maintain an effective circulating volume.
- Recognize the need for colloid support along with crystalloid fluid replacement.
- Anticipate complications of hypovolemia and widespread gastrointestinal mucosal compromise.

ACUTE GENERAL TREATMENT

- Initiate fluid resuscitation with IV fluid therapy:
  - Colloids (e.g., Hetastarch) should be started immediately. Administer a bolus of 5 mL/kg over 20 minutes if the patient is substantially hypovolemic; otherwise begin a continuous rate infusion of 1 mL/kg/h; total daily dose should not exceed 20 mL/kg.
  - Crystalloid fluids should be administered concurrently. Replacement-type fluids should be used (e.g., Normosol-R, lactated Ringer's, Plasmalyte 148, 0.9% NaCl). If necessary, calculate a shock dose of crystalloids (90 mL/kg), and bolus one-third of this amount over 20-30 minutes. Do not administer Normosol-R rapidly, as this fluid contains acetate and may cause refractory hypotension.
  - Aim to replace lost volume (estimated by % dehydration × body weight in kg) over 12 hours.
  - Continue fluids at a rate necessary to replace ongoing losses and meet maintenance requirements.
  - If available, use COP measurement to guide colloid administration.
- Electrolyte disturbances are common; hypokalemia should be addressed specifically, but changes in sodium and chloride should self-correct with standard fluid therapy.
- Antibiotics are recommended, given the potential for bacterial translocation across the intestinal epithelium.
  - Ampicillin: 30 mg/kg IV q 8 h (adequate choice in most cases); *or*
  - Ampicillin/sulbactam (Unasyn): 50 mg/kg IV q 8 h (effective against β-lactamase-producing bacteria); *or*

- Enrofloxacin: 10 mg/kg slow IV q 24 h (if sepsis is suspected)
- Antiemetics should be administered if vomiting is persistent
  - Maropitant (1 mg/kg SQ q 24 h) is an effective first choice (patient must be >16 weeks old); *or*
  - Metoclopramide (1.1-2.2 mg/kg/24 h given as constant rate infusion)
- Antacids and gastric protectants should be administered in patients with hematemesis
  - Famotidine (0.5 mg/kg IV or SQ q 12-24 h); *and/or*
  - Sucralfate (250-1000 mg/dog PO q 8 h); begin when vomiting has stopped

NUTRITION/DIET

- Withhold water until vomiting is adequately controlled, then offer small amounts every 1-2 hours.
- Food should be provided as soon as the patient is interested in eating and vomiting is reduced. Easily digestible diets may be beneficial (e.g., boiled white rice with cottage cheese or boiled chicken), as gastric emptying times are shorter, and fecal volume is minimized.
- Probiotics +/− prebiotics should be considered, as disruption of the normal intestinal flora is both a likely cause and consequence of HGE.

POSSIBLE COMPLICATIONS

- Condition may progress to hypovolemic shock, DIC, and death if not treated appropriately.
- Esophagitis may occur if vomiting is persistent.
- Obtunded patients are vulnerable to aspiration pneumonia.
- Translocation of bacterial across the compromised gastrointestinal mucosa may result in sepsis.
- Cardiac arrhythmias can occur secondary to poor perfusion.

DRUG INTERACTIONS

Metoclopramide is incompatible with many antibiotics (including ampicillin); the infusion must be discontinued while other medications are administered.

RECOMMENDED MONITORING

- Monitor vital parameters (temperature, heart rate, mucous membranes, CRT, pulse quality, blood pressure) and ongoing fluid losses every 2 hours.
- Hematocrit and total solids every 4-6 hours.
- Glucose, BUN, and electrolytes should be checked every 6-8 hours initially.
- COP should be checked every 6-8 hours or as needed to guide decisions about colloid therapy.

PROGNOSIS AND OUTCOME 

- Recovery is usually rapid and complete over 1-2 days; some severely affected dogs may require supportive therapy for several days before return of normal GI function.
- Condition can progress quickly to multiple organ dysfunction syndrome, DIC, and death without appropriate fluid therapy.
- A total of 10% of affected dogs may die despite therapy.

PEARLS & CONSIDERATIONS 

COMMENTS

- The diagnostic hallmark for HGE is a markedly elevated hematocrit with normal to slightly low total protein.
- Colloid support is often essential and should not be overlooked.
- Rule out hypoadrenocorticism, especially in a high-risk breed (e.g., Nova Scotia Duck Tolling Retriever Portuguese water dog, standard poodle, West Highland white terrier).

CLIENT EDUCATION

A total of 10%-15% of dogs will have repeated episodes of HGE.

SUGGESTED READING

Boag AK, Hughes D: Assessment and treatment of perfusion abnormalities in the emergency patient. Vet Clin North Am Small Anim Pract 35:319, 2005.

AUTHOR: AUDREY K. COOK

EDITOR: DEBRA L. ZORAN

1ST EDITION AUTHOR: AMIE KOENIG

Hemorrhage

BASIC INFORMATION

DEFINITION

- The loss of blood from the vascular space into surrounding tissues or from body surfaces
- Clinical signs of hemorrhage result from one of two general mechanisms:
  - Blood loss from damaged or diseased blood vessels
  - Bleeding diatheses: defects causing failure of normal hemostatic processes

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs and cats of all breeds and either sex may be affected, with specific predilections depending on underlying cause. Blood vessel defects are generally acquired disorders, whereas bleeding diatheses may be hereditary traits (e.g., von Willebrand disease) or acquired disorders (e.g., coagulopathy of rodenticide poisoning).

GENETICS & BREED PREDISPOSITION

See pp. 491, , and online chapter: Platelet Dysfunction.

RISK FACTORS: See pp. 491, , and .

ASSOCIATED CONDITIONS & DISORDERS

- Blood vessel defects typically arise from:
  - Traumatic or surgical injuries
  - Inflammatory or neoplastic conditions causing vessel erosion and infiltration
- Bleeding diatheses are classified as:
  - Failure of platelet plug formation (primary hemostatic defects)
  - Failure of fibrin clot formation (secondary hemostatic defects = coagulopathies)
- Disease conditions such as hypertension, anemia, and hyperviscosity alter the normal flow properties of blood (hemorrheology) and are associated with microvascular hemorrhage.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Subtype classification based on:

- Duration: acute versus chronic hemorrhage
- Location: focal or regional versus multiple anatomic sites
- Tissue or vessel involvement: capillary bleeding versus hemorrhage into joint space, body cavities
  - Primary hemostatic defects (failure of platelet plug formation [e.g., from thrombocytopenia or platelet dysfunction] cause signs of hemorrhage involving capillaries and small vessels [arterioles, venules], clinically evident as petechiae, ecchymoses, bleeding from mucosal surfaces, and nonspecific bleeding from surgical and traumatic wounds).
  - Secondary hemostatic defects (coagulopathies; failure of fibrin clot formation [e.g., from coagulation factor deficiency]) generally cause spontaneous hemorrhage into body cavities or potential spaces (i.e., pleural space, intramuscular tissue planes), resulting in hemothorax, hemoabdomen, hemarthrosis, hematoma formation, and nonspecific bleeding from surgical and traumatic wounds.

HISTORY, CHIEF COMPLAINT: Depends on underlying cause. Frank hemorrhage, hematoma formation, and petechiae are obvious signs that may prompt owners to seek veterinary care. Additional signs include pallor and collapse due to acute hemorrhagic shock, or gradual onset of weakness due to chronic blood-loss anemia.

PHYSICAL EXAM FINDINGS

- Physical exam alone may differentiate vessel defects from systemic bleeding diatheses:
  - Frank hemorrhage due to traumatic or surgical blood vessel injury, or vessel infiltration due to solid tumors or inflammatory mass lesions, may be obvious on physical exam or via ancillary diagnostics (endoscopy, radiography).
  - Petechiae evident on cutaneous or mucosal surfaces or funduscopic exam indicate primary hemostatic defect.

    - Retinal hemorrhage and alterations of the normal retinal vasculature may result from abnormal blood flow (hemorrheologic defects such as systemic hypertension, hyperviscosity, anemia).
- Other signs are nonspecific (epistaxis, hematuria, melena, hematemesis, hemothorax, hemoabdomen).
- Hemorrhage from multiple anatomic sites and/or recurrent episodes are suggestive of a bleeding diathesis rather than blood vessel defects.

ETIOLOGY AND PATHOPHYSIOLOGY

- Blood vessel defects: physical disruption, as described above
- Bleeding diatheses:
    - Acquired primary hemostatic defects:
        - Thrombocytopenia is the most common bleeding diathesis.
        - Platelet dysfunction
    - Hereditary primary hemostatic defects:
        - Platelet dysfunction/thrombopathia
        - von Willebrand disease
    - Acquired coagulopathies (secondary hemostatic defects):
        - Vitamin K deficiencies (anticoagulant rodenticide intoxication, biliary obstruction, chronic oral antibiotic administration, warfarin overdose, neonatal)
        - Hepatic synthetic failure (hepatic necrosis, atrophy, portosystemic shunts)
        - Consumptive coagulopathy (disseminated intravascular coagulation [DIC])
        - Drug intoxications, envenomation, complication of heparin, hetastarch, dextran, fibrinolytic drug therapy
        - Dilutional coagulopathy: platelet and/or factor deficiency secondary to massive transfusion with stored blood products or high-volume fluid administration
    - Hereditary coagulopathies (secondary hemostatic defects):
        - Hemophilia
        - Autosomal factor deficiencies

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Vascular injury is by far the most common cause of hemorrhage, and clinicians should begin with a thorough physical exam to identify a source of injury. If history and exam are inconsistent with injury, a prompt evaluation for hemostatic defects is warranted to avoid delays in treatment.

DIFFERENTIAL DIAGNOSIS

Blood vessel defect versus bleeding diathesis:

- Initial physical exam and imaging studies may define the site and cause of vessel defects.
- If a vessel defect cannot be defined on physical exam, blood pressure measurement and screening tests to rule out bleeding diatheses must be performed *before* performing invasive procedures.

INITIAL DATABASE

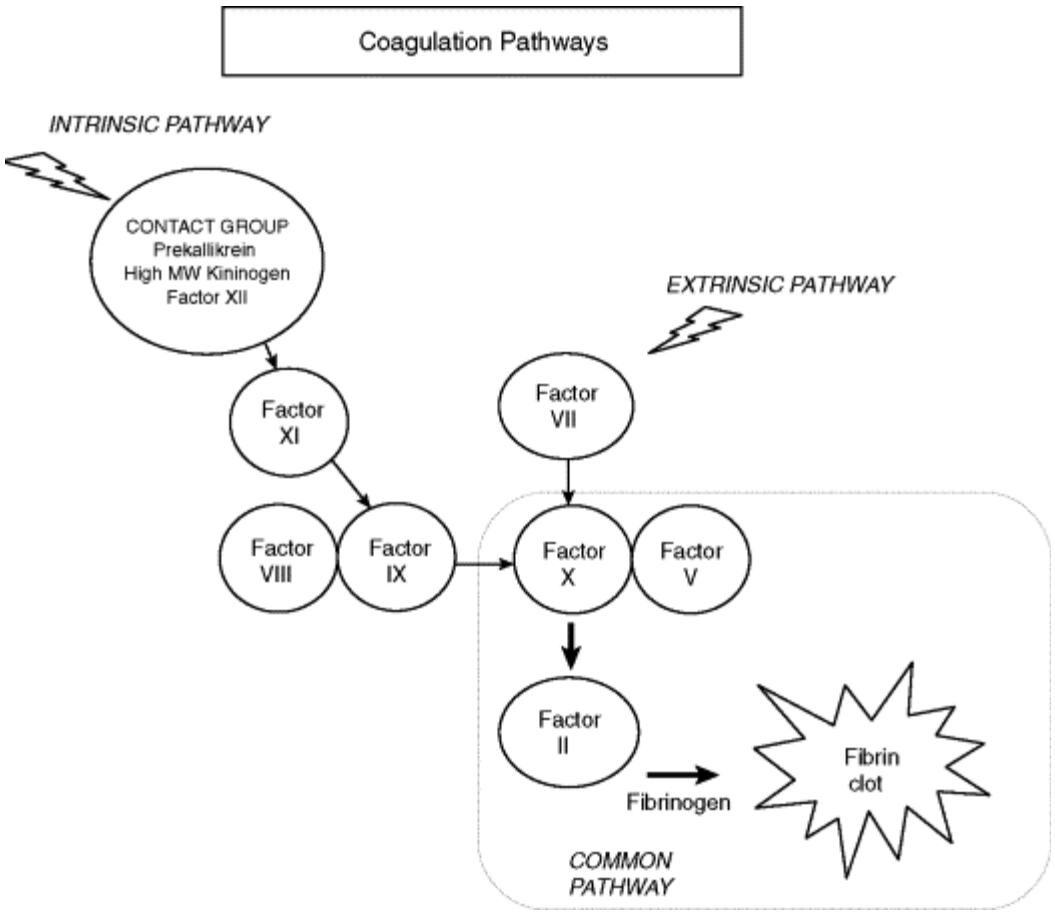
- Thorough physical exam to define nature and location of hemorrhage
- Baseline hematocrit and plasma protein
- Platelet count
- Blood pressure measurement:
    - Normal in calm setting, awake and resting patient, repeatable measures using Doppler: systolic <180 mm Hg (dog, cat)
    - Hypertension and other cause(s) of hemorrhage may coexist.
- Coagulation screening tests: if evidence points to bleeding diathesis:
    - Activated clotting time (ACT; see p. 1440):
        - Expected time to fibrin clot end-point ~120 seconds (dogs and cats)
        - Deficiencies of the intrinsic or common pathway factors cause prolongation of the ACT.
        - Normal values should be established for each test method.
    - Activated partial thromboplastin time (APTT; see p. 1441):
        - The APTT, like ACT, is sensitive to deficiencies of intrinsic or common pathway factors; however, APTT is generally a more specific and reproducible test than the ACT.
        - Long APTT is seen in hereditary coagulopathies such as hemophilia and in combined factor deficiencies such

as rodenticide intoxication and DIC.
        - Prolongation of APTT to a target value of 1.5-2 times baseline is used for adjusting unfractionated heparin dosage.
        - Hemorrhage caused by blood vessel defects or primary hemostatic defects (platelet abnormalities) should not produce abnormal APTT results.
    - Prothrombin time (PT; see p. 1513):
        - Test is sensitive to deficiencies of extrinsic and common pathway factors.
        - Specific prolongation of PT is an indication of factor VII deficiency. Because factor VII is vitamin K–dependent with short plasma half-life (3-6 hours), prolongation of PT develops in conditions causing vitamin K deficiency (e.g., anticoagulant rodenticide, severe hepatopathy).
        - The anticoagulant effect of warfarin and its dosage adjustments are based on prolongation of PT and its standardized derivative, the international normalized ratio (INR).
        - PIVKA (proteins induced by vitamin K absence or antagonism) testing performed using the Thrombotest assay provides information equivalent to the PT.
        - Hemorrhage caused by blood vessel defects or primary hemostatic defects (platelet abnormalities) should not produce abnormal PT results.
    - Thrombin clotting time (TCT) and fibrinogen:
        - Detect a lack of clottable fibrinogen
        - Long TCT and low fibrinogen develop in patients with severe hepatic insufficiency (due to synthetic failure) or dilutional coagulopathy and hemorrhagic DIC (due to depletion of fibrinogen).
        - Vitamin K deficiency does not prolong TCT or decrease fibrinogen values.
        - Hemorrhage caused by blood vessel defects or primary hemostatic defects (platelet abnormalities) should not produce abnormal TCT or fibrinogen results.
- Coagulopathies cause prolongation of one or more coagulation screening tests:
    - The pattern of abnormalities depends on which factor or groups of factors are deficient (see p. 491).
    - Expected coagulation screening test results for common coagulopathies:
        - Vitamin K deficiencies: prolonged ACT, APTT, and PT (but fibrinogen and TCT are normal) due to impaired activation of factors II, VII, IX, and X.
        - Severe hepatic synthetic failure causes deficiencies of all factors and fibrinogen. ACT, APTT, PT, TCT are long and fibrinogen is low.
        - Hemorrhagic DIC typically results in depletion of all factors and fibrinogen. Mild to severe prolongation of clotting times and low fibrinogen accompany hemorrhagic DIC. In contrast, high fibrinogen may accompany thrombotic DIC and other hypercoagulable syndromes.
        - Hemorrhage due to anticoagulant drug overdose or envenomation causes factor inhibition or fibrinogen depletion. All coagulation screening tests will detect severe drug overdose; however APTT and PT are preferentially sensitive to unfractionated heparin and warfarin levels, respectively.

ADVANCED OR CONFIRMATORY TESTING

Based on results of initial database:

- Thrombocytopenia workup may include repeat evaluation, including fresh blood smears, to rule out collection/laboratory artifact; bone marrow, spleen, and lymph node aspiration and cytologic evaluation; serologic evaluation to detect evidence of pathogens; platelet-associated antibody testing.
- Evaluation for platelet dysfunction (see online chapter: Platelet Dysfunction).
- Ancillary diagnostics to differentiate coagulopathies include specific coagulation factor analyses, determinations of antithrombin activity and fibrin breakdown products, and drug detection (e.g., heparin or warfarin levels).



HEMORRHAGE The coagulation cascade.

TREATMENT OVERVIEW

The two main goals are to control active bleeding and stabilize the patient with one or more of the following: local wound care, supportive medical therapy, and/or transfusion therapy. It is important to collect pretreatment samples to perform screening and confirmatory tests.

ACUTE GENERAL TREATMENT

- Hemorrhagic/hypovolemic shock: volume replacement (intravenous fluid therapy), red cell replacement (see p. 1347)
- Blood vessel injuries: control bleeding after visualization of the damaged vessels (physical examination, endoscopic examination, ultrasound examination, or surgical exploration).
- Bleeding diatheses: identify and correct the underlying cause of acquired bleeding diatheses; transfusion if needed to correct hereditary defects or pending response to medical management.

CHRONIC TREATMENT

Depends on underlying cause of hemorrhage

DRUG INTERACTIONS

Avoid drugs with anticoagulant or antiplatelet effects (e.g., nonsteroidal antiinflammatory drugs, clopidogrel, sulfonamides, heparin, warfarin, plasma expanders, estrogens, cytotoxic drugs)

POSSIBLE COMPLICATIONS

- Uncontrolled hemorrhage and hemorrhagic shock are potentially fatal conditions.
- Chronic hemorrhage may result in iron-deficiency anemia, requiring iron supplementation for appropriate bone marrow response.

RECOMMENDED MONITORING

Resolution of hemorrhage is demonstrated by:

- Cessation of active bleeding
- Fading of petechiae, absence of development of new lesions
- Stabilization and normalization of hematocrit/plasma protein
- Correction of low platelet count and/or long clotting times

PROGNOSIS AND OUTCOME

Depends on:

- Initial stabilization and correction of hemorrhagic shock
- Ability to identify and correct vessel defect or cause of acquired bleeding diatheses
- Ability to diagnose and manage hereditary bleeding diatheses

PEARLS & CONSIDERATIONS

COMMENTS

- Blood vessel injury or infiltration is by far the most common cause of hemorrhage.
- Screening for common bleeding diatheses by performing platelet count and ACT (or point-of-care APTT and PT) is indicated early in the diagnostic workup of patients with hemorrhage.
- Anticoagulant rodenticide intoxication is a common acquired coagulopathy. Vitamin K therapy (vitamin K1, 2 mg/kg PO or SQ q 24 h) and plasma transfusion (if severe hemorrhage) should be initiated pending results of coagulation screening, regardless of specific history of product ingestion (see p. 83).
- Results of coagulation tests (PT, APTT) that are below the normal range do not indicate hypercoagulability.

SUGGESTED READING

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AUTHOR: MARJORY B. BROOKS

EDITOR: SUSAN M. COTTER

Hemoptysis

BASIC INFORMATION

DEFINITION

Expectoration or coughing up of blood or blood-stained sputum from the respiratory tract

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dependent on underlying cause
- Young pure-breed animals: coagulopathies
- Young to middle-aged animals: infectious diseases, trauma
- Older animals: neoplasia

GENETICS & BREED PREDISPOSITIONS: von Willebrand disease (many canine breeds; cats: Himalayan), hemophilia (dogs: many breeds; cats: British shorthair, Siamese)

RISK FACTORS

- Coagulopathies:
  - Immune-mediated disease: young to middle-aged, small to medium female dogs
  - Rickettsial disease: dogs living in or traveling to endemic areas
  - Thrombasthenia: otter hounds
  - Thrombopathia: basset hounds
  - von Willebrand disease: Doberman pinschers, Airedales, German shepherds, Scottish terriers, Chesapeake Bay retrievers, and many other breeds; cats
  - Hemophilia A: German shepherds and many other breeds; cats
  - Hemophilia B: Cairn terriers, coonhounds, St. Bernards, and other breeds; cats
- Pulmonary thromboembolism:
  - Neoplasia
  - Hyperadrenocorticism
  - Cardiac disease
  - Immune-mediated hemolytic anemia

CONTAGION & ZOONOSIS: Systemic fungal infections (risk of common-source infection)

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Some or all may be present:

- Coughing up of blood: usually foamy consistency
- Hematemesis: from swallowing blood from the respiratory tract
- With coagulopathy: hematochezia, melena, hematuria, or hemorrhage from other areas of the body
- With pulmonary disease: coughing, exercise intolerance, dyspnea, syncope

PHYSICAL EXAM FINDINGS

- Melena: from swallowing blood
- Nasal hemorrhage
- With coagulopathy: possibly petechiae, ecchymoses, hematomas, hematochezia, melena, hematuria, retinal hemorrhages

ETIOLOGY AND PATHOPHYSIOLOGY

Bleeding disorder:

- Thrombocytopenia:

    - Immune-mediated disease: idiopathic disease, systemic lupus erythematosus, drug reaction
    - Rickettsial disease: ehrlichiosis, Rocky Mountain spotted fever
    - Bone marrow disease: neoplasia, aplastic anemia, infectious (fungal, rickettsial, or viral)
    - Disseminated intravascular coagulation (DIC)
- Thrombopathia:
    - Congenital: von Willebrand disease, thrombasthenia, thrombopathia
    - Acquired: nonsteroidal antiinflammatory drugs, hyperglobulinemia (ehrlichiosis, multiple myeloma), uremia, DIC
- Coagulation factor defect:
    - Congenital: hemophilia A (factor VIIIc deficiency) and hemophilia B (factor IX deficiency)
    - Acquired: anticoagulant rodenticide (warfarin) intoxication, hepatobiliary disease, DIC

Pulmonary Disease:

- Pulmonary hypertension
- Pulmonary thromboembolism
- Trauma
- Foreign body
- Bronchiectasis
- Infection: fungal (blastomycosis, histoplasmosis, coccidioidomycosis), bacterial, or parasitic (*Paragonimus kellicotti*, *Capillaria aerophila*, *Aelurostrongylus abstrusus*, *Filaroides hirthi*)
- Neoplasia: primary or secondary
- Lung lobe torsion

Cardiovascular Disease:

- Heartworm
- Severe cardiogenic pulmonary edema
- Arteriovenous fistula

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is either a part of the chief complaint or is noted during hospitalization. Diagnostic testing first must evaluate the possibility of a systemic disorder (bleeding disorder, systemic hypertension). If none, evaluation of the pharynx and respiratory system typically begins with oral examination, thoracic radiographs, and sedated pharyngeal examination as needed.

DIFFERENTIAL DIAGNOSIS

See Etiology and Pathophysiology above.

INITIAL DATABASE

- CBC:
    - Anemia: if sufficient hemorrhage has occurred
    - Thrombocytopenia
    - Neutrophilia: stress; infection; neoplasia
    - Pancytopenia: bone marrow disease
- Urinalysis:
    - Usually normal
    - Hematuria with coagulopathy
    - Avoid sampling by cystocentesis until coagulation status is known
- Biochemistry profile:
    - Hypoproteinemia: if enough hemorrhage has occurred
    - High blood urea nitrogen with normal creatinine: possible, owing to gastrointestinal blood
    - Hyperglobulinemia: ehrlichiosis, multiple myeloma
    - High alanine aminotransferase (ALT), aspartate aminotransferase (AST), and total bilirubin: severe hepatic disease with coagulopathy possible

ADVANCED OR CONFIRMATORY TESTING

- Other laboratory tests:

- Coagulation profile: prolonged times with coagulation factor defects; normal with thrombocytopenia and thrombopathia
- Platelet function testing (e.g., bleeding time, von Willebrand factor analysis): for suspected coagulopathy despite normal platelet count and coagulation profile
- *Ehrlichia* and Rocky Mountain spotted fever titers/PCR
- Blood gas analysis (pulmonary disease)

- Diagnostic imaging:
  - Thoracic radiographs: pulmonary/cardiac disease, thoracic trauma, metastatic disease
  - CT scan: more sensitive than radiographs for some diseases, but requires general anesthesia
  - Echocardiography
- Other diagnostic procedures:
  - Bronchoscopy: examine lower airways, remove foreign bodies, bronchoalveolar lavage.
  - Cytologic and histopathologic examination and bacterial and fungal culture and sensitivity testing: lung tissue sample
  - Fine-needle aspirate/lung biopsy: pulmonary masses
  - Scintigraphy: ventilation/perfusion scan

TREATMENT

TREATMENT OVERVIEW

Stop the hemorrhage, and treat the primary cause.

ACUTE GENERAL TREATMENT

- Establish a patent airway.
- Oxygen supplementation
- Minimize activity or stimuli that precipitate hemorrhage episodes.
- Whole blood or packed red blood cell transfusion may be needed with severe anemia.

SPECIFIC TREATMENT

- Bleeding disorder:
  - von Willebrand disease: plasma or cryoprecipitate for acute bleeding (see p. 1347)
  - Hemophilia A: plasma or cryoprecipitate for acute bleeding; no long-term treatment
  - Hemophilia B: plasma for acute bleeding; no long-term treatment
  - Anticoagulant rodenticide intoxication: plasma for acute bleeding and vitamin K supplementation
  - Liver disease and DIC: treat and support the underlying cause; plasma may be beneficial.
  - Discontinue all nonsteroidal antiinflammatory drugs.
- Pulmonary disease:
  - Pulmonary hypertension: treat underlying etiology.
  - Pulmonary thromboembolism: treat underlying etiology.
  - Infection: treat specific infectious etiology.
  - Neoplasia: surgery
  - Lung lobe torsion: surgery
- Cardiovascular disease:
  - Heartworm: specific therapy
  - Cardiogenic pulmonary edema: diuretics, venodilators, oxygen supplementation
  - Arteriovenous fistula: surgery

POSSIBLE COMPLICATIONS

- Anemia
- Collapse state
- Respiratory failure

RECOMMENDED MONITORING

- Hematocrit
- Platelet count with thrombocytopenia
- Coagulation profile with coagulation factor defects
- Blood pressure with hypertension
- Monitor clinical signs

PROGNOSIS AND OUTCOME

Dependent on cause.

PEARLS & CONSIDERATIONS

COMMENTS

- Hemoptysis not a diagnosis but a clinical sign.
- Consider systemic diseases and cardiovascular diseases as well as primary pulmonary conditions.

CLIENT EDUCATION

Monitor for recurrence of presenting signs (coughing up of blood, presence of blood-stained sputum).

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Gieger T: Bleeding disorders: epistaxis and hemoptysis. In Ettinger SJ, Feldman EC, editors: Textbook of veterinary internal medicine, ed 6, Philadelphia, 2006, WB Saunders, pp 225–231.

AUTHOR: REMO LOBETTI

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Hemophilias and Other Hereditary Coagulation-Factor Deficiencies

BASIC INFORMATION

DEFINITION

Congenital hemostatic defects caused by mutations that impair the production of active clotting factors

SYNONYMS

Specific defects are classified by the deficient factor, with alternate names in common use for factors I, VII, VIII, and IX:

Hemophilias and Other Hereditary Coagulation-Factor Disorders

Deficient Factor	Alternate Name
Fibrinogen (factor I)	Dysfibrinogenemia, hypofibrinogenemia
Factor II	Prothrombin deficiency
Factor VII	Proconvertin or extrinsic factor deficiency
Factor VIII	Hemophilia A or classic hemophilia
Factor IX	Hemophilia B or Christmas disease
Factor X	Stuart Prower deficiency
Factor XI	Hemophilia C
Factor XII	Hageman trait

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs and cats: severe bleeding disorders typically manifest by age 6-12 months.
- Males almost exclusively affected in hemophilia A and B (factor VIII and factor IX deficiencies)
- Males and females equally affected in all other factor deficiencies

GENETICS & BREED PREDISPOSITION

- X-linked recessive inheritance pattern: hemophilias A and B
- Autosomal recessive (or incomplete dominant): all other factor deficiencies
- Breed predisposition:
  - Dogs: hemophilia A is the most common hereditary coagulation defect and may develop in any purebred or mixed-breed dog (presumably due to de novo mutations). A mild to moderate form of hemophilia A has been propagated widely in German shepherds. Less common defects: factor VII deficiency in beagles, factor X deficiency in Jack Russell terriers, factor XI deficiency in Kerry blue terriers.
  - Cats: hemophilia A and B in any breed and domestic cats. Factor XII deficiency is the most common hereditary factor deficiency in domestic and Siamese cats. Combined deficiency of factors II, VII, IX, and X in Devon rex cats.
  - Note: mutations causing factor deficiencies can arise in any breed.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Severe bleeding tendency: deficiencies of factors I, II, VIII, IX, and X
- Mild to moderate bleeding tendency: deficiencies of factors VII, XI, and some forms of factor VIII and IX deficiency
- No clinical signs: factor XII deficiency

HISTORY, CHIEF COMPLAINT

- Severe forms: spontaneous and recurrent hematoma formation, weakness, or dyspnea due to bleeding into body cavities, lameness due to hemarthrosis, prolonged and potentially fatal bleeding from loss of deciduous teeth or minor wounds
- Mild forms: few spontaneous or severe bleeds, abnormal bleeding typically observed after surgical or traumatic injury

PHYSICAL EXAM FINDINGS

- Abnormal hemorrhage:
  - Manifestations of hemorrhage into body cavities or potential spaces (hemarthrosis, hematoma, hemoabdomen, hemothorax, central nervous system hemorrhage)
  - Bleeding from traumatic/surgical wounds
  - Occasionally epistaxis or intraocular bleeds
  - In contrast to platelet disorders, factor deficiencies rarely cause petechiae or ecchymoses.
- Pallor (blood-loss anemia)

ETIOLOGY AND PATHOPHYSIOLOGY

- Specific factor deficiencies are caused by mutations in the corresponding coagulation factor genes.
- De novo mutations occur most often in the factor VIII gene.
- Mutations causing mild to moderate clinical signs are more likely to become widely propagated in a breed or line.
- Although factor XII deficiency causes prolongation of the activated clotting time (ACT) and activated partial thromboplastin time (APTT) coagulation screening tests, it does *not* cause a clinical bleeding tendency.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Relatively high prevalence of hemophilia warrants coagulation screening tests be performed early in the diagnostic workup of any male with signs of spontaneous or abnormal hemorrhage.

DIFFERENTIAL DIAGNOSIS

- Acquired coagulation disorder (e.g., rodenticide intoxication, liver disease, disseminated intravascular coagulation)
- Thrombocytopenia
- Hereditary platelet function defect or von Willebrand disease
- Bleeding caused by tissue injury or infiltrative disorder
- Defect of fibrinolysis

INITIAL DATABASE

- Thorough physical exam to define site(s) of hemorrhage. Hemorrhage from more than a single site suggests a hemostatic defect rather than blood loss from damaged or diseased blood vessels.
- Baseline hematocrit and plasma protein
- Platelet count: usually normal unless brisk hemorrhage (platelet loss)
- Point-of-care coagulation screening tests (*, markedly abnormal):
  - ACT: prolonged (factors I, II, VIII, IX, X, XI, and XII deficiencies) or normal (factor VII deficiency)
  - APTT: prolonged (factors I, II, VIII, IX, X, XI*, and XII* deficiencies) or normal (factor VII deficiency)
  - Prothrombin time (PT): prolonged (factors I, II, VII, and X deficiencies) or normal (factors VIII, IX, XI, and XII deficiencies)
- Laboratory coagulation panel:
  - APTT, PT: as above
  - Fibrinogen: low (factor I deficiency), normal for others
  - Thrombin clotting time: prolonged (factor I deficiency), normal for others

ADVANCED OR CONFIRMATORY TESTING

Definitive diagnosis based on identifying low levels of specific coagulation factors:

- Clottable fibrinogen (factor I)
- Coagulant activity assays (factors II through XII)

TREATMENT

TREATMENT OVERVIEW

Patients with confirmed factor deficiencies but without clinical signs should receive a prophylactic transfusion prior to surgery. Patients with confirmed factor deficiencies who are actively bleeding may require repeated transfusions and, rarely, withdrawal of blood if compromising vital functions (e.g., large-volume pleural effusion). In both categories of patients, avoidance of unnecessary surgery or trauma are important.

ACUTE GENERAL TREATMENT

- Transfusion to supply hemostatic levels of the deficient factor:
  - Use of plasma components reduces risk of intravascular volume overload and red cell sensitization while maximizing factor replacement.
  - Fresh frozen plasma (10-12 mL/kg IV):
    - "Broad-spectrum" replacement therapy for deficiencies of fibrinogen and factors II through XI
  - Cryoprecipitate (unit dosage varies for different suppliers):
    - Replacement therapy for fibrinogen defects and factor VIII deficiency
  - Cryopoor plasma or cryosupernatant (10-12 ml/kg IV):
    - Replacement therapy for factors II, VII, IX, X, and XI deficiencies
- Replacement of red cells for severe blood-loss anemia:
  - Fresh whole blood (12-20 mL/kg) or packed red cells (6-12 mL/kg) (see p. 1347)

CHRONIC TREATMENT

- Intermittent transfusion as needed to control hemorrhagic events
- Preoperative transfusion to prevent abnormal bleeding
- Avoidance of unnecessary invasive procedures

BEHAVIOR/EXERCISE

- Strenuous activity should be avoided to help limit intraarticular hemorrhage.
- Hemophilic cats should remain indoors, dogs should be supervised when outdoors.
- Owners must balance quality of life with reasonable exercise restriction.

DRUG INTERACTIONS

Avoid drugs with anticoagulant or antiplatelet effects (e.g., nonsteroidal antiinflammatory drugs [NSAIDs], clopidogrel, sulfonamides, heparin, warfarin, plasma expanders, estrogens, cytotoxic drugs)

POSSIBLE COMPLICATIONS

- Red cell sensitization causing transfusion reactions:
  - Transfuse plasma components when possible.
  - Feline transfusion: donor and recipient must be type matched for any transfusion.
  - Canine transfusion: after the first red cell transfusion, perform crossmatch before subsequent transfusions.
- Development of inhibitory antifactor antibodies (rare complication)

RECOMMENDED MONITORING

Adequate factor replacement is demonstrated by:

- Cessation of active bleeding
- Stabilization of hematocrit/plasma protein
- Resolution of lameness and hematoma

PROGNOSIS AND OUTCOME

- Mild to moderate factor deficiencies: good quality of life possible; patient may require occasional transfusion.
- Severe factor deficiencies: fair to poor prognosis due to recurrent bleeds and dependence on repeated transfusion; acute

fatal bleeds may occur.

PEARLS & CONSIDERATIONS

COMMENTS

- Hemophilia A (factor VIII deficiency) is the primary rule out for abnormal bleeding in young male dogs and cats.
- Feline factor XII deficiency does not cause a clinical bleeding diathesis and is typically identified in the course of preoperative workup for an acquired disease process.

PREVENTION

- Factor-deficient dogs and cats should never be used for breeding.
- Familial testing is indicated to identify asymptomatic carriers before they are bred.

TECHNICIAN TIPS

- Consider hereditary bleeding disorders (especially hemophilia) in any dog or cat with abnormal hemorrhage. A blue-top tube (sodium citrate anticoagulant) should be drawn for coagulation screening tests (APTT, PT, fibrinogen).

CLIENT EDUCATION

Definitive diagnosis aids in determining prognosis, selecting appropriate transfusion therapy, and genetic counseling.

SUGGESTED READING

Brooks MB: A review of canine inherited bleeding disorders: biochemical and molecular strategies for disease characterization and carrier detection. J Hered 90:112, 1999.

AUTHOR: MARJORY B. BROOKS

EDITOR: SUSAN M. COTTER

Hemolytic-Uremic Syndrome

BASIC INFORMATION

DEFINITION

An uncommon, severe disease characterized by nonimmune-mediated microangiopathic hemolytic anemia, acute renal failure, and thrombocytopenia. This disease in humans is usually associated with Shiga toxin–producing *Escherichia coli* (STEC) infections and diarrhea or (rarely) other gram-negative bacteria that produce Shiga toxins. A similar syndrome has been reported in dogs and cats.

SYNONYMS

Alabama rot, cutaneous and renal glomerular vasculopathy (CRGV) of greyhounds, Greentrack disease

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Mainly dogs; very rare in cats
- No age or sex predilection

GENETICS & BREED PREDISPOSITION: Reported most frequently and originally in racing greyhounds. Genetic predispositions are difficult to evaluate because of outbreaks in affected kennels among littermates with a common food source.

RISK FACTORS: A diet including inappropriately cooked or raw meat may predispose to STEC infections.

CONTAGION & ZOONOSIS: Contaminated beef ingestion is most widely responsible for hemolytic-uremic syndrome (HUS) in humans, and common-source exposure could occur in pets. There have been reports of outbreaks in children associated with petting zoos.

GEOGRAPHY AND SEASONALITY: First noted in Alabama dog racing tracks

ASSOCIATED CONDITIONS & DISORDERS: Similar condition noted in some cats after renal transplantation. Important to distinguish the thrombotic signs of HUS from those associated with disseminated intravascular coagulation (DIC). Prothrombin time is normal or slightly increased, and fibrinogen is normal or high with HUS.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: HUS and cutaneous/renal glomerular vasculopathy are similar, although HUS typically does not have the cutaneous lesions associated with CRGV.

HISTORY, CHIEF COMPLAINT

- History may include feeding raw or undercooked beef. Usually the initial complaint is hemorrhagic diarrhea, although not always reported. Diarrhea episode could have occurred up to 2 weeks before the onset of clinical signs.
- Lethargy or cutaneous lesions may be the primary complaint, as well as vomiting, limb edema, and anorexia.

PHYSICAL EXAM FINDINGS

- In CRGV, cutaneous lesions are multifocal erythematous swellings commonly located on the tarsus, stifle, medial thigh, and rarely forelimb. Lesions may become ulcerated with serosanguineous discharge.
- Physical findings common to both CRGV and HUS include those typical of anemia and acute renal failure, with hemoglobinuria often present.

ETIOLOGY AND PATHOPHYSIOLOGY

- Shiga toxin–producing *E. coli*, usually serotype 0157:H7, causes endothelial injury via circulating Shiga toxins which generate a systemic prothrombotic response, microangiopathic hemolytic anemia, and renal failure.
- Glomerular disease noted in cutaneous and renal glomerular vasculopathy

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is suspected based on the history of exposure to raw or undercooked meat and the clinical signs of diarrhea, possibly cutaneous lesions, and the laboratory signs of azotemia, anemia, +/- thrombocytopenia. Confirmation requires a positive fecal culture on sorbitol MacConkey agar.

DIFFERENTIAL DIAGNOSIS

- Leptospirosis, sepsis, systemic inflammatory diseases
- Any disease causing acute renal failure or vasculitis
- Immune-mediated hemolytic anemia

INITIAL DATABASE

- CBC, serum biochemistry profile, urinalysis
  - Anemia, presence of schistocytes, and thrombocytopenia are typical.
  - Ensure adequate platelet count if renal biopsy is being considered.
  - Azotemia and isosthenuria may precede, coexist with, or be absent. Generally, increased blood urea nitrogen, creatinine, and phosphorus are seen. Hyperkalemia or other electrolyte changes are possible.
  - Proteinuria possible with glomerular disease (cutaneous and renal glomerular vasculopathy)
  - Hemoglobinuria commonly is present (discolored urine; positive blood result on dipstick but no erythrocytes on sediment exam).
- Coagulation panel with D-dimer or fibrin/fibrinogen degradation product (FDP) analysis: evidence of thrombosis (e.g., increased D-dimer or FDPs, decreased platelet count), normal to slightly prolonged PT, increased or normal fibrinogen
- Urine culture: rule out urinary tract infection as cause of proteinuria.
- Arterial blood pressure measurement: rule out systemic hypertension associated with renal disease.

ADVANCED OR CONFIRMATORY TESTING

- Abdominal ultrasound ± renal biopsy. Assess blood pressure and platelet count first.
- Skin biopsy of representative lesions
- Culture of feces on sorbitol MacConkey agar of STEC 0157:H7

TREATMENT

TREATMENT OVERVIEW

Treatment mainly consists of aggressive intravascular fluid-volume replacement, blood transfusions as needed, blood pressure lowering agents as needed, and general supportive care (e.g., nutrition, soft padded bedding, urinary catheter, etc.). Early referral to a regional dialysis center should be considered for animals in acute renal failure.

ACUTE GENERAL TREATMENT

- Aggressive intravascular volume expansion with crystalloids during the diarrhea phase (early) appears to be preventive for the renal failure component of this disease in children.
- Treat oliguric or anuric renal failure intensively (see p. 1369).
  - Transfusion if severe anemia (hematocrit < 18% or physical/laboratory signs of decreased perfusion such as depressed mentation, weak pulses, cold extremities, increased lactate)
  - Consider early referral to a regional dialysis center.
  - After appropriate volume expansion, if urine output deficient and blood pressure adequate, attempt to increase urine output with either mannitol (0.5 g/kg IV over 30 minutes) or if volume overloaded, furosemide (0.2-0.5 mg/kg/h IV constant rate infusion)
- Avoid antibiotics, as several classes (e.g., fluoroquinolones, trimethoprim-sulfa, β-lactams) lead to increased expression of the Shiga toxin and have been associated with increased risk of developing HUS when used during the diarrhea phase in children.
- Avoid NSAIDS and antimotility agents.
- Analgesia is essential, opioids such as fentanyl or morphine should be considered.
- Nutritional support as needed

CHRONIC TREATMENT

Hypertension may be treated with amlodipine (0.05-0.2 mg/kg PO q 24 h).

POSSIBLE COMPLICATIONS

- Hemorrhage from severe thrombocytopenia or disseminated intravascular coagulation
- Bacterial translocation and sepsis from hemorrhagic diarrhea
- Systemic hypertension
- Chronic glomerulonephritis/protein-losing nephropathy
- Poorly healing cutaneous lesions

RECOMMENDED MONITORING

- Perfusion parameters such as mentation, pulse quality, extremity temperature, lactate, and so forth should be monitored frequently (e.g., q 6 h).
- Renal values on serum chemistry (blood urea nitrogen, creatinine, electrolytes)
- Hematocrit and platelet count
- Urine output
- Blood pressure
- Pain

PROGNOSIS AND OUTCOME

- Often a fatal disease if the patient is in acute renal failure and the owner cannot afford referral to a dialysis center
- Survivors may have chronic kidney disease or glomerular disease.

PEARLS & CONSIDERATIONS

COMMENTS

- There are no data to indicate that plasma exchange (which is used for removing antibodies in a similar syndrome, thrombotic thrombocytopenic purpura, in humans) has any benefit.
- Early intensive therapy with intravascular fluids is the key to survival and perhaps prevention once initial sign of hemorrhagic diarrhea is noted.

PREVENTION

For the cases initiated by ingestion of STEC 0157:H7, prevention depends on removal of inadequately cooked beef from diet.

SUGGESTED READING

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EDITOR: DOUGLASS K. MACINTIRE

1ST EDITION AUTHOR: JEFFREY SIMMONS

Hemoabdomen

BASIC INFORMATION

DEFINITION

Hemoabdomen is characterized by the presence of free blood within the peritoneal cavity.

SYNONYM

Hemoperitoneum

EPIDEMIOLOGY

SPECIES, AGE, SEX: Young dogs are more likely to develop hemoabdomen secondary to trauma. Older large-breed dogs without a history of trauma often develop hemoabdomen due to a ruptured splenic or hepatic mass such as hemangiosarcoma.

GENETICS & BREED PREDISPOSITION: Large-breed older dogs are predisposed to hemangiosarcoma.

RISK FACTORS: Dogs that roam may ingest anticoagulant rodenticides, although this rarely results in hemoabdomen.

ASSOCIATED CONDITIONS & DISORDERS: Animals with hemangiosarcoma can develop pericardial effusion due to rupture of a concurrent right atrial hemangiosarcoma.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- History can range from reports of episodes of acute collapse to mild lethargy. Some dogs will present for evaluation of gastrointestinal signs such as vomiting or a distended abdomen. Many dogs have a history of weakness, collapse, or transient polyuria/polydipsia during the weeks before presentation. Presumptively, this indicates a prior hemorrhagic episode.
- Some but not all dogs with anticoagulant rodenticide toxicosis will have a known history of ingestion of thoison. Anticoagulant rodenticide intoxication much more commonly results in hemothorax, mediastinal, or subcutaneous bleeding rather than hemoabdomen.

PHYSICAL EXAM FINDINGS

- Most physical examination findings are referable to blood loss and hemorrhagic shock. The clinical signs will vary depending on the severity of shock. Dogs may have pale mucous membranes, tachypnea, tachycardia, and bounding pulses. An abdominal fluid wave may be present. In some cases, a discrete abdominal mass (e.g., ruptured neoplasm) may be palpable.
- A traumatic cause for hemoabdomen may be apparent owing to the presence of additional injuries.
- Animals with anticoagulant rodenticide toxicosis may have bruising at venipuncture sites.

ETIOLOGY AND PATHOPHYSIOLOGY

- In dogs without a history of trauma and a normal coagulation profile, hemangiosarcoma is the most likely diagnosis.
- Benign splenic hematomas account for a substantial proportion of canine splenic masses in general but comprise only 5%-10% of the splenic masses seen in dogs with hemoabdomen.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The clinician should work to quickly rule in or rule out hemoabdomen (and/or pericardial effusion) in any middle-aged to older dog presenting with collapse and hypotension. Use of abdominal ultrasound provides the quickest diagnosis of free abdominal effusion and allows for ultrasound-guided centesis.

DIFFERENTIAL DIAGNOSIS

- Ruptured hemangiosarcoma
- Ruptured splenic hematoma
- Other ruptured abdominal mass
- Trauma
- Anticoagulant rodenticide toxicity

INITIAL DATABASE

- Packed cell volume and serum total protein
- Prothrombin time and activated partial thromboplastin time
- CBC with manual platelet count
- Serum biochemical profile
- Abdominocentesis:
    - Nonclotting bloody effusion: if neoplasia or coagulopathy
    - Bloody effusion with clots: if trauma; rarely, with voluminous bleed from mass

ADVANCED OR CONFIRMATORY TESTING

- Abdominal ultrasound to identify the source of hemorrhage in dogs with hemangiosarcoma and splenic hematoma
- Abdominal radiography may be minimally helpful in the presence of free abdominal fluid.
- Whenever possible, thoracic radiographs and echocardiography should be performed before surgery in dogs with hemoabdomen and an abdominal mass (rule out metastasis/poor prognosis).
- Blood rodenticide levels can be performed in cases of suspected toxicosis.

TREATMENT

TREATMENT OVERVIEW

Dogs with hemoabdomen frequently present with severe cardiovascular instability. Once cardiovascular instability is identified (poor pulse quality, cold extremeties, mentation changes, very pale/white mucous membranes), the clinician should work to obtain vascular access and begin resuscitation with intravenous fluids and/or blood products as indicated. Initial treatment should be directed toward reversing the signs of cardiovascular in stability. Further treatment should focus on preventing ongoing hemorrhage.

ACUTE GENERAL TREATMENT

- Intravenous fluids as indicated by the patient's cardiovascular status.
- Blood transfusion in patients with a packed cell volume < 20%-25% that are hemodynamically unstable (e.g., concurrent hypotension, hemorrhagic shock, or rapid sustained ventricular arrhythmia)
- Patients with a coagulopathy should be treated with 15 mL/kg of fresh frozen plasma or 30 mL/kg of fresh whole blood.
- Emergent laparotomy is indicated in dogs with ongoing intraabdominal hemorrhage.
- Dogs with abdominal neoplasia benefit from surgical removal of the bleeding tumor once they are hemodynamically stable, although postoperative survival times may only range from weeks to months, depending on the nature of the neoplasm.

CHRONIC TREATMENT

- Patients with neoplasia may benefit from chemotherapy.
- Anticoagulant rodenticide toxicosis: vitamin K1, 5 mg/kg SQ, then 2.5 mg/kg/d PO for 2-6 weeks as required for the specific toxin ingested.

POSSIBLE COMPLICATIONS

- Ongoing hemorrhage
- Some splenic or liver masses have metastasized by the time of laparotomy, and the masses may not be resectable.
- Severe ventricular arrhythmia may develop and may require antiarrhythmic therapy.

RECOMMENDED MONITORING

- Cardiac electrocardiogram monitoring is indicated owing to the high frequency of arrhythmia in dogs with splenic disease.
- Frequent reassessment of the packed cell volume/total solids is warranted in the initial urgent setting.
- Coagulation times should be rechecked after the completion of plasma transfusions.
- Specific long-term monitoring depends on cause. Typically, dogs with hemoabdomen are reassessed within 10 postoperative

days (history, physical examination, CBC; other tests based on these findings and original etiology), and again 2-4 weeks later barring complications.

PROGNOSIS AND OUTCOME

- Often, exact prognosis is only determined in the postoperative period, with histopathologic assessment of biopsies.
- Dogs with hemangiosarcoma have a poor prognosis, with an average survival of 3-6 months with surgical treatment and 2-3 weeks without surgery.
- Dogs with splenic hematomas may be cured with splenectomy.
- Traumatic hemoabdomen usually responds well to supportive nonsurgical management.

PEARLS & CONSIDERATIONS

COMMENTS

- In patients with acute hemorrhage, the serum total protein will fall before the packed cell volume.
- It is essential to submit large sections of spleen (or the entire spleen) for histopathologic analysis of splenic masses. Otherwise, some splenic biopsies that are interpreted by the pathologist as a hematoma are actually hemangiosarcoma, as the tumor is small and there is a massive hematoma surrounding it.
- Benign splenic hematomas account for a large proportion of canine splenic masses in general, but hematomas make up only 5%-10% of the splenic masses seen in dogs with hemoabdomen.
- Any collapsed large-breed dog should be evaluated for possible hemoabdomen.

PREVENTION

Keep dogs confined or supervised to prevent trauma and rodenticide intoxication.

CLIENT EDUCATION

Advise owner to present older dogs with lethargy for evaluation in a timely fashion.

SUGGESTED READING

Hammond TN, Pesillo-Crosby SA: Prevalence of hemangiosarcoma in anemic dogs with a splenic mass and hemoperitoneum requiring a transfusion: 71 cases (2003-2005). J Am Vet Med Assoc 232:553–558, 2008

Pintar J, et al: Acute nontraumatic hemoabdo-men in the dog: a retrospective analysis of 39 cases (1987-2001). J Am Anim Hosp Assoc 39:518–522, 2003.

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EDITOR: ELIZABETH ROZANSKI

Hematuria

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

The presence of blood (gross or microscopic) in the urine is encountered commonly in dogs and cats.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs or cats of either gender and any age may develop hematuria for a variety of benign or pathologic reasons.

GENETICS & BREED PREDISPOSITION: Welsh corgi (renal telangiectasia), Abyssinian cats (glomerular disease)

RISK FACTORS

- Acquired or hereditary coagulopathies (e.g., rodenticide intoxication, thrombocytopenia, hemophilia)
- Upper or lower urinary tract trauma, neoplasia, infection, or inflammation
- Urolithiasis
- Renal insult (e.g., acute renal failure, glomerulonephritis, renal infarcts)
- Vascular malformation
- Urinary parasites *(Capillaria plica, Dioctophyma renale)*
- Cyclophosphamide administration
- Prostatitis
- Proestrus

ASSOCIATED CONDITIONS & DISORDERS

- Very rarely, urinary obstruction due to blood clots
- Very rarely, anemia accompanies renal hematuria

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Macroscopic hematuria: grossly discolored, bloody urine
- Microscopic hematuria: >5 red blood cells (RBCs)/hpf without overt urine discoloration

HISTORY, CHIEF COMPLAINT

- Gross hematuria may occur at initiation of urination, throughout urination, or at the end of urination:
  - Initial hematuria: lower urinary tract or reproductive origin
  - Total hematuria: origin anywhere along urinary/reproductive tract
  - Terminal hematuria: upper urinary tract, bladder origin
- Depending on causation, any of the following may be reported:
  - Red, pink, or brown urine (macroscopic) (see also p. 312)
  - Dysuria/stranguria (suggestive of lower urinary tract disorders)
  - Pollakiuria (suggestive of lower urinary tract disorders)
  - Bloody discharge from penis or vulva unassociated with urination (suggestive of genital origin)
  - Abdominal pain
  - Systemic signs (e.g., lethargy, anorexia, vomiting) suggestive of upper urinary disorders, obstruction, or rupture

PHYSICAL EXAM FINDINGS: Depending on etiology, findings may include:

- Palpable renal/bladder/urethral mass effect
- Prostatomegaly
- Abdominal pain
- Bleeding unrelated to the urinary/genital tract (e.g., petechiae, ecchymoses, epistaxis), suggesting systemic bleeding disorder

ETIOLOGY AND PATHOPHYSIOLOGY

- Primary (coagulation factors) or secondary (platelet) hemostatic defects or vasculitis may result in hematuria in the absence of urinary or reproductive disorders.
- Bleeding anywhere along the length of the urinary tract or from the reproductive tract may cause hematuria.
- A variety of inflammatory, infectious, neoplastic, traumatic, or toxic insults may result in hematuria. Traumatic cystocentesis can cause iatrogenic hematuria.
- Vascular malformations (e.g., telangiectasia) are a rare but important cause of marked hematuria.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

In most cases, a presumptive diagnosis can be achieved on the basis of history, examination, urinalysis, and abdominal radiographs and/or ultrasound.

DIFFERENTIAL DIAGNOSIS

- Pigmenturia
- Hemoglobinuria
- Myoglobinuria

INITIAL DATABASE

- History reviewed for drugs/toxins (e.g., cyclophosphamide, phenols) or iatrogenic procedures (e.g., urinary catheterization, cystocentesis) that might induce hematuria
    - If microscopic hematuria is observed after cystocentesis, later evaluation of a voided sample is warranted.
- Rectal examination: prostate, intrapelvic urethra
- Digital vaginal exam/cytologic evaluation if vulvar bleeding between urinations
- Urinalysis: hematuria differentiated from hemoglobinuria, myoglobinuria, or pigmenturia (all of which discolor urine and may produce a positive blood result by urine dipstick) by presence of intact RBC on microscopic exam (hematuria only)
    - Cystocentesis is avoided if coagulopathy, ascites, peritonitis, or neoplastic bladder disease is possible.
    - Urethral catheterization: detection of urethral calculi/mass, urine collection
    - Hematuria in samples obtained by catheterization or cystocentesis suggests origin is kidney(s), ureter(s), or bladder. Conversely, if RBC absent from these samples but present in voided urine, source of bleeding is likely urethra or reproductive tract.
- CBC: thrombocytopenia suggests hemostatic defect; neutrophilia suggests upper urinary infection/inflammation; anemia may correlate to degree of blood loss.
- Serum biochemical profile: azotemia and hyperkalemia suggest renal disease or urinary obstruction/rupture.
- Urine culture is indicated when bacteria/pyuria are detected.
- Abdominal radiographs: shape and size of kidneys, bladder, prostate evaluated. Radiopaque stones may be observed.
- Abdominal (urinary and genital) ultrasound: renal parenchyma, bladder wall and luminal content, prostate, uterus, and portions of ureters/urethra evaluated for masses/radiolucent stones.

ADVANCED OR CONFIRMATORY TESTING

- If coagulopathy is suspected, platelet count, bleeding time, prothrombin time, activated partial thromboplastin time, and/or activated coagulation time are indicated.
- Excretory urographic contrast studies (see p. 1265) may delineate masses, stones, or tears in the urinary tract not previously identified.
- Cystoscopy may identify source of bleeding from vagina, urethra, bladder, or either kidney/ureter.
- Traumatic catheterization when urethral/bladder mass detected allows cytologic evaluation.
- Consider biopsy of kidney, bladder, prostate, urethra as appropriate.
- Bladder tumor antigen test unreliable in the face of hematuria

TREATMENT

TREATMENT OVERVIEW

Treatment for hematuria depends entirely on the cause.

ACUTE GENERAL TREATMENT

- Coagulopathy is addressed directly.
- Traumatic injury may require supportive care alone or surgical intervention.
- Urinary calculi are treated via medical dissolution and/or mechanical removal, depending on type and location of stone.
- Urinary tract or reproductive infections are treated with appropriate antibiotics.
- Neoplastic disease may require surgical intervention (e.g., unilateral renal carcinoma) or chemotherapy (e.g., transitional cell carcinoma).
- Drugs (e.g., cyclophosphamide, nonsteroidal antiinflammatory drugs) that might induce hematuria disallowed
- Rarely, renal hematuria may lead to blood loss sufficient to warrant transfusion.

CHRONIC TREATMENT

Dependent on cause

POSSIBLE COMPLICATIONS

Rarely, blood clots lead to ureteral or urethral obstruction.

RECOMMENDED MONITORING

Dependent on cause

PROGNOSIS AND OUTCOME

Dependent on cause

PEARLS & CONSIDERATIONS

COMMENTS

- Generally, hematuria is a sign of underlying disease rather than a primary disorder.
- Renal telangiectasia is an uncommon hereditary condition in Welsh corgi dogs, resulting in potentially profound renal bleeding due to vascular malformations. Diagnosis depends on biopsy, and organs other than the kidney may be involved.
- Benign essential hematuria is an uncommon disorder of young dogs in which no cause for profound, persistent hematuria can be identified. Often it occurs unilaterally; removal of the affected kidney is curative.

TECHNICIAN TIP

- Cystocentesis should not be performed on animals with hematuria until the clinician is reasonably certain that the animal (1) does not have a coagulopathy and (2) does not have a transitional cell carcinoma.

SUGGESTED READING

Moore FM, et al: Telangiectasia of Pembroke Welsh corgi dogs. Vet Pathol 20:203, 1983.

Forrester SD: Diagnostic approach to hematu-ria in dogs and cats. Vet Clin North Am Small Anim Pract 34:849, 2004.

Kaufman AC, et al: Benign essential hematuria in dogs. Compend Contin Educ Pract Vet 16:1317, 1994.

White JD, et al: Persistent haematuria and proteinuria due to glomerular disease in related Abyssinian cats. J Feline Med Surg 10:219, 2008.

AUTHOR & EDITOR: LEAH A. COHN

Hematochezia

BASIC INFORMATION

DEFINITION

The presence of bright red streaks of blood on the surface of or admixed into the stool

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dependent on underlying cause
- Older animals: neoplasia
- Younger animals: parasites

RISK FACTORS: The most common risk factor for hematochezia is colitis. Neoplasia is less commonly responsible. Coagulopathies are a rare cause of hematochezia.

ASSOCIATED CONDITIONS & DISORDERS: Clinically significant anemia very uncommonly occurs as a result of hematochezia.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Animals presenting with hematochezia will also commonly present with mucus in the stool, straining, and difficulty defecating; all are manifestations of colonic disease.
- Animals with hematochezia rarely present signs of systemic illness.

PHYSICAL EXAM FINDINGS

- These animals generally look clinically healthy. Involuntary weight loss should *not* be present; if it is, severe colonic disease (e.g., infiltrative disease) or complications of colonic disease (e.g., malignancy) should be investigated.
- The perianal area may be soiled with blood, fecal material, and/or mucus.
- The anus may be inflamed and ulcerated.
- A mass (neoplasm), swelling (anal gland abscess), or fissure (perianal fistula) around the anus may be visible.
- A rectal examination can confirm the presence of hematochezia and is essential in any patient with a presenting complaint of hematochezia.

ETIOLOGY AND PATHOPHYSIOLOGY

Blood most commonly originates from the anus, rectum, and/or descending colon.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Hematochezia should be suspected in an otherwise healthy dog presenting soft, fresh blood-streaked stool with mucus accompanied by straining and painful defecations. Tests begin with fecal analysis and examination of the patient for signs of rectoanal disease or systemic bleeding disorders.

DIFFERENTIAL DIAGNOSIS

- Diseases involving the anus:
  - Anal sacculitis/abscess
  - Perianal fistula
  - Neoplasia (anal sac tumor)
  - Perineal hernia

    - Rectal stricture
    - Trauma
    - Foreign body
- Diseases involving the rectum and colon:
    - Proctitis
    - Colitis:
        - Idiopathic
        - Inflammatory
        - Infectious *(Campylobacter, Clostridium, Histoplasmosis)*
        - Stress
    - Parasites:
        - Hookworms, whipworms, coccidia, roundworms
    - Neoplasia:
        - Benign: rectal polyp
        - Malignant: lymphoma, carcinoma
    - Rectal prolapse
    - Mucosal trauma (foreign body, hair balls, enemas)
    - Dexamethasone administration (especially in the presence of intervertebral disk disease)
    - Coagulation disorders (usually accompanied by bleeding from other sites)

INITIAL DATABASE

- Rectal examination including anal sac palpation
- Fecal examination for parasites
- Fecal smear, culture, *Clostridium* toxin detection
- Results of trial therapy (see Acute General Treatment below)

ADVANCED OR CONFIRMATORY TESTING

Advanced testing should be considered in patients with systemic signs of illness, persistent or recurrent episodes of hematochezia. Tests are selected based on history, physical exam, and initial database results:

- CBC
- Serum biochemistry profile
- Urinalysis
- Coagulation profile
- Abdominal radiographs
- Abdominal ultrasound
- Colonoscopy

TREATMENT 

TREATMENT OVERVIEW

Initial therapy consists of dietary change, broad-spectrum dewormer, and an antibiotic to control bacterial overgrowth. Unresponsive chronic cases may benefit from referral to a specialist for colonoscopy.

ACUTE GENERAL TREATMENT

- Nonspecific trial therapy can be attempted in an animal without systemic signs:
    - Broad-spectrum dewormer (e.g., fenbendazole, 50 mg/kg PO q 24 h × 5 days)
    - Trial course of metronidazole (e.g., 7-15 mg/kg PO q 12 h × 7 days maximum)
- Dependent on the underlying disease:
    - Perianal fistulas: immunosuppressive therapy
    - Infectious colitis: *Clostridium:* metronidazole, amoxicillin, *Campylobacter:* tylosin
    - Neoplasia: surgical excision, chemotherapy, radiation therapy
    - Stricture: surgery
    - Perianal hernia: surgical correction

CHRONIC TREATMENT

- Dependent on the underlying disease

- Colitis (see pp. 227 and)

NUTRITION/DIET

- Diet containing fermentable fiber
- Low-residue diet

POSSIBLE COMPLICATIONS

Perforated colon:

- Neoplasia
- Dexamethasone therapy (especially in the presence of intervertebral disk disease)

PROGNOSIS AND OUTCOME

Dependent on underlying disease

PEARLS & CONSIDERATIONS

COMMENTS

Hematochezia should not be confused with melena, which refers to the presence of dark, tarry stool caused by digested blood from the upper digestive tract or small intestine.

PREVENTION

Handwashing after caring for patients is essential, as some causes of hematochezia are zoonotic.

SUGGESTED READING

Tams T: Gastrointestinal symptoms. In Handbook of small animal gastroenterology, ed 2, St Louis, 2003, WB Saunders, pp 31–32.

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Hemangiosarcoma

Video Available on Website

BASIC INFORMATION

DEFINITION

A malignant, highly metastatic tumor arising from vascular endothelial cells. Most commonly arises within the spleen, right auricle or right atrium, and skin or subcutaneous tissues.

SYNONYMS

HSA, angiosarcoma, malignant heman-gioendothelioma

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Feline: 8-10 year median, males > females. Uncommon
- Canine: common
  - Cutaneous: adults (range 4-10+ years), no sex predilection
  - Noncutaneous: 8-10 year median, neutered animals may be at increased risk

GENETICS & BREED PREDISPOSITION

- Feline: no genetics or specific breed predisposition known
- Canine:
  - Cutaneous: no genetics known, although breeds with short-haired coats are predisposed (e.g., whippets, pit bulls, dalmatians)
  - Noncutaneous: no genetics known; tend to affect large-breed dogs such as German shepherds and golden retrievers

RISK FACTORS

- Feline: none known
- Canine:
  - Cutaneous: dermal hemangiosarcoma arises on nonhaired skin and is associated with ultraviolet (UV) light exposure. Subcutaneous hemangiosarcoma arises in haired skin and is not associated with UV exposure.
  - Noncutaneous: none known, but breed predisposition suggests a genetic etiology.
  - Cardiac hemangiosarcoma is the most common reason for pericardial effusion.

ASSOCIATED CONDITIONS & DISORDERS

- Feline: none known
- Canine:
  - Cutaneous:
    - UV exposure may also predispose to cutaneous hemangioma or squamous cell carcinoma.
  - Noncutaneous:
    - With either splenic, hepatic, or right atrial/auricular appendage HSA, potentially life-threatening hemorrhage can occur. Occasionally, large subcutaneous hemangiosarcoma tumors may bleed.
    - Pericardial effusion can result in potentially fatal cardiac tamponade.
    - Splenic, hepatic, and right atrial/auricular appendage HSA are associated with cardiac arrhythmias.
    - In any patient with hemangiosarcoma, disseminated intravascular coagulation (DIC) may arise in conjunction with thrombocytopenia and triggering of the coagulation cascade by the formation of abnormal (tumor-related) vascular channels.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Feline: subcutaneous and splenic lesions are most common, but hemangiosarcoma can arise anywhere in the body, including

such diverse tissues as bone, gastrointestinal (GI) tract, and skin.

- Canine:
  - Cutaneous:
    - Tends to arise on lightly haired areas such as the ventral abdomen. Tumors that are <5 cm in diameter and confined to the dermis are classified as stage I. Tumors that are >5 cm in diameter or invade subcutaneous or deeper tissues are classified as stage II or III.
  - Noncutaneous:
    - Splenic lesions are most common, followed by HSA of the right atrial/auricular appendage and skin. Primary HSA of the liver can occasionally occur, but most often, hepatic lesions are metastases from another site. As with cats, hemangiosarcoma can arise anywhere.
    - Cardiac tamponade due to intrapericardial hemorrhage from the tumor site
    - Occasionally can be an incidental finding without associated clinical signs

HISTORY, CHIEF COMPLAINT

- Feline:
  - Cutaneous: bleeding from the mass in a patient that is otherwise well may be the chief complaint.
  - Noncutaneous: typically, nonspecific signs such as inappetence/anorexia, weight loss, lethargy, and vomiting are the basis for seeking veterinary attention.
- Canine:
  - Cutaneous: history of extensive sunlight exposure and development of one or more cutaneous masses
  - Noncutaneous:
    - Often nonspecific complaints (e.g., mild exercise intolerance, mild decrease in appetite, weight loss) commonly attributed at first to “old age,” or environmental change (weather), but then culminating in subacute (days before presentation) or acute (hours before presentation) deterioration with lethargy, weakness, tachypnea, inappetence/anorexia, and/or abdominal distension.
    - Acute onset of weakness or collapse is often mentioned, associated with tumor rupture and hemorrhage.
    - Collapse may be self-resolving by the time the patient is presented for veterinary attention, but physical signs of hemorrhage, abdominal mass, or arrhythmia persist.
    - Cardiac (overlap or combination of the following is possible):
      - Acute collapse with pallor; may have partially resolved over preceding hours or days
      - General malaise, lethargy, anorexia, exercise intolerance
      - Visible abdominal distension

PHYSICAL EXAM FINDINGS

- Feline: Cutaneous or subcutaneous lesions are typically readily identified on physical examination. Visceral disease is often evident on abdominal palpation. Other possible findings include pale mucous membranes, weak pulses.
- Canine:
  - Cutaneous:
    - Single or multiple cutaneous tumors, typically on the ventral abdomen. Usually raised, hairless, smooth, and dark-red lesions, although they may also appear as polypoid, hairless lesions that are the same color as surrounding skin.
  - Noncutaneous:
    - Most often, findings are related to tumor rupture and hemorrhage into a body cavity. The most common physical findings include lethargy, pale mucous membranes, abdominal fluid wave, sinus tachycardia (reflex), and weak pulses.
    - A palpable intraabdominal mass is often present, and such masses should be palpated with great care to avoid further damaging any fragile blood vessels on the surface of the neoplasm and inducing further hemorrhage.
    - Soft heart sounds, cardiac arrhythmia, and signs of circulatory failure may be present either as a result of a ruptured abdominal hemangiosarcoma, cardiac hemangiosarcoma and subsequent pericardial effusion, or both.
    - In some cases: jugular distension, pulsus paradoxus, positive hepatojugular reflux

ETIOLOGY AND PATHOPHYSIOLOGY

- Cutaneous hemangiosarcoma is associated with UV light exposure. Cutaneous hemangiosarcoma is less likely to metastasize and is not usually associated with underlying visceral disease/involvement; subcutaneous hemangiosarcoma may metastasize and may be a marker for underlying visceral disease/involvement.
- Malignant vascular endothelial cells form abnormal vascular channels.
- Microangiopathic disease (abnormal blood vessels in the neoplasm) results in platelet aggregation, red blood cell morphology changes, and DIC
- Tumor rupture leads to anemia, weakness, and inappetence/anorexia.

- Cardiac hemangiosarcoma is usually seen as right atrial/auricular infiltration of neoplastic cells that grow on the epicardial surface and ultimately cause rupture of superficial myocardial vessels of varying sizes, triggering bleeding into the pericardial space. The result is cardiac tamponade when intrapericardial pressure exceeds right atrial and ventricular filling pressures.
- Metastatic disease occurs within the lungs, mesentery, and throughout the body.
- Death is due to uncontrollable bleeding from tumor rupture.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Feline (subcutaneous): abscess, other neoplasia such as injection-site sarcoma, fibrosarcoma
- Feline (splenic): splenic mast cell tumor, lymphoma, nodular hyperplasia, other sarcoma
- Canine (cutaneous/subcutaneous): hemangioma, soft tissue sarcoma, mast cell tumor
- Canine (splenic): splenic torsion, lymphoma, hemangioma, hematoma, extramedullary hematopoiesis, nodular regeneration, other sarcoma
- Canine (hepatic): hepatocellular adenoma/adenocarcinoma, hematoma
- Canine (cardiac): idiopathic benign pericardial effusion, other neoplasia (chemodectoma, mesothelioma, lymphoma), hemopericardium (atrial rupture, anticoagulant rodenticide intoxication), exudative/infectious pericarditis, congestive heart failure (right-sided), diaphragmatic pericardial-peritoneal hernia, hydropericardium due to hypoalbuminemia, pericardial cysts, diseases that cause radiographic enlargement of the cardiac silhouette (dilated cardiomyopathy, severe atrioventricular endocardiosis/valvular heart disease, etc.)

INITIAL DATABASE

- Careful abdominal palpation, assessment for a fluid wave
- Auscult heart and check for synchronous pulses.
- CBC, chemistry profile, urinalysis, coagulation profile
  - Anemia (regenerative or nonregenerative, depending on acuity) and hypoproteinemia are common due to blood loss (e.g., abdominal hemorrhage).
  - Schistocytosis (see pp. 1516 and) may be noted as a result of microangiopathic damage of red blood cells traveling through abnormal vessels in the neoplasm.
- Thoracic and abdominal radiographs
  - Mass effect is commonly apparent on abdominal radiographs; detail may be obscured by abdominal effusion.
  - Pulmonary metastasis of hemangiosarcoma can involve many (hundreds to thousands) 1-to 2-mm nodules, which appear radiographically in the lungs as an interstitial pattern.
  - Cardiac silhouette may be enlarged (globoid), indicating pericardial effusion.
  - Lack of globoid cardiac silhouette does not rule out pericardial effusion.
  - Cardiac silhouette rarely affected by presence of a mass lesion
- Abdominal ultrasound if suspected splenic or hepatic lesion (abdominal effusion/distension, abdominal mass). Utility of ultrasound for patients with a palpable abdominal mass:
  - Confirm presence of the mass, its organ of origin, and likelihood of resectability.
  - Identify lesions suggesting metastasis.
  - Identify abdominal fluid; if small in volume, guide needle abdominocentesis.
  - Identify internal structure of mass, indicating feasibility of fine-needle aspiration/core biopsy (mixed echogenicity and high vascularity contraindicate these procedures in hemangiosarcoma).
- Echocardiography:
  - Right atrial wall collapse (“sail sign;” the right atrial wall motion seen in pericardial tamponade resembles a sail flapping in the wind).
  - Diastolic collapse of RV wall if severe tamponade
  - Tumor mass or blood clot from bleeding tumor may be seen bobbing in fluid adjacent to or involving a thickened (infiltrated) right atrial/auricular wall.
  - Diminished right atrium, right ventricle, left ventricle volume
  - Swinging motion of the heart within the anechoic pericardial fluid
  - Mass seen occasionally within the right atrium; absence of mass does not exclude hemangiosarcoma because of limitations of imaging right auricle with routine (transthoracic) echocardiography.
  - Doppler evaluation of pulmonic flow shows large variation in beat-to-beat peak velocities.
- Electrocardiogram if an arrhythmia is present on physical exam, and if splenic involvement, cardiac involvement, or recent hemorrhage is evident. Most common arrhythmias include electrical alternans (25% of the time), diminished R wave amplitudes (50% of the time), arrhythmias (rare).
- Fine-needle aspiration cytology of regional lymph node in patients with cutaneous HSA.

ADVANCED OR CONFIRMATORY TESTING

- Surgical biopsy is the gold standard for diagnosis. The entire spleen should be submitted; some laboratories request it to be shipped chilled on ice (not frozen), whereas others request it be fixed in 10:1 ratio of formalin/tumor for 24-48 hours, after which the fixed tissues can be sent to the laboratory in a small amount of formalin.
- Contrast ultrasonography is becoming more widely used to assess the nature of ultrasonographically identified splenic and hepatic nodules. Metastatic liver nodules are characterized by a hypoechoic appearance, in contrast to benign nodules which are isoenhancing.
- Fine-needle aspiration cytology or cytologic evaluation of hemorrhagic fluids is rarely diagnostic. Fine-needle aspiration cytology of visceral masses may result in hemorrhage and is not recommended in cases of suspected splenic, cardiac, and any other noncutaneous form of hemangiosarcoma (see Pearls & Considerations below).
- Pericardial fluid pH: controversial. One study indicated pericardial pH > 7 as highly indicative of neoplasia and pericardial pH < 7 as highly indicative of benign effusion, whereas another study showed no such differentiation.
- Serum troponin-1 elevation suggests hemangiosarcoma. This blood test may be performed locally at a human hospital (human assay is accurate in dogs) or may be performed at referral veterinary laboratories.

TREATMENT

TREATMENT OVERVIEW

- Reduce tumor burden and prevent/minimize future hemorrhagic episodes.
- Relief of tamponade (palliative)
- Control metastatic disease.
- Prolong survival.

ACUTE GENERAL TREATMENT

- Cutaneous (either species):
  - Surgery to remove tumor
- Noncutaneous (either species):
  - If evidence of recent or ongoing hemorrhage: IV fluids ± oxygen ± transfusion (see p. 489)
  - Pericardiocentesis (see p. 1325) if pericardial effusion causing cardiac tamponade is present
  - Diuretics: contraindicated in acute pericardial effusion/cardiac tamponade
  - Once the patient is stable, surgery to remove the tumor or pericardectomy to prevent recurrence of tamponade

CHRONIC TREATMENT

- Feline and canine (cutaneous): surgery alone may be curative in most patients with dermal HSA. Margins should be at least 1-3 cm wide and 1 or more fascial planes deep.
- Feline and canine (noncutaneous and stage II cutaneous HSA):
  - Chemotherapy with a protocol of five doses of doxorubicin (dog, 30 mg/m^2 IV; cat, 25 mg/m^2 IV) given every 3 weeks. Special handling requirements and potentially severe or life-threatening adverse patient effects exist with this chemotherapeutic drug. Concerns and rapid evolution of protocols warrant consultation with/referral to an oncologist.
  - Consider adjuvant radiation therapy for patients with incompletely excised subcutaneous stage-II HSA.
- Canine visceral/noncutaneous HSA:
  - Metronomic chemotherapy with piroxicam (0.3 mg/kg PO q 24 h), etoposide (50 mg/m^2 PO q 24 h for 21 days, alternating every 3 weeks with cyclophosphamide), and cyclophosphamide (12.5-25 mg/m^2 PO q 24 h for 21 days, alternating every 3 weeks with etoposide) was more effective than 5 doses of doxorubicin (dosed as above) in one study.
- Canine cardiac HSA:
  - Subtotal pericardectomy (usually performed following second event of tamponade)
  - Right auricular ablation: removal of tumor mass (difficult and may not prolong life)
  - Right auricular ablation plus chemotherapy (see Prognosis and Outcome below)
  - Repeated pericardiocenteses

POSSIBLE COMPLICATIONS

- General chemotherapy toxicities: myelosuppression, GI upset
- Specific doxorubicin toxicities: allergic reaction during administration, perivascular sloughing with drug extravasation, cumulative myocardial toxicity (dogs) and heart failure, cumulative renal toxicity (cats)
- Specific cyclophosphamide toxicities: sterile hemorrhagic cystitis; administration concurrent with furosemide (1-2 mg/kg with each dose of cyclophosphamide) may prevent this side effect.
- Etoposide is a chemotherapy drug not widely used in veterinary medicine. No specific toxicities were noted in dogs treated at

the aforementioned dose.

RECOMMENDED MONITORING

- Feline and canine (cutaneous): recheck physical examination every 3-4 months.
- Feline and canine (noncutaneous): weekly CBC initially, thoracic radiographs every 1-2 months, abdominal ultrasound every 1-2 months
- Echocardiography 24 hours after pericardiocentesis; 1 week after pericardiocentesis, monthly thereafter

PROGNOSIS AND OUTCOME

- Feline and canine (cutaneous): <30% of patients with dermal (stage I) HSA will develop metastases, so complete surgical excision can be curative.
- Feline and canine (noncutaneous and stage II cutaneous):
  - Highly metastatic, so when treated with surgery alone, median survival may be only 2-3 months. There are occasional reports of patients surviving several months, but survival up to or beyond 1 year is very uncommon.
  - If all grossly detectable neoplastic tissue can be removed surgically, adjuvant chemotherapy may extend survival to a median time of 6 months.
  - If grossly apparent neoplastic tissue persists in postoperative period, median survival time approximates 2 months.
  - Adjuvant radiation therapy can be considered for patients with incompletely excised stage II cutaneous hemangiosarcoma, but limited data prevent any clear conclusions regarding benefit.
  - Right auricular ablation plus chemotherapy may prolong life (median survival in 8 dogs with right auricular ablation alone, 42 days versus in 8 other dogs with right auricular ablation plus chemotherapy, 175 days)

PEARLS & CONSIDERATIONS

COMMENTS

- Hemangiosarcoma is a locally aggressive, highly metastatic tumor that most often arises within the spleen, right atrium, or skin in dogs.
- Most often hemangiosarcoma of the liver is due to metastatic disease, since primary hepatic hemangiosarcoma is uncommon.
- Nodules of ectopic splenic tissue on the omentum, and regenerative hepatic nodules, are benign, dark-red/brown tissue nodules that must not be misinterpreted as hemangiosarcoma metastases during laparotomy in a patient with a splenic mass. Biopsy is advised to avoid misdiagnosis.
- Although rare in cats, this tumor has a similarly aggressive biological behavior.
- Fine-needle aspiration/cytologic evaluation and core biopsy are often unrewarding because of poor cellular yield and blood dilution. Both carry the real possibility of causing rupture of the tumor and potentially life-threatening hemorrhage and are therefore *contraindicated* for evaluation of masses when hemangiosarcoma is on the differential diagnosis list: masses of splenic, hepatic, renal, or cardiac origin that, on ultrasound exam, are of mixed echogenicity and may be highly vascularized based on color flow Doppler assessment.
- Fine-needle aspiration and cytologic evaluation may be considered for evaluation of skin masses for which hemangiosarcoma is on the differential diagnosis list, but diagnostic yield may be limited for the same reasons.
- Cutaneous hemangiosarcoma in both dogs and cats has a less metastatic behavior, and surgical excision may be curative.
- Even with doxorubicin chemotherapy, reported survivals are short (~6 months) in both species. The best chemotherapy protocol for the treatment of hemangiosarcoma remains unknown, as no randomized clinical trials have compared reported protocols. Combining doxorubicin with cyclophosphamide appears to be well tolerated and may provide longer survival times than doxorubicin alone. Adding vincristine to a doxorubicin and cyclophosphamide protocol is associated with more significant toxicity than with doxorubicin and cyclophosphamide or doxorubicin alone. Alkylating agents such as lomustine and ifosfamide may prove to have activity against this disease; however, large studies documenting efficacy are lacking. Experimentally, immunotherapy appears to be of benefit, but no effective immunotherapies are commercially available.

CLIENT EDUCATION

- Watch for recurrent signs associated with return of tamponade.
- Watch for signs of respiratory embarrassment associated with pulmonary metastasis.

PREVENTION

The development of cutaneous hemangiosarcoma is related to UV light exposure. Minimize sun exposure in animals with white or thin haircoats.

SUGGESTED READING

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Johannes C, et al: Hemangiosarcoma in cats: 53 cases (1992-2002). J Am Vet Med Assoc 231:1851–1856, 2007.

Lana S, et al: Continuous low-dose oral chemotherapy for adjuvant therapy of splenic hemangiosarcoma in dogs. J Vet Intern Med 21:764–769, 2007.

AUTHOR: RUTHANNE CHUN

EDITOR: KENNETH M. RASSNICK

Hemangiosarcoma, Cardiac

Video Available on Website

BASIC INFORMATION

DEFINITION

Malignancy of vascular endothelial origin involving cardiac tissue as either a primary or metastatic site. The neoplasm usually is located in the right auricle but may be seen also in the atria and ventricles. Regardless of location, it usually causes a hemorrhagic pericardial effusion.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs: older adults, both sexes. Extremely rare in the cat.

GENETICS & BREED PREDISPOSITION: Dogs: genetics unknown, but golden retriever, German shepherd, rottweilers, greyhounds, and other large-breed dogs are overrepresented. Cats: rarely.

RISK FACTORS: Dogs: most common reason for pericardial effusion

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Cardiac tamponade due to intrapericardial hemorrhage from the tumor site
- Occasionally can be an incidental finding on echocardiography without associated clinical signs

HISTORY, CHIEF COMPLAINT: Three forms of presenting complaints (some overlap/combination possible):

- Acute collapse with pallor; may have partially resolved over preceding hours or days
- General malaise, lethargy, anorexia, exercise intolerance
- Visible abdominal distention

PHYSICAL EXAM FINDINGS

- Tachycardia, muffled heart sounds, thready/weak pulse, abdominal distension
- In some cases: jugular distension, pulsus paradoxus, positive hepatojugular reflux

ETIOLOGY AND PATHOPHYSIOLOGY

- *Primary*: usually seen as right atrial/auricular infiltration of neoplastic cells that grow on the epicardial surface and ultimately cause rupture of superficial myocardial vessels of varying sizes, triggering bleeding into the pericardial space. The result is cardiac tamponade when intrapericardial pressure exceeds right atrial and ventricular filling pressures.
- *Systemic:* seen as metastatic site from primary involvement of liver or spleen.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Recent-onset abdominal distension, and/or weakness coupled with physical exam findings of dull or muffled heart sounds and a thready weak pulse provide sufficient evidence to pursue thoracic radiography and echocardiography early in the patient evaluation process.

DIFFERENTIAL DIAGNOSIS

Other causes of pericardial effusion:

- Idiopathic benign pericardial effusion
- Other tumors such as chemodectoma, mesothelioma, lymphoma, pericardial teratoma

- Pericardial lipoma, granuloma, or abscess
- Hemopericardium (atrial rupture, anticoagulant rodenticide intoxication)
- Exudative/infectious pericarditis
- Congestive heart failure (right-sided)
- Peritoneopericardial diaphragmatic hernia
- Hydropericardium due to hypoalbuminemia
- Pericardial cysts
- Diseases that cause radiographic enlargement of the cardiac silhouette (dilated cardiomyopathy, severe, advanced atrioventricular endocardiosis/valvular heart disease, severe right ventricular enlargement)

INITIAL DATABASE

- CBC: regenerative anemia
- Serum chemistry: usually unremarkable unless hepatic involvement
- Electrocardiogram: electrical alternans (25% of cases), diminished R wave amplitudes (50% of cases), arrhythmias (rare)
- Thoracic/abdominal radiographs: enlarged globoid cardiac silhouette possible (80% of time), caudal vena caval distention, pleural effusion, ascites, hepatomegaly. With hemangiosarcoma, multifocal pulmonary metastases may appear as an interstitial pattern.
- Echocardiography: most accurate diagnostic test. (see two video clips)
  - Confirm presence of fluid accumulation between the epicardium and the pericardium.
  - Right atrial wall collapse (“sail sign”; the right atrial wall motion seen in pericardial tamponade resembles a sail flapping in the wind).
  - Diastolic collapse of RV wall if severe tamponade
  - Tumor mass or blood clot from bleeding tumor may be seen bobbing in fluid adjacent to or involving a thickened (infiltrated) right atrial/auricular wall.
  - Diminished right atrium, right ventricle, left ventricle volume
  - Swinging motion of the heart within the anechoic pericardial fluid
  - Mass seen occasionally in/on the right atrial wall in 83% of cases with skilled echocardiographer; absence of mass does not exclude hemangiosarcoma because of limitations of imaging right auricle with routine (transthoracic) echocardiography.
  - Doppler evaluation of pulmonic flow shows large variation in beat-to-beat peak velocities.
- Abdominal ultrasonography: evaluate liver, spleen, omentum for presence of primary neoplasia.

ADVANCED OR CONFIRMATORY TESTING

- Pericardial fluid cytology:
  - Typically indicates extensive bleeding and minimal exfoliation
  - Mainly useful to exclude infectious pericardial effusion and lymphoma
  - Cytologic evaluation alone is highly unreliable: 74% of malignancies not detected; 13% of benign pericarditis cases erroneously classified as malignant.
- Pericardial fluid pH: controversial. One study indicated pericardial pH > 7.0 as highly indicative of neoplasia and pericardial pH < 7.0 as highly indicative of benign effusion, whereas another study showed no such differentiation.
- Serum troponin-1 elevation suggests hemangiosarcoma. This blood test may be performed locally at a human hospital (human assay is accurate in dogs) or may be performed at some referral veterinary laboratories.
- Contrast CT/cardiac MRI/magnetic resonance angiography (MRA), transesophageal echocardiography (TEE)

TREATMENT

TREATMENT OVERVIEW

Pericardiocentesis with drainage of the pericardial effusion is a mandatory first step once the diagnosis is confirmed. Complete patient evaluation for evidence of neoplasia elsewhere is imperative once the emergency correction of tamponade has been achieved.

ACUTE GENERAL TREATMENT

- Pericardiocentesis and drainage of accumulated effusion (see p. 1325)
- Diuretics: contraindicated in acute pericardial effusion/cardiac tamponade

CHRONIC TREATMENT

- Subtotal pericardectomy (usually performed following second event of tamponade)

- Right auricular ablation: removal of tumor mass (difficult and may not prolong life)
- Right auricular ablation plus chemotherapy (see Prognosis and Outcome below)
- Repeated pericardiocenteses

POSSIBLE COMPLICATIONS

- Almost all cases have pulmonary metastasis at time of initial diagnosis even though they may not be detected by thoracic radiography.
- Additional tumor sites: liver, spleen, skin, ventricle, brain, kidney

RECOMMENDED MONITORING

- Echocardiography 24 hours after pericardiocentesis; 1 week after pericardiocentesis, monthly thereafter
- Thoracic radiographs monthly

PROGNOSIS AND OUTCOME

- Poor to grave: most patients have recurrent bleeding from the tumor site, requiring repeat pericardiocentesis; metastatic disease usually present.
- Right auricular ablation plus chemotherapy: may prolong life (median survival in 8 dogs with right auricular ablation alone, 42 days versus in 8 other dogs with right auricular ablation plus chemotherapy, 175 days)

PEARLS & CONSIDERATIONS

COMMENTS

- Life expectancy < 6 months
- Often the mass seen bobbing around within the pericardial fluid is actually an organized blood clot associated with tumor tissue invading the right atrial/auricular wall.

CLIENT EDUCATION

- Watch for recurrent signs associated with return of tamponade.
- Watch for signs of respiratory embarrassment associated with pulmonary metastasis.

SUGGESTED READING

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Hemangiopericytoma

BASIC INFORMATION

DEFINITION

A common, locally invasive, slowly progressive tumor that occurs most commonly on the limbs of large-breed dogs; carries a fair to good prognosis with either complete excision or incomplete excision combined with radiation therapy

SYNONYMS

Malignant schwannoma, neurofibrosarcoma, peripheral nerve sheath tumor

EPIDEMIOLOGY

SPECIES, AGE, SEX: Common in middle-aged to older dogs; rare in cats

GENETICS & BREED PREDISPOSITION: Large-breed dogs may be overrepresented.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Most animals are presented for evaluation of a progressively enlarging mass noticed by the owner. Pets with hemangiopericytoma in certain locations may be presented because of clinical signs related to the location of the tumor (e.g., limb tumors may result in lameness).

PHYSICAL EXAM FINDINGS

- Visible or palpable mass, more commonly on the limbs (any location on the limbs)
- Mass is usually firm and fixed to underlying tissues. Occasionally, the mass can be hairless or ulcerated.
- Regional lymphadenopathy may be present secondary to inflammation caused by the tumor or (rarely) lymph node metastasis.
- The remainder of the physical examination typically is unremarkable.

ETIOLOGY AND PATHOPHYSIOLOGY

- Hemangiopericytoma has some histologic features similar to the tumor of the same name in humans, but the actual cell of origin of this tumor is disputed.
- Hemangiopericytomas are spontaneously occurring in most cases in dogs.
- Disturbance caused by hemangiopericytomas depends on the location of the primary tumor and invasion into and destruction of surrounding normal structures.
- Hemangiopericytomas are typically slow growing and slow to metastasize. Over time they can invade into surrounding soft-tissue structures.
- It is still unclear whether hemangiopericytomas, schwannomas, and nerve sheath tumors are identical or related but distinct tumors. Immunohistochemistry may be able to differentiate these similar tumor types, but since they have similar biological behavior, differentiating the specific tumor type may not add useful information.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Definitive diagnosis can only be confirmed via histopathology, although additional tests such as diagnostic imaging (e.g., CT or MRI) are often helpful in defining the extent of the tumor.

DIFFERENTIAL DIAGNOSIS

- Other soft-tissue sarcomas
  - Fibrosarcoma
  - Malignant fibrous histiocytoma

    - Others
- Mast cell tumors
- Other skin and subcutaneous tumors
- Benign or nonneoplastic masses
    - Benign tumor (e.g., lipoma)
    - Abscess
    - Elbow hygroma

INITIAL DATABASE

- Fine-needle aspiration and cytologic evaluation may help identify the tumor type before other diagnostics.
- Three-view thoracic radiographs to rule out pulmonary metastases
- Radiographs of the affected area may rarely reveal involvement of underlying bone.
- Fine needle aspirate of draining lymph nodes help rule out metastasis.

ADVANCED OR CONFIRMATORY TESTING

- Biopsy is the diagnostic procedure of choice.
    - Definitive diagnosis of hemangiopericytoma is based on histopathologic evaluation of the tumor tissue.
    - Biopsy is typically excisional, with removal of the entire tumor if possible or removal of the greatest feasible extent of tumor mass if not entirely resectable.
    - Incisional biopsy may be performed to obtain the diagnosis before treatment, especially in cases where multiple treatment modalities might be necessary (e.g., preoperative radiation).
    - Occasionally, special immunohistochemical stains may be necessary to differentiate hemangiopericytoma from other types of soft-tissue sarcomas, especially with poorly differentiated tumors.
- CT or MRI may be necessary to delineate the local extent of the tumor and plan for surgery or radiation therapy.
- Histopathologic grade of the tumor is necessary for determining prognosis and treatment of most soft-tissue sarcomas (see p. 1034). Although most hemangiopericytomas are low to intermediate grade, high-grade tumors can occur and may be more likely to metastasize.

TREATMENT

TREATMENT OVERVIEW

Definitive treatment is based on complete eradication of the primary tumor whenever possible. Since metastasis of this type of tumor is rare, additional treatment such as chemotherapy is rarely used but could be considered for high-grade tumors or tumors that have already metastasized. Palliative treatment options, such as palliative radiation, may help control pain or discomfort in patients with advanced tumors or in patients where definitive treatment cannot be tolerated.

ACUTE AND CHRONIC TREATMENT

- Aggressive surgical resection (aim: 3-cm margins; often not possible, especially on distal limb). Radiation therapy, and/or chemotherapy may be used (see p. 1034).
- Tumors that are incompletely resected or cannot be surgically resected (e.g., highly invasive or metastatic) may be treated with a combination of radiation therapy and surgery, which is associated with favorable long-term outcomes.
- Radiation therapy alone provides good long-term outcomes, although tumor control rates are higher with combined surgery-radiation therapy.
- Chemotherapy may be indicated for hemangiopericytomas that are high grade based on histologic features.

POSSIBLE COMPLICATIONS

Complications of treatment for hemangiopericytomas depend on types of treatments and location of primary tumor.

RECOMMENDED MONITORING

- Following appropriate local treatment of the primary tumor, routine followup up examination is indicated to monitor for local recurrence and metastasis. High-grade tumors may require more frequent monitoring for metastases during and after chemotherapy administration.
    - Dogs likely to develop metastasis (splenic tumors, high-grade tumors) should be monitored closely (every 2-3 months) with physical exam, including lymph node palpation and thoracic radiographs.
    - Dogs with low-or intermediate-grade tumors that have adequate treatment should have physical examinations done every 2-3 months or more frequently depending on risk of side effects from treatment. Thoracic radiographs could be

done less frequently (6 months and 1 year after therapy).

PROGNOSIS AND OUTCOME

- Prognosis is excellent for most hemangiopericytomas with appropriate treatment. This includes either complete surgical resection with clean histopathologic margins or incomplete resection combined with radiation therapy.
    - Combined surgery-radiation therapy treatment results in long-term tumor control in 86% of dogs with hemangiopericytoma. Survival times for dogs treated this way were >5 years, with 85% tumor free at 3 years.
    - Radiation therapy alone has resulted in 1-year tumor control rates of up to 75% at higher doses. However, these studies used suboptimal radiation dose schedules. In certain situations where surgery is not indicated, radiation may be used for providing some degree of tumor control.
- High-grade hemangiopericytoma is rare and information is limited regarding prognosis.

PEARLS & CONSIDERATIONS

COMMENTS

Despite uncertainty about the cell of origin for these tumors, hemangiopericytoma, peripheral nerve sheath tumor, schwannoma, and neurofibrosarcoma generally have the same biological behavior and should be treated in the same way.

CLIENT EDUCATION

Pet owners can be educated to monitor their pets for the occurrence of masses under the skin and have such masses evaluated in a timely fashion. Early detection may allow for easier treatment via surgery and may help avoid the need for radiation therapy.

SUGGESTED READING

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Chijiwa, et al: Immunohistochemical evaluation of canine peripheral nerve sheath tumors and other soft tissue sarcomas. Vet Pathol 41:307–318, 2004.

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Helicobacter Gastritis

DEFINITION

EPIDEMIOLOGY

RISK FACTORS: Environmental conditions may play a role, as higher infection rates are found in shelter and colony dog and cats as compared to pets.

- The mode of transmission is unknown, although oral-oral and fecal-oral routes may occur. Vector transmission (flies) may occur. Waterborne infections may be important in certain areas' supplies. *Helicobacter* gastritis has zoonotic potential.
- One of the most important reasons for concern about *Helicobacter* infections in dogs and cats is the zoonotic potential for transmission to humans. Careful consideration is warranted because of the association of human *Helicobacter pylori* infection with human peptic ulcer disease and an increased risk of gastric cancer. Most evidence suggests this potential is very low, and although several species of *Helicobacter* may affect dogs and cats, *H. pylori* is very uncommonly isolated from cats and has not been isolated from dogs.

CLINICAL PRESENTATION

- Chronic vomiting, intermittent inappetence, and pica may be seen.

PHYSICAL EXAM FINDINGS: There are no specific findings on physical examination suggestive of *Helicobacter* gastritis.

- Multiple species of *Helicobacter* have been isolated from dogs and cats:
  - Cat: *H. felis, H. pamatensis, H. pylori, H. heilmanii*. Approximately 41%-100% of healthy cats and 57%-100% of vomiting cats have *Helicobacter*-like organisms.
  - Gastritis, erosion, and ulceration occur as a consequence of ammonia production (the bacteria produce urease) and other secretory products of the organism that damage epithelial cells and induce gastric acid secretion.

DIAGNOSTIC OVERVIEW

DIFFERENTIAL DIAGNOSIS

        - Gastric parasites
        - Foreign body
    - Nongastric diseases causing vomiting:
    - Systemic diseases (hypoadrenocorticism, hyperthyroidism, heartworm disease, renal disease, liver disease, neoplasia)
    - Drug therapy

      CBC, serum biochemistry profile, urinalysis, and fecal flotation are normal in *Helicobacter* gastritis but are indicated to identify other (systemic) causes of vomiting.

    - Noninvasive studies:
    - Serologic titers: not commercially available; specificity of 95% and sensitivity of 79% when ELISA and immunoblotting were used in combination.
  - Invasive studies:
  - Biopsy (endoscopic or surgical) and histologic evaluation: Warthin-Starry silver stains, Giemsa, or toluidine blue improve identification over routine H&E staining. Squash preps stained with Diff-Quik are useful for rapid identification.
  - Culture: least sensitive method, difficult to culture. Can identify antimicrobial sensitivity.

TREATMENT

Identification of *Helicobacter* organisms or other evidence of helicobacteriosis in dogs and cats warrants treatment if signs of gastritis are present and there is concurrent evidence of chronic gastritis. Eradication of the organism should be the goal for long-term resolution of clinical signs.

- Triple therapy: amoxicillin, 20 mg/kg PO q 12 h; metronidazole, 10 mg/kg PO q 12 h; and clarithromycin, 7.5 mg/kg PO q 12 h for 14 days (first choice)
- It should be noted that although combination antibiotic therapy is the treatment of choice, a combination of amoxicillin,

metronidazole, and bismuth subsalicylate resulted in eradication in only 75% at 4 weeks and 43% of treated dogs at 6 months. It is unknown whether therapeutic failure (lack of eradication) is related to an inability to clear the organism or reinfection. There are no studies reported on the efficacy of the author's listed first choice.

The prognosis is good for initial resolution of clinical signs if the gastritis is due to *Helicobacter* spp. infection. The chance for recurrence is high owing to failure to eradicate the infection or reinfection.

COMMENTS

CLIENT EDUCATION

SUGGESTED READING

Bruchim Y, Klement E, Saragusty J, et al: Heat

stroke in dogs: a retrospective study of 54

cases (1999-2004) and analysis of risk

factors for death. J Vet Intern Med 20(1):38–46, 2006.

AUTHOR: GEOFF HEFFNER

EDITOR: ELIZABETH ROZANSKI

1ST EDITION AUTHOR: KRISTEN AARBO

Heat Stroke/Hyperthermia

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Hyperthermia: elevation of the core body temperature. May occur as a result of exposure to endogenous pyrogens (i.e., fever) or may be the result of excessive external (heat stroke) or internal (muscle fasciculations, seizures) heat.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs, cats. Pediatric or geriatric animals are at higher risk.

GENETICS & BREED PREDISPOSITION: Increased likelihood in:

- Brachycephalic dog breeds; other upper airway obstructions such as laryngeal paralysis
- Obese patients
- Dark-colored or long haired dogs

RISK FACTORS

- Excessive muscle fasciculations:
  - Status epilepticus
  - Metaldehyde or garbage (mycotoxin) intoxication
  - Hypocalcemic tetany
- Excessive external heat/inadequate heat dissipation:
  - Exposure to high ambient temperatures, including enclosure in small spaces such as clothes dryers or cars
  - Vigorous exercise
  - Respiratory abnormalities such as brachycephalic syndrome or laryngeal paralysis
  - Obesity
  - Cardiopulmonary disease
- Endogenous pyrogens:
  - Sepsis
  - Febrile paraneoplastic syndrome
- Other:
  - Drugs such as phenothiazines, opioids (cats), cardiac medications, inhalant anesthetics (halothane), amphetamines, or macadamia nuts
  - Central nervous system lesions

GEOGRAPHY AND SEASONALITY: More common in early summer before heat acclimatization occurs (e.g., outdoors) or on hottest summer days (e.g., trapped in closed car)

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Hemodynamic and respiratory stabilization of the patient is a priority and may need to precede the complete history taking.
- Dogs generally present due to excessive panting or collapse or after being found overheated.
- Most commonly, animals will present with a history of environmental exposure (outside on a hot day without access to shade, left in a car) or recent strenuous physical activity such as hunting, chasing, or seizures.
- It is helpful to obtain information suggesting laryngeal paralysis (recent voice change, upper respiratory stridor), dysphagia, cardiac medications, or prior seizure history to identify an underlying risk factor if possible

PHYSICAL EXAM FINDINGS

- Elevated rectal temperature:
  - Generally >40°C (105.8°F). Note that emergency treatment by owner before arrival may lower the rectal temperature so that the actual peak temperature is not known.
  - Altered mental status
- Hyperemic mucous membranes

- Increased respiratory effort and loud upper airway sounds
- Petechiae

ETIOLOGY AND PATHOPHYSIOLOGY

- Elevation of core body temperature results in activation of inflammatory cytokines, alters mitochondrial function, breaks down lipids within cell walls, denatures proteins and enzymes, and leads to cell necrosis.
- Pulmonary: disruption of pneumocytes of the alveolar endothelium and pulmonary capillary beds leads to protein-rich fluid accumulating within the alveolar space, altering surfactant and inciting additional inflammation, which in turn reduces gas exchange, increases the shunt fraction, and reduces pulmonary compliance. This can lead to noncardiogenic pulmonary edema (), severe hypoxemia, and acute respiratory distress syndrome ().
- Cardiovascular: hyperthermia, hypoperfusion and acidosis cause ischemia and necrosis of cardiac myocytes and Purkinje fibers, leading to ventricular arrhythmias (), conduction disturbances, and myocardial dysfunction.
- Hematologic: endothelial cells are particularly prone to thermal injury. When damaged, these cells release procoagulant factors, activate and/or destroy platelets, activate complement and clotting cascades, which causes a systemic inflammatory response and coagulation. Disseminated intravascular coagulation (DIC;) is a common cause of death in severely affected patients.
- Renal: acute kidney injury can occur as a result of direct thermal injury, microemboli, hypoxia, and hypoperfusion. Renal failure is common in severe heatstroke.
- Neurologic: excess inflammatory and endogenous cytokines and microemboli can result in cerebral edema and neuronal tissue death.
- Malignant hyperthermia is an extremely rare genetically based disorder involving rapid-onset hyperthermia, usually triggered by such specific agents as halothane or succinylcholine.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis of hyperthermia is generally straightforward (markedly elevated body temperature), and diagnostic efforts are mainly aimed at identifying and monitoring secondary complications that occur in severe cases, and an inciting cause if one is not known from the history alone.

DIFFERENTIAL DIAGNOSIS

Hyperthermia: heat stroke, fever

INITIAL DATABASE

- Complete physical exam including neurologic examination (see p. 1311)
  - In heat stroke, mental status is important prognostically, as dogs that are obtunded are less likely to survive.
- CBC: hemoconcentration is common and can be severe. The presence of nucleated red blood cells occurs in up to 68% of cases. A neutrophilic leukocytosis is most common, but patients can also be leukopenic due to peripheral neutrophil chemotaxis and migration. Most animals (62%) are thrombocytopenic at admission, and 83% become thrombocytopenic during hospitalization.
- Serum biochemistry profile: elevation in creatinine kinase from muscle damage is the most common abnormality noted, occurring in nearly every case. Elevations in ALT, AST, and ALP are also very common but rarely affect patient outcome. Hypoglycemia and elevated creatinine values can occur in more than 50% of patients and are negative prognostic features.
- Prothrombin time (PT), activated partial thromboplastin time (APTT) are frequently prolonged in severely affected patients and these elevations are of negative prognostic value.

TREATMENT

TREATMENT OVERVIEW

Treatment goals:

- With obtunded/comatose patients, immediate intubation to secure a patent airway is paramount to improve gas exchange, provide additional oxygen supplementation, reduce the risk of aspiration. and allow for additional heat dissipation.
- Active cooling
- Determine etiology and treat underlying cause as needed.
- Manage complications such as DIC, acute renal failure, sepsis, or cerebral edema.

ACUTE GENERAL TREATMENT

- Lukewarm (room temperature) IV fluids and cool water baths to decrease temperature while avoiding excessive peripheral vasoconstriction. Additional cooling techniques can include infusing the bladder with sterile, lukewarm fluid or cold water gastric lavage. Peritoneal lavage invasive, time consuming, and not clearly superior.
  - Active external cooling should be discontinued once the rectal temperature reaches 103-103.5°F (39.2-39.4°C) to reduce the risk of severe hypothermia.
- Treat hypoglycemia () if present.
- Mannitol (20% injectable solution [200 mg/mL]: 0.5-1 g/kg given IV slowly over 15-20 minutes) may be used if increased intracranial pressure is suspected.
- Seizure activity should be managed with diazepam, 0.2-0.5 mg/kg IV, repeated up to three times; if ineffective, either phenobarbital (4 mg/kg IV q 30 minutes up to 16 mg/kg) or propofol continuous rate infusion (CRI) (6 mg/kg IV bolus followed by 0.1-0.2 mg/kg/min).
- Ventricular arrhythmias (see p. 1165) should be triaged and treated if necessary.
- Fresh frozen plasma (10-15 mL/kg) should be administered if coagulation times are prolonged or there is clinical evidence of bleeding.
- Broad-spectrum antibiotics such as cefazolin (22 mg/kg IV q 8 h), enrofloxacin (5-20 mg/kg IV q 24 h), and metronidazole (10-15 mg/kg IV q 12 h) are indicated empirically owing to venous pooling within the splanchnic circulation and risk for bacterial translocation.

POSSIBLE COMPLICATIONS

- DIC
- Acute renal failure
- Gastrointestinal sloughing/bacterial translocation
- Hepatic failure
- Other components of multiple organ dysfunction syndrome (MODS)
- Cerebral edema
- Bone marrow dysfunction may result in leukopenia and circulating nucleated red blood cells.

RECOMMENDED MONITORING

- Continuous ECG monitoring for changes in heart rate or worsening arrhythmia
- Frequent respiratory monitoring and blood gas evaluation as clinically indicated
- Serial neurologic evaluation
- Blood pressure monitoring (try to maintain systolic at >100-120 mm Hg) and blood glucose assessment (aim for 80-140 mg/dL) q 2-4 h as clinically indicated)
- Urine output (goal of >1-2 mL/kg/h)
- Coagulation times if initially prolonged or evidence of bleeding
- Platelet count

PROGNOSIS AND OUTCOME

- The prognosis associated with heatstroke varies widely depending on clinical severity at hospital admission. Animals recovering from heatstroke do not generally have any long-term side effects but may be at increased risk of future heatstroke.
- Initial body temperature has NOT been correlated with outcome.
- The following have been associated with a poor prognosis:
  - Coagulopathy (PT >18 sec, APTT >30 sec) at admission
  - Nucleated red blood cells >18/100 WBC
  - Hypoglycemia (<47 mg/dL)
  - Serum creatinine (>1.5 mg/dL) after 24 hours
  - Seizures
  - Delayed admission
  - Obesity

PEARLS & CONSIDERATIONS

COMMENTS

- Aggressive early cooling warranted

- Avoid overcorrection/hypothermia.
- Multiple organ failure including DIC is possible.

PREVENTION

Avoid exposing the animal to high ambient temperature or prolonged physical activity.

TECHNICIAN TIPS

- Avoid jugular venipuncture until patient coagulation status can be ascertained.
- Avoid hypothermia by discontinuing active cooling when temperature reaches 103°F-103.5°F (39.2-39.4°C).
- Monitor for recurrent respiratory distress upon extubation, particularly in those animals with brachycephalic syndrome or laryngeal paralysis. Prolonged intubation, temporary tracheotomy (see p. 1344) or definitive airway correction may be required.
- Placement of a urinary catheter and closed collection system allows for frequent, accurate calculation of urine output and characterization.

CLIENT EDUCATION

- Educate clients about the dangers of leaving dogs in cars on hot days, or prolonged exercise on hot days, or if upper airway diseases exist.
- Clinical signs such as weakness and panting in hot weather may be an emergency; institute cooling measures and consult a veterinarian.

SUGGESTED READING

Bruchim Y, Klement E, Saragusty J, et al: Heat stroke in dogs: a retrospective study of 54 cases (1999-2004) and analysis of risk factors for death. J Vet Intern Med 20(1):38– 46, 2006.

AUTHOR: GEOFF HEFFNER

EDITOR: ELIZABETH ROZANSKI

1ST EDITION AUTHOR: KRISTEN AARBO

Heartworm Disease, Dog

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

- Heartworm disease is the clinicopathologic manifestation of infestation with *Dirofilaria immitis,* an intravascular parasite that resides in the pulmonary arteries, and less often the right side of the heart and venae cavae. It results in pneumonitis, pulmonary endarteritis, pulmonary hypertension (PH), pulmonary thromboembolism (PTE), and/or cor pulmonale.
- An occult heartworm (HW) infection is defined as an infection in which microfilariae are not detectable in blood.

SYNONYM

Heartworm (HW) infection

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Wild and domestic canids most commonly; lower prevalence in cats
- Most dogs are 3-6 years old when diagnosed (uncommon in dogs <1 year old).

GENETICS & BREED PREDISPOSITION

- Sporting breeds are predisposed.
- Caval syndrome occurs most commonly in spring and early summer in middle-aged males housed outdoors.

RISK FACTORS

- Lack of HW-preventive drug administration in endemic areas. Most dogs become infected in summer.
- Signalment and lifestyle: for example, male outdoor dogs are more likely to become infected than female indoor dogs.

CONTAGION & ZOONOSIS: Human infections are rare (typically with aberrant migration), not directly associated with a specific heartworm-infected pet, and usually innocuous.

GEOGRAPHY AND SEASONALITY

- Throughout the United States, especially within 150 miles of the Gulf of Mexico and Atlantic coastlines and along the Mississippi River and its tributaries
- Also endemic in Australia, Japan, and some Mediterranean countries
- HW transmission is unlikely in regions or seasons where the ambient temperature does not average more than 65°F (18°C) during a 30-day period.
- Prophylactic failures (often with presumed good client compliance) have been noted along the Mississippi River Delta. One explanation is macrolide resistance, although this has yet to be confirmed.

ASSOCIATED CONDITIONS & DISORDERS

- Aberrant migration of larvae can result in neurologic, dermatologic, and ophthalmic complications.
- Retrograde migration of part of the worm burden into the right atrium and cavae can result in heartworm caval syndrome (common in highly endemic areas), a serious complication involving entanglement of a worm mass in the tricuspid valve apparatus, causing intravascular hemolysis, an acute-onset murmur of tricuspid regurgitation, and signs of forward (hypoperfusion) and backward (congestive) heart failure.
- PTE may be due to dead worms (natural or pharmacologic death) or intravascular thrombi formed as a consequence of the infection.
- PH can occur secondary to pulmonary vascular disease and may result in congestive heart failure (CHF), hemoptysis, and exercise intolerance.
- CHF (uncommon) with signs of right-sided heart failure (ascites and occasionally pleural effusion)
- Allergic pneumonitis (somewhat common) and eosinophilic granulomatosis (rare)
- Glomerulonephritis (virtually all dogs with HW infection; typically mild)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Class 1: few or no overt clinical signs. Class 2: moderate clinical signs. Class 3: severe clinical signs. Class 4: caval syndrome.

HISTORY, CHIEF COMPLAINT

- Most dogs with HW infection are in class 1 and show no clinical signs. HW infection is detected as part of routine blood screening.
- When clinical signs exist, coughing is the most common complaint.
- Other complaints include exercise intolerance, weight loss, syncope or collapse, and manifestations of right-sided congestive heart failure induced by pulmonary hypertension.
- Acute dyspnea secondary to PTE.

PHYSICAL EXAM FINDINGS

- Dogs not showing overt clinical signs to the owner usually have no abnormal physical examination findings.
- Spontaneous or inducible cough possible upon tracheal palpation.
- A split second (S^2) heart sound may be heard if severe pulmonary hypertension is present.
- Jugular venous pulsations and a right apical holosystolic murmur indicate tricuspid regurgitation (a harsh-sounding murmur is often present with caval syndrome).
- Palpable fluid wave (ballottement) if abdominal distention (ascites), and jugular venous distention if CHF
- Discolored urine (from hemoglobinuria), murmur of tricuspid regurgitation, tachypnea/dyspnea, collapse, and right-sided CHF and/or left-sided forward failure indicate caval syndrome.

ETIOLOGY AND PATHOPHYSIOLOGY

- Female mosquitoes serve as intermediate hosts after feeding on microfilaria-positive dogs.
- Microfilariae develop within the mosquito into L3 larvae and can infect another dog within 2-2.5 weeks.
- Patent infection (microfilaremia) occurs 6-7 months after inoculation of susceptible host by infective (L3) larvae.
    - Occult (amicrofilaremic) infections exist during this a prepatent period; other causes of occult infection include immune-mediated microfilarial destruction, unisex infections, acute high-dose or chronic macrolide prophylactic administration.
- Disease severity is determined in part by the duration of infection, number of adult HW, the host's response to live and dead heartworms, and amount of exercise.
- *Wolbachia* sp. (an obligate intracellular gram-negative bacterium) appears to have a symbiotic relationship with *D. immitis* and may exacerbate the inflammatory response by releasing endotoxins and antigens associated with worm death.
    - *Wolbachia* sp. are necessary for *D. immitis* reproduction.
    - Microfilariae produced in absence of *Wolbachia* sp. do not become infective in the mosquito.
- Response of the pulmonary arteries:
    - Damage from direct contact and other mechanisms (e.g., immune mediated) to vessel intima
    - Villous proliferation of the intima and subintimal smooth muscle
    - Pulmonary hypertension: results from obstruction to blood flow (PTE) and reduced vascular compliance induced by endothelial and medial thickening and probably biological incompetence (failure of damaged vessels to respond to vasodilatory stimuli)
    - Results in dilated pulmonary arteries that can be tortuous and truncated
- Response of the pulmonary parenchyma:
    - Deposition of HW antigen within the microvasculature causes parenchymal immune/allergic reactions (periarterial edema and inflammation).
    - Corticosteroid-responsive allergic pneumonitis in 14% of HW infections
    - Severe chronic HW infection causes irreversible pulmonary fibrosis with PH.
- Cardiac response:
    - Right ventricular enlargement secondary to moderate-severe PH and subsequent tricuspid regurgitation and myocardial failure
    - Right-sided congestive heart failure (ascites) in up to 50% of severe HW infections
- Systemic response:
    - Renal: glomerulonephritis, proteinuria, hypoalbuminemia, and decreased antithrombin III (increases pulmonary thromboembolic risk)

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is made in one of two contexts: an incidental finding of a positive antigen test in an overtly healthy dog (more common) or overt clinical signs caused by infection-related secondary lesions. The antigen test is the confirmatory test of choice, and additional testing is indicated based on severity of physical signs and thoracic radiographic changes.

DIFFERENTIAL DIAGNOSIS

- Microfilaria: *Acanthocheilonema reconditum* (formerly *Dipetalonema reconditum)* microfilariae are shorter, narrower, and have a blunted head when compared to *D. immitis* microfilariae.
- Coughing: primary bronchointerstitial disease, collapsing trachea, infectious tracheobronchitis, pneumonia, left-sided congestive heart failure
- Pulmonary hypertension: PTE (due to other causes); chronic pulmonary disease; cyanotic right-to-left shunting cardiac disease such as patent ductus arteriosus and ventricular septal defect with primary or secondary PH; and primary PH.
- CHF: primary or secondary myocardial failure, chronic congenital or acquired valvular disease
- Pulmonary granulomas: primary and metastatic neoplasia

INITIAL DATABASE

- CBC, serum biochemistry profile, urinalysis: evidence of hemolysis and hemoglobinuria if class 4 (caval syndrome). Pathologic proteinuria common due to glomerulonephritis; may be reversible with treatment.
- Electrocardiography may demonstrate a right axis shift (prominent S waves in leads I, II, III, and V3, indicating PH and right ventricular enlargement) and/or atrial or ventricular arrhythmias in moderate to severe cases.
- Thoracic radiographs
    - Dilated and sometimes tortuous, truncated pulmonary arteries
    - Patchy mixed interstitial-alveolar pattern with perivascular infiltrates demonstrated primarily in caudal lung lobes
    - Right heart enlargement
    - Enlarged caudal vena cava if CHF is present or imminent

ADVANCED OR CONFIRMATORY TESTING

- HW antigen tests (ELISA and immuno-chromatographic) are specific, sensitive, and some are semiquantitative.
    - False-negative results with low female worm burdens or immature infections
- Microfilaria: filter and modified Knott's tests preferred over wet direct blood smear.
    - Only indicated if no history of macrolide heartworm prophylaxis and patent infection is suspected
    - Indicated to ascertain presence of microfilariae in dogs with HW infection before institution of therapy
- Echocardiography for moderate to severe HW infection to assess PH and caval syndrome:
    - Dilated pulmonary arteries
    - Parallel linear hyperechoic densities in pulmonary arteries (and sometimes the right heart and venae cavae) with large worm burdens
    - Right ventricular eccentric and concentric hypertrophy with flattened intraventricular septum in severe cases
    - High-velocity tricuspid regurgitation or pulmonic insufficiency on echo-Doppler with PH (TR Vmax greater than 3 m/s)

TREATMENT

TREATMENT OVERVIEW

- Eliminate worm burden and microfilariae (if present).
- Address complications.
- Prevent future infection.

ACUTE GENERAL TREATMENT

- Pulmonary thromboembolism:
    - Oxygen therapy (oxygen cage at 40% O2 or nasal insufflation at 50-100 mL/kg) (see p. 1318)
    - Cage rest
    - Corticosteroids (prednisone, 1 mg/kg PO q 24 h for 7-10 days)
    - Antithrombotic therapy (aspirin, 2.5-5 mg/kg PO q 12 h; or heparin, 75 IU/kg SQ q 8 h for 5 to 7 days or until the platelet count normalizes) is controversial.
- Allergic pneumonitis: cage rest and corticosteroids (prednisone, 1 mg/kg PO q 24 h for 7-10 days)
- Adulticide therapy:
    - Melarsomine (Immiticide):
        - Up to 96% efficacy after two doses; 50% of worm burden killed after a single dose
        - Plan A: melarsomine administered once at 2.5 mg/kg IM, followed by two injections at 2.5 mg/kg 24 hours

apart, given 1-3 months later (authors' preference)
- Plan B: melarsomine administered as two 2.5 mg/kg IM injections given 24 hours apart
- Strict adherence to manufacturer's instructions for intramuscular injection of arsenical agent.
- Consider corticosteroids (prednisone, 1 mg/kg PO q 24 h) or administration of a nonsteroidal antiinflammatory drug (NSAID) at manufacturer's recommended dosage at the time of IM injections to reduce injection site inflammation.
- Ideally, during the transmission season, adulticide therapy should follow 2-3 months of prophylactic therapy.
- Doxycycline (10 mg/kg PO q 24 h) may be administered for 1 month prior to and possibly for 2 weeks after each round of adulticide therapy.
- Exercise restriction for 4-6 weeks after melarsomine injections

- Macrolides as adulticides:
  - Recent studies suggest that an aggressive (off-label) macrolide protocol (ivermectin 6 mcg/kg PO weekly), coupled with a complex regimen of doxycycline (10 mg/kg PO q 24 h from weeks 0-6, 10-12, 16-18, 22-26, and 28-34) will hasten worm death (~80% within 8-9 months) in experimental transplanted HW infections.
  - Ivermectin and selamectin at preventive dosages have a 40%-100% efficacy against young HW infections when administered continuously for 18 or 31 months, respectively.
  - Milbemycin: modest adulticide activity
  - Pulmonary and vascular manifestations of HW infection still result during macrolide adulticide therapy, especially if patient is active.
  - Ivermectin at preventive dosage, with or without doxycycline, is reserved for cases in which financial constraints or concurrent medical problems prohibit melarsomine therapy; should be used only after assurance that microfilariae are cleared (to reduce risk of parasite resistance).

- Worm embolectomy:
  - Blind or fluoroscopically (or sonographically) guided surgical removal of HW from the venae cavae and right heart with alligator forceps, an endoscopic basket retrieval device, or loop snare device
  - Avoid damaging the HW when extracting them (PTE and/or anaphylactoid reaction)
- Microfilaricide therapy:
  - No agent is currently approved by the U.S. Food and Drug Administration for the elimination of microfilariae.
  - Macrolide therapy:
    - Ivermectin: 0.05 mg/kg (about eight times the preventive dose). Ivermectin (Ivomec) diluted 1:9 in propylene glycol or sterile water, administered orally at 1 mL/20 kg. Strongly discouraged by the American Heartworm Society.
    - Milbemycin: 0.5-0.99 mg/kg PO (same as preventive dose)
  - Adverse reactions in approximately 10% receiving microfilaricidal dosage:
    - Shock, depression, hypothermia, and vomiting
    - Fluid and corticosteroid (dexamethasone, 2-4 mg/kg IV) therapy if severe
    - Diphenhydramine (2 mg/kg IM) and dexamethasone (0.25 mg/kg IV) administered prophylactically to prevent adverse reactions
  - The authors' recommendation for microfilaricidal therapy is to initiate routine macrolide prophylactic therapy at the time of diagnosis, to be accompanied or followed by adulticide therapy, depending on season (see Adulticide therapy, above). The clearance of microfilariae should be confirmed.
    - Ivermectin, selamectin, or moxidectin may be used (see Chronic Treatment below) as "slow microfilaricides."
    - Milbemycin is more rapidly microfilaricidal at the preventive dosage. Patients should be hospitalized, pretreated as described above using diphenhydramine and dexamethasone, and observed for 8 hours for adverse reactions.

CHRONIC TREATMENT

- Preventive therapy:
  - Wide window of efficacy with up to 2-month "reachback effect" (elimination of developing larvae that have been in the dog for 2 months).
    - "Reachback effect" can be extended to 3 months with continuous 12-month administration. Extent of "reachback effect" may vary temporally and geographically.
  - Ivermectin (Heartguard): 6-12 mcg/kg PO monthly; *or*
  - Selamectin (Revolution): 6-12 mg/kg topically monthly; *or*
  - Milbemycin (Interceptor): 0.5-0.999 mg/kg PO monthly; *or*
  - Moxidectin/imidacloprid topical (Advantage Multi; imidacloprid 10 mg/kg, moxidectin 2.5-6.8 mg/kg topical monthly) or moxidectin injectable (Proheart 6; 0.17 mg/kg SQ every 6 months)
    - Preventive doses are gradually microfilaricidal; see above for precautions.
    - Package insert states that injectable moxidectin should not be administered to HW+ dogs.
- Congestive heart failure: see pp. 468, 470
- Pulmonary hypertension: see p. 935
  - Adulticidal therapy when deemed safe

POSSIBLE COMPLICATIONS

- Injection site inflammation (adulticide)
- PTE

PROGNOSIS AND OUTCOME

- Good in mild to moderate HW infections
- Fair to guarded in severe cases
- Poor to grave even with treatment in caval syndrome, severe PTE, and CHF

PEARLS & CONSIDERATIONS

COMMENTS

- Virtually all infected dogs are candidates for adulticide therapy (exception: surgical removal of worms in class 4/caval syndrome patients or those undergoing severe PTE or CHF in which increasing worm death will worsen situation).
- Macrolide “slow-kill” adulticide method using preventive drugs rather than melarsomine is easier but does not prevent pathologic response and potentially permanent or life-threatening lesions from HW infection. It also may contribute to the problem of resistance.
- Exercise restriction is an extremely important part of HW infection therapy.

CLIENT EDUCATION

- HW infection is a preventable disease.
- Most preventives are broad-spectrum antiparasitic drugs.
- Importance of year-round preventives:
    - Enhanced “reach-back effect”
    - Adulticidal effect
    - Other parasiticidal effects
    - Reduced issues of compliance

SUGGESTED READING

Atkins CE: Heartworm disease. In Ettinger SJ, Feldman EC, editors: Textbook of veterinary internal medicine, ed 7, St Louis, 2010, Elsevier Saunders, pp 1353–1380.

Current guidelines for diagnosis and treatment from the American Heartworm Society. www.heartwormsociety.org/

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Heartworm Disease, Cat

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Heartworm disease (HWD) is the clinico-pathologic manifestation of infestation with *Dirofilaria immitis,* an intravascular parasite that resides in the pulmonary arteries, the right side of the heart, and venae cavae. This infestation results in pneumonitis, pulmonary endarteritis, pulmonary thromboembolism (PTE), and uncommonly, pulmonary hypertension (PH) with/without cor pulmonale.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Felids are atypical hosts for this canine parasite.
- There is no age predilection (range 1-17 years).
- Male cats generally have an increased risk of exposure and have a higher incidence than females when infected experimentally.

RISK FACTORS

- Cats not receiving heartworm (HW) preventative in endemic areas are at risk, with varying seasonal individual risk determined by season of the year and geographic location.
- Outdoor cats are predisposed, but indoor cats are also at risk (up to one quarter of cats with HWD are indoor cats).
- Feline leukemia virus and feline immunodeficiency virus are not predisposing factors.

CONTAGION & ZOONOSIS: Cats with mature heartworm infection do not provide a threat of transmission to other cats, dogs, or humans (see p. 477).

GEOGRAPHY AND SEASONALITY

- The frequency of feline HW infection correlates with that of dogs in the same geographic region but at a lower incidence (infection rate is 5%-20% that of the dog).
- Reported worldwide and is endemic throughout most parts of the United States
- HW transmission is unlikely in regions or seasons where the ambient temperature does not average over 65○F (>18°C) during a 30-day period.
- Prevalence: in shelter cats (up to 14%) and 9% in pet cats presented for cardiorespiratory signs (26% of these cats were HW antibody positive, indicating HW exposure). Nationwide in the United States, exposure rate likely exceeds 12%.
- Clinical signs associated with early infection occur in late fall and early winter.

ASSOCIATED CONDITIONS & DISORDERS

- Aberrant migration of larvae more common in cats (neurologic, dermatologic, and ophthalmic complications)
- Heartworm-associated respiratory disease (HARD): clinical and histopathologic findings of cats when they abort infections before heartworm maturation (“pulmonary larval dirofilariasis”).
- Pulmonary thromboembolism (PTE) may be due to dead worms (natural or pharmacologic death) or intravascular thrombi formed in response to the infection, resulting in vascular occlusion, infarction, and sometimes acute respiratory death.
- Pulmonary edema, often fulminant, with pulmonary thromboembolism possibly representing acute respiratory distress syndrome (ARDS). This may result acutely after adult worm death.
- Eosinophilic pneumonitis with cough, wheezing, dyspnea
- Congestive heart failure (CHF) is uncommon; signs of right-sided heart failure occur, usually a pleural effusion (either hydrothorax or chylothorax) and/or ascites.
- *Wolbachia* sp. (see p. 477): vital for filariae reproduction and possible contributor to pulmonary lesions; elimination of this symbiotic bacterium may play a role in adulticide therapy.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Clinical classification: (1) no clinical signs, (2) acute or peracute, and (3) chronic (most common)
- Most feline HW infections are occult infections, defined as an infection in which microfilaria are not detectable; microfilaremia in cats is uncommon (<20%), inconsistent, and transient.

HISTORY, CHIEF COMPLAINT

- ≈28% of cats with HW infection show no clinical signs.
- Chronic signs usually predominate (cough [38%], dyspnea [48%], vomiting, anorexia, weight loss, lethargy, exercise intolerance, and rarely, right-sided CHF).
- Acute signs include tachypnea/dyspnea secondary to PTE or severe pneumonitis or ARDS. Sudden death occurs in approximately 10%.

PHYSICAL EXAM FINDINGS

- Usually nonspecific. There appears to be no correlation between the clinical signs, physical examination, and radiographic changes.
- Adventitial lung sounds may be present.
- An audible heart murmur and/or gallop rhythm is uncommon and CHF is rare. Jugular venous distention, dyspnea, diminished lung sounds, and (rarely) ascites may be detected if CHF is present.

ETIOLOGY AND PATHOPHYSIOLOGY

- Female mosquitoes serve as intermediate hosts after feeding on microfilaria-positive dogs.
- Being an atypical host, cats have an inherent resistance.
    - Lower worm burdens (usually fewer than 6, typically 1 to 3)
    - Shortened worm patency period
    - High frequency of amicrofilaremia or low microfilaria counts
    - Shortened lifespan of adult heartworms (2-3 years, although some new information suggests that worms may live up to 4 years).
- Disease severity is determined in part by the number of adult HW and the host's response to live and dead heartworms.
    - Pulmonary response is more severe in cats compared to dogs.
    - Clinical signs can be seen prior to maturation of the larvae (HARD).
- Response of the pulmonary arteries, pulmonary parenchyma, and air spaces
    - Eosinophilic infiltrates predominate.
    - Pulmonary arterial medial and intimal hypertrophy with or without thrombosis, often resulting in obliteration of the vascular lumen
    - Altered vascular permeability allows plasma leakage, producing noncardiogenic pulmonary edema (ARDS) which is typically fatal.
    - Chronic changes can result in diminished pulmonary function, hypoxemia, dyspnea, and cough.
- Acute or sudden death of affected cats is typically associated with adult worm death and resultant respiratory failure.
    - Lungs are considered to be the “shock organ” in feline HW disease.
    - Immune-mediated reaction to HW antigens produces bronchiolar and bronchial constriction, pulmonary congestion and interstitial edema, acute inflammatory interstitial disease, superficial pulmonary hemorrhage, and periarterial hemorrhage with subsequent fatal respiratory failure.
    - Heartworm embolism
        - Smaller feline pulmonary arterial tree with less collateral circulation is more susceptible to worm embolization with subsequent pulmonary infarction.
        - May contribute to episodes of dyspnea and/or sudden death

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

The diagnosis should be suspected when a cat in an endemic geographic area demonstrates signs of respiratory dysfunction or other systemic signs if differential diagnoses that are more likely have been ruled out. Serum antibody testing, thoracic radiography, and echocardiography each may contribute to confirming the diagnosis, and the tests are selected in sequence depending on availability and cost.

DIFFERENTIAL DIAGNOSIS

- Cat with respiratory signs:
    - Bronchitis or asthma

- Lungworms *(Aelurostrongylus abstrusus)*
- *Paragonimus kellicotti* infection
- Pleural effusions (pyothorax, hydrothorax, chylothorax, or neoplastic)
- Pneumothorax

- Cat with neurologic signs (brain or spinal cord):
  - Various inflammatory, ischemic, neoplastic, or degenerative diseases of central nervous system
- Cat with gastrointestinal (GI) signs:
  - Various systemic diseases such as primary GI disease, neoplasia, hyperthyroidism, and renal failure

INITIAL DATABASE

- CBC, chemistry profile, urinalysis
  - Mild nonregenerative anemia or eosinophilia in about 33%
  - Basophilia is highly suggestive, but rare.
- Tracheal wash or bronchoalveolar lavage may contain eosinophils with or without the presence of peripheral eosinophilia.
- Fecal examination for lung parasites (flotation, sedimentation, Baermann procedure)
- Electrocardiography may demonstrate a right axis shift and/or atrial or ventricular arrhythmias in severe cases (uncommon).
- Imaging:
  - Thoracic radiographs (variable findings depending on duration of infection and HW infection severity).
    - Enlarged and sometimes torturous, truncated caudal pulmonary arteries. Right heart enlargement, common in dogs, is unusual in cats.
    - Patchy mixed interstitial-alveolar pattern with perivascular infiltrates (primarily in caudal lung lobes)
    - Radiographic vascular findings are transient.
    - Mimics asthma with bronchovascular pattern and pulmonary hyperinflation

ADVANCED OR CONFIRMATORY TESTING

- The diagnosis of HW infestation/disease in cats can be difficult and often requires an elevated index of suspicion and serial application of diagnostic tests.
- Microfilaria: Most cats are amicrofilaremic. Filter and modified Knott's tests preferred over wet direct blood smear. A positive result is uncommon but diagnostic.
- HW antibody tests:
  - Used in the detection of *exposure* to HW and possible HARD or mature HWI; does not prove ongoing infection
  - Used for “ruling out” HW infection in cats with compatible signs. However, at least 14% of cats with mature HW infection may be antibody-negative.
  - Approximately 2% of HW-infected, antibody-negative cats are HW antigen positive.
- HW antigen tests (ELISA and immuno-chromatographic; assess for antigen elaborate by adult female HW) are specific, and some are semiquantitative. A positive result is diagnostic.
  - High number of false-negative results due to low female worm burdens or immature infections.
  - Recently an antigen test for felines has been marketed (adaptation of the canine test with reported 15% increase in sensitivity; IDEXX SNAP Feline Heartworm Antigen test).
  - Clinical signs can occur *before* the presence of detectable HW antigen.
- Echocardiography:
  - Dilated pulmonary arteries
  - Parallel linear hyperechoic densities in pulmonary arteries, the right heart and/or the venae cavae
  - HW found with echocardiography in 78% of 9 naturally infected cats in one study.

TREATMENT

TREATMENT OVERVIEW

- Address complications.
- Prevent future infection.
- Adulticide therapy is generally not recommended.

ACUTE GENERAL TREATMENT

- Cats with HW infection should receive HW preventive medication (see Chronic Treatment, below) and short-term corticosteroids (prednisone, 1-2 mg/kg PO q 8-48 h) can be used for managing respiratory signs.
- Emergency therapy for acute dyspnea:
  - Oxygen therapy (oxygen cage at 40% O2 or nasal insufflation at 50-100 mL/kg; see p. 1318)
  - Cage rest

- Corticosteroids (dexamethasone, 1 mg/kg IV or IM; or prednisolone sodium succinate, 50-100 mg/cat IV)
- Bronchodilator therapy (aminophylline, *6.6* mg/kg IM q 12 h)
- Antithrombotic therapy: aspirin (80 mg PO q 72 h) is controversial.

- Worm embolectomy
  - Can be considered, although mortality rates in one report (2 of 5) thought to be unacceptable
- Microfilaricide therapy
  - No agent is currently approved by the U.S. Food and Drug Administration for the elimination of microfilaria.
  - The authors' recommendation for microfilaricidal therapy is to initiate macrolide prophylactic therapy at the time of diagnosis.
    - Ivermectin (Heartguard): 25 mcg/kg PO monthly, *or*
    - Selamectin (Revolution): 6-12 mg/kg topically monthly, *or*
    - Milbemycin (Interceptor): 2 mg/kg PO monthly
      - Preventive doses are microfilaricidal.
      - Patients with microfilaria should be observed at home or hospitalized possibly, pretreated with diphenhydramine and dexamethasone, and observed for 8 hours for adverse reactions.
  - Imidacloprid-moxidectin (Advantage Multi): 10 mg/kg imidacloprid and 1 mg/kg moxidectin applied topically monthly

CHRONIC TREATMENT

- Preventive therapy:
  - Ivermectin (Heartguard): 25 mcg/kg PO monthly
  - Selamectin (Revolution): 6-12 mg/kg topically monthly
  - Milbemycin (Interceptor): 2 mg/kg PO monthly
    - Preventive doses are microfilaricidal; risk of anaphylactic reaction in cats with microfilaremia (although infrequent owing to low microfilarial numbers).
  - Imidacloprid-moxidectin (Advantage Multi): 10 mg/kg imidacloprid and 1 mg/kg moxidectin applied monthly
- CHF:
  - Conventional therapy, individualized to patient needs:
    - Furosemide (2-3 mg/kg PO q 8-12 h)
    - Spironolactone (1-2 mg/kg PO q 12-24 h)
    - Angiotensin-converting enzyme inhibitor (enalapril, 0.5 mg/kg PO q 12-24 h)
    - Periodic abdominocentesis/thoracocentesis
    - Oxygen therapy
    - Extreme exercise restriction
    - Amlodipine (0.1-0.2 mg/kg PO q 24 h) to reduce pulmonary hypertension
- Eosinophilic pneumonitis:
  - Corticosteroids (prednisone, 2 mg/kg/day, tapering over 4 weeks; reinstitute as needed at lowest q 48 h dosage that maintains the cat free of clinical signs).
  - Bronchodilators (optional; aminophylline, *6.6* mg/kg IM q 12 h)

PROGNOSIS AND OUTCOME

- Good in mild to moderate HW infestations.
  - For most patients that survive the initial insult, the median survival time may be much greater than 1 year.
- Fair to guarded in severe cases.
- Overall, prognosis similar to hypertrophic cardiomyopathy, which shares a median age of diagnosis with HW infection of roughly 6 years.
- Recent studies suggest that some cats remain asymptomatic and self-cure, with the infection often unrecognized.

PEARLS & CONSIDERATIONS

COMMENTS

- Preventive therapy is indicated in cats that are in HW-endemic areas.
- Signs may be peracute, acute, chronic, or absent in cats with HWI.
- Most often signs are respiratory.
- Consider HWI whenever feline bronchial disease is suspected.
- Cats which resist mature infection may still develop clinical signs produced by immature heartworms.
- Adulticide therapy is generally not recommended.
- Diagnosis may be difficult, requiring a high index of suspicion and multiple tests including HW antibody tests, HW antigen tests, thoracic radiography, and echocardiography.

CLIENT EDUCATION

- HW infection is a preventable disease.
- Most preventatives are broad-spectrum antiparasitic drugs.
- Importance of year-round preventatives
    - Issues of compliance

SUGGESTED READING

Atkins CE: Heartworm disease. In Ettinger SJ, Feldman EC, editors: Textbook of veterinary internal medicine, ed 7, St Louis, 2010, Elsevier Saunders, pp 1353–1380.

Current guidelines for diagnosis and treatment from the American Heartworm Society. www.heartwormsociety.org/

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EDITOR: ETIENNE CÔTÉ

Heart Murmurs

BASIC INFORMATION

DEFINITION

Normal blood flow in the circulatory system is laminar in nature and very quiet. When laminar flow through the heart is altered, turbulence develops, causing a sound that can be heard: a heart murmur. This can be most easily likened to a slow-flowing, wide river undulating quietly back and forth. Suddenly an obstruction such as a large boulder is placed in the river, and now the quiet river becomes a noisy one as the water flows around the rock creating turbulence.

EPIDEMIOLOGY

SPECIES, AGE, SEX: A heart murmur is a clinical sign which may develop in any animal. Pathologic murmurs caused by structural heart lesions generally increase in intensity with age and disease progression. “Benign” heart murmurs of young, growing dogs and cats are noted to be:

- Soft (grade II/VI or less)*
- Systolic*
- Point of maximal intensity: left hemithorax*
- Abolished with an increase in heart rate or change in body position
- Disappear by age 16 weeks

* Can also occur with a murmur caused by a congenital heart malformation

GENETICS & BREED PREDISPOSITION: Many breeds are predisposed to congenital heart malformations that are associated with heart murmurs (e.g., patent ductus arteriosus, subaortic stenosis, pulmonic stenosis, ventricular septal defect, tricuspid dysplasia, etc.) and adult-onset disorders, some of which have a heritable basis (myxomatous mitral valve disease, dilated cardiomyopathy etc.).

RISK FACTORS

- Heart murmurs are associated with diseases of the heart (myocardium, heart valves, the endothelial lining of the heart) and great vessels.
- Heart murmurs of secondary cardiac origin are associated with noncardiac entities such as fever, anemia, hyperthyroidism, extreme thinness or obesity, and pregnancy. These murmurs are systolic, soft (<III/VI), and more intense on the left side.
- Heart murmurs develop with congenital and acquired heart defects.
- Physiologic murmurs are rare in adult dogs and cats; this is a murmur present in the absence of any cardiac or systemic abnormalities. Dynamic right ventricular outflow turbulence (dRVOT) has been described in the cat, and is associated with obstruction to flow in the ventricle; clinical consequences may develop over time.
- Murmurs may also be identified in the veins and arteries under circumstances that cause nonlaminar flow, such as arteriovenous fistulas or extravascular partial obstructions.
- Systemic infection may cause bacterial endocarditis (see p. 346).

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Heart murmurs may be noted during a routine examination in a patient that is otherwise well. The goal is to identify the cause of the murmur (may be highly suggestive based on signalment, history, and exam, or may require diagnostic testing).
- Heart murmurs may be noted in a patient that is systemically ill (e.g., anemic). Ascertain whether the murmur can be explained by the systemic illness alone (see Risk Factors) or whether an underlying heart problem is coexistent (e.g., endocarditis).
- Heart murmurs may be noted in patients with overt signs compatible with heart disease (dyspnea, exercise intolerance, collapse, signs of thromboembolism). The murmur is a clue that these generalized signs may be caused by a heart problem, and that cardiac diagnostic testing is indicated.

PHYSICAL EXAM FINDINGS

- Murmurs should be identified during the physical examination process. Using the stethoscope, the dog or cat's thorax is thoroughly auscultated first using the diaphragm and then the bell of the instrument. All four valve areas—mitral, tricuspid, pulmonic and aortic regions—are ausculted listening for abnormalities of the heart rate and rhythm, as well as alterations in the heart sounds (see p. 433) and most commonly, a heart murmur. If a murmur exists, it must be identified with respect to timing, intensity, and musical tonality as well as where it is heard on the thorax and if the sounds spread to other parts of the thorax or into the jugular region of the neck.
- Murmurs are described as to their intensity, using a grading system of VI maximum, with a I/VI being the least intense and barely heard; II/VI being soft but unmistakenably heard; III/VI being easily distinguished; IV/VI being intense but without a palpable thrill; V/VI being loud, intense, and associated with a precordial vibration (thrill) on the thorax where it is auscultated; and a VI/VI being so loud it is heard with the stethoscope off the thorax and so intense a thoracic thrill is present.
- The murmur is identified as to when it occurs—in systole, diastole, or seamlessly through both of these physiologic periods of the heart cycle (“continuous”). Murmurs are also noted as being early, mid, or late (within systole or diastole) and are then characterized by their musical quality or tone such as high frequency, midrange, or low frequency. While not always true, usually the intensity of the murmur correlates with the severity of the disease.

ETIOLOGY AND PATHOPHYSIOLOGY

- Systolic murmurs are associated with congenital conditions such as aortic stenosis, pulmonic stenosis, septal defects, atrioventricular valve dysplasia, tetralogy of Fallot, and other less common congenital lesions.
- Acquired systolic murmurs are auscultated with mitral valvular heart disease (insufficiency), cardiomyopathies, anemia, fever, hyperthyroid disease, heartworm disease, endocarditis, and diastolic dysfunction syndromes.
- Diastolic murmurs in small-animal veterinary medicine are unusual but are associated with mitral stenosis, aortic valvular insufficiency, pulmonic valvular insufficiency.
- Continuous murmurs are heard with patent ductus arteriosus or A-V vascular shunting lesions, either centrally or in the peripheral vascular system.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Heart murmurs must be differentiated from breath sounds. In animals with particularly noisy breathing, respiratory distress, or anxiety, the breath sounds may be confused with heart murmurs because of the noise occurring from the thorax or upper respiratory system during auscultation and physical examination.

INITIAL DATABASE

- Depends on the context in which the murmur is noted (see History, Chief Complaint)
- Thoracic radiographs: diagnostic test of choice for left-sided congestive heart failure (pulmonary edema)
- Echocardiography: diagnostic test of choice for pinpointing the cardiac lesion responsible for the murmur
- CBC, serum chemistry panel, urinalysis, abdominal imaging: as indicated for systemic disorders
- Cardiac biomarkers (particularly NT-proBNP): helpful in distinguishing cardiac from noncardiac thoracic disease; may have significance in correlating with the phase of cardiac disease, especially in the cat and possibly in the dog.

TREATMENT

TREATMENT OVERVIEW

Treatment of heart murmurs is not an option. The veterinarian must identify the murmur first, then the cause of the murmur, and then make associations with the disease condition present. The presence of a murmur does not mean the animal requires therapy. The intensity of the murmur usually directly relates to the severity of the disease; increased radiographic vertebral heart score together with a murmur is usually a good indication of the severity of the cardiac disease.

PROGNOSIS AND OUTCOME

Highly variable, depending on the underlying cause of the murmur. The prognosis of a patient with a heart murmur is influenced by the disorder causing the murmur, not by the murmur itself.

PEARLS & CONSIDERATIONS

COMMENTS

- In dogs that are panting, anxious, sniffing, or whining, closure of the mouth and intermittent occlusion of the dog's nostrils for 2-3 seconds at a time is useful for intermittently masking breath sounds that interfere with auscultation of the heart.
- In cats, the sound of running water, or “scruffing” (lifting the skin of the nape of the neck) helps abolish purring.
- A systolic whoop is an uncommon but strikingly loud (VI/VI) systolic murmur produced by resonance of the mitral valve. It may appear or disappear spontaneously and is not related to the presence or severity of any underlying heart problem, although further monitoring is indicated.

SUGGESTED READING

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Heart Failure, Chronic

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

- Heart failure (HF) is a syndrome that results from impaired filling or emptying of the heart, typically manifesting with cardiogenic edema or effusion.
- A new classification system can be applied to heart failure in small-animal practice. In this schema, patients with heart failure are staged as follows:
  - Class A—patients at risk for heart failure (no overt or occult signs of heart disease)
  - Class B—patients that have structural heart disease but have not developed heart failure
  - Class C—patients that have *or previously have had* clinical signs of heart failure
  - Class D—patients with refractory heart failure
- Here, the term *chronic HF* is used as a synonym for Class C heart failure as described above. Urgent therapy of acute or decompensated heart failureis addressed elsewhere (see p. 468).

SYNONYM

Congestive heart failure

EPIDEMIOLOGY

SPECIES, AGE, SEX: HF is a syndrome that can result from practically any cardiac disease; signalment reflects predispositions for the causative disorder:

- Geriatric small-breed dogs: chronic mitral and tricuspid regurgitation due to myxomatous valve disease
- Adult large-and giant-breed dogs: dilated cardiomyopathy (DCM)
- Cats: hypertrophic cardiomyopathy (HCM; males > females), restrictive/unclassified cardiomyopathy

GENETICS & BREED PREDISPOSITION

- DCM: Doberman pinschers, Great Danes, Irish wolfhounds, and other large-and giant-breed dogs
- Mitral and tricuspid regurgitation due to chronic myxomatous valve disease: geriatric small-breed dogs including Cavalier King Charles spaniels, dachshunds, and many others
- HCM: inherited in Maine coon cats and Ragdoll cats. It is possible that feline HCM generally is a genetic disease

RISK FACTORS: Electrocardiographic and echocardiographic variables that predict the development of HF in Doberman pinschers have been described. In Irish wolfhounds and other giant-breed dogs, atrial fibrillation sometimes precedes the development of HF. In small-breed dogs, a murmur caused by myxomatous mitral degeneration is a risk factor for development of HF, but there is great interindividual variability in the rate at which valvular disease progresses. In cats, echocardiographically evident left atrial enlargement is associated with the development of HF.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Left-sided HF results in pulmonary edema.
- Right-sided HF causes ascites and sometimes concurrent pleural effusion.
- In cats, pleural effusion results from left-, right-, or biventricular HF; ascites is uncommon.

HISTORY, CHIEF COMPLAINT: Clinical signs such as respiratory distress generally have improved or resolved with initial treatment, but signs such as progressive abdominal distension, syncope, lethargy, and weight loss may persist. Patients with chronic heart failure are subject to episodes of acute/decompensated heart failure.

PHYSICAL EXAM FINDINGS

- Patients with HF due to mitral/tricuspid myxomatous valve disease have a cardiac murmur; usually the murmur is loud, and its intensity is generally not affected by treatment.

- An audible third or fourth heart sound—a gallop—reflects high atrial pressures and reduced ventricular compliance. In dogs, it is a relatively specific marker of HF.

ETIOLOGY AND PATHOPHYSIOLOGY

- Congestive signs result when high venous pressures cause the development of edema or cavitary effusions.
- In dogs, HF that results primarily from systolic dysfunction—failure of the ventricle to completely empty—is most common.
- HF in cats usually results from diseases that impair ventricular filling; diastolic ventricular pressures are abnormally high when ventricular volume is normal or small.
- High filling pressures are reflected upstream to the venous circulation, resulting in edema or pleural effusion.
- HF is associated with neuroendocrine activation: specifically, impaired cardiac performance leads to increased activity of the renin-angiotensin-aldosterone system (RAAS) and the adrenergic nervous system (ANS).
- Angiotensin II (ATII) is the biologically active product of a biochemical cascade for which the final step is catalyzed by angiotensin-converting enzyme (ACE).
- ATII is a vasoconstrictor, but it also stimulates the release of aldosterone, augments activity of the ANS, and acts as a cardiomyotrophic factor.
- Activation of the RAAS and ANS serves to temporarily maintain perfusion pressure and cardiac output.
- Vasoconstriction increases vascular resistance so that blood pressure is maintained when cardiac output is subnormal. In patients with mitral/tricuspid myxomatous valve disease or DCM, vascular resistance is high, causing a detrimental increase in after-load; this partly explains the beneficial effect of vasodilators.
- It is now generally accepted that neuroendocrine activation associated with cardiac dysfunction is initially beneficial but ultimately detrimental and contributes importantly to the pathogenesis of progressive cardiac dysfunction. Current therapies for chronic HF reflect this conceptual framework.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Chronic heart failure is present when acute/decompensated heart failure is treated successfully, but the underlying cause cannot be cured. Therefore, clinical features of chronic heart failure include a history of acute/decompensated heart failure, with partial or complete resolution of signs with treatment but persistence of the underlying cardiac lesion.

DIFFERENTIAL DIAGNOSIS

Other causes of respiratory distress, cough, abdominal distension, lethargy, inappetence, and weight loss (cardiac cachexia)

INITIAL DATABASE

- Thoracic radiography:
  - Left atrial enlargement with pulmonary opacities is diagnostic of left-sided HF (see p. 468).
  - With diuretic treatment of decompensated HF, clinical improvement is usually rapid (minutes to hours), but radiographic resolution of pulmonary infiltrates may take 12-24 hours.
  - Cats commonly develop pleural effusion in association with left-sided cardiac disease.
- Electrocardiography (ECG) is indicated when arrhythmias complicate the presentation. Atrial fibrillation is commonly associated with heart failure in large-breed dogs, but tachyarrhythmia of virtually any type may complicate the presentation of heart failure (see p. 468).
- Noninvasive estimation of systemic blood pressure using the Doppler cuff or oscillometric method should be considered. The finding of systemic hypertension (SH) provides evidence of concurrent disease; that is, SH may complicate HF, but it is not a result of HF. However, documented SH should be treated, since untreated SH may accelerate the progression of the primary cardiac disorder.
- Serum biochemistry profiles: provide useful ancillary information and are important in monitoring the effects of therapy (especially renal and electrolyte effects).

ADVANCED OR CONFIRMATORY TESTING

B-type natriuretic peptide (BNP) is released by cardiomyocytes in response to increases in ventricular filing pressures. Elevated circulating BNP is a marker of the heart failure state, but the diagnostic utility assay has yet to be fully clarified.

Echocardiography generally provides the diagnosis of the underlying cardiac disorder. Echocardiography is complementary to physical examination and thoracic radiography but does not replace them.

TREATMENT

TREATMENT OVERVIEW

- Correction/cure of the underlying cause when possible
- In all cases, increase in quality and duration of life
- Although individual patient characteristics must be taken into account, poly-therapy consisting of furosemide, an ACE inhibitor, and pimobendan with or without digoxin has become standard treatment for management of class C HF in the dog.
- There is uncertainty regarding optimal therapy for cats with HF resulting from diastolic dysfunction; furosemide and an ACE inhibitor, with or without beta-blockade, are widely used.

CHRONIC TREATMENT

- Diuretics. Furosemide is the most effective agent for management of congestive signs.
  - In dogs, a dose of 1 mg/kg PO q 12 h is often initially adequate when given concurrently with ancillary agents such as ACE inhibitors and pimobendan. Cats with HF generally require lower initial doses (0.5-1 mg/kg PO q 12-24 h).
  - Furosemide is used first, but the progressive nature of the HF state generally requires adjustment of doses. If clinical signs suggest diuretic resistance or if electrolyte derangements are documented, other diuretics such as hydrochlorothiazides (2-4 mg/kg PO q 12 h) or spironolactone (1-2 mg/kg PO q 12 h [dog]) can be added. Doing so allows for synergistic diuretic action: Different diuretics act in different parts of the nephron, which minimizes the negative effects of long-term (weeks or more) administration of high doses of a single diuretic (e.g., >3-4 mg/kg q 8-12 h furosemide).
  - Diuretic dose should be determined by clinical response; the optimal dose is the lowest one that eliminates congestive signs.
  - Excessive diuretic administration may decrease renal perfusion, creates electrolyte imbalances, and contributes to potentially harmful neuroendocrine activation.
  - Most patients require lifelong diuretic administration; progression of the underlying disorder generally necessitates increases in furosemide dose and/or the use of additional diuretics.
  - Furosemide administration sometimes can be tapered or temporarily discontinued in cats with hypertrophic cardiomyopathy.
- ACE inhibitors partially blunt the effects of RAAS activation and reduce afterload.
  - ACE inhibition has proven benefits for patients with chronic HF caused by systolic dysfunction; preliminary evidence suggests a benefit for patients with chronic HF caused by diastolic dysfunction (e.g., cats with HF caused by hypertrophic or restrictive/unclassified cardiomyopathy).
  - Of the ACE inhibitors, veterinary experience is greatest with enalapril (0.5 mg/kg PO q 12-24 h [dog]), benazepril (0.25-0.5 mg/kg PO q 24 h [dog], 0.5-1 mg/kg PO q 24 h [cat]), and ramipril (0.125 mg/kg PO q 24 h [dog]).
- Digoxin:
  - 0.22 mg/m^2 PO q 12 h [dog]; 0.03125 mg/cat PO q 48 h
  - Weak positive inotrope that has potentially beneficial neuroendocrine effects; digoxin inhibits adrenergic activity and increases vagal tone.
  - Important in management of patients with both systolic dysfunction (e.g., dilated cardiomyopathy) and atrial fibrillation; benefit to patients with sinus rhythm is uncertain. Digoxin is generally contraindicated in HCM.
- Pimobendan (0.1-0.3 mg/kg PO q12 h administered when stomach is empty) is a phosphodiesterase inhibitor that acts as an “inodilator.” It is indicated for the treatment of dogs that have developed Class C heart failure due to valvular disease or dilated cardiomyopathy.
  - Pimobendan decreased mortality when compared to benazepril in patients with HF due to valvular disease. The evidence that pimobendan decreases mortality in Doberman pinschers with class C heart failure due to DCM is strong.
  - Unfortunately, information that relates to the effect of pimobendan in dogs receiving standard therapy of an ACE inhibitor and furosemide is sparse. While it is accepted that these drugs can and probably should be used together, there are unanswered questions that relate to staging of therapy.
  - The concurrent use of pimobendan, an ACE inhibitor, and furosemide as initial therapy can be justified, as can staged therapy in which an ACE inhibitor or pimobendan is used as rescue therapy in the event of clinical deterioration.
  - Adverse effects associated with the administration of pimobendan are apparently uncommon, although there is some evidence that pimobendan might harm patients with mild subclinical valvular disease. Accordingly, the use of this drug should be reserved for patients with Class C or D HF due to valvular or myocardial disease. A proarrhythmic effect is possible but appears uncommon, if it even exists in dogs.
- β-Blockers (BB). There is experimental evidence that supports the use of BB in dogs with dilated cardiomyopathy or advanced mitral/tricuspid valve disease.
  - BB are negative inotropes that can induce acute HF if given at an inappropriately high initial dose or if the dose is increased too quickly; dose must be gradually titrated over weeks from a low initial dose to a target dose, typically beginning at 0.1 mg/kg PO q 12 h (carvedilol) or 0.1-0.2 mg/kg PO q 12 h (metoprolol).
  - BB are never started before a patient's pulmonary edema has resolved.

- Spironolactone (1-2 mg/kg PO q 12 h [dog])
  - In chronic HF, excess aldosterone may contribute to the development of myocardial fibrosis.
  - Spironolactone is an aldosterone antagonist, and as such it may limit the detrimental effects of hyperaldosteronemia; careful monitoring of electrolytes is advised.
  - Minimal diuretic efficacy as monotherapy in the dog.
  - Severe facial dermatitis in 30% of cats makes this drug relatively contraindicated in this species.
- Cautious addition of amlodipine (0.0625-0.25 mg/kg PO q 24 h [dog],0.125 mg/kg-0.25 mg/kg PO q 24 h [cat]) to conventional therapy can be considered for patients with refractory HF or for those in which SH complicates the clinical presentation. Blood pressure monitoring is essential.
- Moderate dietary sodium restriction generally is indicated. If palatable to the patient, low-sodium diets may reduce diuretic requirements.

NUTRITION/DIET

Moderate sodium restriction, adequate protein and energy content, and palatability are important attributes of an optimal diet for HF patients (see p. 168).

POSSIBLE COMPLICATIONS

- "Cardiorenal syndrome": azotemia associated with diuretic administration and diminished cardiac performance
  - When azotemia is encountered in patients receiving furosemide and ACE inhibitors, *furosemide* is first decreased by 50%, provided the patient is free of congestive signs. If creatinine does not decrease, diuretic therapy is discontinued, provided congestive signs are not evident. Only if this is unsuccessful is the ACE inhibitor discontinued.
  - There are unfortunately few alternatives for patients that develop clinical signs specifically due to azotemia when congestive signs are present concurrently; this may reflect medically intractable heart failure. However, caution must be exercised, as "overinterpretation" of radiographs or abnormal lung sounds (e.g., pulmonary rales/crackles due to interstitial lung fibrosis, not edema) can lead to inappropriately high diuretic doses, volume depletion, and azotemia.

RECOMMENDED MONITORING

- Serum urea, creatinine, and electrolytes
- Serum digoxin concentration

PROGNOSIS AND OUTCOME

Despite favorable initial response, heart failure is generally associated with a poor long-term prognosis unless the causative disorder is curable.

PEARLS & CONSIDERATIONS

COMMENTS

- Current therapy of heart failure reflects the understanding that activation of the ANS and RAAS is central to the pathogenesis of the syndrome.
- When the causative disorder is not curable, chronic HF is a progressive and terminal syndrome. Therefore attempts to identify a correctable cause are important; some patients with dilated cardiomyopathy respond to supplementation with nutraceuticals such as taurine and L-carnitine.

PREVENTION

- In patients with clinically silent dilated cardiomyopathy, the onset of heart failure may be delayed by the administration of ACE inhibitors and BB.
- ACE inhibition has a modest but probably positive effect on the time to development of class C HF in canine patients with left atrial enlargement due to mitral valve regurgitation.
- Evidence that medical therapy slows the progression HCM is currently lacking.

CLIENT EDUCATION

Management of the veterinary patient with chronic HF requires careful monitoring and relatively frequent adjustment of medical therapy.

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Heart Failure, Acute/Decompensated

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Acute (or decompensated) congestive heart failure (HF) is characterized by the sudden onset of clinical signs associated with pulmonary edema or cavitary effusions that develop as a consequence of heart disease. Acute/decompensated HF is a common cause of respiratory distress that is most often associated with worsening cardiac performance in patients with chronic heart disease.

SYNONYMS

Acute congestive heart failure, decompensated heart disease, overt heart failure

EPIDEMIOLOGY

SPECIES, AGE, SEX: Signalment reflects predispositions for the causative heart disorder. Examples:

- Geriatric small-breed dogs: chronic mitral/tricuspid regurgitation (myxomatous valve disease)
- Cats: hypertrophic cardiomyopathy (HCM)

GENETICS & BREED PREDISPOSITION

- Dilated cardiomyopathy (DCM): Doberman pinschers, Great Danes, Irish wolfhounds, and other large-and giant-breed dogs
- Mitral/tricuspid myxomatous valve disease: Cavalier King Charles spaniels, dachshunds, many others
- HCM: inherited in Maine coon cats and in Ragdoll cats; it is possible that feline HCM generally is a genetic disease.

RISK FACTORS

- In patients with underlying heart disease:
  - Dietary sodium excess
  - Acute intravascular volume load (e.g., parenteral fluids)
  - Possibly corticosteroids (HCM cats)
  - Possibly ketamine/tiletamine (HCM cats)
- Electrocardiographic, echocardiographic variables: predictive of likelihood of future HF or sudden, unexpected death in Doberman pinschers with DCM

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Left-sided HF results in pulmonary edema.
- Right-sided HF causes ascites and sometimes concurrent pleural effusion.
- In cats, pleural effusion may result from left-and/or right-sided heart disease.

HISTORY, CHIEF COMPLAINT

- Respiratory signs predominate. Specifically, the characteristic manifestations include tachypnea, dyspnea, and, in the dog, cough. Heart failure seldom causes coughing in cats.
- Clients may report that the patient appears to be uncomfortable, restless, or unwilling to lie down.

PHYSICAL EXAM FINDINGS

- Tachycardia is a relatively consistent, although nonspecific, finding in dogs with HF. Heart rate of cats with acute HF differs little from heart rate of healthy cats. Some cats with acute HF have bradycardia.
- The presence of respiratory sinus arrhythmia is generally inconsistent with acute HF; other explanations for the clinical signs should be considered.
- In patients with pulmonary edema, tachypnea and respiratory distress are usually apparent during the physical examination.
- Dogs with acute HF due to mitral or tricuspid regurgitation caused by myxomatous valve disease have a cardiac murmur;

usually the murmur is loud (=III/VI).
- An audible, low-frequency third or fourth heart sound—a gallop—reflects high atrial pressures and reduced ventricular compliance. Relatively specific marker of acute HF in dogs.

ETIOLOGY AND PATHOPHYSIOLOGY

- Congestive signs result when high venous pressures cause the development of edema or cavitary effusions.
- In dogs, HF that results primarily from systolic dysfunction—failure of the ventricle to completely empty—is most common.
- HF in cats usually results from diseases that impair ventricular filling (diastolic dysfunction).
- HF is associated with neuroendocrine activation that temporarily maintains perfusion pressure and cardiac output through vasoconstriction and increases in heart rate and contractility.
- In patients with systolic dysfunction, systemic vascular resistance rises disproportionately, causing a detrimental increase in after load; this explains the beneficial effect of vasodilators.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Heart failure is a clinical or radiographic diagnosis:

- Left heart failure is defined by the presence of radiographic pulmonary opacities in association with left atrial enlargement.
- Right heart failure is defined by the finding of ascites in association with jugular venous distension and/or evidence of right atrial/right ventricular enlargement from imaging studies.

DIFFERENTIAL DIAGNOSIS

Other causes of respiratory distress and/or cough:

- Chronic sterile bronchitis
- Collapsing trachea
- Allergic airway disease
- Noncardiogenic pleural effusion
- Intrathoracic mass
- Pneumonia
- Pneumothorax

INITIAL DATABASE

- Thoracic radiographs: radiographic findings of left atrial enlargement together with pulmonary opacities are diagnostic of left-sided HF.
- Electrocardiography (ECG) is indicated when arrhythmias complicate the presentation.
- Serum biochemistry profile and urinalysis: in all cases, preferably before initiating treatment

ADVANCED OR CONFIRMATORY TESTING

- Echocardiography defines the causative disorder.
    - Elevated circulating NT-proBNP is a marker of HF; the diagnostic utility of the assay has yet to be fully clarified.

TREATMENT

TREATMENT OVERVIEW

The goal of treatment is to restore ventilatory function by eliminating lung edema or pleural effusion, and in some cases, improving cardiac performance.

ACUTE GENERAL TREATMENT

- Rest
- Judicious/minimal restraint and other measures for reducing anxiety are essential.
- Furosemide: diuretic of choice in acute HF. Dose and dosage interval are best determined by clinical response.

    - Initially: relatively high dose (2-6 mg/kg IV, IM). If no overt (e.g., respiratory) evidence of effect, this dose can be repeated within 45-60 minutes.
    - If respiratory rate and effort decrease: 1-2 mg/kg IV or IM q 1-6 h until respirations normalize.
    - The effect of furosemide is rapid but short lived; low doses at short intervals may limit adverse effects.
    - Constant rate infusion of furosemide is an alternative to frequent bolus administration, but advantages in veterinary patients are uncertain; dosage = total projected daily dosage of furosemide divided by 24 as the hourly rate of the infusion.
    - In general, cats require lower doses than dogs.
- Supplementary oxygen
- Morphine (0.05-0.3 mg/kg SQ, IM, or IV) should be considered for dogs that are anxious from respiratory distress.
- Thoracocentesis (see p. 1338) if physical or radiographic findings indicate that pleural effusion is likely responsible for respiratory distress.
- Transdermal nitroglycerin (0.5-3 cm q 12 h) may reduce venous pressures. Efficacy undetermined.
- Patients with systolic dysfunction and evidence of diminished cardiac output at rest may benefit from intravenous administration of nitroprusside (0.5-15 mcg/kg/min) and/or dobutamine (2-15 mcg/kg/min) constant rate infusion. Careful monitoring required.
- Dogs with acute/decompensated HF due to valvular disease or dilated cardiomyopathy may benefit from administration of the inodilator pimobendan (0.25 mg/kg PO q 12 h), particularly if there are findings such as prerenal azotemia, hyponatremia, or hypothermia that suggest diminished cardiac output. The use of pimobendan in acute (or decompensated) HF has not been systematically evaluated.
- IV or SQ fluid administration is generally contraindicated unless used as a vehicle for the administration of drugs or electrolytes.
- Angiotensin-converting enzyme inhibitors, other diuretics: considered once patient is stable (see p. 470).

POSSIBLE COMPLICATIONS

- Hypovolemia/impaired renal perfusion due to excessive diuresis
- Hypotension

RECOMMENDED MONITORING

- Frequent monitoring of vital signs, mucous membranes, body weight
- ECG if arrhythmias
- Flow-directed (Swan-Ganz) pulmonary artery catheterization and/or arterial cannula can be considered for hemodynamic monitoring of severely affected dogs admitted to an intensive care unit; rarely performed.

PROGNOSIS AND OUTCOME

- Most patients presented for first treatment of acute HF respond promptly to conservative therapy consisting of rest, supplemental oxygen, furosemide, and in some cases nitroglycerin.
- Despite favorable initial response, HF is generally associated with a poor long-term prognosis unless the causative disorder is curable.

PEARLS & CONSIDERATIONS

COMMENTS

- Although ancillary therapy including vasodilators and inotropes may speed recovery from acute HF, most patients that are destined to recover respond to conservative management.
- Response to empirical therapy is diagnostically useful. When treatment is based on a presumptive diagnosis, failure to respond to diuretic suggests the possibility that clinical signs are due to primary respiratory tract disease or that the patient has refractory HF.

CLIENT EDUCATION

Chronic medical therapy is generally required even after apparent recovery.

SUGGESTED READING

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Luis Fuentes V: Management of feline myocar-dial disease. In Bonagura JD, Twedt DC, editors: Kirk's current veterinary therapy XIV, St Louis, 2009, Saunders Elsevier, pp 809–815.

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Heart Base Tumor

BASIC INFORMATION

DEFINITION

A general term describing a cardiac tumor of any type located at the base of the heart in association with the ascending aorta and/or pulmonary trunk, but without right atrial involvement

SYNONYMS

Chemoreceptor cell tumor: chemodectoma, aortic body tumor, nonchromaffin paraganglioma

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs: second most common cardiac tumor, mean age 10 years (range (5-15 years), males may be overrepresented in predisposed breeds.
- Cats: reported but rare

GENETICS & BREED PREDISPOSITION: Brachycephalic breeds (English bulldogs, boxers, Boston terriers) appear to be predisposed.

RISK FACTORS: Chronic hypoxemia may be a contributing factor.

ASSOCIATED CONDITIONS & DISORDERS: Pericardial effusion, right-sided congestive heart failure

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Most commonly causes clinical signs due to pericardial effusion and cardiac tamponade
- May be an incidental finding

HISTORY, CHIEF COMPLAINT

- Acute collapse
- Lethargy/exercise intolerance
- Abdominal distension
- Anorexia/inappetence
- Cough or tachypnea/dyspnea

PHYSICAL EXAM FINDINGS

- Findings associated with pericardial effusion (tachycardia, weak peripheral pulses, and muffled heart sounds)
- Findings consistent with right-sided congestive heart failure (ascites, hepatomegaly jugular distention/pulsation)
- ± Tachypnea/dyspnea

ETIOLOGY AND PATHOPHYSIOLOGY

- Chemodectoma:
  - Tumor of specialized neuroepithelial cells within the adventitia of the aortic arch; majority of heart base tumors in dogs
  - Typically benign and slow growing but may be very large at the time of diagnosis; occasionally locally invasive and rarely metastatic
- Ectopic thyroid carcinoma:
  - 5%-10% of heart base tumors in dogs; usually nonfunctional
  - Biological behavior not well characterized
- Mesothelioma may occasionally form a mass lesion at the heart base (dogs).

- Regardless of type, heart base tumors typically result in pericardial effusion, causing cardiac tamponade and right-sided congestive heart failure.
- Compression of cardiac structures and great vessels impeding inflow or outflow is possible with a large mass.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is most often made with echocardiographic identification of a mass at the heart base. While a presumptive diagnosis of chemodectoma is often based on echocardiographic appearance, Definitive diagnosis of the tumor type requires histopathologic evaluation of tissue.

DIFFERENTIAL DIAGNOSIS

- Other intrapericardial tumors (hemangiosarcoma, mesothelioma, lymphoma, rare primary cardiac tumors, metastatic tumors)
- Other causes of pericardial effusion (see p. 854)

INITIAL DATABASE

- Echocardiography: diagnostic test of choice. Heart base tumors typically originate from the ascending aorta, most commonly the left cranial aspect, and lie between the aorta and the main pulmonary artery. They are usually homogeneous with smooth margins. Presence and severity of pericardial effusion is also assessed.
- Thoracic radiographs: enlarged or globoid cardiac silhouette in most but not all cases of pericardial effusion (80%). A soft-tissue mass effect at the heart base; may cause dorsal and lateral deviation of the trachea.
- Electrocardiogram: normal sinus rhythm or sinus tachycardia with low amplitude QRS complexes. Electrical alternans is suggestive but insensitive for pericardial effusion (50%).
- CBC, serum biochemistry profile, and urinalysis: often unremarkable

ADVANCED OR CONFIRMATORY TESTING

- Cytology and pH of the pericardial effusion: not generally useful. Heart base tumors typically do not exfoliate cells, reactive mesothelial cells mimic malignant cells, and there is much overlap in pH between causes.
- Histopathology of the tumor: allows a Definitive diagnosis of tumor type.

Requires surgical biopsy and often does not alter treatment plan.

TREATMENT

TREATMENT OVERVIEW

Treatment is generally aimed at removal of pericardial fluid when cardiac tamponade occurs and eliminating recurrent effusion. When a heart base tumor is an incidental finding, initially no treatment may be necessary.

ACUTE GENERAL TREATMENT

- Pericardiocentesis (see p. 1325) is essential when cardiac tamponade is present but may not be necessary if only mild effusion is present and not causing hemodynamic effects.
- Diuretics are contraindicated in acute treatment of cardiac tamponade.

CHRONIC TREATMENT

- Repeated pericardiocentesis as needed for recurrent pericardial effusion
- Diuretics to delay effusion recurrence are controversial.
- Pericardiectomy alone is an effective palliative treatment for recurrent pericardial effusion. Less-invasive alternatives to surgical pericardiectomy include thoracoscopic pericardiectomy (see p. 1340) and percutaneous balloon pericardiotomy.
- Complete surgical resection is rarely possible owing to high vascularity of the tumor and close association with great vessels.

POSSIBLE COMPLICATIONS

- Pericardiocentesis related (see p. 1325)

- Surgical complications related to pericardiectomy. Surgical resection carries substantial risks.
- As most heart base tumors are benign, metastasis is rare but has been reported.

RECOMMENDED MONITORING

- Follow-up exams and echocardiography to assess for recurrent pericardial effusion and tumor progression
- Thoracic radiographs and possibly abdominal ultrasound for tumor staging

PROGNOSIS AND OUTCOME

- Guarded to fair without pericardiectomy
- Pericardiectomy alone improves survival time considerably.

PEARLS & CONSIDERATIONS

COMMENTS

- Characteristic echocardiographic findings lead to the presumptive diagnosis of a heart base tumor and the possibility of a better prognosis with pericardiectomy than with other cardiac tumors such as hemangiosarcoma.
- Cytologic and biochemical evaluation of pericardial fluid are unreliable.

CLIENT EDUCATION

- Pericardiocentesis and pericardiectomy are both palliative and not curative.
- Pericardiectomy will likely lead to longer survival time, with fewer clinical signs in the interim.

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Head Trauma

BASIC INFORMATION

DEFINITION

Traumatic injury resulting in damage to soft tissues of the head, the skull, intracranial structures, or some combination of these

EPIDEMIOLOGY

SPECIES, AGE, SEX: Animals of any age or breed. Young animals may be overrepresented (lifestyle, increased risk of traumatic injury).

ASSOCIATED CONDITIONS & DISORDERS

- Traumatic injuries affecting other body systems
- Head trauma may increase the risk for future seizure disorders.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- History of traumatic event
- Owners may report loss of consciousness, inappropriate behavior, or seizure activity.

PHYSICAL EXAM FINDINGS

- Signs of hypotensive shock (e.g., tachycardia, hypotension, pale mucous membranes) may be present.
- Neurologic exam (see p. 1311): indicators of intracranial injury:
  - Pupil asymmetry, abnormal pupil reactivity (excluding ocular trauma).Dilated unresponsive pupils (in the absence of ocular trauma or atropine) indicate severe neurologic injury and a poor outcome.
  - Diminished or absent oculocephalic (doll's eye) reflex
  - Postural reaction deficits (may be due to spinal injury [see p. 1039]; note remainder of neurologic findings).
  - Diminished or altered consciousness (may be due to shock; note remainder of physical exam).
- Skull fractures may be palpable.
- Respiratory, musculoskeletal, and other body systems may show signs of traumatic injury.

ETIOLOGY AND PATHOPHYSIOLOGY

- Cerebral blood flow (CBF) is mainly determined by blood pressure. Auto-regulation maintains blood flow to brain over a variety of pressures but is lost when systolic arterial blood pressure <50 mm Hg or during neuronal injury (at which time arterial blood pressure dominates control of blood flow to the brain).
- Cerebral perfusion pressure (CPP = mean arterial pressure [MAP] – intracranial pressure [ICP]) is used for estimating CBF. As ICP rises or MAP drops, cerebral perfusion decreases.
- Trauma can result in primary (at the time of incident, due to direct neuronal damage and hemorrhage) or secondary (hours or days after the incident, due to energy depletion, free radical generation, cytokine release) insults to the brain. Treatment aims to prevent or limit secondary effects.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is based on a history of trauma with physical signs of intracranial injury. Complete neurologic evaluation is essential for establishing treatment plan and prognosis. Concurrent traumatic injuries affecting other body systems are common and should be ruled out as part of the diagnostic plan.

DIFFERENTIAL DIAGNOSIS

- Rule out other causes of intracranial disease (i.e., neoplasia, infectious, inflammatory, congenital), especially when trauma is suspected but was not witnessed.
- Animals in hypotensive shock may manifest altered consciousness without neurologic damage. Await full neurologic assessment until initial stabilization has been completed.
- Metabolic diseases (e.g., hypoglycemia, liver disease) may also affect neurologic exam and should be considered as differentials if no traumatic event is reported or if the history is uncertain.

INITIAL DATABASE

- Baseline tests (packed cell volume/total solids, blood glucose, blood urea nitrogen); initial assessment of some metabolic causes of altered mentation:
  - Consider transfusion if necessary (severe anemia/hemorrhage) to support adequate oxygen delivery to tissues.
  - Avoid causing hyperglycemia, which may be associated with poor outcome in head injury.
  - With azotemia or dehydration, diuretics (mannitol/furosemide) should be used with caution if at all; tissue perfusion (normotension) is most important.
- Blood pressure:
  - Identify and correct hypotension.
  - Systemic hypertension may be seen with elevated intracranial pressures or a consequence of pain or anxiety.
- Blood gas or pulse oximetry:
  - Identify hypoxemia (e.g., Pao2 <80 mm Hg when breathing room air) to provide supplemental oxygen.
  - Identify and correct hypercarbia (elevated PaCO2, e.g., >35 mm Hg).
- Heart rate/electrocardiogram
  - Sinus tachycardia common with shock or volume depletion; ventricular arrhythmias possible (see p. 1165)
  - Bradycardia may be seen with elevated ICP; in a comatose patient, it suggests brain herniation.

ADVANCED OR CONFIRMATORY TESTING

- Radiographs
  - May be useful in identifying skull fractures
  - Of limited value in the overall assessment of intracranial injury
- CT
  - Ideal imaging modality if available; requires general anesthesia, but some comatose/obtunded patients have been imaged without anesthesia.
  - Evaluate for skull fractures, hemorrhage, or other injuries
- ICP monitoring
  - Useful for directing therapies and limiting consequences of elevated intracranial pressures
  - May also be prognostic
  - Infrequently used in veterinary medicine
  - Requires skill and advanced care

TREATMENT 

TREATMENT OVERVIEW

Treatment is aimed at ensuring adequate cerebral perfusion. Important goals include maintaining adequate systemic blood pressure and systemic oxygenation (oxygen delivery to tissues).

ACUTE TREATMENT

- Maintain mean blood pressure above 60 mm Hg (generally signifies that systolic blood pressure >90 mm Hg): essential in management of head trauma, managed via titration of intravenous fluids. Options:
  - Crystalloids (e.g., 0.9% NaCl or lactated Ringer's solution) at shock doses IV (60-90 mL/kg for dog, 45-60 mL/kg for cat), unless renal/cardiovascular/dilutional contraindication; exact dose is titrated to blood pressure.
    - Concurrent use of colloids or hypertonic saline may limit cerebral edema that can occur with aggressive fluid administration.
    - Avoid fluids with excessive free water (maintenance fluids, 5% dextrose in water, 0.45% saline).
  - Colloids, e.g., hetastarch, pentastarch (10-20 mL/kg/d IV). Oncotic effect draws free water from the interstitium into the vasculature. May potentiate effects of lower molecular weight substances (i.e., mannitol). Useful for intravascular support with limited fluid volumes.
  - Hypertonic saline (7.5%), 4 mL/kg IV slowly. Short-lived osmotic action draws fluid from cerebral interstitium; combination with crystalloids prolongs osmotic effect.
    - May also limit other secondary effects of head injury. Only used if patient is adequately hydrated.

- Decrease intracranial pressure:
  - Mannitol (0.5-1 g/kg IV q 6-8 h; limit to three bolus injections/24-h period). Osmotic diuretic with free-radical scavenging properties. Increases intravascular osmolarity and draws fluid in from cerebral tissue. Decreases blood viscosity, increases cerebral blood flow. Potential adverse effects:
    - Diuresis may decrease blood volume and consequently blood pressure (ensure adequate blood pressure and volume status before administration).
    - May result in "reverse osmotic shift." In areas of hemorrhage, mannitol may leak into interstitium, worsening cerebral edema. The effects of mannitol on lowering ICP may outweigh these potential effects on damaged areas.
  - Furosemide (2-5 mg/kg IV in coordination with mannitol). Decreases production of cerebrospinal fluid and causes diuresis; may potentiate effects of mannitol and decrease ICP. Caution: diuretic action may also worsen intravascular volume contraction and lead to hypovolemia.
- Maintain adequate oxygenation:
  - Supplemental oxygen as needed (see p. 1318)
  - Ensure adequate oxygen-carrying capacity (hematocrit/hemoglobin) and delivery (adequate blood pressure).
- Miscellaneous therapies:
  - Surgery:
    - Craniotomy may be indicated for removal of hematomas, control of hemorrhage in the case of depressed skull fractures, or for removal of penetrating objects.
    - Results in a substantial decrease in ICP (15% with craniotomy and an additional 65% reduction with durotomy) and is superior in relief of elevated ICP compared to any medical therapy.
    - CT is useful for evaluation of injuries and determining need for surgical intervention.
  - Hyperventilation:
    - Has been advocated in head injury, although its use is controversial
    - Lowers CO2. Resultant vasoconstriction decreases cerebral perfusion pressure and decreases ICP. However, decreased perfusion to brain parenchyma may have deleterious consequences.
    - Current recommendation: ventilate patient such that Paco2 = 30-35 mm Hg.
  - Barbiturates:
    - Can use pentobarbital to effect (4-16 mg/kg IV titrated for induction, then 0.2-1 mg/kg/h to maintain sedation
      - Decreases cerebral metabolic rate and vasoconstricts, decreasing ICP
      - Studies evaluating efficacy controversial
      - May cause respiratory or cardiac depression, which is severely problematic in the head-injured patient
      - If used, intensive nursing care is essential to monitor respiration (intubation and mechanical ventilation may be necessary) as well as blood pressure and temperature.
      - Often discussed as "last resort"
      - May be beneficial for seizure control or in an extremely agitated animal
  - Hypothermia:
    - Results in decreased cerebral metabolic rate, decreased cerebral perfusion via reflex vasoconstriction, and consequently decreases ICP
    - May also limit secondary brain injury by limiting neuroexcitatory activities and suppression of local inflammatory response
    - Can be associated with coagulation abnormalities, cardiac disturbances, and hypotension
    - Moderate hypothermia (32-33°C) has been reported to be efficacious in human trials and animal models of brain injury. Clinical use in veterinary patients is uncertain
  - Glucocorticoids:
    - Methylprednisolone sodium succinate (30 mg/kg slow IV over 10 minutes) after initial resuscitation may be best choice
    - Use of corticosteroids in head injury is highly controversial and generally not recommended. Human studies have failed to show benefit.
    - Potential benefits due to antiinflammatory and free radical scavenging effects
    - May be associated with several complications (hyperglycemia, gastric ulceration, decreased wound healing, and infection)

NUTRITION/DIET

- Supplemental nutrition may be needed in severely compromised patients.
  - Enteral route preferred if possible/safe (see p. 1267)
  - Parenteral nutrition (see p. 1322) may be needed in patients at risk for aspiration pneumonia.

BEHAVIOR/EXERCISE

- Animals with severe neurologic deficits may be recumbent with limited mobility.
  - Range-of-motion exercises and physical rehabilitation (see p. 1329) may be beneficial for these patients.

POSSIBLE COMPLICATIONS

- Infection (aspiration pneumonia, nosocomial infection)
- Seizures
- Renal failure
- Persistent neurologic deficits

RECOMMENDED MONITORING

- Assess neurologic status:
  - Repeated examination may aid in the evaluation of efficacy of therapy.
  - Imaging (CT scan) may be helpful in assessing injury.
  - Therapy to decrease intracranial pressure if indicated
- Monitor oxygenation (arterial blood gas/pulse oximetry).
- Ensure adequate blood pressure.

PROGNOSIS AND OUTCOME

- Prognosis is dependent on severity and type of injury:
  - Fair to good with minor, nonprogressive injury
  - Severely injured animals have poorer short-term recovery rates and may have longer rehabilitation/recovery periods if they survive.
- Modified Glasgow Coma Score (MGCS; see box) has been used for scoring injury severity in head trauma and has been correlated to outcome.

PEARLS & CONSIDERATIONS

COMMENTS

- Head trauma is a common and serious injury in dogs and cats.
- Clinicians must recognize the signs of progressive neurologic injury.
  - The MGCS may be helpful as a monitoring tool.

Modified Glasgow Coma Score

Motor Activity	
Normal gait, normal spinal reflexes	6
Hemiparesis, tetraparesis, or decerebrate activity	5
Recumbent, intermittent extensor rigidity	4
Recumbent, constant extensor rigidity	3
Recumbent, constant extensor rigidity with opisthotonos	2
Recumbent, hypotonia of muscles, depressed or absent spinal reflexes	1
Brainstem Reflexes	
Normal pupillary light reflexes and oculocephalic reflexes	6
Slow pupillary light reflexes and normal to reduced oculocephalic reflexes	5
Bilateral unresponsive miosis with normal to reduced oculocephalic reflexes	4
Pinpoint pupils with reduced to absent oculocephalic reflexes	3
Unilateral unresponsive mydriasis with reduced to absent oculocephalic reflexes	2
Bilateral unresponsive mydriasis with reduced to absent oculocephalic reflexes	1

Level of Consciousness	
Occasional periods of alertness, responsive to environment	6
Depression or delirium, capable of responding to environment but response may be inappropriate	5
Stupor, responsive to visual stimuli	4
Stupor, responsive to auditory stimuli	3
Stupor, responsive only to repeated noxious stimuli	2
Coma, unresponsive to repeated noxious stimuli	1

Total: _____

- Assessment
  - Good prognosis 15-18
  - Guarded prognosis 9-14
  - Grave prognosis 3-8

TECHNICIAN TIPS

- Diligent monitoring and nursing care are important for an optimal outcome.
  - Even subtle changes in neurologic assessment can be important and should be brought up with the attending veterinarian.
  - Comprehensive nursing care is important to prevent complications such as nosocomial infection or aspiration pneumonia.

CLIENT EDUCATION

- Clients must be informed of the potential for long recovery periods with severely injured animals.
- Clients should also be made aware of the need for intensive treatment and monitoring of animals with head injury.
- The MGCS may be helpful in quantitating injury severity in order to provide the client with a prognosis.

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Head Tilt

BASIC INFORMATION

DEFINITION

Tilting of the head in a clockwise or counterclockwise direction along the long axis of the body. The head may be tilted due to a disorder of balance (vestibular disease) or due to discomfort from a dermatologic problem (acute moist dermatitis of the lateral face, or otitis externa). Head tilt due to an orthopedic problem (torticollis) is rare in small animals.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Idiopathic vestibular disease dogs >8 years; any age in cats

GENETICS & BREED PREDISPOSITION

- Otitis externa/dermatitis: usually “floppy eared” breeds of dogs with long pinnae (e.g., spaniels, retrievers)
- Congenital vestibular disease (uncommon): Doberman pinscher, cocker spaniel, German shepherd, others

GEOGRAPHY AND SEASONALITY: Idiopathic vestibular disease in cats may predominate in late summer/early fall

ASSOCIATED CONDITIONS & DISORDERS

- If head tilt is of vestibular origin, concurrent nystagmus, ataxia, circling, and/or vomiting may occur.
- If head tilt is associated with otitis externa/dermatitis, concurrent vigorous head shaking is common.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Vestibular disease (peripheral or central)
- Associated with discomfort (e.g., otitis externa or dermatitis ventral to the ear)

HISTORY, CHIEF COMPLAINT

- Head tilt associated with idiopathic vestibular disease; usually acute onset:
  - Vomiting followed by head tilt, ataxia, and circling/rolling for the next 1-2 hours is common
  - Owners may not report nystagmus.
- Head tilt associated with otitis externa/dermatitis:
  - Signs of pain of the affected ear/dermatitis lesion
  - Scratching of ear/affected skin
  - Rubbing of face on the floor

PHYSICAL EXAM FINDINGS

- Head tilt associated with peripheral vestibular disease (one or more maybe present):
  - Head tilt is always toward the side of the lesion.
  - Nystagmus (horizontal or rotary) with fast phase away from the side of the head tilt (see p. 772).
  - Circling
  - Ataxia with falling to the side of the head tilt
- Head tilt associated with central vestibular disease (one or more may be present):
  - Head tilt is toward the side of the lesion.
  - Nystagmus (horizontal, rotary, or vertical) with fast phase away from the side of the head tilt (see p. 772)
  - Circling
  - Ataxia
  - Proprioceptive deficits, motor weakness on the side of the lesion
  - Rarely, central vestibular disease may cause paradoxical signs (head tilt away from the side of the lesion). Proprioceptive deficits indicate the true side of the lesion (ipsilateral).
  - Other cranial nerve deficits (V, VI, VII)

- Head tilt associated with otitis externa/dermatitis:
  - Otitis externa (frequently suppurative)
  - Moist dermatitis ("hot spot") just ventral to the ear but covered by the pinna

ETIOLOGY AND PATHOPHYSIOLOGY

- Peripheral vestibular disease:
  - Idiopathic
  - Infection (otitis media/interna)
  - Neoplasia
  - Hypothyroidism (rare)
  - Post middle ear surgery
  - Intoxication (e.g., aminoglycoside antibiotics; rare)
  - Congenital/hereditary
- Central vestibular disease:
  - Infection
  - Inflammation
  - Neoplasia
  - Trauma
- Otitis externa/dermatitis:
  - Dogs: secondary to atopy, food hypersensitivity/allergy, hypothyroidism
  - Bacterial
  - Yeast
  - Mites (cats)

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Head tilt is most commonly caused by vestibular dysfunction. Therefore, the diagnostic process should seek to identify whether the brain (central) or inner/middle ear (peripheral) is the site of the lesion, which can usually be determined with a clinical neurologic exam. Further testing is selected based on a differential diagnosis list elaborated from history, physical exam, and neurologic exam findings.

INITIAL DATABASE

- CBC, serum chemistry profile, and urinalysis: usually normal
- Otoscopic exam:
  - Otitis externa, polyp, blood (head trauma) are possible.
  - Careful examination may reveal fluid in the middle ear with infectious causes.
- Tympanic bulla radiographs
- In otitis externa, consider evaluation for atopy, food hypersensitivity/allergy, and hypothyroidism

ADVANCED OR CONFIRMATORY TESTING

- Serum thyroid assays if cutaneous, biochemical, or other signs suggesting hypothyroidism are present (dogs).
- MRI or CT if inner ear or intracranial lesion is suspected based on case information to date.
- Cerebrospinal fluid analysis if intracranial disease is considered.

TREATMENT

TREATMENT OVERVIEW

- Improve the clinical condition by decreasing nausea, anorexia, skin and external ear irritation, and pain.
- Treat primary cause when possible.

ACUTE GENERAL TREATMENT

- Vestibular:
  - No specific therapy is available for treatment of idiopathic vestibular syndrome in dogs or cats. Glucocorticoids do not

appear to help.
    - Other specific causes will require treatment based on etiology.
    - It may be difficult for the animal to walk or stand, so good nursing care including ability for the animal to get to food and water as well as appropriate care to prevent urine or fecal scalding are very important.
- Dermatologic:
    - In cases of moist dermatitis, clipping the hair of the affected area and gentle cleaning with an antiseptic are recommended (see p. 30).

PROGNOSIS AND OUTCOME

- Vestibular:
    - The prognosis for idiopathic vestibular disease is excellent (dog and cat), but recurrence is possible.
    - With idiopathic vestibular disease, a head tilt may remain after resolution of all other signs.
    - The prognosis for neoplasia and all causes of central vestibular nystagmus is guarded to poor, depending on the exact cause, ability to treat, and response to therapy.
- Dermatologic:
    - The prognosis for otitis externa is good, but chronic cases may require advanced treatment or occasionally surgery.
    - Moist dermatitis ventral to the ear has an excellent prognosis.

PEARLS & CONSIDERATIONS

COMMENTS

- In a majority of cases in dogs and cats, acute-onset head tilt is caused by idiopathic peripheral disease and will resolve spontaneously in 1-2 weeks.
- Idiopathic vestibular disease is a diagnosis of exclusion.
- Nearly all central vestibular disease cases will have other central nervous system signs (proprioceptive defects, weakness, other cranial nerve involvement).

CLIENT EDUCATION

- When idiopathic vestibular disease is the primary consideration, the owners need to know that the problem will usually resolve with time.
- Otitis externa may become a chronic problem; owners should be advised that rechecks are needed even if the animal appears normal.

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Halitosis

BASIC INFORMATION

DEFINITION

An offensive odor emanating from the oral cavity, which may arise from intraoral or extraoral causes

SYNONYMS

Bad breath, oral malodor

EPIDEMIOLOGY

SPECIES, AGE, SEX: Any species, age, and sex may be affected.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Halitosis is a leading concern of pet owners, as it can negatively affect their relationship with the beloved pet.

PHYSICAL EXAM FINDINGS

- A complete physical examination must always include a thorough oral examination.
- Most intraoral disorders that cause halitosis are apparent upon examination of the oral cavity and surrounding tissues.
- General physical findings can vary greatly depending on the underlying disease process. For example, oral manifestations of leptospirosis vary depending on the serovar and may include halitosis, petechiae, oral hemorrhages, ulceration, glossitis with necrosis, and sloughing of the tongue.
- Attention should also be paid to the prepuce/vulva via inspection and to the anal sacs via palpation, because licking of these structures or their secretions is a recognized cause of halitosis in dogs and cats.

ETIOLOGY AND PATHOPHYSIOLOGY

- Intraoral causes:
  - Plaque and calculus accumulation, gingivitis, periodontitis, stomatitis
  - Cheilitis, lip fold pyoderma
  - Osteomyelitis, osteonecrosis
  - Oral tumors (particularly those that outgrow their blood supply and become necrotic, e.g., malignant melanoma, osteosarcoma)
  - Foreign bodies, oral implants
  - Oronasal communications
- Extraoral causes: see Differential Diagnosis

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Physical examination helps differentiate between intraoral and extraoral causes; further diagnostic tests are selected accordingly.

DIFFERENTIAL DIAGNOSIS

The DAMNIT scheme can be utilized as a guide to differential diagnosis:

- *D*evelopmental, degenerative: congenital and acquired palate defects/oronasal communications
- *A*utoimmune, anatomic, allergic: pemphigus vulgaris, systemic lupus erythematosus, erythema multiforme, drug eruption; “mouth breathing” associated with brachycephalic head conformation
- *M*etabolic, mechanical: diabetic ketoacidosis, uremia/renal failure, hepatic dysfunction causing hyperammonemia; retention of food debris

- *N*utritional, neoplastic: gastroesophageal reflux; oral, pharyngeal, esophageal, gastric neoplasia; dietary indiscretion/consumption of spoiled food
- *I*nfectious, inflammatory or idiopathic: dental plaque/calculus (oral bacteria), periodontal disease (gingivitis and periodontitis), gingival hyperplasia, contact mucositis and contact mucosal ulceration, stomatitis; leptospirosis; local and systemic fungal diseases; cheilitis and lip fold pyoderma; bronchitis, pneumonia; infection with feline leukemia virus (FeLV), feline immunodeficiency virus (FIV), feline calicivirus (FCV) or feline herpesvirus (FHV)
- *T*oxic, traumatic: toxic epidermal necrolysis, trauma from malocclusion, tooth fracture, jaw fracture, nonhealing oral wounds, oral foreign body

INITIAL DATABASE

Sensory evaluation and complete physical examination (including oral examination in the awake patient)

ADVANCED OR CONFIRMATORY TESTING

- CBC, chemistry panel, urinalysis: if history and physical examination suggest an extraoral cause
- Viral testing: FeLV and FIV in cats with stomatitis (feline coronavirus and feline herpesvirus testing uncommonly performed because of great number of clinically healthy carriers, and positive results likely would not change treatment plan).
- General anesthesia, oral examination, and biopsy of suspicious lesions
- Case-specific advanced diagnostics centered on the mouth and upper airway when an intraoral cause is suspected (e.g., dental radiography, CT, thoracic radiographs for metastasis check of suspected oral neoplasms) and systemic evaluations (e.g., leptospirosis testing) when an extraoral diagnosis is suspected.
- Identify and quantify volatile sulfur compounds or volatile organic compounds with gas chromatography, mass spectroscopy, and sulfide meters (in research settings).

TREATMENT

TREATMENT OVERVIEW

The goal of treatment is to control halitosis by addressing its underlying intraoral or extraoral causes. For intraoral causes, primary treatment is often followed by preventive care. For extraoral causes, treatment of the underlying disorder is the basis of therapy.

ACUTE GENERAL TREATMENT

- Improve oral hygiene via professional dental cleaning and periodontal therapy, with specific attention to treatment of oral disease associated with halitosis (e.g., extraction of teeth with severe periodontitis).
- Specific treatment for halitosis caused by extraoral disorders is directed towards the underlying disorder.

CHRONIC TREATMENT

- Maintain a healthy periodontium via routine home oral hygiene (daily tooth brushing, application of chlorhexidine products onto teeth and gums, use of diets, treats, and chew toys that help control plaque and calculus accumulation) and professional dental cleaning and periodontal therapy.
- Treat extraoral causes of halitosis.

NUTRITIONAL/DIETARY THERAPEUTICS

Home oral hygiene products, diets, treats, and toys proven to control plaque and calculus accumulation (see the Veterinary Oral Health Council website: http://vohc.org/)

RECOMMENDED MONITORING

Follow-up as indicated for routine management of underlying intraoral or extraoral cause

PROGNOSIS AND OUTCOME

Generally depends on the ability to eliminate underlying cause

- Fair to good prognosis: periodontitis, gingival hyperplasia, anal sac disease when treatment and prophylaxis are implemented properly and maintained consistently (active disorders that usually require ongoing care)

- Guarded prognosis: oral neoplasia, leptospirosis, opportunistic infection secondary to retroviral disease; the severity of the causative problem may make halitosis difficult to control.

PEARLS & CONSIDERATIONS

COMMENTS

A nonmalodorous oral cavity improves the human-animal bond as well as the pet's health and well-being.

PREVENTION

- Plaque accumulation on teeth, a major cause of halitosis, can easily be prevented by daily home oral hygiene and yearly professional dental cleaning and periodontal therapy.
- Other intraoral causes of halitosis can be recognized early by means of home oral examination by the owner and professional oral examination by the veterinarian during wellness visits.

TECHNICIAN TIPS

Technicians are on the frontline of identifying oral disorders pathologies including halitosis in at least two important ways: bringing oral abnormalities to the attention of the clinician and demonstrating proper home oral hygiene techniques to the owner.

CLIENT EDUCATION

- The oral cavity can be easily assessed by most owners.
- Halitosis is obvious, abnormal, and requires appropriate veterinary intervention.
- Home oral hygiene is important to general health.

SUGGESTED READING

Tonzetich J: Production and origin of oral malodor: a review of mechanism and methods of analysis. J Periodontol 48:13, 1977.

Veterinary Oral Health Council (VOHC): http://vohc.org/

AUTHOR: JAMIE G. ANDERSON

EDITOR: ALEXANDER M. REITER

Ivermectin Toxicosis

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Clinical syndrome associated with exposure to the macrocyclic lactone antiparasitic drug, ivermectin

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Very young animals may be at increased risk: immature blood-brain barrier.
- Dogs more likely to be involved; however, some sensitive cats may show clinical signs at the recommended doses.

GENETICS & BREED PREDISPOSITION

A defect in p-glycoprotein multidrug transporter in the blood-brain barrier has been identified as an autosomal recessive trait (MDR-1/ABCB1 gene mutation) in some individuals of several dog breeds including collies, Shetland sheepdogs, Australian shepherds, English shepherds, and Old English sheepdogs (see p. 706). Some German shepherds and greyhounds or other breeds may be relatively more sensitive to ivermectin and may show clinical signs at doses lower than previously reported.

RISK FACTORS

- Use of large-animal formulations in small animals holds risks of dilution errors and accidental overdosage.
- Animals with preexisting central nervous system (CNS) disease or disruption of the blood-brain barrier (e.g., due to trauma) may be at increased risk of toxicosis.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Acute: onset of signs within 4-12 hours of exposure
- Subacute: onset of signs within 48-96 hours, especially with exposure by injection or after multiple daily doses

HISTORY, CHIEF COMPLAINT

- History of exposure to ivermectin-containing product
- Depression, disorientation, vocalization, stupor, ataxia, tremors, vomiting, anorexia, recumbency, blindness, coma, seizure, death

PHYSICAL EXAM FINDINGS

- Mydriasis (bilateral) ± blindness (clinical: pupillary light reflexes generally intact)
- CNS depression: mild to stupor or coma
- Ataxia (proprioceptive)
- Disorientation
- Hypersalivation
- Tremors
- ± Bradycardia
- ± Vomiting
- ± Seizures
- Hypothermia (recumbency) or hyperthermia (tremor/seizure)

ETIOLOGY AND PATHOPHYSIOLOGY

Macrocyclic lactones enhance the release of γ-aminobutyric acid (GABA), an inhibitory neurotransmitter:

- In insects, GABA-mediated neurons are present throughout the peripheral nervous system, and enhanced GABA release

results in paralysis.
- In mammals, GABA-mediated neurons are restricted to the CNS, and in normal mammals the blood-brain barrier excludes ivermectin at therapeutic dosages.
- In overdose situations or in mammals with blood-brain barrier defects, ivermectin enters the CNS and exerts an inhibitory effect, resulting in CNS depression.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The combination of suspected or known exposure (acute or repeated) and CNS signs (progressive ataxia, weakness, mydriasis, seizures, coma) 12-96 hours after exposure is sufficient to establish a working diagnosis and begin treatment. There is no specific confirmatory test.

DIFFERENTIAL DIAGNOSIS

- Other intoxications (marijuana, benzodiazepines, barbiturates, ethylene glycol, isoxazole mushrooms)
- Brain neoplasia
- Encephalitis
- Hepatic encephalopathy

INITIAL DATABASE

- Neurologic exam (see p. 1311): asymmetric neurologic deficits are *inconsistent* with intoxication.
- No specific clinical pathologic alterations expected
- Baseline CBC, serum chemistry profile, urinalysis, postprandial bile acids (± thoracic/abdominal diagnostic imaging) to rule out other possible etiologies

ADVANCED OR CONFIRMATORY TESTING

- A comatose animal may return to temporary consciousness after physostigmine administration (1 mg/40 lb or 0.06 mg/kg IV). This should not be considered confirmatory, as physostigmine can reverse depression from many CNS depressants.
    - Physostigmine should be used with care; may trigger seizure activity.
- Ivermectin sensitivity testing (see p. 706)
- Ivermectin can be detected in liver, adipose tissue, brain, or serum.
    - Serum levels may not correlate well with clinical signs, however. Presence of ivermectin in the serum can help confirm exposure (if uncertain/ unknown).

TREATMENT

TREATMENT OVERVIEW

First priority is given to managing critical CNS abnormalities (seizures, coma). If signs are less severe or absent, treatment consists of inducing vomiting (within 2 hours of ingestion) and giving activated charcoal (within 8–12 hours of ingestion). Experimental treatments exist for severe toxicoses.

ACUTE GENERAL TREATMENT

- Manage seizures (see p. 1009):
    - Diazepam (0.25–2 mg/kg IV) PRN
    - Gas anesthetics, propofol if diazepam ineffective
    - Avoid barbiturates because of residual CNS depression.
    - Minimize sensory stimuli.
- Manage comatose animals:
    - Maintain airway, assist respiration as needed.
    - Thermoregulation essential
    - Atropine (0.01–0.02 mg/kg IV) for bradycardia
    - Frequent turning to prevent decubital ulcers
    - Urinary catheter and hygiene to avoid urine scald
    - Physostigmine (as above)

        - Duration of action 30-90 minutes (may allow time for feeding animal). Does not shorten recovery time.
- Decontamination of patients:
    - Emesis (see p. 1364)
        - Not recommended in animals already showing clinical signs (risk of aspiration).
    - Gastric lavage (see p. 1281)
        - For large ingestions
    - Activated charcoal (majority of ingested ivermectin is excreted in feces):
        - Initial dose: 1-4 g/kg PO or labeled dosage of commercial product when ingestion occurred <12 h earlier
        - Repeat administration q 8-12 h in animals showing overt signs.
        - Subsequent doses: half initial dosage is used to avoid osmotic fluid shifts and hypernatremia; monitor serum sodium.
- Experimental therapy: Intralipid 20% (dogs):
    - 1.5 mL/kg given IV over 10–15 minutes, followed by IV continuous rate infusion of 15 mL/kg over 30–60 minutes. Repeat bolus q 4 h for 3 doses. Monitor for lipemia prior to each dose. If evidence of lipemia, wait 2 hours, then recheck prior to redosing.
    - Intralipid may help trap (bind) highly lipophilic medications like ivermectins, thus making them unavailable. Efficacy and safety of this therapy has not been determined in dogs. Consider using when other treatment methods are not working.
    - Monitor for pancreatitis.

CHRONIC TREATMENT

- Repeated dosing of activated charcoal; check serum sodium 3 h after dosage if repeated doses, due to hypernatremia risk.
- Nursing care:
    - Frequent turning
    - Prevent urine scald.
    - Thermoregulation

NUTRITION/DIET

Tube feeding may be needed for recumbent/comatose animals for several days.

DRUG INTERACTIONS

Avoid drugs that may contribute to CNS depression (e.g., barbiturates).

POSSIBLE COMPLICATIONS

- Decubital ulcers
- Aspiration of activated charcoal or food
- Retinopathy has been reported in two dogs.

RECOMMENDED MONITORING

- Respiration
- Body temperature
- Heart rate
- Fluid/electrolyte balance

PROGNOSIS AND OUTCOME

- No specific antidote
- Prognosis depends on dose, relative individual sensitivity, and provision of good nursing care. Most animals recover with good supportive/nursing care.
    - Animals surviving >24 hours have reasonable prognosis, even though supportive care may be necessary for days or possibly weeks.

PEARLS & CONSIDERATIONS

COMMENTS

- Other macrocyclic lactones with similar mechanisms of action and clinical effects include milbemycin, moxidectin, selamectin, doramectin, eprinomectin, and abamectin.
- In general, doses up to 10 times the recommended *heartworm preventive doses* of milbemycin and ivermectin are well tolerated, even by sensitive (e.g., MDR-1 mutant) dogs.
- Toxic dose of ivermectin in collies and other sensitive breeds ranges between 0.1 and 0.2 mg/kg (15–30 times the therapeutic heartworm preventative dose but equal to the doses sometimes recommended for dermatologic or heartworm microfilaricide treatment) and 2.5–40 mg/kg (>200 times) in beagles.
- Because ivermectin is eliminated primarily through the bile and undergoes enterohepatic recirculation, activated charcoal can be of benefit even if the exposure was parenteral.
- Animals receiving repeated high doses of ivermectin for dermatologic or other reasons should be closely monitored for mydriasis or ataxia that may develop after several doses.
- Very high risk of moxidectin overdose when some equine moxidectin products containing 1.87% moxidectin (18,700 mcg/mL) are used in dogs.

PREVENTION

- Avoid large-animal products (concentration: 10 mg/mL which equals 10,000 mcg/mL) in companion animals to avoid risk of dilution errors. To prevent accidental exposure of dogs to spilled product, keep dogs out of area while horses are being dewormed.

TECHNICIAN TIPS

- Ivermectin toxicosis is less common (and therefore, more easily overlooked), owing to the wide availability of other effective antiparasitics.
- Profoundly affected patients may be comatose, and in such cases, the patient's life can depend on good airway protection (when tube feeding or if vomiting), hygiene (to prevent urine scald and fecal contamination), and pressure sore prevention (turning, topical therapy PRN).

SUGGESTED READING

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AUTHOR: CAROLINE DONALDSON

EDITOR: SAFDAR A. KHAN

1ST EDITION AUTHOR: SHARON M. GWALTNEY-BRANT

Iris Abnormalities

BASIC INFORMATION

DEFINITION

Iris abnormalities include any change in the color, character, or appearance of the iris, including acquired changes secondary to anterior uveitis, neoplasia, ocular melanosis, or cyst formation, as well as developmental changes (e.g., persistent pupillary membranes [PPMs]). Other relevant definitions include those for rubeosis iridis (blood vessel formation on the surface of the iris) and synechia (adhesion of iris-to-cornea [anterior] or iris-to-lens [posterior]).

SYNONYMS

Uveal disease, ocular melanosis (once termed pigmentary glaucoma)

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs and cats
- Anterior uveal neoplasia usually is seen in middle-aged to older animals.
- Ocular melanosis is seen in Cairn terriers and does not demonstrate age or sex predisposition.
- Uveal cysts most frequently are found in middle-aged to older animals (rare in cats).
- PPMs are congenital; pupillary membranes usually atrophy by 6 weeks of age in most puppies, but if not PPMs may be detected in all age groups (rare in cats).

GENETICS & BREED PREDISPOSITION

- Uveal melanoma has a suspected genetic predisposition in the Labrador retriever, golden retriever, and German shepherd.
- Ocular melanosis is an inherited, probably autosomal dominant condition in Cairn terriers.
- Uveal cysts: predisposed breeds include golden retrievers, Labrador retrievers, Boston terriers, Great Danes, rottweilers; see p. 1149).
- Heritable cause suspected for PPMs in basenjis, Pembroke Welsh corgis, chow chows, mastiffs, and others.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Uveitis (see p. 1151)
- Uveal neoplasia (see p. 620)
- Uveal cysts (see p. 1149)
- PPMs

HISTORY, CHIEF COMPLAINT

- Anterior uveitis: see p. 1151
- Uveal neoplasia: see p. 620
- Ocular melanosis: any or all of the following:
  - Change in color of the iris to dark brown
  - Cloudy/hazy appearance to the eye in cases of secondary glaucoma
- Uveal cysts: see p. 1149
- PPMs: any or all of the following:
  - Usually incidental findings
  - Cloudiness of eye
  - Cloudiness/opacities in pupil

PHYSICAL EXAM FINDINGS

- See History, Chief Complaint above.

- Ocular melanosis: any or all of the following:
  - Dark pigment-colored thickening of the iris root/base
  - Episcleral/scleral pigment plaques
  - Release of pigment into aqueous humor, with pigment deposition in aqueous drainage pathways
  - Pigmentation of the tapetal fundus +/− on the surface of the optic disk
  - Secondary glaucoma in severe cases
- PPMs: any or all of the following:
  - Single or multiple fine strands (rarely sheets) of iris tissue originating from the iris collarette and inserting on:
    - Adjacent iris; typically benign, incidental finding
    - Anterior lens; often associated with anterior capsular cataracts
    - Corneal endothelium; associated with varying degrees of corneal scarring and/or edema
    - Iris sheets; most severe form (sheet of tissue bridging pupil); associated with vision impairment

ETIOLOGY AND PATHOPHYSIOLOGY

- The uveal tract (or vascular layer) of the eye is composed of the iris, ciliary body, and choroid (see figure,p. 1151). The iris is the most anterior of these and is a thin diaphragm containing blood vessels, connective tissue, melanocytes, and two muscles—the iris sphincter and the iris dilator. In the center of the iridal diaphragm is a circular aperture, the pupil.
- Anterior uveitis (see p. 1151)
- Uveal neoplasia (see p. 620)
- Ocular melanosis: inherited thickening and pigmentation of the iris caused by increased melanocytes and (to a lesser extent) melanophages, with release of pigmented material into the aqueous humor and pigment deposition in the episclera/sclera ± posterior segment. Secondary glaucoma can result from extensive pigment deposition in the aqueous drainage pathways.
- Uveal cysts (see p. 1149)
- PPMs: nonvascular remnants of the tunica vasculosa lentis, which appear as iris strands or sheets originating in the iris collarette (midway point between iris base and pupillary margin). PPMs extend across the iris to insert on adjacent iris, lens, or cornea. When they insert on lens or cornea, opacification of these structures may occur. PPMs are a developmental defect that may have a heritable component in some breeds.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is generally suspected via the chief complaint or emerges as an incidental finding on physical exam. Characterization of an iris problem is based on a careful examination of the anterior chamber and iris surface with magnifying head loupes and diffuse and focal light sources.

DIFFERENTIAL DIAGNOSIS

- Discoloration of iris:
  - Pigmentation:
    - Uveal melanoma (variable appearance in the dog [focal] versus cat [mainly diffuse]; solid tissue; may cause dyscoria [misshapen/distorted pupil] and/or anisocoria [unequal or asymmetric pupils])
    - Ocular melanosis of Cairn terriers
    - Uveal cyst (round to ovoid, single or multiple, often translucent; see p. 1151)
    - Chronic anterior uveitis
  - Depigmentation:
    - Chronic anterior uveitis
    - Uveal neoplasm
  - Reddening:
    - Rubeosis iridis
    - Iridal hemorrhage
    - Uveal neoplasm
- Iris mass:
  - Uveal neoplasm
  - Uveal cyst
- Iris strands:
  - PPMs (arise from iris collarette; typically fine strands)
  - Synechiae (anterior: typically arise from base of iris or pupillary margin; posterior: arise from pupillary margin or posterior aspect of iris; often result in dyscoria [abnormal pupil shape])

INITIAL DATABASE

- Complete ophthalmic examination
- Variable depending on underlying condition

ADVANCED OR CONFIRMATORY TESTING

Variable depending on underlying condition:

- Ocular ultrasound (differentiate uveal neoplasm from cyst)

TREATMENT

TREATMENT OVERVIEW

Treatment of iris abnormalities varies widely, but fortunately diagnosis and subsequent treatment decisions are usually straightforward based on clinical signs.

ACUTE GENERAL TREATMENT

- Directed at underlying condition and, when possible, cause
- PPMs do not generally require treatment unless substantial corneal and/or lens opacification is/are present:
  - Iris-to-cornea PPMs may cause significant corneal edema which may benefit from topical 5% hypertonic saline ophthalmic solution or ointment q 6–12 h; continued long-term if clinical improvement noted.
  - Iris-to-lens PPMs can lead to cataract formation; if cataract is causing vision impairment, cataract surgery may be warranted (see p. 181).

POSSIBLE COMPLICATIONS

- Variable depending on underlying condition
- Cataracts and corneal edema associated with PPMs are rarely progressive.

PROGNOSIS AND OUTCOME

- Prognosis for *anterior uveitis* depends on severity at presentation, individual variation on severity and frequency of recurrences, underlying etiology, and client compliance.
- Primary intraocular neoplasia usually carries a poor prognosis for saving the eye but good prognosis for systemic health.
- Ocular melanosis has a variable rate of progression and usually carries a poor prognosis for saving the eye if secondary glaucoma develops.
- Uveal cysts and PPMs rarely cause problems with vision or ocular comfort.

PEARLS & CONSIDERATIONS

COMMENTS

- Most iridal abnormalities can be readily diagnosed on basis of clinical signs.
- Anterior uveitis requires immediate therapeutic intervention.

PREVENTION

Avoid breeding affected or closely related dogs predisposed to breed-related iris abnormalities.

SUGGESTED READING

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Petersen-Jones SM, Forcier J, Mentzer AL: Ocular melanosis in the Cairn terrier: clinical description and investigation of the mode of inheritance. Vet Ophthalmol 10(1):63–69, 2007.

AUTHOR: STEVEN R. HOLLINGSWORTH

EDITOR: CHERYL L. CULLEN

Ionophore Toxicosis

BASIC INFORMATION

DEFINITION

- Ionophores are antiparasitic fermentation products of *Streptomyces* fungi. They are used primarily as feed additives to increase feed efficiency and weight gain, and as coccidiostats in ruminants and poultry.
- Toxicosis results from accidental ingestion of livestock or poultry feed containing ionophores and is character-ized by acute central nervous system (CNS) dysfunction within 12 hours of large ingestions. Signs relate mainly to muscle damage within 24-96 hours of smaller ingestions.

SYNONYMS

Some of the commonly available ionophores are monensin (Rumensin, Coban), lasalocid (Bovatec, Avatec), salinomycin (Sacox, Bio-Cox), narasin (Monteban), semduramicin (Aviax), laidlomycin propionate (Cattlyst)

EPIDEMIOLOGY

SPECIES, AGE, SEX

- All animals susceptible; dogs mainly involved compared to cats
- Dogs are attracted to livestock or poultry feed that may contain the ionophore. Cats rarely attracted to these products.

GENETICS & BREED PREDISPOSITION

Farm dogs have greater access to ionophore-containing poultry or cattle feed.

RISK FACTORS

- Ionophore premix formulations (concentrated) are much more dangerous than ready-to-feed products.
- Patients with underlying cardiac or myopathic conditions could be at heightened risk of toxic effects.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Acute onset from high doses (<12 hours): acute CNS depression, ataxia, recumbency
- Subacute onset from lower doses (24-96 hours): generalized weakness, lethargy, anorexia
- Duration of effect: acute exposures, 2-10 days. Significant muscle involvement may produce permanent myopathy to variable degree. Cardiac lesions not commonly reported in dogs and cats (versus horses).

HISTORY, CHIEF COMPLAINT

- History of exposure to ionophore (livestock or poultry feed)
- Combination of possible access to ionophore and acute onset of progressive CNS depression, hind limb or full body weakness, or collapse
- Anorexia, diarrhea

PHYSICAL EXAM FINDINGS

- As listed above, plus ataxia, triplegia, hyporeflexia, tachypnea/dyspnea, tachycardia/arrhythmia, hyperthermia, tongue laxity
- Urine discoloration (myoglobin)

ETIOLOGY AND PATHOPHYSIOLOGY

Ionophore-induced cation transport across cell membranes results in intracellular calcium overload, mitochondrial disruption, catecholamine release, skeletal and myocardial muscle ischemia, necrosis and fibrosis, and acute renal tubular failure from myoglobin deposition.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is from history or evidence of exposure and clinical signs of ataxia, CNS depression, muscle weakness within 12 hours of exposure. No timely testing is available to confirm diagnosis. Presence of high amounts of ionophores in the feed can help determine exposure.

DIFFERENTIAL DIAGNOSIS

- Other intoxications (e.g., ivermectin, amitraz, bromethalin, macadamia nuts, alcohols, muscle relaxants [e.g., baclofen], hypoglycemic agents [e.g., xylitol, artificial sweetener], cardiac glycosides, sedatives, or painkillers [e.g., opioids, barbiturates, benzodiazepines, phenothiazines], and phenoxy herbicides)
- Rhabdomyolysis
- Neuromuscular disease (botulism, myasthenia gravis, polyradiculoneuritis, tick paralysis)
- Hypoadrenocorticism

INITIAL DATABASE

- Baseline serum biochemistry profile, including electrolytes and calcium
- Electrocardiogram (ECG); early indicator of myocardial involvement. ECG alterations (S-T segment depression, atrial fibrillation, paroxysmal atrial tachycardia), sinus tachycardia possible.
- Baseline and follow-up monitoring of skeletal muscle enzymes: creatine kinase (CK), aspartate aminotransferase (AST), and lactate dehydrogenase (LDH). Also note increase in alanine aminotransferase. CK is the most sensitive indicator, noted within 4-6 hours of acute insult, maximum at 6-12 hours. AST rises more slowly, may persist for several days. LDH is less dramatic, reaches maximum levels within 48-72 hours.
- Myoglobin (serum and urine). Absent in serum/urine of the healthy animal, released rapidly from damaged muscle/tissue; sensitive indicator of myone-crosis.
- Blood pressure
- Arterial blood gas

ADVANCED OR CONFIRMATORY TESTING

- Feed analysis may help determine ionophore concentration and dose consumed by the animal. Beneficial to affected patient (confirmation of toxic exposure) if known at time of intoxication; otherwise, retrospective confirmation.
- Histopathologic exam of tissues: various stages of focal myocyte degeneration, vacuolation, necrosis, and fibrosis.

TREATMENT

TREATMENT OVERVIEW

Goals of treatment are to induce emesis (within 2 hours of exposure) and administer activated charcoal followed by supportive care (intravenous fluids). Do not induce emesis if clinical signs are present. Administration of charcoal and fluids depends on the risk (dose), and most sus-

pects or confirmed cases should receive them because dose of exposure usually is not known.

ACUTE GENERAL TREATMENT

- Reduce gut absorption:
  - Induce emesis (dogs) if exposure is within 2 hours (seep. 1364).
  - Activated charcoal with a cathartic (1-4 g/kg PO, repeat in 6-8 hours if initial exposure is high).
- Supportive care:
  - Intravenous fluids 0.9% saline, typically at 1.5 to 2 times maintenance rate; caution if exhibiting cardiopulmonary signs. Ensure adequate perfusion to avoid/reduce renal tubu-lar damage (myoglobin-associated), and assist compensation of expected low-moderate degree of acidosis.
  - Urine alkalinization with sodium bicarbonate to reduce myoglobin deposition in renal tubules is controversial but not necessarily contraindicated; ensure acid-base, electrolyte, and cardiac monitoring.
  - Treat cardiac abnormalities as indicated from abnormal ECG tracings (see p. 1165). CAUTION: lidocaine may potentiate monensin toxicity.
  - Correct electrolyte imbalances, assess and manage expected metabolic acidosis.

- Oxygen support as indicated from pulse oximetry readings and pulmonary condition.
- Dialysis benefit unknown but may be indicated if severe renal failure is of concern.
- Calcium channel blockers, calcium antagonists or modulators are *not* recommended.

CHRONIC TREATMENT

Patient should not be stressed (minimize activity) and should be rested for several weeks (muscle recovery).

DRUG INTERACTIONS

Concurrent administration of chloramphenicol, tiamulin, erythromycin, sulfonamides, or cardiac glycosides is contraindicated: can potentiate ionophore toxicosis.

POSSIBLE COMPLICATIONS

Skeletal muscle fibrosis, vacuolization of peripheral sensory and motor nerves possible

RECOMMENDED MONITORING

- Selected cardiac, renal, acid-base, and muscle chemistries
- ECG

PROGNOSIS AND OUTCOME

- Poor if extensive damage to skeletal muscle occurs
- The relative degree of myofibrosis will determine the long-term prognosis.
- May require retirement of high-performance patients (e.g., breeding, sporting, trial dogs)

PEARLS & CONSIDERATIONS

COMMENTS

- Occurrence of ionophore toxicosis in dogs and cats is low.
- Monensin: canine acute oral LD50 = 10-20 mg/kg. Lasalocid: field cases reported at 166-210 mg/kg/d of dog food (10-15 mg/kg/d of lasalocid). Salinomycin: reported oral toxicosis in cats at 440 mg/kg in cat food.
- Relay (secondary) toxicosis has been reported in dogs consuming dead chickens containing ionophores (lasalocid).
- Intoxication from accidental ionophore adulteration of dog food has also been reported.

TECHNICIAN TIP

Subtle signs of muscle pain (myalgia), including mild lameness or new-onset tenderness or resentment of palpation over thigh or lumbar muscles, may not be apparent in the exam room and may first be detected during handling or longer interaction with an affected dog.

PREVENTION

Do not allow dogs and cats to enter cattle or poultry farms where ionophores are stored or being fed.

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Intussusception

BASIC INFORMATION

DEFINITION

- Invagination of one segment of the gastrointestinal (GI) tract into the lumen of an adjacent segment
- *Intussusceptum* is the invaginated segment, and the *intussuscipiens* is the outer or enveloping segment.

SYNONYMS

Intestinal telescoping, enteroenteric intussusception (also called *intestinal intussusception)*

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Intestinal intussusception usually occurs in animals <1 year unless associated with neoplasia.
- Gastroesophageal intussusception is most common in dogs <3 months old.

GENETICS & BREED PREDISPOSITION

Siamese and Burmese cats, German shepherds, and shar-peis may be predisposed.

RISK FACTORS

Infectious gastroenteritis (parasitic, bacterial, or viral); foreign-body ingestion; intestinal mass/neoplasia; previous surgery; canine renal transplantation, peritonitis; organophosphate intoxication

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Any of the following sites can be involved: gastroesophageal (see p. 527), pylorogastric, enteroenteric, enterocolic.
- Intussusception most commonly occurs in direction of normal peristalsis, with intussusceptum as proximal segment, but reverse can also occur (e.g., gastroesophageal intussusception).
- More than one site can be involved, or two invaginations may occur at the same site.

HISTORY, CHIEF COMPLAINT

- Diarrhea, hematochezia, vomiting, anorexia, lethargy, and weight loss
- Respiratory distress if gastroesophageal intussusception
- Signs can be acute or chronic.

PHYSICAL EXAM FINDINGS

- Palpable, sausage-shaped abdominal mass is characteristic but may not be present (or may be precluded by guarding/abdominal wall tension).
- Signs of pain on abdominal palpation
- Dehydration, tachycardia (more severe signs associated with more proximal obstruction)
- Poor body condition can be seen in chronic cases.
- Intussusception may protrude from

ETIOLOGY AND PATHOPHYSIOLOGY

- Proposed cause is structural or functional heterogeneity within the bowel wall, resulting in an alteration of intestinal pliability or motility.
- Intussusception produces partial or complete intestinal obstruction.

- Increased intraluminal pressure and kinking causes collapse of mesenteric blood vessels. Avulsion of vessels can also occur.
- Bowel wall becomes edematous and may become ischemic.
- Necrosis of the bowel wall, with leakage of contents contained by a fibrin seal between the layers of the intussusception, may occur. If leakage is not contained, peritonitis develops.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

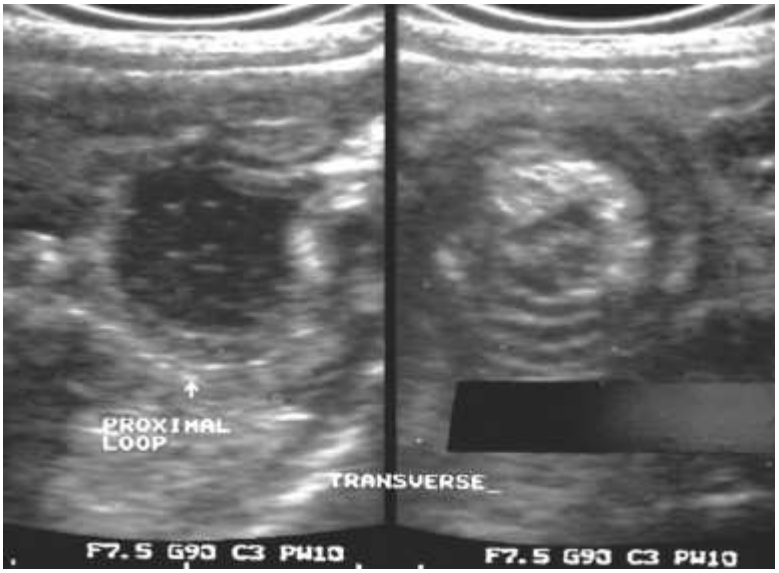
The diagnosis of enteroenteric (intestinal) intussusception is suspected based on history and typical physical examination findings if present. Confirmation is obtained with abdominal ultrasound exam or surgical exploration (either one is pathognomonic).

DIFFERENTIAL DIAGNOSIS

- Gastroenteritis associated with infection or dietary indiscretion
- Intestinal obstruction associated with foreign body, neoplasia, abscess, or granuloma
- Physiologic ileus
- Rectal prolapse if intussusception protruding through anus (see p. 963)

INITIAL DATABASE

- CBC may show evidence of a stress leukogram or anemia. Increased red blood cell count may be seen with dehydration.
- Serum chemistry profile may show evidence of dehydration (increased total protein, azotemia), hypokalemia, hypochloremia, hyponatremia, or hypoproteinemia. Alkalosis may be seen with proximal obstructions.
- Abdominal radiographs: fluid- or gas-distended intestinal loops. Tubular mass effect (sausage shape) of the intussusception may be seen in the small intestine or in a gas-filled colon.
- Thoracic radiographs: soft-tissue density within esophagus if gastroesophageal intussusception
- Fecal flotations (serial until positive result or total of three): indicated in all cases of intussusception, to assess possible parasitic causes



INTUSSUSCEPTION Ultrasound appearance of small-intestinal intussusception. *Left,* Dilated, poorly motile jejunum located proximal to the intussusception. *Right,* Characteristic multilayered, “target” appearance of intussuscepted small intestine. Horizontal bar below intussuscepted bowel is artifactual.

(Courtesy Dr. Richard Walshaw.)

ADVANCED OR CONFIRMATORY TESTING

- Contrast radiography with upper GI radiographic contrast study or barium enema: filling defect caused by intussusceptum seen within intussuscipiens
- Ultrasonography: concentric rings seen in transverse plane (“target sign”)

TREATMENT

TREATMENT OVERVIEW

Hypovolemia should be corrected prior to surgical intervention. At surgery, an attempt is made to reduce the intussusception. If it is not reducible or there is bowel damage, a resection and anastomosis is indicated. Enteroplication may be considered to prevent recurrence.

ACUTE GENERAL TREATMENT

- Intravenous crystalloids to correct dehydration or treat for shock. Colloids may be helpful with hypoproteinemia. If severe hypochloremia/hyponatremia, treat with 0.9% NaCl. Provide potassium supplementation if hypokalemic.
- Perioperative antibiotics (e.g., cefazolin, 22 mg/kg IV q 2 h) during perioperative period
- Enteroenteric or enterocolic intussusceptions; at the time of surgical exploration, reduce intussusception by applying pressure to intussuscipiens while *gently* pulling on intussusceptum:
    - Resection and anastomosis if unable to reduce intussusception, a mass is present, or there is nonviable bowel
- With enteroenteric intussusception, perform enteroplication if recurrence appears likely based on inability to correct underlying disease.
- With gastroesophageal intussusception, perform gastropexy of fundus and pylorus to prevent recurrence.

CHRONIC TREATMENT

- Opioid analgesia after surgery may decrease risk of recurrence.
- Treat infectious enteritis that may have caused intussusception.
- Antibiotics should be continued after surgery if peritonitis is present.
- Enteroplication if not performed at first surgery and postoperative intussusception recurs

POSSIBLE COMPLICATIONS

- Recurrence of intussusception occurs in 11%–25% of patients.
- Peritonitis associated with bowel rupture
- Leakage or dehiscence of intestinal suture line
- Entrapment and strangulation of bowel between enteroplication sutures
- Foreign body entrapment in bend of intestine created by enteroplication

RECOMMENDED MONITORING

- Monitor hydration status and serum electrolyte concentrations.
- Monitor for signs of intestinal suture line dehiscence and peritonitis (increased body temperature, abdominal pain, hypoglycemia).
- If clinical signs recur after surgery, repeat imaging to evaluate for possible recurrence of intussusception or complication associated with enteroplication.

PROGNOSIS AND OUTCOME

- Depends on cause, location, and duration of intussusception.
    - Good if fluid and electrolyte abnormalities are corrected and there is immediate surgical intervention.
    - Patients with proximal GI tract intussusception, generalized peritonitis, or underlying malignant intestinal neoplasia have a worse prognosis.
- Up to 25% recurrence is reported if enteroplication is not performed in association with surgical correction of intestinal intussusception.
- Severe complications are associated with enteroplication in 19% of dogs.

PEARLS & CONSIDERATIONS

COMMENTS

For each patient, the risk of recurrence must be weighed against the risk of complications associated with enteroplication:

- The decision is based largely on whether an underlying cause that can be corrected has been identified.
- If enteroplication is performed, create gentle loops along entire length of small intestine (from duodenocolic ligament to ileocolic junction); sutures 5-10 cm apart.
- Spontaneous reduction of intussusception has been reported in dogs; however, recurrence that requires surgical intervention may occur.

SUGGESTED READING

Burkitt JM, Drobatz KJ, Saunders M, et al: Signalment, history and outcome of cats with gastrointestinal tract intussusception: 20 cases (1986-2000). J Am Vet Med Assoc 234:771, 2009.

Applewhite AA, Hawthorne JC, Cornell KK: Complications of enteroplication for the prevention of intussusception recurrence in dogs: 35 cases (1989-1999). J Am Vet Med Assoc 219:1415, 2001.

Applewhite AA, Cornell KK, Selcer BA: Diagnosis and treatment of intussusceptions in dogs. Compend Contin Educ Pract Vet 24:110, 2002.

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EDITOR: RICHARD WALSHAW

Intraocular Neoplasia

BASIC INFORMATION

DEFINITION

- Primary intraocular neoplasms arise from the vascular intraocular tunic (iris, ciliary body, choroid). In cats, primary undifferentiated sarcoma arises from undetermined cell population, most likely lens epithelium. Neoplasia of the fibrous tunic, adnexa (eyelids, conjunctiva, lacrimal glands), and orbit are covered in additional detail elsewhere (see p. 1045 ,p. 711 , and p. 790).
- Secondary intraocular neoplasia occurs through metastasis or (rarely) by extension from adjacent tissues.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Melanoma/melanocytoma affects dogs and cats, usually older adults (>7 years), although also seen in young dogs <4 years old
- Medulloepithelioma usually affects animals 1–4 years of age.
- Primary sarcoma occurs only in cats, of any age.

GENETICS & BREED PREDISPOSITION

- Uveal melanoma has demonstrated genetic predisposition in Labrador retrievers, suspected in golden retrievers, German shepherds.
- Mode of inheritance suspected to be autosomal dominant

ASSOCIATED CONDITIONS & DISORDERS

Uveitis, glaucoma, retinal detachment, intraocular hemorrhage can occur secondary to intraocular neoplasia.

CLINICAL PRESENTATION

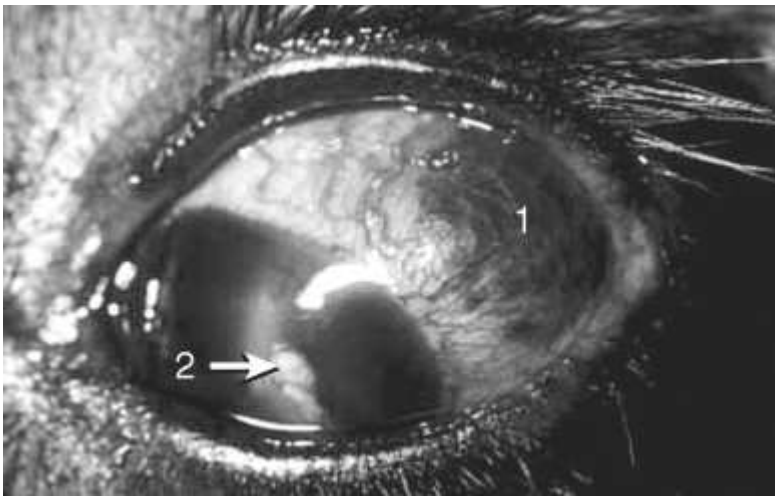
HISTORY, CHIEF COMPLAINT

- Change in appearance of the eye: redness, cloudiness, swelling, darkening of iris, mass noted
- Pain, blepharospasm
- Loss of vision

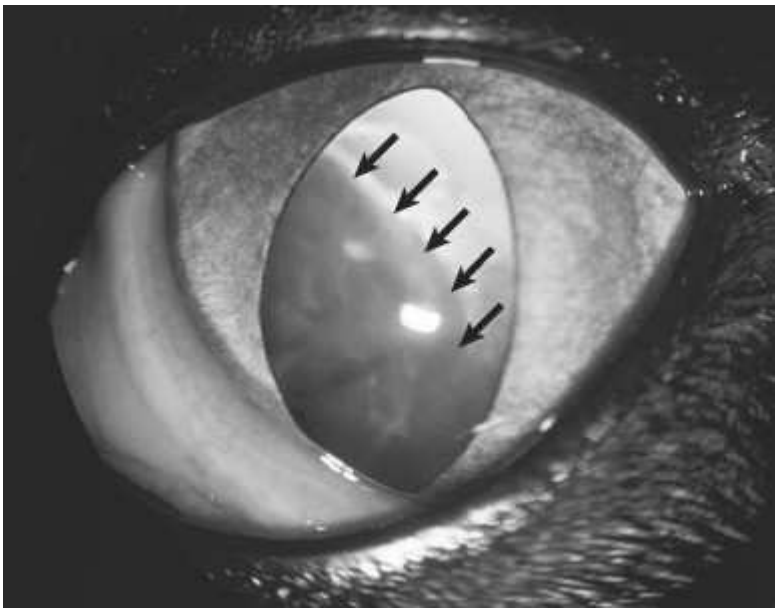
PHYSICAL EXAM FINDINGS

- Findings directly associated with tumor:
  - Mass which may be pigmented (melanoma/melanocytoma) or pink in color (more likely ciliary body adenoma/adenocarcinoma, or metastatic neoplasia) within the iris or pupil
  - Not all melanomas are pigmented, nor are all pigmented masses melanomas (histologic diagnosis).
  - Extension of mass through sclera
  - Diffuse hyperpigmentation of iris (more often in cats)
  - Dyscoria (abnormally shaped pupil), anisocoria (pupil of different size than the contralateral pupil)
  - Shallow anterior chamber
  - Intraocular hemorrhage
  - Displacement of lens (see p. 644)
- Findings associated with secondary glaucoma/uveitis:
  - Elevated intraocular pressure (glaucoma)
  - Fixed, dilated pupil
  - Corneal edema
  - Scleral injection
  - Aqueous flare
  - Hyphema
  - Lens luxation

- If chronic, retinal degeneration and peripapillary (area around the optic disc) hyperpigmentation



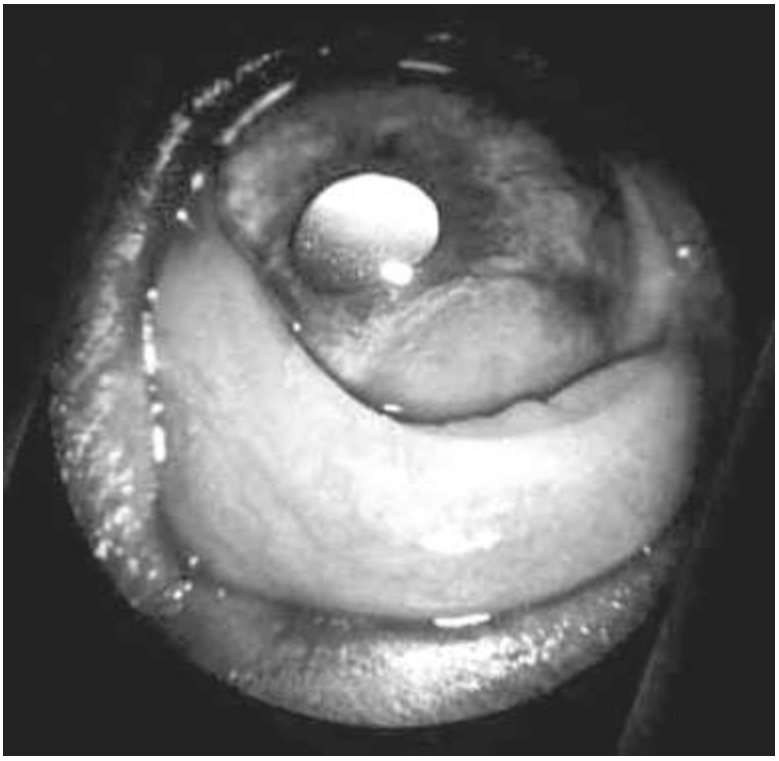
INTRAOCULAR NEOPLASIA Uveal melanoma in a dog with corneal and extrascleral extension *(1).* Note white area of calcific corneal degeneration at leading edge of corneal extension *(2).* Enucleation is recommended.



INTRAOCULAR NEOPLASIA Pink, vascular mass visible within the pupil in a cat. Appearance is typical of a ciliary body adenoma/adenocarcinoma, but metastatic neoplasia is also possible.

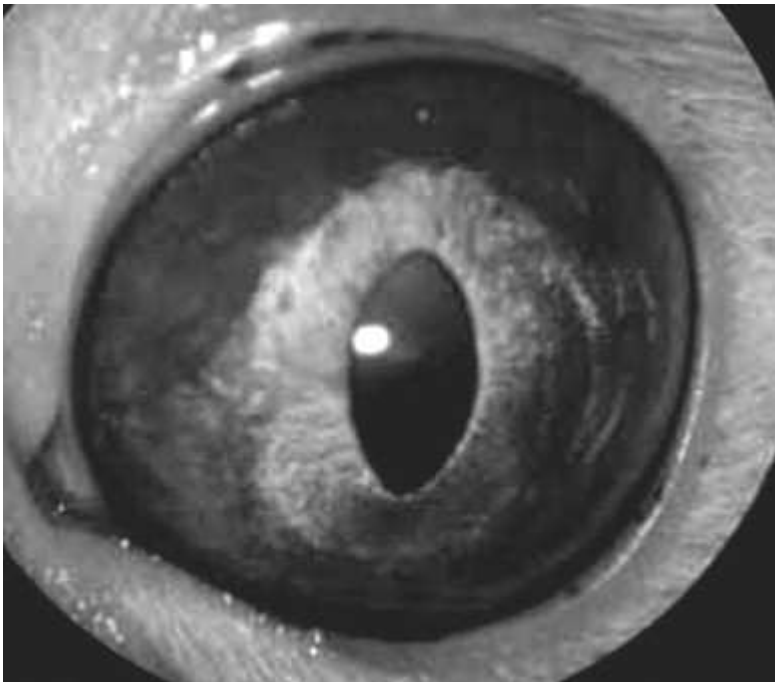
ETIOLOGY AND PATHOPHYSIOLOGY

- Proliferation of uveal melanocytes or ciliary body epithelium, cause unknown
- Melanoma originates most commonly in the anterior uvea (iris and ciliary body), unlike humans, where most are of choroidal origin.
- Undifferentiated sarcoma in cats occurs months to years after blunt or penetrating trauma to the eye. Damage to lens epithelium is implicated as initiating factor.
- Primary tumors in dogs are benign and although locally invasive, rarely metastasize.
- Ciliary body tumors rarely metastasize.
- Uveal melanoma in cats may metastasize.
- Primary intraocular sarcoma in cats frequently metastasize.



INTRAOCULAR NEOPLASIA Lymphoma metastatic to the iris and third eyelid in a dog. Diagnosis was made by biopsy of the third eyelid.

(Photograph from Dr. Robert L. Peiffer, Jr. with permission.)



INTRAOCULAR NEOPLASIA Diffuse iris melanoma in a cat. Note the raised, “velvety” appearance distinguishing this from benign iris hyperpigmentation. Enucleation is recommended.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Goals of diagnosis are to confirm neoplasia versus other processes and differentiate primary versus secondary and malignant versus

benign intraocular neoplasm.

DIFFERENTIAL DIAGNOSIS

- Iris cyst
- Diffuse iris melanocytosis, hyperpigmentation
- Granulomatous uveitis with accumulation of inflammatory nodules within iris stroma
- Other causes of uveitis, glaucoma, intraocular hemorrhage

INITIAL DATABASE

- Ophthalmic examination (see p. 1313) including evaluation of vision and pupillary light reflexes, measurement of intraocular pressure; direct visualization of mass may allow conclusive diagnosis.
- Ocular ultrasonography may confirm and delineate mass that cannot be directly visualized because of location or lack of clarity of ocular media. Tumor appears as a hyperechoic mass within iris or ciliary body and may be difficult to differentiate from organized hemorrhage.
- Systemic evaluation to rule out metastatic disease (CBC, serum biochemistry panel, urinalysis, thoracic and abdominal radiographs and ultrasonography)

ADVANCED OR CONFIRMATORY TESTING

- Aqueocentesis may not be diagnostic, as tumors often do not exfoliate cells into the aqueous; most valuable for lymphoma.
- Fine-needle aspirate of mass is often nondiagnostic owing to inadequate size of sample.
- Biopsy of mass may be accompanied by hemorrhage.

TREATMENT

TREATMENT OVERVIEW

Treatment is based on assessment of presence of vision and potential to preserve comfortable globe. Goals are to prevent progressive growth of tumor (preserving vision and comfort) and alleviate discomfort caused by secondary glaucoma in blind eye.

ACUTE GENERAL TREATMENT

- Primary intraocular tumors:
  - Enucleation is indicated if irreversible blindness and pain due to secondary glaucoma
  - Due to their metastatic potential, enucleation is indicated for iris melanoma and primary sarcoma in cats.
  - Conservative monitoring alone may be justified in older dogs, based on likely slow growth of primary tumor.
  - Sector iridectomy may provide incomplete excision and is often accompanied by hemorrhage and secondary glaucoma; may be only surgical option for nonpigmented tumors.
  - Diode laser treatment, transcorneally or through a limbal incision, is effective for pigmented tumors.
- Secondary intraocular tumors: treatment is directed at primary neoplasm if possible. If systemic prognosis warrants, enucleation may be indicated for comfort.

POSSIBLE COMPLICATIONS

- Laser treatment of large lesions may be accompanied by significant inflammation and may precipitate secondary glaucoma.
- Regrowth of tumor is possible following laser treatment.

RECOMMENDED MONITORING

Long-term monitoring to detect recurrent growth is indicated after laser treatment.

PROGNOSIS AND OUTCOME

- Primary neoplasms of the iris and ciliary body in dogs are nearly always benign and very rarely metastasize.
- Iris melanomas in cats are malignant tumors and may metastasize.
- Primary intraocular sarcomas in cats are locally aggressive and often metastasize.

PEARLS & CONSIDERATIONS

COMMENTS

- Assessment of vision is a primary factor in determining treatment recommendation. If eye has functional vision, laser treatment should be considered for localized lesions; if eye is blind, enucleation is recommended.
- For malignant melanoma and sarcoma in cats, enucleation is advisable.

PREVENTION

Iris melanoma in dogs: avoid breeding affected or closely related individuals.

SUGGESTED READING

Cook CS, Wilkie DA: Treatment of presumed iris melanoma in dogs by diode laser pho-tocoagulation: 23 cases. Vet Ophthalmol 2:217, 1999.

Dubielzig RR: Ocular neoplasia in small animals. Vet Clin North Am Small Anim Pract 20:837, 1990.

AUTHOR: CYNTHIA S. COOK

EDITOR: CHERYL L. CULLEN

Intervertebral Disk Disease

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Degeneration and displacement of disk material into the vertebral canal or intervertebral foramen, causing variable clinical signs that include discomfort (ranging from mild to excruciating) and/or gait disturbance (ranging from mild ataxia to paralysis)

SYNONYMS

Disk herniation, disk protrusion, disk extrusion, disk rupture, disk prolapse

EPIDEMIOLOGY

SPECIES, AGE, SEX

Most common in young to middle-aged, chondrodystrophic breeds, owing to chondroid metaplasia of the intervertebral disks. Cats: most commonly seen in older cats, with predilection for the lumbar spine, although cervical disk displacements have been reported.

RISK FACTORS

In both dogs and cats, these disk displacements usually occur spontaneously and are not associated with external trauma.

CLINICAL PRESENTATION

HISTORY/CHIEF COMPLAINT

- Discomfort is produced chiefly by the attenuation of dorsal nerve roots as they pass to the spinal cord via the intervertebral foramina.
- Discomfort associated with thoracolumbar and lumbar disk disease may be severe (general stiffness) and may be misinterpreted by the client and/or veterinarian as evidence of intraabdominal pain.
- Reluctance to jump, climb, or engage in other forms of activity
- Paresis (weakness): caused by disruption of normal nerve transmission between the brain and nerves to the limbs. Ataxia (incoordination) and knuckling/tripping on digits (conscious proprioception deficits).

PHYSICAL EXAM FINDINGS

- Focal discomfort on palpation of the area
- Ataxia and/or proprioceptive deficits in limbs
- Paresis. The type of paresis seen in the affected limb(s) (i.e., upper motor neuron versus lower motor neuron) is determined by the longitudinal location of the spinal cord lesion produced by the displaced disk. The severity of paresis is linked to the amount of spinal cord compression.
- Segmental reflex alterations help with neuroanatomic (longitudinal) localization.
- Nociception. Alterations in perception of and response to noxious stimuli are of localizing and prognostic significance.

ETIOLOGY AND PATHOPHYSIOLOGY

- Hansen type I disk disease represents displacement of nucleus pulposus through a rent in the annulus fibrosis, producing a relatively focal mass effect within the vertebral canal and/or intervertebral foramen. It is typically associated with chondroid disk metaplasia as seen in chondrodystrophic breeds. This is usually associated with acute/ subacute clinical signs.
- Hansen type II disk disease represents a bulging of the annulus fibrosis and herniation of nucleus pulposus within the annulus to produce a somewhat more diffuse mass effect within the vertebral canal. It is more typically seen with fibroid metaplasia in non-chondrodystrophoid breeds. Clinical signs tend to develop more slowly and progressively.
- So-called Hansen type III disk disease, or “gunshot” disk/high velocity displacement of nucleus pulposus

DIAGNOSIS

OVERVIEW STATEMENT

Diagnosis is based on results of physical, neurologic, and imaging (myelography, CT, or MRI) examinations.

DIFFERENTIAL DIAGNOSIS

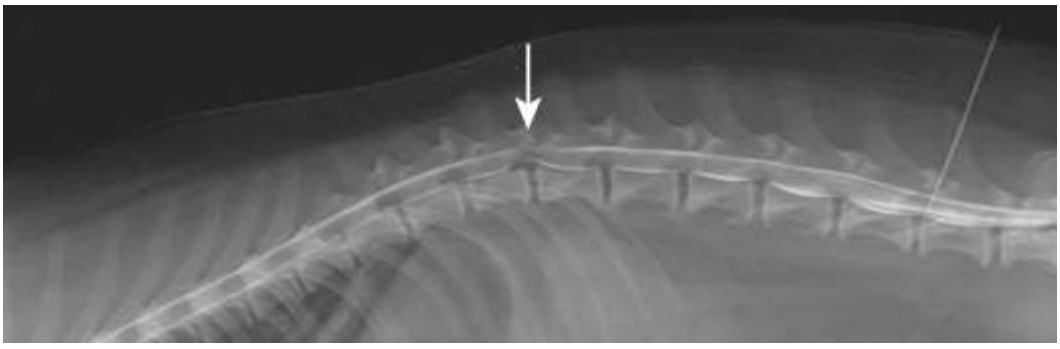
Spinal fracture/luxation; spinal cord, nerve root, epidural or vertebral neoplasia; fibrocartilaginous embolism; spinal cord inflammation (myelitis); diskospondylitis (intradiskal osteomyelitis); degenerative myelopathy; caudal occipital malformation syndrome with syringomyelia

INITIAL DATABASE

- Neurologic examination (see p. 1311):
  - Findings are consistent with a single focal spinal cord lesion (i.e., mentation and cranial nerve responses are within normal limits).
  - Deficits help to localize the lesion:
    - Upper motor neuron signs in fore-limbs and hind limbs: C1-C5 segments lesion
    - Lower motor neuron signs in fore-limbs, upper motor neuron signs in hind limbs: C6-T2 segments (cervical intumescence) lesion
    - Forelimbs normal, upper motor neuron signs in hind limbs: T3-L3 segments lesion
    - Forelimbs normal, lower motor neuron signs in hind limbs (femoral nerve distribution, diminishment of patellar reflex): L3-L6 segments lesion
    - Forelimbs normal, normal to increased patellar reflex (pseudohyperreflexia). Lower motor neuron signs in hind limbs (sciatic nerve distribution, diminishment of withdrawal and cranial tibial reflexes): L6-S1 segments lesion
    - Limbs normal (or mild LMN and CP deficits in pelvic limbs), decreased tail tone, decreased anal tone, decreased perineal reflexes: S2-coccygeal segments lesion
    - Cutaneous trunci (“panniculus”) reflex may help further localize in dogs with signs referable to a T3-L3 segment lesion, and might also help determine which side the lesion is preferentially affecting.
    - Palpation of epaxial muscles and vertebrae to determine if discomfort present and location of discomfort
    - Determination of a line of hypalgesia or analgesia (sensory level) if possible
  - Location of deficits helps determine the site of the lesion but does not confirm that intervertebral disk disease is the cause.
- CBC, serum biochemistry panel, urinalysis (possible dysuria/urine retention and infection), electrocardiogram (potential anesthesia for imaging studies and surgery).
- Survey radiography with orthogonal views of heavily sedated, properly positioned patient will rule out fractures/luxations, and severe bone neoplasia Calcified disks in situ are abnormal (degenerated) but may not be clinically significant.

ADVANCED OR CONFIRMATORY TESTING

- Myelography (see p. 1300, CT (see p. 1233), CT combined with myelography or MRI (see p. 1302) may reveal location of spinal cord compression due to disk displacement. Cerebrospinal fluid (CSF) analysis may be done in conjunction with myelography or after CT or MRI, especially if something other than a disk displacement is suspected to be the cause for myelopathy.
- Advanced imaging is usually done where surgery is contemplated as a possible treatment. If a client has ruled out surgical intervention, the results of any imaging study (including plain radiography) will only be of academic value and may have little to no influence on further treatment planning or prognostication.



INTERVERTEBRAL DISK DISEASE Myelogram in a dog with intervertebral disk disease, lateral view. Spinal needle used for injecting contrast agent is in the L5-L6 interspace *(right of image).* A dorsal deviation in the contrast column is seen at T13-L1, consistent with disk displacement *(arrow).* As an incidental finding, mineralization of the nucleus pulposus is seen in several intervertebral disks (T10-T11, T12-T13, L5-L6).

(Courtesy Dr. LeeAnn Pack.)

TREATMENT

TREATMENT OVERVIEW

Goals of treatment are to alleviate discomfort, reverse neurologic dysfunction, and prevent secondary complications such as those associated with urine retention and incontinence.

ACUTE GENERAL TREATMENT

- Based on severity and progression of neurologic dysfunction and discomfort
- Patients with discomfort alone and no neurologic deficits, or those with mild neurologic deficits that are not progressing rapidly: STRICT cage rest for 2–6 weeks (only activity = short walks to go to urinate/defecate) regardless of perceived improvement.
- Treatment with muscle relaxants and analgesics (nonsteroidal antiinflammatory drugs [NSAIDs], opiates).
    - Muscle relaxant (e.g., methocarbamol [Robaxin] 15–22 mg/kg PO or 44 mg/kg IV as needed up to q 4 h, not to exceed 330 mg/kg/day)
    - NSAIDs: meloxicam 0.1 mg/kg IV, SQ, or PO q 24 h; *or* carprofen 2 mg/kg PO q 24 h; *or* deracoxib 2–4 mg/kg PO q 24 h; *or* etodolac 10–15 mg/kg PO q 24 h. Do not use more than one NSAID at a time, or an NSAID concurrently with corticosteroids (risk of severe gastric ulceration).
- Patients with more severe neurologic signs and imaging evidence of cord compression: surgical decompression.
- Corticosteroids:
    - Time honored but increasingly unpopular with neurosurgeons due to frequent adverse effects and lack of proven efficacy
    - Corticosteroids do not eliminate the primary lesion and cannot be considered equivalent to surgical decompression.
    - Protocols advocated by other sources include methylprednisolone (Solu-Medrol) 30 mg/kg IV once, within 12 hours of onset of clinical signs; *or* dexamethasone 0.5-1 mg/ kg IV once within 6-8 hours of onset of clinical signs.
- If acutely paraplegic/tetraplegic: IV fluids to maintain hydration for optimal spinal cord perfusion

CHRONIC TREATMENT

- For animals that have lost motor function, the single most important aspect of treatment is bladder management to reduce the risk of urinary tract infection and bladder detrusor muscle damage from chronic overdistention. This may entail manual expression of the bladder every 4-6 hours or catheterization. In some cases, medication to help decrease urethral sphincter tone (e.g., phenoxybenzamine 0.25 mg/kg PO q 12 h; avoid if hypotension) may be helpful.
- Reducing antiinflammatory medications and analgesics after the acute phase, based on patient comfort
- Confined, padded rest areas, slings for assisted ambulation, hydrotherapy for cleanliness and to stimulate ambulation
- Control of body weight to avoid obesity
- Avoidance of climbing and jumping activities that stress the spine
- Physical rehabilitation including underwater treadmill use (see p. 1329) to strengthen axial and appendicular musculature and help retrain the nervous system
    - Acupuncture (see p. 1195): provides analgesia but does not alter the primary lesion; controversial.
    - Chiropractic maneuvers are highly controversial and may worsen neurologic status.

DRUG INTERACTIONS

Concurrent usage of corticosteroids and NSAIDs may lead to severe gastrointestinal ulceration and is contraindicated.

POSSIBLE COMPLICATIONS

- Urinary tract infection from incontinence/long dwell times or improper catheter use/care
- Detrusor atony from chronic overdistention of the bladder
- Urine scalding of skin from overflow incontinence
- Worsened neurologic status due to iatrogenic spinal cord trauma or vascular changes during decompressive surgery
- Ascending-descending myelomalacia: a devastating complication that occurs in <1% of acutely paraplegic dogs (mostly dachshunds). Focal lesion, commonly T3-L3, rapidly deteriorates to expanding cord necrosis, causing signs of ascending and descending cord dysfunction over a period of hours. There is no known treatment for this complication, and the key is early recognition so humane euthanasia can be performed.

RECOMMENDED MONITORING

Discomfort level, bladder/bowel evacuations, evidence of pressure sores, and neurologic status should be assessed frequently.

PROGNOSIS AND OUTCOME

- The most important prognostic indicator for paralyzed dogs (i.e., no voluntary motor function) is the presence or absence of nociception (deep pain), because the unmyelinated pain fibers in the spinal cord are the least vulnerable to ischemic injury. This assessment is always subjective, but apparent loss of sensation below the level of spinal cord injury suggests the possibility for permanent paralysis, regardless of treatment. Approximately 50% of dogs in this condition will recover if treated with decompressive surgery within 12 hours of the loss of nociception. Beyond 12 hours, the recovery rate decreases rapidly to between zero and 5%.
- For dogs with intact nociception, even if paraplegic (no motor function), approximately 80%–90% will recover fully or nearly fully with surgical decompression. However, the time frame for recovery is extremely variable (few days to many weeks or months).
- The recurrence rate (i.e., a new disk displacement at a different level) is almost nil in nonchondrodystrophic breeds, although some of these dogs (especially German shepherds) may have initial signs attributable to Hansen type II disease at multiple levels simultaneously.
- For chondrodystrophic breeds and Hansen type I displacements, the published recurrence rates vary widely, but the best estimates for a severe recurrence of signs that would require a second operation are in the 3%-5% range. A higher percentage of postdecompression dogs may suffer new signs that are less severe and can be managed medically.
- Patients treated without surgery may recover as well, regardless of severity of deficits. However, such recoveries usually take longer than in those dogs receiving surgery, and the recurrence rate for similar or worse clinical signs is much higher.
- Relapse of signs is seen in approximately 30%–50% of dogs managed nonoperatively and is likely due to more nucleus pulposus from the same disk displacing into the vertebral canal at a later time, rather than multiple disks displacing.
- Dogs with signs attributable to ascending-descending myelomalacia have a hopeless prognosis and should be humanely euthanized.

PEARLS & CONSIDERATIONS

COMMENTS

- Strict cage rest is critical for recovery in nonsurgical patients treated only with analgesics and antiinflammatory medications. Physical rehabilitation, weight control, and avoidance of jumping activities can reduce the risk of recurrence and future need for surgery.
- There is no direct correlation between severity of signs and amount of disk material displaced. It is a grievous mistake to assume that surgery is not indicated in dogs with pain as their only sign or those with only mild deficits (thinking that such mild signs imply only a small amount of displaced disk), since these patients may have huge amounts of displaced disk and marked spinal cord/nerve root compression. Conversely, some of the most severely affected dogs (e.g., acutely paraplegic/no deep pain) may have suffered a Hansen type III disk displacement (“gunshot disk”), and will not likely be improved by surgery, even if done on an emergency basis.
- Options for a patient with suspected disk disease include medical management, hospitalization versus home care, referral for 24-hour observation, or referral for possible surgery. Ongoing monitoring is essential to determine whether the current course should be continued or if failure to improve, relapse of signs, or worsening of signs make a new strategy advisable.

PREVENTION

- Avoidance of obesity and jumping activities for chondrodystrophic breeds may lessen the tendency for recurrence.
- Prophylactic disk fenestration or chemonucleolysis may reduce the risk for treated disk spaces to undergo later displacement, but risks and the true benefit are unproven at this time.

CLIENT EDUCATION

- See Prevention above
- For paralyzed patients, clients should be informed of bladder involvement in addition to the limb paralysis to understand this component of management.

SUGGESTED READING

Seim HB: Surgery of the cervical and thoraco-lumbar spine. In Fossum TW, editor: Small animal surgery, ed 3, St Louis, 2007, Mosby Elsevier, pp 1418–1426, 1469–1479.

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EDITOR: JOSEPH HARARI

1ST EDITION AUTHOR: JOSEPH HARARI

Interstitial Lung Diseases

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

A heterogeneous group of uncommon lung diseases centered on the pulmonary interstitium, and that result from exaggerated inflammatory and/or reparative (fibrotic) responses to inhaled or hematogenous insults

SYNONYMS

Examples of interstitial lung diseases (ILDs) include:

- Bronchiolitis obliterans with organizing pneumonia (BOOP); recently renamed to cryptogenic organizing pneumonia (COP) in human medicine
- Endogenous lipid pneumonia
- Eosinophilic pneumonia (also called eosinophilic bronchopneumopathy *and* pulmonary infiltrates with eosinophilia [PIE]; see p. 350)
- Idiopathic pulmonary fibrosis
- Lymphocytic interstitial pneumonia
- Pulmonary alveolar proteinosis
- Silicosis and asbestosis

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs or cats; usually middle-aged to older; eosinophilic pneumonia often occurs in younger animals.
- No sex predisposition

GENETICS & BREED PREDISPOSITION

Some specific syndromes have a breed predisposition:

- Pulmonary fibrosis in West Highland white terriers and Staffordshire bull terriers
- Eosinophilic pneumonia in Siberian huskies, Alaskan malamutes and rottweilers (usually associated with hypereosinophilic syndrome in rottweilers).

RISK FACTORS

Generally unknown; exceptions may include:

- Pulmonary toxicant drugs (e.g., bleomycin)
- Inhaled chemical fumes (e.g., hydrocarbons)
- Mineral fibers
- Dusts
- Allergens

ASSOCIATED CONDITIONS & DISORDERS

- Eosinophilic pneumonia may occur alone or as part of the hypereosinophilic syndrome (e.g., rottweilers).
- Lymphocytic interstitial pneumonia has only been reported in cats with feline immunodeficiency virus infection.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Respiratory signs can include:
  - Cough

    - Tachypnea
    - Respiratory distress
    - Exercise intolerance
    - Hemoptysis
- Nonrespiratory signs can include:
    - Fever
    - Lethargy
    - Anorexia
    - Weight loss

PHYSICAL EXAM FINDINGS

- Spontaneous or elicited cough:
    - May be productive or nonproductive
- Audible pulmonary crackles on ausculation (inspiratory; with pulmonary fibrosis)
- Increased respiratory rate and/or effort
- Fever
- Poor body condition

ETIOLOGY AND PATHOPHYSIOLOGY

- Disease is believed to result from injury to the alveolar epithelial cells, leading to a cycle of inflammation and host reparative responses that proceed unchecked.
    - In humans, injury can be triggered by:
        - Inhalation of toxins, irritants, or allergens
        - Vascular damage from drugs
        - Collagen-related vascular diseases
        - Systemic immune-mediated diseases
        - Infection
        - Neoplasia
    - Many veterinary cases are idiopathic.
- Alveolar epithelial cell injury leads to:
    - Inflammatory cell influx
    - Release of proinflammatory and fibrogenic mediators
    - Deposition of extracellular matrix
    - Structural changes including fibrosis
- Idiopathic pulmonary fibrosis appears to be a fibroproliferative disorder that can originate independent of inflammation (i.e., inflammation is secondary).
    - Injured alveolar epithelial cells are still critical for triggering and sustaining fibrogenesis.

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

Diagnosis is suspected in patients with clinical signs and radiographic features consistent with ILD in which there is no evidence of infectious and neoplastic causes of respiratory disease; definitive confirmation requires lung biopsy for histopathologic examination.

DIFFERENTIAL DIAGNOSIS

- Physical examination (cough/respiratory distress):
    - Other airway diseases (e.g., chronic bronchitis, eosinophilic bronchitis)
    - Pneumonia (infectious, aspiration, foreign body)
    - Neoplasia
    - Pulmonary thromboembolism
    - Cardiogenic or noncardiogenic pulmonary edema
    - Pleural effusion or pneumothorax
- Radiographic:
    - Infectious pneumonia (bacterial, fungal, viral, protozoal, parasitic)
    - Noncardiogenic pulmonary edema
    - Neoplasia

INITIAL DATABASE

- CBC:
  - Inflammatory leukogram and eosinophilia possible
- Thoracic radiographs:
  - Interstitial, alveolar (especially in severe disease), or bronchointerstitial patterns
  - Interstitial nodules
  - Hypoinflation of the lungs
  - Hilar lymphadenopathy possible
  - Right-sided cardiomegaly from corpulmonale possible
- Arterial blood gas may show:
  - Hypoxemia
  - Hypocarbia
- Fecal flotation or sedimentation (Baermann): respiratory parasites
- Serologic titers: infectious agents endemic to the patient's area

ADVANCED OR CONFIRMATORY TESTING

- CT provides more specific information on the extent, pattern, and location of disease. High-resolution CT (HRCT) has become an important imaging modality for the diagnosis and staging of ILDs in humans, but key features of ILDs using HRCT have yet to be thoroughly characterized in small animals.
- Bronchoscopy, bronchoalveolar lavage, and fine-needle aspiration (all for cytologic evaluation and culture) can provide evidence of underlying infection or neoplasia only when microorganisms or neoplastic cells are identified:
  - Nonspecific inflammatory cells or poor cellularity is seen with ILDs.
  - Absence of microorganisms or neoplastic cells does not rule out these causes of respiratory disease.
- Lung biopsy is the only definitive means for diagnosis:
  - Can be performed by a keyhole technique, thoracoscopy, or thoracotomy
  - Special stains are indicated to rule out infectious agents.

TREATMENT

TREATMENT OVERVIEW

Treatment consists of removing or addressing the inciting cause if it can be identified. If no underlying cause can be identified, treatment is focused on decreasing inflammation. No specific treatments have been found which will directly halt the progression of fibrosis.

ACUTE GENERAL TREATMENT

Oxygen supplementation is indicated for hypoxemic patients, particularly those in respiratory distress (see p. 1318). Many affected patients are comfortable with mild to moderate arterial hypoxemia.

CHRONIC TREATMENT

- Remove any potential inciting cause:
  - Consider discontinuation of any drug not immediately critical for the patient's health.
- For eosinophilic pneumonias, treat underlying etiology (e.g., heartworm, other parasites, or fungi) if identified. If none found, treat with immunosuppressive doses of glucocorticoids.
- For most other ILDs, immunosuppression has been advocated (provided infection is definitively ruled out), starting with glucocorticoids (e.g., prednisone, 2 mg/kg PO q 24 h).
  - Empirically (i.e., without scientific evidence of their efficacy), other immunosuppressive drugs have also been tried in refractory cases.
    - Azathioprine (dogs, 1–2 mg/kg PO q 24 h for 10–14 days, then q 48 h)
    - Cyclophosphamide (50 mg/m^2 PO q 24 h for 3–4 days/week)
    - Cyclosporine (3–5 mg/kg PO q 12 h; monitor serum concentrations; see p. 1471)

BEHAVIOR/EXERCISE

Minimize exposure to inhalant fumes, chemicals, or dusts.

POSSIBLE COMPLICATIONS

- Decompensation during and after bronchoscopy or lung biopsy, especially in patients with a significant degree of respiratory compromise at rest

- Immunosuppression can predispose to secondary infections.
    - After lung biopsy, allow the incision to heal before immunosuppressive medication administration.

RECOMMENDED MONITORING

- Clinical signs
- Physical examination
- Arterial blood gas (if significant respiratory compromise)
- Thoracic radiographs

PROGNOSIS AND OUTCOME

- For eosinophilic pneumonia (without hypereosinophilic syndrome), with appropriate treatment, prognosis is fair to excellent.
- For BOOP, if the insult is removed and the animal responds well clinically and radiographically to glucocorticoids, the prognosis is good.
    - Relapse is common if glucocorticoids are tapered too quickly.
    - For animals with BOOP that do not respond well to therapy, prognosis is guarded to poor.
- For other ILDs, including idiopathic pulmonary fibrosis, prognosis depends on stage of the disease and rapidity of progression.
    - In general, long-term outcome is guarded to poor.

PEARLS & CONSIDERATIONS

COMMENTS

- Lung biopsy is critical for appropriate diagnosis of interstitial lung diseases.
- Pulmonary crackles on auscultation are common with interstitial fibrosis and therefore are not exclusive to pulmonary edema.
- Advanced imaging (e.g., HRCT) may serve as a useful noninvasive diagnostic technique as ILDs gain further recognition in veterinary medicine.

TECHNICIAN TIPS

It is important to minimize stress and provide appropriate oxygen supplementation when handling patients. Serial evaluation of arterial blood gases may be useful as a means of assessing oxygenation and addressing the oxygen needs of each individual patient.

CLIENT EDUCATION

Over time, most interstitial lung diseases are associated with permanent architectural changes, and treatment cannot reverse fibrosis. The likelihood that clinical signs will resolve depends on the balance of “active” inflammatory and reparative events, which can be addressed, versus fibrosis, which cannot.

SUGGESTED READING

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EDITOR: RANCE K. SELLON

Insulinoma

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

A functional pancreatic β-cell tumor that secretes excess insulin, causing clinical signs associated with hypoglycemia

SYNONYMS

β-cell tumor, hyperinsulinism, insulin-secreting tumor, islet cell adenocarcinoma, islet cell tumor

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs: uncommon; middle-aged to older (mean 10 years, range 3–14 years); no sex predilection; most reports are of medium- to large-breed dogs.
- Cats: rare; older (mean 14.7 years, range 12–17 years); no sex predilection

GENETICS & BREED PREDISPOSITION

- Dogs: increased incidence suggested for Labrador retrievers, golden retrievers, Irish setters, boxers, German shepherds, standard poodles, fox terriers, and collies.
- Cats: 3 of 5 reported cases were Siamese cats.

ASSOCIATED CONDITIONS & DISORDERS

Obesity

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Dogs: seizures (48%–62%), weakness (40%), and collapse (30%–40%) are most common.
  - Ataxia, disorientation, mental dullness, tremors/muscle fasciculations, polyphagia, restlessness, and nervousness may also be seen. An associated peripheral polyneuropathy may lead to hyporeflexia or areflexia.
- Cats: seizures, weakness, ataxia, and muscle twitching

PHYSICAL EXAM FINDINGS

- Usually unremarkable
- Obesity/overweight is seen in some dogs.
- Signs listed under History, Chief Complaint above may be found if marked hypoglycemia is present at the time of presentation.

ETIOLOGY AND PATHOPHYSIOLOGY

- In normal animals, when blood glucose concentrations decrease below 60 mg/dL (<3.2 mmol/L), insulin secretion stops, and catecholamines and glucagon are released to help return the blood glucose concentration to normal.
  - Cortisol and growth hormone have more chronic antihypoglycemic effects.
- In animals with insulinoma, the neoplastic β cells do not respond appropriately but continue to secrete insulin despite hypoglycemia.
- The excess insulin causes increased glucose uptake and use and decreased hepatic glucose production.
- The clinical signs of insulinoma are the result of neuroglycopenia and/or hypoglycemia-induced release of catecholamines.
- In dogs, insulinoma develops within the right and left pancreatic lobes with equal frequency. Solitary nodules are most common, but multiple nodules and occult nodules can also occur.
- Insulinomas are notorious for masking their malignant tendencies in the dog. Virtually all β-cell tumors in dogs are malignant (95%), and up to 64% have metastatic lesions at the time of surgery. Metastasis to the liver, regional lymph nodes, and

omentum is most common.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Appropriate clinical signs, hypoglycemia and concurrent hyperinsulinemia, and the presence of a pancreatic tumor support the diagnosis. Immunocytochemical staining of the tumor during histopathologic analysis is confirmatory.

DIFFERENTIAL DIAGNOSIS

- Fasting hypoglycemia:
  - Neonatal and juvenile hypoglycemia
  - Insulin overdose
  - Sepsis
  - Xylitol toxicity
  - Extrapancreatic tumors (e.g., hepatocellular carcinoma, leiomyosarcoma, oral melanoma)
  - Endocrine (i.e., hypopituitarism, hypoadrenocorticism, glucagon deficiency)
  - Hepatic (i.e., vascular shunts, glycogen storage diseases, cirrhosis)
  - Pregnancy
  - Uremia
  - Severe polycythemia
- Seizures (see p. 1009)
- Collapse/weakness (see p. 230)
- Tremors/twitching (see p. 1116)

INITIAL DATABASE

- CBC, serum chemistry profile, and urinalysis may show hypoglycemia or may be normal.
  - A normal blood glucose concentration does not rule out insulinoma.
- Simultaneous measurement of serum glucose and insulin concentrations should be made when the blood glucose concentration is <60 mg/dL (<3.2 mmol/L).
  - At this blood glucose concentration, insulin secretion is normally suppressed.
- If insulinoma is suspected but the blood glucose concentration is normal, fast the patient and assess a blood glucose concentration every 1–2 hours, with collection of a sample for concurrent insulin measurement when hypoglycemia occurs.
- A low serum fructosamine concentration can also provide evidence of chronic/recurrent hypoglycemia.
- Hyperinsulinemia during hypoglycemia is supportive of the diagnosis of insulinoma.
  - An insulin concentration in the middle to upper-normal range (in the face of hypoglycemia) is also suggestive but not diagnostic of insulinoma.
- Amended and other insulin/glucose ratios (AIGR) do not improve diagnostic accuracy.
- Thoracic and abdominal radiographs are usually normal with insulinoma but may help identify other disorders causing hypoglycemia.
  - Insulinomas rarely metastasize to the lungs.
- Abdominal ultrasound may be helpful (tumor visible in 30%–50% of affected dogs) but should be used in conjunction with other diagnostic tests.

ADVANCED OR CONFIRMATORY TESTING

- Histologic evaluation and immunohistochemical staining of the tumor is confirmatory.
- Abdominal CT or MRI can identify the location of the tumor in up to 70% of cases.
- Scintigraphy and angiography have poor reliability in detecting insulinomas.
- Endoscopic ultrasonography used in humans has a reported sensitivity of 77%-93% but is not readily available in small animal medicine.

TREATMENT

TREATMENT OVERVIEW

Urgent management of hypoglycemia may be done during transport of the patient to the hospital if insulinoma was previously documented or is suspected. In-hospital correction of hypoglycemia should be sufficient to control clinical signs but not excessive (avoid stimulating insulin release). Definitive treatment consists of removal of the tumor.

ACUTE GENERAL TREATMENT

- Emergency therapy:
  - If signs are present but the patient is able to eat, feed a small meal (see Chronic Treatment below).
  - If seizure or severe collapse/weakness is present, administer intravenous dextrose bolus (1–2 mL/kg of 50% dextrose solution diluted with saline in the ratio 5 parts saline to 1 part 50% dextrose, IV). A rapid clinical improvement should be seen. Follow with an infusion of 2.5%–5% dextrose IV (1–2 mL/kg/h), or if the patient is able to eat, feed a small meal. Solutions with >5% dextrose should be sufficient to control clinical signs but only given via a central line to avoid thrombophlebitis.
  - Glucagon can be used in refractory hypoglycemic patients in an acute crisis. Initial infusion rate is 5–10 ng/ kg/min. Adjust as needed to maintain normoglycemia.
  - If seizures persist, also administer diazepam 0.5–1 mg/kg IV or another anticonvulsant medication (see p. 1009).
  - The goal is to abolish clinical signs; blood glucose levels may remain below normal, and acute treatment should not aim to fully normalize blood glucose levels because doing so may elicit greater insulin secretion from the tumor.
- Surgery:
  - Remove the tumor if possible.
  - Perform a partial pancreatectomy for multiple adenomas or if a nodule cannot be palpated.
    - Insulinomas have no predisposition for one lobe of the pancreas over the other.
- After surgery, treat for potential pancreatitis (see pp. 817 and 820).

CHRONIC TREATMENT

- Because metastasis is common, signs often continue or recur after surgery and require long-term management.
- Dietary therapy: feed 4-6 small meals/ day of a diet high in protein, fat, and complex carbohydrates. Simple sugars, often found in semimoist pet foods, should be avoided.
- Limit exercise.
- When frequent feedings no longer control the signs, prednisone (0.25 mg/ kg PO q 12 h) can be added. This dose can be increased up to 2 mg/kg q 12 h if needed.
- When frequent feedings and prednisone no longer control the signs, or signs of iatrogenic hyperadrenocorticism are causing problems, diazoxide (5 mg/kg PO q 12 h, with a gradual increase up to a maximum of 40 mg/ kg divided q 8-12 h) can be added to the treatment regimen. This drug inhibits insulin release, enhances glycogenolysis and gluconeogenesis, and decreases glucose tissue uptake. It is expensive and not readily available.
- When these treatments are no longer effective, the following treatments may be considered:
  - Octreotide (somatostatin analog): 10–50 mcg/dog SQ q 8–12 h; questionable efficacy reported.
  - Streptozotocin: selectively destroys β cells but is extremely nephrotoxic. If used, a 3-hour diuresis with 0.9% saline is done before drug administration (500 mg streptozotocin/ m^2 IV in 0.9% saline over 2 hours) and for 2 hours after the streptozotocin infusion. This may be repeated every 3 weeks until hypoglycemia resolves or adverse reactions occur.
  - Alloxan: also selectively destroys β cells but is nephrotoxic and may cause sudden acute respiratory distress syndrome. If used (65 mg/ kg IV), concurrent fluid therapy is needed.

POSSIBLE COMPLICATIONS

- The most common postoperative complication is pancreatitis in dogs.
- Recurrent or progressive episodes of hypoglycemia may occur postoperatively secondary to residual and/or metastatic disease.
- Iatrogenic hyperadrenocorticism may result from prednisone therapy.
- Anorexia, vomiting, and ptyalism are uncommon potential side effects of diazoxide therapy.
- Renal failure can occur with streptozotocin or alloxan therapy.

RECOMMENDED MONITORING

- At home: return or progression of clinical signs of hypoglycemia
- In hospital: serum glucose concentrations

PROGNOSIS AND OUTCOME

- Malignancy is common, and many patients have metastasis at time of surgery.
- Surgery improves survival time.
- Dogs: median survival time of 12 months after surgery. Younger dogs have shorter survival times. Only 20% of dogs with metastatic disease live longer than 1 year.
- Cats: median survival time of 6 months

PEARLS & CONSIDERATIONS

COMMENTS

- Insulinoma, although rare, is the most common islet cell tumor in small animals.
- Administration of new methylene blue 3 mg/kg diluted in 100–500 mL 0.9% saline and given IV over 30 minutes may make insulinomas more visible especially at the end of the infusion (insulinoma becomes reddish purple, versus blue-gray background of pancreas), but severe hemolysis is common 24–72 hours postoperatively and therefore this approach is controversial.
- Treatment of insulinoma is generally palliative and improves the quality of life for most patients.
- There is no predisposition for one lobe of the pancreas over the other.
- Recommend referral to a specialty center, as surgery and perioperative management can be complicated.

TECHNICIAN TIP

When treating severe hypoglycemia, remember to administer enough dextrose to abolish clinical signs but not more, as this stimulates the tumor to secrete more insulin.

CLIENT EDUCATION

The owner should be aware of the clinical signs of hypoglycemia and seek immediate veterinary attention if they occur.

SUGGESTED READING

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EDITOR: SHERRI IHLE

Insect Growth Regulator Toxicosis

BASIC INFORMATION

DEFINITION

- Insect growth regulators (IGRs) are relatively safe insecticides in dogs and cats when used correctly and rarely cause concern for intoxication except under unusual circumstances.
- Oral ingestion of IGRs can cause mild stomach upset (hypersalivation, vomiting, and diarrhea), whereas sprays or spot-on formulations can result in dermal irritation, redness, itching, or rubbing.

SYNONYMS

Third-generation insecticides, growth inhibitors, juvenoids, juvenile hormone I, II, and III

EPIDEMIOLOGY

GEOGRAPHY AND SEASONALITY

Year-round in areas where target pests (usually fleas) are a nuisance

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Dogs and cats are typically presented for evaluation of signs caused by other flea and tick insecticides combined with the IGR (especially pyrethroid/ pyrethrin, organophosphate/carbamate insecticides).
    - Acute-onset gastrointestinal upset (presence of central nervous system [CNS] signs usually attributed to other pesticides present in the formulation)
- Dogs uncommonly access an IGR-containing livestock product, which typically involves the client noting the packaging disturbed and the dog showing signs of gastrointestinal upset.

PHYSICAL EXAM FINDINGS

- Patient vital signs should be within normal limits, as no direct systemic effect is expected following casual exposure to an IGR-only agent.
- Hypersalivation (common), mild vomiting
- Clinical signs from IGR-only products are typically due to other ingredients contained in the product.
- Dermal irritation, redness, itching, or rubbing could result from the carrier, the IGR, or other pesticides present in the formulation.

ETIOLOGY AND PATHOPHYSIOLOGY

Source:

- IGRs are used for controlling fleas, ants, mosquitoes, and roaches and are typically found in combination with other insecticides such as pyrethrins/ pyrethroids, organophosphates, carbamates (some of these are commonly encountered in clinical practice).
- They are available in sprays, foggers, monthly spot-on products, liquids, collars, or granules.
- IGRs are commonly added to flea control products sold for on-animal use and in the pet's environment (inside the home, yard, kennel areas, etc.).
- IGRs are subclassed, generally based by physiologic action or effect.
    - Chitin synthesis inhibitors: cyromazine, diflubenzuron, lufenuron, hexaflumaron, penflumaron, teflubenzuron, triflumaron
    - Juvenile hormone mimics: fenoxycarb, hydroprene, methoprene, pyriproxyfen
    - Molting hormone agonists: halofenozide, tebufenozide, methoxyfenozide
    - Others, like precocenes
- See online version of this chapter for a detailed table of IGRs, their toxic doses, and expected clinical signs.

Mechanism of Toxicosis:

- IGRs break the life cycle of the insect by disrupting normal activity of the endocrine or hormone system.
- IGRs have a much slower mode of action than “knock-down” insecticide (such as cholinesterase inhibitors and pyrethrins/pyrethroids that kill immediately).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Given the mild degree of signs and abnormalities associated with IGR intoxication, diagnostic testing is not necessary unless the patient was simultaneously coexposed to other toxic substances (in compound formulations). Therefore, the diagnosis rests on history of exposure, with or without supportive physical signs.

DIFFERENTIAL DIAGNOSIS

Toxicologic:

- Many household chemicals, cleaners, nontoxic plants that can cause acute hypersalivation and vomiting (see p. 880 and p. 217)

Spontaneous, Nontoxicologic:

- Dietary indiscretion, mild viral gastritis

INITIAL DATABASE

- If IGR is combined with other active ingredients, select diagnostic tests based on this information:
  - If product packaging is not available, begin with physical examination alone; if no abnormalities are present, consider conservative monitoring approach versus additional tests (below).
  - If presenting signs are not compatible with mild, IGR-only signs, consider baseline serum biochemistry profile, CBC, urinalysis, and abdominal and thoracic radiographs.

TREATMENT

TREATMENT OVERVIEW

IGR intoxication is typically very mild in degree and easily managed. It is important to know the ingredients for any product containing an IGR, as most are combined with insecticides that may be more toxic.

ACUTE GENERAL TREATMENT

- Antiemetic if significant vomiting (most IGR-only cases are self-limiting):
  - Metoclopramide, 0.1-0.2 mg/kg SQ; *or*
  - Maropitant, l mg/kg SQ; *or*
  - Dolasetron, 0.5–1 mg/kg IV
- Activated charcoal generally not indicated unless exceptionally large or complex (polytoxic) exposure
- Replacement fluids as needed
- Gastric protection, depending on severity of vomiting:
  - Famotidine (Pepcid), 0.5 mg/kg PO q 12 h × 3–4 treatments
  - Sucralfate (Carafate), optional, 0.5 mg/kg PO q 12 h × 48 hours

DRUG INTERACTIONS

IGRs do not interact to a negative degree with other insecticides or drugs.

PROGNOSIS AND OUTCOME

- Generally excellent (IGR-only agent exposures); unusual cases (e.g., ingesting large amounts of IGR-containing livestock feed) may require hospitalization for general supportive care.

PEARLS & CONSIDERATIONS 

COMMENTS

- Most IGR exposures result in very mild and transient clinical signs.
- Some clients ask about cyromazine (melamine precursor).
    - Should be no concern for systemic toxicosis following single exposure to any agent containing an IGR as the only active ingredient

PREVENTION

Keep any pesticide under lock when not being used, and avoid applying in an area where the pesticide could be accessible to a pet.

TECHNICIAN TIPS

- IGRs are not effective against adult insects; many clients are confused about this and mistakenly think the product “is not working” when adult fleas persist.
- IGRs may be sold as stand-alone products but typically are combined with a knock-down insecticide to kill fleas in later stages of maturity.

SUGGESTED READING

Compendium of pesticide common names: http://www.alanwood.net/pesticides/class_ insecticides.html. Accessed December 16, 2009.

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Injection Site Sarcoma

BASIC INFORMATION

DEFINITION

Commonly occurring tumors that arise from mesenchymal tissue secondary to vaccine administration or other injection

SYNONYMS

Vaccine-site sarcoma, vaccine-associated fibrosarcoma, vaccine-associated sarcoma (all outdated terms)

EPIDEMIOLOGY

SPECIES, AGE, SEX

Almost exclusive to cats; rare reports involving dogs. Younger age (7–9 years) compared with cats that develop sarcomas at nonvaccine sites.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Many different tumor types have been identified at vaccination sites in cats, including fibrosarcoma, malignant fibrous histiocytoma, neurofibrosarcoma, nerve sheath tumor, hemangiopericytoma, schwannoma, leiomyosarcoma, rhabdomyosarcoma, undifferentiated sarcoma, osteosarcoma, chondrosarcoma, liposarcoma, and myofibroblastic sarcoma.

HISTORY, CHIEF COMPLAINT

- Cats are usually presented for veterinary attention because their owners have noticed a progressively enlarging mass.
- A vaccination history should be obtained. Often cats with vaccine-site sarcomas will have a known prior history of having been vaccinated in a site near the tumor.

PHYSICAL EXAM FINDINGS

Cats usually present with a palpable firm cutaneous mass. Typical locations include the interscapular area, dorsal lumbar area, flank, or lateral thorax. Less commonly they can be found on extremities. Often the mass is hairless and/or ulcerated.

ETIOLOGY AND PATHOPHYSIOLOGY

- Vaccine-site sarcomas have been clearly linked to vaccination with certain inactive vaccines, particularly vaccines that contain aluminum hydroxide adjuvants. It is believed that inflammation at injection sites causes local cell proliferation which may lead to tumor development.
- Small numbers of case reports and anecdotal reports suggest that these tumors may result from subcutaneous injection of medications or fluids.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Definitive diagnosis can only be confirmed histopathologically, although adjunctive tests such as diagnostic imaging are often helpful in defining the extent of the tumor. Since an aggressive first surgery is more likely to result in tumor control, an incisional biopsy should be used for confirming the tumor type prior to planning definitive treatment (rather than tumor removal with incomplete margins histologically, requiring reoperation).

DIFFERENTIAL DIAGNOSIS

- Local inflammatory vaccine reaction
- Other subcutaneous tumor
- Abscess

INITIAL DATABASE

- Fine-needle aspirate (FNA) and cytologic examination may help identify the tumor type prior to other tests.
- Thoracic radiographs to rule out pulmonary metastases
- Radiographs of the affected area may reveal involvement of underlying bone.
- Fine needle aspirate of draining lymph nodes to help rule out metastasis.

ADVANCED OR CONFIRMATORY TESTING

- Histopathologic examination of an incisional biopsy specimen. Markers that may link the tumor with vaccine administration include peripheral lymphocytic infiltrate or macrophages within the tumor that contain aluminum adjuvant. In the absence of these markers, the location of the tumor, vaccination history, and diagnosis of a sarcoma also can suggest that the tumor was caused by vaccination.
- Simple excisional biopsy is not recommended as a first step in obtaining a diagnosis for this tumor because such reaction is often inadequate. Reports suggest that aggressive surgical resection or multimodality therapy at the time of the first intervention is more likely to result in local disease control.
- Advanced imaging (i.e., CT scan or MRI) to delineate the local extent of the tumor. Many of these tumors have a peripheral region that is contrast enhancing, with a nonenhancing center. They also often have fingerlike projections that extend far into surrounding normal tissues, and identifying these helps with complete excision.

TREATMENT

TREATMENT OVERVIEW

Treatment goals are to eradicate the local tumor and, in some cats, to prevent or delay metastasis.

ACUTE AND CHRONIC TREATMENT

- Radical surgical excision is the treatment of choice if physically possible.
  - Tumors on the distal limbs and tail may be successfully treated with amputation alone.
  - Tumors on the trunk are usually not amenable to radical excision. For these cases, a combination of radiation and surgery (excision with as wide a margin as possible based on physical examination and advanced imaging) is usually indicated for successful treatment of the local tumor.
  - Rarely, surgery with complete excision may be possible and result in adequate local control of the tumor; however, in one report, 31% of cats with complete excision of the tumor based on histopathologically clean margins developed a recurrence.
- Radiation therapy prior to surgery allows for adequate treatment of the microscopic tumor extensions with smaller radiation fields; however, therapy interferes with the histopathologic evaluation of the primary tumor mass and the margins, and it may slightly increase risk of wound complications after surgery.
- The role of chemotherapy in the treatment of vaccine-site sarcoma is not well defined. Studies have not shown a definite advantage to using chemotherapy if local therapy (surgery, radiation) is adequate. Nevertheless, many oncologists recommend chemotherapy (doxorubicin, cyclophosphamide, carboplatin, or ifosfamide).

POSSIBLE COMPLICATIONS

- Complications of surgery may include wound dehiscence or infection.
- Complications of radiation depend on the location of the tumor in relation to critical normal structures (e.g., spinal cord, kidneys) and the amount of radiation delivered to those structures.
- Chemotherapy complications: see p. 188

RECOMMENDED MONITORING

Owing to the aggressive local nature of these tumors and the low risk of metastasis, long-term monitoring should include:

- Routine examination by a veterinarian to monitor for local recurrence or side effects of treatment
- Routine thoracic radiographs to monitor for pulmonary metastases

PROGNOSIS AND OUTCOME

- Prognosis depends on the stage and location of the tumor.
  - Cats with tumors that can be resected with a wide margin of normal tissue (tumors on the tail or distal limbs, small localized tumors) may have an excellent prognosis.
  - Cats with larger tumors that can still be removed with an aggressive surgery and are treated with multimodality therapy (radiation, surgery, and chemotherapy) may still have an excellent prognosis for long-term tumor control; however, some of these cats will still develop metastases or recurrence of the primary tumor.
  - Cats with large nonresectable tumors or metastases at the time of diagnosis have a poor prognosis regardless of treatment.
- Another factor shown to affect recurrence of vaccine-site sarcoma is the extent of surgery performed at the first intervention after identification of the tumor. Cats that had the first excision of their tumor at a referral institution had a longer time to recurrence than cats that had surgery performed by their regular veterinarian. This is likely due to the relatively aggressive nature of surgery performed at the referral institutions.

PEARLS & CONSIDERATIONS

COMMENTS

- Treatment of cats with vaccine-site sarcoma is usually best performed using a team approach. Specialists, including a surgeon, oncologist, and radiation oncologist, should be consulted early in the course of diagnostic testing to determine the best multimodality approach.
- Many different types of sarcoma have been identified at vaccine sites.

TECHNICIAN TIP

For routine vaccination, it is helpful to record the location of administration (which site) of each vaccine to allow long-term monitoring and follow-up of local adverse reactions.

PREVENTION

- Early detection of these tumors may lead to more successful treatment.
  - Guidelines have been established by the American Veterinary Medical Association (AVMA) Vaccine Associated Sarcoma Task Force for approaching a cat that has a mass in an injection site after vaccination. According to these guidelines, the following masses should be investigated with an incisional biopsy to determine if further diagnostics or treatment are necessary:
    - A mass that is increasing in size after 1 month postinjection
    - A mass that is >2 cm in diameter
    - A mass that persists >3 months postinjection
- Vaccination of cats in areas of the body that may allow for an aggressive surgical removal if a tumor develops may prevent these tumors from requiring radiation or chemotherapy or from becoming life threatening.
- Critical evaluation of vaccination protocols for animals that have a low risk of contracting infectious disease may help decrease the risk of vaccine-associated sarcomas.

CLIENT EDUCATION

- Educate clients about the risks of tumor development following vaccination, as well as other risks of vaccination compared with the benefits of vaccination.
- Clients may also be educated on the importance of examining their cats regularly for new masses to allow for early detection and treatment of these tumors.

SUGGESTED READING

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Vaccine-associated feline sarcoma task force: vaccines and sarcomas: a concern for cat owners. Accessed February, 2010: http://www.avma.org/vafstf/ownbroch.asp.

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Inguinal Hernia

BASIC INFORMATION

DEFINITION

Protrusion of an organ or tissues through a weakened inguinal ring into the subcutaneous space at the level of the caudalmost portion of the ventral abdomen

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Middle-aged intact female dogs: acquired inguinal hernia
- Male and female puppies

GENETICS & BREED PREDISPOSITION

- Congenital:
  - Males: testicular descent may delay narrowing of inguinal ring.
  - Predisposed breeds may include basenji, Pekingese, poodle, basset hound, cairn terrier, Cavalier King Charles spaniel, Chihuahua, cocker spaniel, dachshund, Pomeranian, Maltese, West Highland white terrier.
- Heritability: may be polygenic in cocker spaniels and dachshunds
- No breed predilection for acquired (trauma-associated) inguinal hernia

RISK FACTORS

Obesity, trauma, pregnancy

ASSOCIATED CONDITIONS & DISORDERS

Umbilical hernia

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Indirect inguinal hernia:
  - Abdominal viscera enter the cavity of the vaginal process. o Males: uncommonly, may progress to scrotal hernia
- Direct inguinal hernia:
  - More common form in small animals
  - Organs pass through inguinal rings adjacent to the normal evagination of the vaginal process.
  - Usually large
  - Usually not associated with incarceration/strangulation

HISTORY, CHIEF COMPLAINT

- Chief complaint generally involves one of two categories: either the owner has noticed an inguinal enlargement incidentally, or there are systemic signs of illness due to abdominal organ entrapment/strangulation within the hernia.
- Indirect inguinal hernia in male dogs; often causes organ dysfunction:
  - Vaginal process narrows considerably at the inguinal ring.
    - Potential organ incarceration/ strangulation
- Direct inguinal hernia usually larger
  - Less commonly associated with clinical problems
- If organ incarceration in hernia, small intestine, bladder, or uterine entrapment:
  - Abdominal pain, vomiting, dysuria, vaginal discharge/hemorrhage may be noted.
- Vomiting, abdominal pain, or depression:
  - Vomiting for several days' duration is predictive of strangulated, nonviable small intestine.
  - Overall, risk of strangulated intestines is <5% of cases of inguinal hernia.

PHYSICAL EXAM FINDINGS

Vary with size of the hernia and its contents:

- Uncomplicated inguinal hernia:
  - Soft, painless unilateral or bilateral mass
  - Mass reducible into abdomen
  - Enlarged inguinal ring palpable
  - May appear more caudally in the female
- Complicated inguinal hernia:
  - Firm, nonreducible inguinal mass
  - Painful on palpation
  - Bruising/erythema of overlying tissues

ETIOLOGY AND PATHOPHYSIOLOGY

- Nontraumatic inguinal hernia:
  - Anatomic: Females may be predisposed:
    - Entrance to the vaginal process remains open.
    - Inguinal canal is shorter and larger in diameter.
  - Hormonal:
    - Most inguinal hernias become clinically apparent during estrus or pregnancy.
    - Inguinal hernias occur less frequently in spayed females.
      - Estrogen may play a role in development of inguinal hernias (alters strength and character of connective tissue).
  - Nutritional/metabolic:
    - Weakening of abdominal wall
    - Obesity:
      - Increased intraabdominal pressure
      - Fat forced into the inguinal canals
        - Dilation of canal and vaginal process
- Blunt abdominal/pelvic trauma:
  - Disruption/weakening of caudal abdominal muscles
  - Enlargement of inguinal canal

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis usually is established on physical examination alone.

DIFFERENTIAL DIAGNOSIS

- Perineal hernia: hernia is adjacent to anus.
- Scrotal hernia (male): most dogs with inguinal hernias present with a fluctuant, painless, unilateral or bilateral mass, whereas scrotal hernias usually appear as a firm, cordlike mass that extends into the scrotum.
- Mammary neoplasia or mastitis: firm, enlarged, possibly painful mammary gland(s)
- Hematoma: ecchymosis; nonreducible (gentle pressure only)
- Abscess: may be inflamed; nonreducible (gentle pressure only)

INITIAL DATABASE

- CBC, serum biochemistry profile, urinalysis: if systemic clinical signs exist or as part of preoperative screening
- Avoid fine-needle aspiration unless performed with ultrasound guidance:
  - Risk of perforation of intestinal loop or gravid uterus

ADVANCED OR CONFIRMATORY TESTING

- Survey abdominal radiographs:
  - Displaced gravid uterus, small or large intestine, urinary bladder, or spleen
  - Loss of intraabdominal detail in the caudal abdominal and inguinal regions
- Contrast radiography:

- Cystogram to determine position of bladder
- Ultrasound examination:
  - Determine position of organs in abdomen and contents of hernia.

TREATMENT

TREATMENT OVERVIEW

- All inguinal hernias should be surgically corrected at the time of diagnosis, regardless of size. Delay may make surgery more difficult and increase the risk of complications (visceral strangulation, devitalization, and rupture).
- Inability to reduce strangulated organs (particularly bladder, intestines, or uterus), clinical signs of peritonitis, and pain are indications for immediate surgical intervention.

ACUTE GENERAL TREATMENT

- Treatment for inguinal hernia is herniorrhaphy, performed at the time of diagnosis to prevent complications and improve ease of surgical repair.
  - Tension-free apposition of tissue and ligation of the hernia sac
  - Generally performed via an external approach to the inguinal ring
  - In more complicated cases in the older female, herniorrhaphy via an abdominal approach (include ovariohysterectomy) may be most appropriate.

POSSIBLE COMPLICATIONS

- Hernia associated:
  - Incarceration/strangulation of abdominal organ(s): peritonitis, cellulitis
  - Edema, pain
- Associated with the surgical repair:
  - Hematoma/seroma: inadequate hemostasis, excessive tissue dissection, excessive activity after repair
  - Infection: herniorrhaphy site or peritonitis
  - Swelling or edema caused by incorporation of neurovascular bundle into repair
  - Overall postoperative complication rate for herniorrhaphy: 17%

RECOMMENDED MONITORING

- Postoperative exercise restriction for 10–14 days
- Surgical site should be monitored for swelling and discharge.

PROGNOSIS AND OUTCOME

- Excellent in uncomplicated inguinal hernia with successful repair
- Prognosis may be less favorable in complicated cases.
  - Intestinal incarceration/strangulation, peritonitis, pyometra
- There is no information in the literature to suggest that these hernias close spontaneously.

PEARLS & CONSIDERATIONS

COMMENTS

- Inguinal hernias are most commonly seen in middle-aged, intact female dogs.
- Prompt repair is recommended to minimize complications.
  - Surgical repair is easier with smaller hernias.
- Proper postoperative pain control and exercise restriction are necessary for good outcome.

PREVENTION

- Ovariohysterectomy may decrease risk.
- Obesity may increase risk.

- Dogs that have nontraumatic inguinal hernia should not be used for breeding purposes.

CLIENT EDUCATION

- Proper weight management is recommended.
- Nonbreeding female dogs should be neutered.

SUGGESTED READING

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Waters DJ, Roy RG, Stone EA: A retrospective study of inguinal hernia in 35 dogs. Vet Surg 22:44–49, 1993.

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Influenza, Canine

BASIC INFORMATION

DEFINITION

An uncommon but highly contagious respiratory pathogen which is a mutation of the equine influenza A subtype H3N8

SYNONYMS

Dog flu, H3N8 influenza virus

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dog, no age or sex predilection. Since this is an emerging disease with no pre-exposure, all ages are susceptible.

RISK FACTORS

High-density canine populations (e.g., kennels, shelters, pet stores)

CONTAGION & ZOONOSIS

Dog-to-dog transmission, no known zoonotic transmission

GEOGRAPHY AND SEASONALITY

Confirmed diagnosis in 25 U.S. states and the District of Columbia. Several “hot spots” have been identified in New York, southern Florida, northern Colorado, and southern Wyoming.

ASSOCIATED CONDITIONS & DISORDERS

Bacterial pneumonia

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Three forms exist:

- Mild subclinical form; no clinical signs.
- Mild upper respiratory disease that is similar to typical infectious tracheobronchitis/“kennel cough.”
- Severe form (occurs in 5%-20% of dogs) with life-threatening pneumonia.

HISTORY, CHIEF COMPLAINT

- Recent exposure to high-density dog populations
- Moist cough (productive or nonproductive), nasal discharge, lethargy, fever, and tachypnea/dyspnea

PHYSICAL EXAM FINDINGS

Soft, moist paroxysmal cough (can be a dry cough that is mistaken for kennel cough complex). Mucopurulent nasal discharge. Lethargy, fever, tachypnea and/or dyspnea. Harsh lung sounds/crackles and cyanosis can occur with pneumonia.

ETIOLOGY AND PATHOPHYSIOLOGY

- Incubation time is 2 to 5 days.
- Clinical infection generally lasting 2-4 weeks.

- Virus is typically shed in respiratory secretions for 4–10 days.
- Postexposure immunity may last up to 2 years.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The presence of clinical signs with a history of exposure to high-density dog populations, especially within the known hot spots, is suggestive of canine influenza. Confirmation requires positive canine influenza titer from serologic testing.

DIFFERENTIAL DIAGNOSIS

- *Bordetella bronchiseptica*
- Canine parainfluenza virus
- Canine distemper virus
- Canine adenovirus 2
- Bacterial pneumonia *(Pasteurella multocida, Klebsiella pneumonia, Escherichia coli, Streptococcus* spp., or *Mycoplasma* spp.)
- Canine reovirus

INITIAL DATABASE

- CBC: stress leukogram +/− immature neutrophils
- Serum biochemistry profile: nonspecific
- Urinalysis: nonspecific
- Thoracic radiographs: +/− interstitial to alveolar pattern
- Transtracheal wash or bronchoalveolar lavage (typically performed when suspecting other disorder, or to characterize secondary bacterial infection): neutrophilic infiltrate +/− bacteria

ADVANCED OR CONFIRMATORY TESTING

- Antibody titer: most commonly used method. Not detectable during first week. Positive titer confirms exposure in most cases, as most affected dogs develop a positive titer. Because vaccination has only recently become available, and its use is not widespread, a positive titer in the presence of clinical signs usually indicates disease. If a dog is vaccinated, titer will no longer be useful to confirm disease.
- PCR: nasal and pharyngeal swab samples; very sensitive and specific but can be variably rewarding depending on stage of disease
- Influenza A ELISA: less sensitive than PCR
- Virus isolation: taken from affected lung samples

TREATMENT

TREATMENT OVERVIEW

Canine influenza has a viral etiology, so treatment consists of supportive care and prevention/management of secondary bacterial infections.

ACUTE GENERAL TREATMENT

- Isolate from other dogs, and/or treat as outpatient if possible because of highly contagious nature.
- Maintain hydration (PO, SQ, or IV).
- Culture bronchoalveolar lavage fluid in dogs with pneumonia.
- Antibiotic therapy:
  - Doxycycline: 5–10 mg/kg PO q 12 h; *or*
  - Clindamycin: 5–11 mg/kg IM, SQ, or PO q 12 h; or 11 mg/kg IV q 12 h for sepsis; *or*
  - Ampicillin: 22 mg/kg IV or PO q 8 h; *or*
  - Chloramphenicol: 45–60 mg/kg PO, IM, SQ, or IV q 6–8 h; *or*
  - Enrofloxacin: 5–20 mg/kg IV q 24 h
- Nebulization and coupage q 6–8 h (can add gentamicin and/or albuterol to nebulizer)
- Oxygen supplementation if necessary

- Oseltamivir phosphate (Tamiflu): 1 mg/ kg PO q 24 h. Not approved for dogs; controversial because of concerns about creating resistant strains of influenza and using drugs on dogs that should be reserved for human outbreaks.
- Combinations of antimicrobials may be necessary for a broader spectrum of coverage while waiting for culture and susceptibility results.

CHRONIC TREATMENT

- Continue antibiotics for 2 weeks after resolution of clinical signs.
- Cough suppressants: case dependent and contraindicated with pneumonia or productive cough; useful for mild upper respiratory form

POSSIBLE COMPLICATIONS

Development of pneumonia +/− sepsis

RECOMMENDED MONITORING

- Auscultation of the patient multiple times daily to access lung sounds
- Repeat thoracic radiographs.
- Pulse oximetry (Spo2)
- Arterial blood gases, A: a gradient, Pao2/Fio2 ratio in dogs with pneumonia

PROGNOSIS AND OUTCOME

Good with supportive care and antibacterial therapy. Morbidity is estimated at 80% and mortality from l%–8%.

PEARLS & CONSIDERATIONS

COMMENTS

- Use proper isolation precautions, as with parvovirus.
- If possible, treat as an outpatient to prevent contamination of the veterinary clinic.
- Monitor the patient closely for signs of developing pneumonia.
- Maintain adequate hydration.
- Normal progression to pneumonia is 5-10 days.
- Continue medications for at least 2 weeks after the resolution of clinical signs.
- Coughing can continue for 10–30 days.

PREVENTION

- Restricted access to high-density dog populations
- If showing clinical signs, isolation from other dogs

TECHNICIAN TIPS

- Wear gloves, wash hands, strictly isolate patients to prevent spread to other hospitalized dogs.
- Clean nasal and ocular discharge with a warm moist disposable cloth.
- Warm food to enhance smell when offering food (nasal congestion) (see p. 80).

CLIENT EDUCATION

If treating at home, monitor for fever, loss of appetite, increased coughing and breathing effort.

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EDITOR: DOUGLASS K. MACINTIRE

Inflammatory Bowel Disease

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Common intestinal disease of dogs and cats. Characterized by chronic (>3 weeks) gastrointestinal signs of idiopathic origin, with inflammatory infiltration of small and/or large intestinal mucosa.

SYNONYMS

IBD. Depending on the infiltrating cell type: lymphocytic-plasmacytic, eosinophilic, suppurative, or granulomatous enteritis, colitis, or enterocolitis

EPIDEMIOLOGY

SPECIES, AGE, SEX

Most prevalent among middle-aged and old dogs and cats (median age 5–6 years) but can affect patients of all age categories

GENETICS & BREED PREDISPOSITION

Dog: chronic enteropathies are frequent in German shepherd dogs and shar-peis. IBD and protein-losing enteropathy occur frequently in soft-coated wheaten terriers and Lundehunds. Histiocytic ulcerative colitis is common in boxers.

ASSOCIATED CONDITIONS & DISORDERS

- Dog: soft-coated wheaten terriers often have concurrent protein-losing nephropathy.
- Cat: “triaditis” with concurrent IBD, cholangiohepatitis, and pancreatitis; relatively common

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Clinical signs vary depending on which segment of the intestine is involved. In cats, suspect concomitant small-intestinal involvement even in patients showing exclusively large-bowel signs.

HISTORY, CHIEF COMPLAINT

- Mild IBD may cause intermittent clinical signs, whereas severe IBD is characterized by progressive and severe clinical signs.
- Dogs are presented for evaluation of chronic diarrhea which can be of small- and/or large-bowel origin. Vomiting may also occur.
    - Small-intestinal disease may be associated with decreased appetite, weight loss, and lethargy.
    - Large-intestinal disease is often limited to typical diarrhea and occasional vomiting.
- Cats are usually presented for evaluation of chronic vomiting which may or may not be associated with diarrhea. Inappetence/anorexia, weight loss, and lethargy are common.

PHYSICAL EXAM FINDINGS

- Small-intestinal disease:
    - Poor body condition with poor hair coat is frequent with severe disease.
    - Dehydration is possible.
    - Thickened small intestinal loops may occasionally be palpated.
    - Animals may occasionally show pain or discomfort on abdominal palpation.
    - Ascites, hydrothorax and peripheral edema may occur in case of significant protein loss.
- Large-intestinal disease:
    - Often unremarkable; may be associated with abdominal discomfort in severe cases.
    - Mucoid and/or bloody stool during rectal exam

ETIOLOGY AND PATHOPHYSIOLOGY

- Abnormal interactions between intestinal microflora and innate/adaptive immune systems
- Penetration of luminal antigens into the lamina propria, with subsequent uncontrolled immune response
- Protein loss may reflect poor absorptive function or inflammatory exudation or ulceration.
- In some instances, associated with the presence of mucosa-adhesive bacteria such as *Escherichia coli* (feline IBD, canine histiocytic ulcerative colitis)

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis of IBD is reached by exclusion.

DIFFERENTIAL DIAGNOSIS

- General differentials
  - Chronic intestinal foreign body
  - Intestinal parasites: hookworms, whipworms, *Giardia* and *Tritrichomonas* (cat)
  - Chronic kidney disease
  - Chronic liver disease
  - Chronic pancreatitis
  - Endocrine diseases (hypoadrenocorticism [dog], hyperthyroidism [cat])
  - Cecal intussusception (dog, rare)
- Differentials that may result in GI signs and histologic evidence of GI inflammation:
  - Adverse reactions to food (food intolerance, food allergy)
  - Antibiotic-responsive diarrhea (dog)
  - Fungal enterocolitis (e.g., *Histoplasma)*
  - Colitis associated with *Pythium insidiosum* infection
  - Histiocytic ulcerative colitis (HUC) in boxer and other dogs
  - Bacterial enterocolitis (e.g., in dogs, *Campylobacter* spp., *C. perfringens, C. difficile)*
  - Infiltrative intestinal neoplasia (alimentary lymphoma, particularly cat)
- Differentials to consider for intestinal protein loss:
  - Intestinal lymphangiectasia (Yorkshire terrier, Lundehund), histoplasmosis, alimentary lymphoma
  - Liver, kidney or dermal origin

INITIAL DATABASE

- Fecal parasitology to rule out nematodes, protozoa
- Fecal *Giardia* antigen test to rule out giardiasis
- In endemic areas for fungal diseases: rectal scraping (see p. 1334)
- CBC, especially in dogs and cats with small-intestinal signs; useful to rule out differential diagnoses
- Serum biochemistry: panhypoproteinemia may be associated with severe disease, hypocalcemia reflects hypoalbuminemia and possibly malabsorption of fat-soluble vitamin D, concomitant liver disease (cat); useful to rule out differential diagnoses.
- Serum thyroxin concentration (cat)
- Consider ACTH stimulation test (dog)
- Abdominal radiographs to rule out intestinal obstruction (e.g. in vomiting cats)
- Abdominal ultrasound: may be normal or show focal or diffuse intestinal wall thickening, loss of layering, presence of mucosal striation or spicules, enlarged and/or hypoechoic mesenteric lymph nodes. Localization of lesions may help decide best approach for biopsies (endoscopy or celiotomy). Ultrasound-guided fine-needle aspiration of abnormal lymph nodes or intestinal wall can be useful.
- Serum trypsinlike immunoreactivity, cobalamin, and folate concentrations: recommended to identify concurrent pancreatic disease and cobalamin deficiency (especially in cats)

ADVANCED OR CONFIRMATORY TESTING

- Upper and/or lower gastrointestinal endoscopy: assess mucosa, sample eight deep (include upper submucosal layer) biopsies per anatomic site.
- Celiotomy if lesions are inaccessible by endoscopy or if full-thickness biopsies are desirable (e.g., to rule out lymphoma in cats)
- Histopathologic analysis: beware of differences between pathologists; objective is to confirm inflammatory mucosal infiltration and diagnosis of IBD.

TREATMENT

TREATMENT OVERVIEW

- Treatment of IBD most commonly centers on immune suppression with glucocorticoids. Other immune-suppressive drugs can be added as needed.
- The goal of therapy is to control the clinical signs, as a cure may be unattainable.

ACUTE GENERAL TREATMENT

- Supportive treatment as necessary if patient not stable (IV fluids, antiemetics, etc.)
- Ensure the following has been done before instituting immunosuppressive therapy for IBD:
  - Empirical deworming (e.g., with fenbendazole, 50 mg/kg PO q 24 h × 3 days
  - Elimination diet: novel protein or hydrolyzed peptide-based diet for 2 weeks or more
  - Modify intestinal microflora: especially in dogs, antimicrobial treatment with metronidazole (10–15 mg/ kg PO q 12 h), tylosin (25 mg/kg PO q 12 h), or tetracycline (20 mg/ kg PO q 8 h) for 2–6 weeks.
- In case of canine colitis (not HUC; see p. 228):
  - Sulfasalazine (10–30 mg/kg PO q 8 h) for 2 weeks, then taper to same dose q 12 h for 2 weeks, then half dose q 12 h for 2 weeks, and so on. Alternatively, olsalazine (10–20 mg/kg PO q 12 h). Monitor tear production (risk of keratoconjunctivitis sicca with sulfa drugs).
  - Consider adding soluble fiber (psyllium 1-2 teaspoons/10 kg per meal).
- In severe cases, in cases with protein-losing enteropathy, or in cases in which the above approach has failed, treatment with immune-suppressive doses of glucocorticoids is indicated:
  - Prednisone, 2 mg/kg PO initially q 12 h for a few days, then q 24 h for 2 weeks, then 1 mg/kg PO q 24 h, then 1 mg/kg q 48 h, then decrease dose by half every 2 weeks. Treatment and weaning period usually last for at least 8–12 weeks. Cats may respond better to prednisolone (up to 4 mg/kg PO q 24 h in the initial 10- to14-day phase).
  - Budesonide (dog, 3 mg/m^2 PO q 24 h; cat, 1 mg/cat PO q 24 h) can be substituted for prednisone. Budesonide undergoes some first-pass hepatic metabolism, and low systemic drug concentrations may cause fewer side effects.
- In steroid-refractory cases:
  - Cyclosporine A, 5 mg/kg PO q 24 h can be helpful (dog, cat); *or*
  - Dogs only: azathioprine, 2 mg/kg PO q 24 h for 2 weeks, then q 48 h (can be decreased to 1 mg/kg q 48 h) is another alternative; *or*
  - Cats: chlorambucil may be used as supplemental immune-suppressive therapy (2 mg/cat PO q 48 h).
- Supplement hypocobalaminemic patients with SQ vitamin B12 (see p. 220).
- Patients with PLE can be at increased risk for thromboembolism. Low-dose aspirin (0.5 mg/kg PO q 12 h in dogs; 5–81 mg/cat PO q 72 h in cats) is recommended if antithrombin levels are low. Gastroprotection with omeprazole (0.5–1 mg/kg PO q 24 h) or famotidine (0.5 mg/kg PO q 24 h) is recommended.

CHRONIC TREATMENT

The goal is to wean the patient off immune-suppressive therapy. If this is not feasible, the goal becomes finding the lowest-dose regimen that will allow reasonable control of clinical signs.

NUTRITION/DIET

- An elimination diet with novel proteins (requires good nutritional history) or hydrolyzed peptides is recommended in most dogs and cats with IBD.
- Alternatively, an easily digestible diet with low fat content is recommended in cases with IBD and severe PLE.

POSSIBLE COMPLICATIONS

- High doses of glucocorticoids may cause multiple systemic side effects (e.g., polyuria/polydipsia, iatrogenic hyperadrenocorticism)
- Side effects reported with cyclosporine use in dogs include decreased appetite and vomiting.
- Azathioprine may cause bone marrow suppression and has been associated with acute pancreatitis in dogs. Regular monitoring of CBC is advised. Avoid use in patients with previous history of pancreatitis.
- Immunosuppressive medications predispose animals to secondary infections.
- Metronidazole toxicosis may cause neurologic signs in cats.

RECOMMENDED MONITORING

Regular evaluation of the body weight and overall clinical condition are recommended. Consider rechecking serum albumin.

PROGNOSIS AND OUTCOME

- Short-term prognosis is usually good in mild to moderate cases of IBD.
- In dogs, negative prognostic factors include hypoalbuminemia and hypocobalaminemia, as well as severe mucosal lesions in the duodenum (noticed during endoscopy).
- Cases refractory to steroid treatment are not uncommon (l6%-55%) in dogs with non-food-responsive IBD. Cyclosporine therapy was successful in 25% of steroid-refractory patients.
- Treatment failures may be due to incorrect diagnosis, severe disease, presence of concurrent disease, or poor owner compliance. In cats, lack of response to treatment should motivate the clinician to reconsider the possibility of alimentary lymphoma.

PEARLS & CONSIDERATIONS

COMMENTS

IBD is a diagnosis of exclusion. It is essential to address possible intestinal parasites and initiate a dietary elimination trial in dogs and cats with chronic GI signs before making this diagnosis. Additionally, in dogs, consider antimicrobial treatment.

CLIENT EDUCATION

- A realistic goal for your pet's treatment is to manage the intestinal disease. As a definitive cure may not be attainable, our goal is to control the clinical signs while limiting the side effect of therapy.
- Your pet's diet is of central importance for the treatment. Please make every effort to adhere closely to our dietary recommendations.

SUGGESTED READING

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Infertility, Male

BASIC INFORMATION

DEFINITION

- This chapter is limited to discussion of abnormalities of the spermiogram, which may be categorized as follows:
  - Asthenozoospermia: decreased numbers of progressively motile spermatozoa per ejaculate (<30%–50%)
  - Teratozoospermia: increased numbers of morphologically abnormal spermatozoa per ejaculate (>40%–50%)
  - Oligozoospermia: abnormally low numbers of spermatozoa per ejaculate <22 million spermatozoa/kg body weight in the dog; or <5 million total spermatozoa in the tom)
- Other causes of male infertility are listed on .

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dog or cat, intact males, any age

GENETICS & BREED PREDISPOSITION

Some etiologies may have a hereditary component.

RISK FACTORS

Age, systemic disease (especially those resulting in increased body temperature), endocrinopathy, testicular disease or trauma

CONTAGION & ZOONOSIS

Brucella canis possible (see p. 162)

GEOGRAPHY AND SEASONALITY

Lower total number of spermatozoa and lower percentage of morphologically normal spermatozoa in summer months are expected in North American dogs

ASSOCIATED CONDITIONS & DISORDERS

May be associated with poor libido

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Reversible versus irreversible
- Compensatory versus noncompensatory

HISTORY, CHIEF COMPLAINT

- Declining or consistently poor fertility
- Recent episode of malaise or fever is possible.
- Prior history of physical training (possibility of performance-enhancing drugs)
- History of bloody penile or preputial discharge or pain with ejaculation
- History of chronic respiratory disease (asthenozoospermia)

PHYSICAL EXAM FINDINGS

- ± Fever

- Libido may be normal or decreased.
- Testes may be small and soft or normal in size and consistency.
- Testes, epididymides, or spermatic cords may be enlarged (inflammation or neoplasia), and/or thickened.
- Scrotum may be enlarged or thickened (dermatitis, trauma, edema or fluid accumulation).
- Prostatomegaly possible (symmetric or asymmetric; painful or nonpainful)
- In dogs with asthenozoospermia due to primary ciliary dyskinesia/immotile cilia syndrome, additional signs may include recurrent nasal discharge and/ or cough, hydrocephalus (open fontanelle, domed calvaria), or situs inversus (spleen is palpated on the right side of the abdomen; heartbeat is strongest on right hemithorax).

ETIOLOGY AND PATHOPHYSIOLOGY

- Causes (all categories):
  - Infectious or inflammatory (orchitis, epididymitis, prostatitis including infection with *B. canis,* mycoplasmas or other aerobic bacteria, or feline infectious peritonitis [FIP])
  - Scrotal hyperthermia (due to fever, obesity with increased intrascrotal fat, hydrocele, hematocele, scrotal edema, or neoplasia)
  - Toxin exposure or exogenous drug administration (corticosteroids, anabolic steroids [human estrogen or testosterone patches or creams], other steroid hormones, chronic nonsteroidal antiinflammatory drug [NSAID] usage, gonadotropin-releasing hormone [GnRH] agonist/antagonists, chemotherapeutic agents)
  - Testicular degeneration (primary or secondary)
  - Immune mediated (lymphocytic thyroiditis or spermatozoal autoantibodies)
  - Unilateral or partial epididymal or tubular obstruction (granuloma, spermatocele)
  - Congenital
- Additional causes (specific to individual categories):
  - Primary ciliary dyskinesia with abnormal spermatozoal midpiece formation (asthenozoospermia)
  - Prostatic disease: benign prostatic hyperplasia, prostatitis, or squamous metaplasia (oligozoospermia, asthenozoospermia)
  - Neoplasia (oligozoospermia, teratozoospermia)
  - Hyperadrenocorticism (oligozoospermia)

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is based on history (generally of suboptimal fertility), physical exam findings, semen evaluation, and cultures of semen or prostatic fluid in many cases. Remainder may require more advanced diagnostic testing.

DIFFERENTIAL DIAGNOSIS

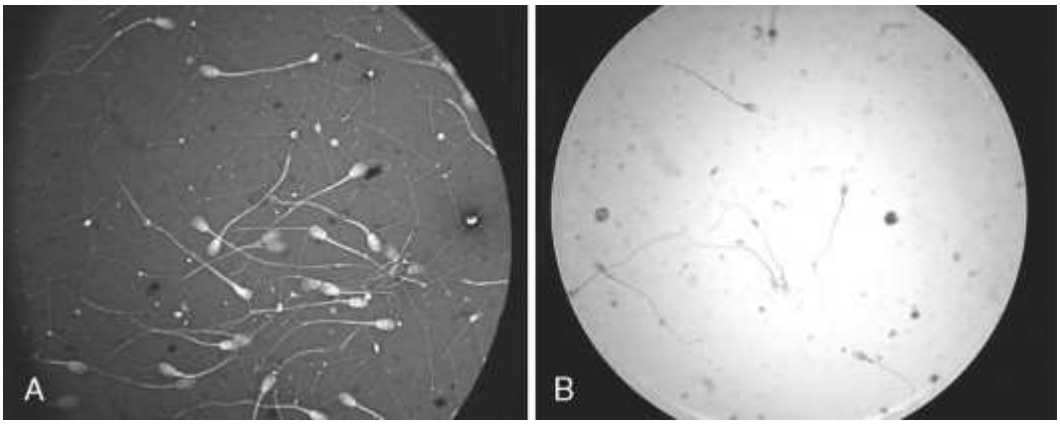
- Asthenozoospermia:
  - Contaminated or improperly washed ejaculate collection equipment (e.g., disinfectant residues)
  - Excessive use of lubricants
  - Prolonged exposure of ejaculate to latex, heat, or cold
  - Urine contamination of the ejaculate
  - Infrequent ejaculate collection, with accumulation of dead sperm in the epididymis and/or vas deferens
- Teratozoospermia:
  - Poor handling of semen after collection (especially if coiled tails or detached heads are present)
  - Improper microscopic interpretation
  - Prolonged sexual abstinence (increase in detached heads) or overuse, pubertal and geriatric patients (increases in cytoplasmic droplets)
- Oligozoospermia:
  - Retrograde ejaculation
  - Fear or apprehension of mating (i.e., presence of dominant female, timid male, first time breeding)
  - Overuse of males, resulting in depletion of epididymal sperm reserves

INITIAL DATABASE

- Physical examination, including palpation of the scrotal contents, spermatic cords, and prostate
- Semen collection and evaluation (including motility, morphology, concentration, volume) and libido evaluation
  - Seminal and prostatic fluid cytologic analysis and culture (see p. 1332)
  - CBC, serum biochemistry panel, urinalysis
  - Serology: *B. canis,* feline coronavirus/FIP

ADVANCED OR CONFIRMATORY TESTING

- All categories:
  - Scrotal and prostatic ultrasonography for structural lesions
  - Endocrine testing: baseline testosterone, estradiol, and follicle-stimulating hormone concentrations
  - Endocrine stimulation testing:
    - Administer 2.2-3.3 mcg/kg GnRH IM or 44 IU/kg human chorionic gonadotropin (hCG) IM in dogs with baseline testosterone and luteinizing hormone (LH) and then sample for LH (10 minutes post injection) and testosterone (1 hour post injection); *or* 250-500 IU hCG IM or IV; or 25 mcg GnRH IM in toms with baseline testosterone and poststimulation samples taken 2 and 4 hours later for hCG or 1 hour after GnRH
    - Normal response: a minimum of a twofold to fourfold increase in testosterone concentrations
    - Negligible or inappropriate response indicates either a primary testicular lesion or a lesion of the hypothalamic-pituitary axis, resulting in failed feedback loop mechanisms
  - Testicular biopsy or aspirate to be considered if noninvasive testing is unrewarding or if a structural lesion (e.g., mass) is present.
  - Advanced semen diagnostics: sperm chromatin structure assay, electron microscopy, in vitro functional assays
- Asthenozoospermia:
  - Radiography of the thorax, respiratory tract cultures, biopsy and electron microscopy of nasal or respiratory epithelium or spermatozoal midpieces for evaluation for primary ciliary dyskinesia (see p. 916)
  - Examination of ejaculate for pH and/or presence of urine crystals, indicating urine contamination
  - Collection directly into semen extender at body temperature, with fractionation of ejaculate
- Teratozoospermia:
  - Detailed morphologic examination using special staining and microscopic techniques such as Spermac, toluidine blue, or Coomassie blue stains, phase contrast, differential interference contrast or electron microscopy
- Oligozoospermia:
  - Urinalysis after ejaculation to assess for retrograde ejaculation. Sample may be obtained by cystocentesis or catheterization.
  - Seminal plasma alkaline phosphatase concentrations to confirm that ejaculation actually occurred with azoospermia



INFERTILITY, MALE Sperm morphology slides made with either an eosin-nigrosin (viability) stain **(A)** or Romanowsky stain (Diff-Quik) **(B)**. With the viability stain, sperm that have damaged cell membranes (dead) stain red (pink), whereas sperm with normal cell membranes (live) do not take up the eosin and therefore appear white. With the Romanowsky stain, increased incubation time (at least 5 minutes for each stain instead of the typical 10 dips within the stain jar) is required for the sperm cells to take up adequate amounts of stain to determine morphology.

TREATMENT

TREATMENT OVERVIEW

- Increase the number of total sperm, the number of total motile cells, and/ or the number of normal cells per ejaculate.
- Manage the use of the male to maximize fertility.

ACUTE GENERAL TREATMENT

- All:
  - Bacterial infections should be treated with appropriate antibiotics based on culture and sensitivity. Individuals positively confirmed to be infected with brucellosis should also be neutered and all kennelmates tested.

    - Hemicastration for unilateral inflammatory, obstructive, or neoplastic conditions
    - Cats that meet the clinical and laboratory criteria for FIP should be removed from catteries/multicat environments (see p. 383)
- Asthenozoospermia:
    - Careful cleaning, rinsing (at least twice with distilled water), and drying of artificial insemination equipment
    - Sparing use of nonspermicidal lubricants
    - Have males urinate immediately prior to collection to avoid urine contamination of ejaculate.
- Teratozoospermia:
    - With scrotal overheating, waiting a minimum of 65 days from onset of insult should result in return to normal spermatozoal morphology.
    - Weight reduction in obese males
    - Centrifugation with sperm gradients to remove abnormal sperm
- Oligozoospermia:
    - With scrotal overheating, waiting a minimum of 65 days from onset of insult should result in return to normal spermatozoal morphology.
    - For retrograde ejaculation: in dogs, phenylpropanolamine (1.1 mg/kg PO q 8–12 h) or pseudoephedrine (0.2–0.4 mg/kg PO q 8 h or 1 to 3 hours before breeding; in toms, phenylproponolamine 6.25–12.5 mg/cat PO q 8–12 h (contraindicated in systemic hypertension)
    - Administration of GnRH (Cystorelin) at 2.2 mcg/kg IM to increase libido, 20-30 minutes prior to collection; or dinoprost tromethamine (Lutalyse) at 0.025-0.05 mg/kg SQ 20 minutes prior to collection (results in sperm-rich ejaculate only +/− full erection)
    - Weight reduction in obese males
    - Positive reinforcement for behavioral issues

CHRONIC TREATMENT

- Asthenozoospermia:
    - Immediate centrifugation of the ejaculate in cases of urine contamination, followed by reextension with semen extender or centrifugation with sperm gradients
    - Depo-Testosterone enanthate (testosterone) plus pregnant mare serum gonadotropin (PMSG) every 2 weeks for 6 weeks has been advocated, but dosages, efficacy, and safety have not been established (50 mg/dog testosterone enanthate + 250 IU/dog PMSG have been used successfully in 15 kg dogs).
- Teratozoospermia, oligozoospermia + asthenozoospermia:
    - If testicular degeneration is present, long-term administration of GnRH (3.3 mcg/kg) IM once weekly or hCG (500-1000 IU IM) every 2 weeks in dogs; or hCG 250-500 IU IM every 2 weeks in toms has shown some positive effects

NUTRITION/DIET

- Administration of daily glucosamine, omega-3 fatty acid, and DHA supplement may be of benefit for asthenozoospermia.
- Administration of daily zinc sulfate and vitamin E supplement may be of benefit for all conditions.

BEHAVIOR/EXERCISE

Excessive exercise and stress may result in infertility from chronic stress or overheating.

DRUG INTERACTIONS

Ketoconazole, cimetidine, long-term NSAID therapy, sulfasalazine, amitriptyline

RECOMMENDED MONITORING

- Routine (monthly) microscopic reevaluation of the spermiogram and reassessment of endocrine function as indicated, beginning 2 to 3 months after initiation of treatment
- Monitor pregnancy rates and litter size.

PROGNOSIS AND OUTCOME

The prognosis for fertility is guarded if no response to treatment occurs within 3 months, poor if no response to treatment occurs within 6 months, and grave if no response to treatment occurs within a year.

PEARLS & CONSIDERATIONS

COMMENTS

- Optimize available sperm:
  - Accurate breeding management and ovulation timing
  - Reduce the number of matings per cycle.
  - Use of transcervical or surgical insemination (surgical insemination preferred)
  - Breeding to young, fertile females
- Avoid overuse:
  - Do not collect more than every other day.
  - Collection of males 7-10 days before anticipated matings in animals that have had prolonged abstinence, to flush the ejaculatory tract of dead sperm
  - Avoid strict raw-meat diets, as they may result in amino acid or vitamin/mineral deficiencies.
- Never diagnose sterility after a single exam.

PREVENTION

- Brucellosis screening biannually (dogs)
- Coronavirus/FIP screening of all new entries into catteries (see p. 383 and p. 258).

CLIENT EDUCATION

- Monitor semen quality regularly for breeding males.
- Freeze semen when dogs are young and fertile.

SUGGESTED READING

Johnston SD, et al: Clinical approach to infertility in the male dog. In Canine and feline theriogenology. Philadelphia, 2001, WB Saunders, pp 381–382.

Meyers-Wallen VN: Clinical approach to infertile male dogs with sperm in the ejaculate. Vet Clin North Am Small Anim Pract 21:609–633, 1991.

AUTHOR: CHERYL LOPATE

EDITOR: MICHELLE A. KUTZLER

Infertility, Female Dog

BASIC INFORMATION

DEFINITION

The failure to ovulate, accept the male, become pregnant, maintain pregnancy, or deliver live puppies at term

SYNONYMS

Infecundity, sterility

EPIDEMIOLOGY

SPECIES, AGE, SEX

Canine, anytime after puberty (6 months and older), female

GENETICS & BREED PREDISPOSITION

More prevalent in inbred families of purebred dogs. Anecdotal information indicating that some breeds of dogs have poor fertility (e.g., Norwich terriers, some sight hounds). Some have been bred to have conformations requiring assistance with breeding and parturition (e.g., bulldogs).

RISK FACTORS

- Advancing age can decrease fertility. Peak fertility is 2-4 years of age.
- Poor or incomplete breeding management is responsible for most apparent infertility in the bitch (see p. 155).
- Previous hormone therapy, abnormal hormone concentrations, and uterine disease also increase the risk of infertility.
- Anestrus, silent heat, persistent estrus, irregular estrus, abnormal sexual behavior, uterine disease, hypoluteoidism, structural abnormalities of the female reproductive tract, systemic illness, and inappropriate nutrition (excessive or inadequate caloric intake, raw diets contaminated with *Salmonella* spp. and/or *E. coli)* all may predispose to infertility.

CONTAGION & ZOONOSIS

Several bacterial and viral agents contributing to infertility are contagious and can be spread both by inhalation and venereally, including β-hemolytic *Streptococcus, Mycoplasma,* and *Ureaplasma* spp., and herpesvirus. The most significant canine venereal disease is *Brucella canis* (see p. 162).

GEOGRAPHY AND SEASONALITY

Female domestic dogs are nonseasonal, with the exception of the basenji that only enters proestrus in the late summer/ early fall.

ASSOCIATED CONDITIONS & DISORDERS

Pseudocyesis (see p. 929) occurs in many bitches whether they are pregnant or not and has not been linked to infertility. Vaginal hyperplasia (see p. 1156) may contribute to infertility by limiting or preventing natural service (does not interfere with artificial insemination).

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Breeding management issues
- Abnormalities of the estrous cycle
- Uterine abnormalities

HISTORY, CHIEF COMPLAINT

Varies with the client; medical history is the most important tool in the approach to infertility. Important elements in the history include:

- General health history: vaccination status of the bitch; current medications; past medications, vitamins, and herbal supplements, including heartworm-preventative and topical medications
- Housing details: kennel, home, indoor, outdoor, and number of bitches in the household
- Bitch's age at first estrous cycle
- Length of each cycle from onset of vulvar swelling to diestrus cytology
- Intercycle interval? Details of cycle: onset of vulvar swelling and vulvar discharge, onset of estrous behavior (flagging), dates of mating.
- Method of mating: natural service or artificial insemination by bitch owner, stud owner, or veterinarian
- Artificial insemination: with fresh, chilled, or frozen semen? Was the semen deposited into the vagina or the uterus?
    - Stud dog status
- Dates of last *B. canis* serologic testing for both the bitch and the stud dog
- Method of pregnancy diagnosis: palpation, hormone assay, ultrasound, or radiographs
- Were hormone assays performed during the cycle? Was vaginal cytologic and/or progesterone testing performed to time the breedings? If progesterone testing was done, was it quantitative or qualitative?
- Was the bitch being campaigned or under any other stressful event such as a new home?
- History in infertility in the pedigree if any

PHYSICAL EXAM FINDINGS

Physical examination is usually within normal limits. Special attention should be paid to the external genitalia and mammary glands.

- Ambiguous genitalia may be an indicator of an intersex state (clitoral enlargement suggestive).
- Digital vaginal examination (see p. 1360): to assess patency and accessibility of the vulva and caudal vagina
- Vaginal examinations should be performed gently and atraumatically; may not be feasible in toy-breed bitches that are anestrous at the time of examination.
- Vaginal septae and circumferential strictures may interfere with natural service and with artificial insemination into the vagina as well.
- Visual inspection and palpation of the mammary glands

ETIOLOGY AND PATHOPHYSIOLOGY

- Mistimed breeding is by far the most common cause of infertility.
- Ovarian dysfunction: abnormalities in ovulation and maintenance of the corpus luteum, persistent estrus, and primary anestrus
- Uterine dysfunction: lesions of the uterus (cystic endometrial hyperplasia/ pyometra), subclinical uterine infection, shortened interestrus interval, resulting in implantation failure. The canine uterus requires 130 to 150 days following the onset of proestrus for endometrial repair to occur.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is based on a compilation of history (most important), physical examination, and results of laboratory evaluation. Historical information provided by the client is the cornerstone of the diagnostic process and must be elicited comprehensively.

DIFFERENTIAL DIAGNOSIS

- Pregnancy loss
- Ovulation failure
- Silent heat
- Stud dog infertility

INITIAL DATABASE

- CBC, serum biochemistry profile, thyroid panel, *B. canis* serology, vaginal cytologic examination, vaginal culture if in estrus or if discharge present
- Hypoproteinemia and/or or renal dysfunction may contribute to infertility.

ADVANCED OR CONFIRMATORY TESTING

- Vaginoscopy
- Progesterone testing to document ovulation and assess luteal function. Progesterone testing is recommended monthly to assess cyclicity if the client has not observed cycles.
- Ultrasonography of the uterus and ovaries
- Herpesvirus titer
- Ovarian and/or uterine biopsy with histopathologic evaluation could be used in select cases.
- In cases of primary anestrus, it is wise to determine the karyotype of the bitch to assess her actual chromosomal makeup. Trisomy X, XO females and other abnormal chromosome combinations have been reported. Many normal sight hound bitches do not cycle until near 24 months old.

TREATMENT 

TREATMENT OVERVIEW

Targeted treatment is based on the underlying cause of the infertility. In most cases, it is improper breeding management, and client education is the critical issue.

ACUTE AND CHRONIC TREATMENT

- Shortened interestrus interval: mibolerone, 30–180 mcg (small to large dog) PO q 24 h (schedule IV controlled substance)
- Treatment for cystic endometrial hyperplasia/pyometra if present (see p. 954)
- Treatment for persistent estrus if present (see p. 916)
- There is no reliable therapy to induce fertile estrus in the bitch. There are many protocols in use with varying outcomes, but no controlled studies have been published. The most commonly attempted protocols include the use of Ovuplant (a deslorelin implant) or the oral antiprolactinic medication, cabergoline.

NUTRITION/DIET

- Diet with an Association of American Feed Control Officials statement that this diet is complete for all life stages, based on feeding trials.
- If feeding a puppy food during the second half of gestation, it should be a small-breed puppy food.
- No controlled studies to support any claims of over-the-counter supplements that purportedly increase litter size, regulate estrous cycles, promote normal delivery, and so on; some may result in infertility.
- Avoid calcium supplementation pre-partum.

BEHAVIOR/EXERCISE

- A bitch that is removed from her litter too early or a singleton puppy may never demonstrate normal breeding behavior because of her lack of appropriate interaction with littermates at an early age. These bitches may or may not demonstrate normal maternal behavior after whelping. A bitch that is the first canine within a household may not accept a male that is added to the household at a later date. Artificial insemination will overcome this difficulty.
- Performance bitches may be allowed to continue training in the venue in which they compete, provided consideration is allowed for temperature, confinement, stress, and the physical demands of the activity. Special consideration should be made for the potential for exposure to viral and bacterial pathogens for which there is no prophylaxis available. Show grounds, training fields, and training facilities are likely to be a source of many challenges to normal reproduction.

DRUG INTERACTIONS

Use care in the selection of any medication used in a breeding bitch. For example, topical corticosteroids can be absorbed systemically and are not recommended. Use reference list for appropriate drug selection in pregnancy.

POSSIBLE COMPLICATIONS

- Mibolerone causes clitoral hypertrophy, epiphora, and tear staining and may increase aggression towards other dogs. This drug can exacerbate existing liver enzyme elevation. Dogs with normal liver enzymes rarely have changes as a result of the drug.
- The progestational compounds may cause masculinization of female fetuses. Failure to withdraw progestational compounds at the appropriate time can unduly prolong gestation, resulting in fetal death. Progestational compounds can also cause mammary masses to increase in size.

RECOMMENDED MONITORING

Confirm pregnancy using ultrasonography at 30 days post breeding. One can measure progesterone concentrations at that time and weekly if there is any indication of variability in embryonic vesicle size or embryonic loss.

PROGNOSIS AND OUTCOME

Good to excellent for clients who will comply with breeding management recommendations. Guarded for bitches with uterine disease and/or ovarian dysfunction.

PEARLS & CONSIDERATIONS

COMMENTS

- Infertility of the stud dog is the second most common cause of female infertility after improper breeding management. The stud dog must also be evaluated and demonstrated to produce adequate numbers of motile and morphologically normal sperm, and the semen must be inseminated properly.
- Failure to cycle is often a failure to observe the bitch adequately for physical changes consistent with proestrus. The client should blot the vulva daily to detect vaginal discharge and change in vulvar size and shape +/— monthly progesterone assays to detect ovulation with unobserved estrus.

TECHNICIAN TIPS

Be prepared for many questions from clients whose dogs fail to produce puppies. Many clients think that all bitches should be bred on a particular (10th/12th/other) pair of days from the onset of proestrus or every day while she is receptive, and such preconceived notions need to be anticipated and addressed with medical fact, as described above.

CLIENT EDUCATION

- Suggest a reproductive workup before the next anticipated estrous cycle.
- Vaginal cytologic evaluation, vaginal culture, and serum progesterone testing
- Importance of good semen and proper insemination technique

SUGGESTED READING

Edens M, et al: Breeding management in the bitch and queen. In Root-Kustritz M, editor: Small animal theriogenology. St Louis, 2003, Butterworth Heinemann, pp 33–60.

Gobello C, et al: Noninfectious/spontaneous pregnancy loss in bitches. Compend Contin Educ Pract Vet 24(10):778–783, 2002.

AUTHOR: FRANCES SMITH

EDITOR: MICHELLE KUTZLER

Incontinence, Urinary

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Lack of voluntary control over the passage of urine

EPIDEMIOLOGY

SPECIES, AGE, SEX

- With young animals, congenital disorders are more likely.
- Female dogs: older, spayed females are prone to incontinence due to urethral incompetence.

GENETICS & BREED PREDISPOSITION

- Ectopic ureter: Siberian huskies, miniature and standard poodles, Labrador retrievers, Newfoundlands, fox terriers, West Highland white terriers, collies, and Welsh Corgis

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Dribbling urine
- Incontinence while sleeping: a hallmark of urethral incompetence in spayed female dogs and ectopic ureter(s) in puppies

PHYSICAL EXAM FINDINGS

- Urine staining or scalding in perineum
- Neurologic deficits
- Bladder should be palpated before and after urination.
- Bladder expression:
  - Easy: decreased outflow resistance
  - Difficult: normal or increased outflow resistance
- Rectal examination
  - Urethral thickening (inflammation or infiltration)
  - Prostatomegaly (see p. 1420)
  - Bladder trigone abnormalities

ETIOLOGY AND PATHOPHYSIOLOGY

- Neurogenic:
  - Lower motor neuron (LMN; lesion at S1-S3 spinal cord segment, or peripheral nerve disorder)
  - Upper motor neuron (UMN; lesion cranial to sacral spinal cord segment S1)
- Non-neurogenic:
  - Anatomic
  - Functional

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Any patient with a chief complaint of urinary incontinence should have a complete medical history (notably to assess the possibility of behavioral causes and determine whether polyuria or pollakiuria is present); a physical examination including abdominal palpation, rectal palpation when feasible, neurologic examination, and examination of the genitalia and reproductive tract; a urinalysis; and a bacterial culture and sensitivity of urine. Additional tests are selected based on results of these evaluations and may include

monitoring response to treatment.

DIFFERENTIAL DIAGNOSIS

- Neurogenic:
  - LMN disorder (S1-S3 segment or peripheral nerve disorder):
    - Sacral fracture/malformation
    - Trauma to pelvic nerve
    - Lumbosacral disease
  - UMN disorder (cranial to S1); usually characterized by urine retention; overflow incontinence can occur:
    - Intervertebral disk disease
    - Spinal trauma
    - Fibrocartilaginous embolism
    - Spinal neoplasia
- Non-neurogenic:
  - Urethral sphincter mechanism incompetence:
    - Most common cause in adult female dogs
  - Urge incontinence/detrusor hyperspasticity:
    - Associated with lower urinary tract signs
  - Anatomic abnormalities:
    - Ectopic ureters
    - Patent urachus
    - Vaginal stricture

INITIAL DATABASE

- Neurologic examination:
  - UMN:
    - Firm, difficult to express bladder
  - LMN:
    - Flaccid, easily expressed bladder
    - Decreased/absent anal tone, bulbospongiosus reflex, perineal sensation
  - Pain on tail lift: associated with lumbosacral disease
  - Pain on spinal palpation; ataxia, proprioceptive deficits: associated with intervertebral disk disease
- Laboratory tests:
  - Urinalysis:
    - Cystocentesis preferred
    - Pyuria suggests infection of inflammation, leading to increased urge
    - Hematuria suggests inflammation or neoplasia
  - Urine culture and sensitivity
  - CBC/serum biochemistry panel

ADVANCED OR CONFIRMATORY TESTING

- Diagnostic imaging:
  - Abdominal radiographs/ultrasound: structural lesions
  - Cystourethrography/vaginography: radiolucent defects
  - Spinal radiography/myelogram/CT/MRI: spinal cord lesions
- Endoscopy:
  - Direct visualization of ectopic ureters and other anatomic defects
  - Evaluate, and if indicated, biopsy vaginal vault and mucosa of urethra and bladder.
- Urodynamic studies: urethral pressure profilometry
  - Measure pressure, volume, and flow in the urethra and bladder. Improves localization of anatomic site of dysfunction.
  - Generally only available at referral/ research facilities
  - Should be considered in patients refractory to treatment

TREATMENT

TREATMENT OVERVIEW

Some dogs may respond better to one medication than another. If there is no response to a medication, review the diagnosis and if unchanged, consider adding a second medication, changing to a medication in another class of action, and/or pursuing further

diagnostic testing. Goals of treatment are to correct any underlying anatomic defects, treat secondary conditions (e.g., infection), and palliate incontinence if persistent despite these measures.

CHRONIC TREATMENT

- When an underlying disorder is present (e.g., urinary tract infection, prostatic disease, urethral neoplasia), treatment is directed at improvement or resolution of this primary cause.
- If no underlying disorder is found and the patient is an adult female spayed dog with a history consistent with urethral incompetence, the following treatments may be considered.
- α-Agonists:
  - Phenylpropanolamine (PPA) used as first line treatment.
    - When given at 1.1–1.5 mg/kg PO q 8 h, effective in 85%–90% of female dogs with urethral sphincter mechanism incompetence
    - Much more effective when given q 8 h than q 12 h; if there is treatment failure, check dosing frequency with clients before changing medications.
  - Pseudoephedrine and ephedrine
    - Generally used when PPA is unavailable
    - Efficacy appears to be similar to PPA but not as well researched.
    - Incidence of side effects may be higher than with PPA.
- Reproductive hormones/estrogen:
  - Diethylstilbestrol (DES).
    - 0.1–0.2 mg/kg PO q 24 h for 5 days, then same dose PO reduced to 1–2 times per week
    - Efficacy 50%-65% in female dogs with urethral incompetence
    - Excessive doses associated with bone marrow suppression; monitor CBCs.
  - Estriol
    - Possible substitute to DES
    - Dosage for a medium-sized (20 kg) dog is 2 mg PO/day for 7 days, then reduced at weekly intervals to minimum effective dose.
    - Studies are limited, but bone marrow suppression has not been reported.
    - Efficacy and safety need to be further evaluated.
  - Estradiol cypionate (ECP) should not be used, owing to significant risk of bone marrow suppression.
- Surgical and endoscopic therapies:
  - Colposuspension/urethropexy:
    - Resolves incontinence in 50% of dogs
    - Remaining patients may respond to medication.
  - Bulking agents:
    - Endoscopic injection of collagen bulking agents into periurethral tissue
    - Repeat injections may be needed for satisfactory results.
    - Addition of PPA improves response rate.
    - Success rates of approximately 50% with mean duration of 17 months have been reported in preliminary studies.

PROGNOSIS AND OUTCOME

- Outcome for dogs and cats with correctable structural abnormalities is good to excellent.
- Treatment is generally successful with urethral incompetence, although dosage adjustment is often required and urinary tract infections must be identified and treated.
- Although not an inherently life-threatening disorder, urinary incontinence may lead to the consideration of euthanasia in refractory cases.

PEARLS & CONSIDERATIONS

COMMENTS

- Combination therapy of α-agonists and reproductive hormones is synergistic.
- Female dogs resistant to single-agent therapy should receive combination therapy.
- Treatment failure with PPA may result from inadequate dosing. Studies show three-times-daily therapy is effective, but owners may only administer twice a day.
- Multiple therapies may be needed to control refractory patients.

SUGGESTED READING

Barth A, Reichler IM, Hubler M, et al: Evaluation of long-term effects of endoscopic injection of collagen into the urethral sub-mucosa for treatment of urethral sphincter incompetence in female dogs: 40 cases (1993-2000). J Am Vet Med Assoc 226(1): 73–76, 2005.
Hoelzler MG, Lidbetter DA: Surgical management of urinary incontinence. Vet Clin North Am Small Anim Pract 34(4):1057– 1073, 2004.

AUTHOR: CLAIRE WEIGAND

EDITOR: ETIENNE CÔTÉ

Incontinence, Fecal

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Inability to retain feces

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Young animals: inappropriate house training, congenital disorders
- Old animals: senility/cognitive dysfunction, neoplasia

GENETICS & BREED PREDISPOSITION

- German shepherd: degenerative lumbosacral stenosis, perianal fistulas
- English bulldogs, Manx cats: congenital spinal malformations

RISK FACTORS

- Perineal surgery, radiation therapy
- Pelvic or lumbosacral trauma
- Perianal diseases
- Tail avulsion fractures

ASSOCIATED CONDITIONS & DISORDERS

Urinary incontinence

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Anal sphincter incontinence
  - Non-neurogenic
  - Neurogenic
- Reservoir incontinence
- Behavior
- Other

HISTORY, CHIEF COMPLAINT

- Sphincter incontinence:
  - Unaware of fecal elimination; unassociated with defecation behavior
  - Small amounts of normal or abnormal feces dribble out, especially when intraabdominal pressure increases suddenly (e.g. coughing).
  - Paraparesis
  - Urinary incontinence may be present.
  - Perineal soiling
  - Dogs with spinal lesions and episodic incontinence may be aware of the need to defecate but are unable to control the urge.
- Reservoir incontinence:
  - Animal aware of incontinence; defecation behavior present, but is unable to control the time and place of elimination.
  - Abnormal feces, suggestive of rectocolonic disease (diarrhea, mucoid, hematochezia)
  - Defecation associated with signs of rectocolonic disease (tenesmus, dyschezia)
- Behavior:
  - Housesoiling with normal feces and defecation

- Destructive behavior

PHYSICAL EXAM FINDINGS

- Sphincter incontinence:
  - Non-neurogenic:
    - Perineal/anal sphincter tumors, erosions, fistulas, trauma, anal sac disease, strictures, scarring
  - Neurogenic:
    - Spinal, lumbosacral pain
    - Hyperesthesia of hind limbs or perineum
    - Lower motor neuron signs: paresis/paralysis with decreased muscle tone, decreased spinal reflexes, decreased anal tone; abnormal bulbocavernosus, rectal inflation, or anal reflexes; + loss of tail tone and voluntary movement
    - Upper motor neuron signs: increased spinal reflexes, ataxia
    - Intracranial disease: abnormal behavior or mentation, abnormal cranial nerve examination
- Reservoir incontinence:
  - Abnormal feces: diarrhea, constipation
  - Rectal masses, mucosal changes, pain on digital rectal examination
  - Signs of gastrointestinal disease (weight loss, anorexia, vomiting)
- Behavior: normal physical exam

ETIOLOGY AND PATHOPHYSIOLOGY

- Sphincter incontinence: diseases of the anal sphincter or adjacent structures
  - Non-neurogenic: anatomic disruption of the anal sphincter preventing functional seal. Anal tone and reflexes normal.
  - Neurogenic:
    - Peripheral (either focal pathology or a polyneuropathy): sphincter dysfunction due to inadequate sensory or motor nerve supply, with normal sphincter anatomy (lower motor neuron deficits)
    - Central: loss of subconscious or conscious modification of reflex defecation (upper motor neuron deficits)
- Reservoir incontinence; diseases of the colon/rectum:
  - Diseases impairing colonic-rectal compliance, capacity, or causing irritation
  - Normal sphincter anatomy and neural supply
  - Altered fecal consistency or excessive volume: feces enter into rectum too rapidly for normal control to take place.
  - Urge incontinence
  - “Overflow incontinence”: liquid feces seeping around constipated fecal material

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Fecal incontinence is a sign, not a diagnosis. The underlying cause must be identified for optimal treatment and accurate prognostication. Neurologic exam, behavioral history, and rectal palpation are indicated in all cases.

DIFFERENTIAL DIAGNOSIS

- Sphincter incontinence:
  - Non-neurogenic:
    - Damage to the levator ani, coccygeal, internal and external anal sphincters
    - Perianal trauma, tumors, infections, fistulas; perineal surgery, hernias
  - Neurogenic sphincter incompetence:
    - Degenerative lumbosacral stenosis (“cauda equina syndrome”)
    - Spinal cord disease: trauma, neoplasia, compressive lesions, degenerative and inflammatory conditions
    - Autonomic dysfunction: dysautonomia
    - Peripheral neuropathies
    - Myopathies
    - Cerebral conditions
- Reservoir incontinence:
  - Inflammatory (colitis, proctitis) and noninflammatory (neoplasia) colorectal disease
  - Diets or diseases causing diarrhea, constipation (overflow incontinence)
- Behavior:
  - Inadequate or inappropriate housetraining
  - Cognitive dysfunction

- Conditions affecting locomotion: inability/unwillingness to walk to the elimination area (e.g., severe arthritic pain)
- Separation anxiety, litter box aversion, location preferences/aversions, inadequate privacy

- Other: rectovaginal fistulas

INITIAL DATABASE

- Physical examination including perineal and digital rectal examination
- Fecal analysis
- Complete neurologic examination, especially:
  - Bulbocavernosus, anal, and rectal inflation reflexes
  - Perineal and tail sensation
  - Anal sphincter and tail tone
- CBC
- Serum biochemistry panel
- Urinalysis ± culture and sensitivity

ADVANCED OR CONFIRMATORY TESTING

- Sphincter incontinence:
  - Electromyography
  - Nerve conduction velocity assessment
  - Muscle and nerve biopsies
  - Spinal radiographs + myelography, epidurography
  - Spinal CT, MRI
  - Cerebrospinal fluid analysis
- Reservoir incontinence:
  - Colonoscopy, proctoscopy
  - Rectal-colonic mucosal biopsy: cytologic, histopathologic analysis

TREATMENT

TREATMENT OVERVIEW

- Treat the primary cause.
- Supportive care

ACUTE GENERAL TREATMENT

Generally not required

CHRONIC TREATMENT

- Intestinal motility altering agents: loperamide, diphenoxylate
- Amitriptyline has been successful in an open-label trial in humans with idiopathic fecal incontinence.
- Maintain low intrarectal pressures:
  - Warm water enemas + laxatives (lactulose): may help decrease inappropriate fecal dribbling by keeping rectum empty in some cases.
  - Frequent opportunities to defecate if some control is present
  - Induction of reflex defecation: warm moist washcloth on anus/perineum
  - Avoid evening feedings.
- Prevent fecal scalding (clip and clean perineum, intermittent tail wrap if longhaired, barrier cream).
- Change in environment to make incontinence more acceptable, “doggy diapers”
- Surgical: consider referral to a board certified surgeon.
  - Anorectal reconstruction
  - Silicon elastomer sling
  - Neosphincter
  - Fecal diversion procedures: colonostomy
  - Semitendinous muscle transfer flap

NUTRITION/DIET

May respond to a therapeutic diet trial: either low-residue or high-fiber (soluble or insoluble) diets can be tried. Success is variable

and depends on the underlying etiology.

POSSIBLE COMPLICATIONS

- Fecal soiling predisposes to perineal dermatitis and urinary tract infections (females).
- Constipation possible with motility-modifying medication

RECOMMENDED MONITORING

Medical management must be regarded as a therapeutic trial; response guides subsequent treatment and diagnostic testing if necessary.

PROGNOSIS AND OUTCOME 

- Guarded to poor with:
  - Many neurogenic sphincter causes (degenerative neuropathies, dysautonomia, lumbosacral stenosis)
  - Severe anal sphincter lesions
  - Underlying cause not found
- Fair to good with:
  - Controlled rectocolonic disease
  - Behavioral causes
  - There have been some encouraging results with surgical correction of even long-standing focal UMN spinal lesions.

PEARLS & CONSIDERATIONS 

COMMENTS

- Fecal incontinence caused by UMN spinal cord lesions may develop prior to limb deficits.
- Fecal incontinence is a common reason for client-requested euthanasia.
- Response and client satisfaction are highly variable and based on client expectation and ability.

PREVENTION

Precise and atraumatic technique when performing perineal surgery

CLIENT EDUCATION

Discuss prognosis and complications early with clients to avoid unrealistic expectations.

SUGGESTED READING

Chen AV, Bagley RS, West CL, et al: Fecal incontinence and spinal cord abnormalities in seven dogs. J Am Vet Med Assoc 227:1945, 2005.

AUTHOR: FRANK KETTNER

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Inappropriate Elimination, Dog

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

- Urination or defecation in a location other than areas acceptable to the client
- Marking: urination (or less commonly defecation) for hierarchical purposes or as part of an anxiety disorder. Usually involves small amounts of urine deposited in several places, often vertical surfaces.
- Incontinence: inadvertent passage of urine or feces as a clinical manifestation of illness.

SYNONYMS

Housesoiling, incomplete housebreaking, incomplete housetraining, soiling, toileting issues

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Can affect dogs of any age and either sex
- Sexually intact dogs may have increased rates of urine marking.
- Puppies first develop physical abilities to inhibit elimination and cognitive abilities to make associations with a preferred substrate (i.e., surface onto which they eliminate) at 8.5 weeks of age. Therefore, between 7 and 9 weeks of age is the ideal age to housetrain a dog.
- Older dogs (particularly young neutered females) may experience urinary incontinence associated with age-related joint laxity and urethral sphincter mechanism incompetence. These problems are medical disorders, not behavioral abnormalities.

GENETICS & BREED PREDISPOSITION

Toy breed dogs eliminate small volumes and therefore may not be as strictly supervised or confined until fully housetrained as would be larger dogs, in which case treatment may be more protracted or difficult. Small bladder volume and greater metabolic rate also mean that smaller dogs need more frequent access to appropriate areas for elimination.

RISK FACTORS

- Sexually intact status
- Presence of intact animals, especially if in estrus (provokes urinary marking by neutered and intact animals)
- Re-homed street and kennel-raised dogs (may never have learned to inhibit their elimination behaviors and will have to learn inhibition and appropriate substrate and location preferences as adults).
- Urinary and fecal marking and increased urgency can be nonspecific signs associated with anxiety disorders. Many dogs with chronic generalized anxiety disorder, for example, have sporadic or chronic diarrhea. Any dog given a diagnosis of “inflammatory bowel disease” should be fully screened for behavioral problems.

CONTAGION & ZOONOSIS

If the inappropriate elimination is due to incomplete housetraining, marking by other dogs in the household may occur.

GEOGRAPHY AND SEASONALITY

- Harsh weather may inhibit a dog's willingness to eliminate outside. Snow and ice should be cleared in a way that allows access and traction.
- Dogs should be exposed to a variety of surfaces/substrates (e.g., grass, cement, sand, stones, sawdust) that will meet the seasonal and lifestyle requirements in which the dog is expected to live.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

House soiling may involve inappropriate urination, inappropriate defecation, marking with urine, marking with feces, or a combination.

Not all urinary marking is vertical. Both males and females can use a variety of positions to mark, and leg cocking is more associated with unfamiliar social stimuli than with sex-based behaviors.

HISTORY, CHIEF COMPLAINT

- Client finds urine or feces inside the home.
- Client may report that the dog was taken out and returned to eliminate in the house.
- Information on volume, frequency, appearance, and when the house soiling occurs is critical in determining underlying cause.

PHYSICAL EXAM FINDINGS

- Findings should be unremarkable in cases with a behavioral etiology (including rectal palpation).
- Abnormal physical exam findings should raise the possibility of medical disorders causing urinary or fecal incontinence (see pp. 599 and 598).

ETIOLOGY AND PATHOPHYSIOLOGY

- Inappropriate elimination is a nonspecific sign that may be “normal” (e.g., incomplete housetraining) or abnormal and associated either with medical or behavioral disturbances, specifically with anxiety disorders.
- Any condition that triggers a fight or flight response can lead to involuntary voiding that may be misinterpreted by the client as purposeful, malicious, or vengeful.
- Olfactory stimulation for normal elimination and marking behaviors is extremely important to dogs and poorly understood by humans.
- Meeting the individual dog's age- and size-specific needs is the key to understanding the root of house soiling and therefore to addressing it.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Inappropriate elimination in itself is a complaint, not a diagnosis, and not always a sign of abnormality, as when the problem is that the pet's choice of location for voiding is incompatible with the owner's wishes. The goal of diagnosis is, through careful behavioral history taking and after ruling out medical problems, to determine whether the behavior is normal but requires some modification to better fit living within a human household or if the elimination is a marker of an anxiety disorder.

DIFFERENTIAL DIAGNOSIS

- Behavioral differential diagnoses:
  - Incomplete housetraining: occurs regardless of client presence or absence, large volume of urine is voided. Normal stool is deposited. Certain areas of the house may be sought preferentially.
  - “Submissive” or excitement urination: occurs upon greeting a person or when the dog is excited. The dog often crouches down and starts to roll over when approached.
  - Marking behaviors: urine marking typically involves small quantities in several locations in the absence of another medical problem. Urine may be deposited in vertical (most common), horizontal, or a combination of surfaces. Fecal marking is less well understood, but small amounts of feces are deposited in response to the presence of unfamiliar animals. Texture and content of feces changes with frequency of marking.
  - Separation anxiety (see p. 1012)
  - Storm phobia (see p. 875)
  - Panic disorder
  - Generalized anxiety disorder
- Medical differential diagnoses:
  - Urinary and fecal incontinence (see pp. 599 and 598)

INITIAL DATABASE

CBC, serum chemistry panel, thyroid function evaluation (see and p. 562), urinalysis, and fecal flotation to assess possible etiologies for polyuria, pollakiuria, and abnormal stool consistency that may lead to inappropriate voiding

ADVANCED OR CONFIRMATORY TESTING

- Once any medical disorders are resolved, a behavioral diagnosis and treatment plan can be pursued if the inappropriate elimination persists, because the inciting causes may be medical, but the maintenance causes may be behavioral.

- Behavioral diagnosis may be achieved using detailed history; consultation with a veterinary behaviorist can be very rewarding.

TREATMENT

TREATMENT OVERVIEW

Treat underlying medical disorder(s). If inappropriate elimination persists, address behavioral sequelae to restore housetraining.

ACUTE AND CHRONIC TREATMENT

- Incomplete housetraining: fully confine or supervise when indoors, using a leash or crate. If the dog is “caught” eliminating, calmly take outside to the chosen elimination area, allow the dog to finish, and praise lavishly. Take to eliminate after eating, after play, after any slowing in play, and after awakening. Any yelling or punishment is likely to hasten the voiding process and is entirely counterproductive.
- Submissive or excitement urination: Owner should maintain an emotionally calm approach, especially when greeting the dog. It may be necessary to ignore the dog until it is very calm and then guide it outside to greet after elimination. Cornerstones of successful treatment are to keep the dog's bladder empty through frequent, well-timed walks outside to eliminate, and to use positive methods and rewards for teaching the dog to sit without leaking or cringing. Use rule structures that guide the pet to learn which behaviors are considered correct in the home and in social interactions. This approach lessens the dog's need to signal submission with urination. The owners should teach the dog that calm behaviors like sitting and lying down get praise, and attention will lessen overall reactivity and encourage the dog to react calmly.
- Clients should be advised against punishing after the fact. This makes no sense to the dog, may force it to housesoil out of sight, and eliminates the opportunity to praise for correct behavior.
- For small dogs with higher metabolic rates, or less agile or ill dogs, canine litter boxes may be a good solution, especially in urban areas. Accustoming the dog to the substrate to be used in the box at an early age may help. Commercially available boxes or homemade ones that accommodate the dog's size and mobility (low edges for arthritic dogs) can be filled with cat litter, especially made artificial turf or lined with paper. Owners' objections tend to dissipate when it is pointed out that litter boxes, even large ones, are easier to clean than carpets and rugs.
- For marking behaviors within the house, it is important to address the social interactions between the animals. Screening for overt and covert aggression (see p. 48) and other anxiety-related conditions in all of the household pets should be undertaken.
- For marking behaviors outside the house, exposure to other stimuli is the only feasible management approach. If feral and roaming animals are triggers, owners can contact local animal control and shelter organizations to arrange for humane trapping, neutering, and adoption.
- For intact male dogs who become distracted in the presence of female urine: a problem for many working (e.g., service, assistance, explosives detection) dogs, castration as early in the development of the marking behavior as is possible largely resolves the situation in most cases.
- Because of the learning component, veterinarians should screen all dogs at all visits for elimination complaints. Early intervention decreases the effect of the learning component.

BEHAVIOR/EXERCISE

- Taking a dog out twice daily often is insufficient. Encourage clients to think of how often they eliminate every day and to understand the dog's metabolism is just like theirs.

POSSIBLE COMPLICATIONS

Punishment will either be useless in resolving the problem or will make the problem worse, especially if anxiety is contributory.

PROGNOSIS AND OUTCOME

- Prognosis is excellent in cases of incomplete housetraining or “submissive” or excitement elimination, so long as proper identification of underlying cause and thorough behavior modification are carried out.
- Prognosis for problematic marking behaviors is excellent if the associated behavioral concerns of the household are competently addressed.
- Prognosis is guarded for an adult male dog that has urine marked for his entire life. The learning component is likely far more important at this stage than the hormonal component.

PEARLS & CONSIDERATIONS

COMMENTS

- Abuse of puppies and abuse of human children often starts with abusive behavior surrounding housetraining/ toilet training (see online chapter: Abuse). Veterinarians should be aware of the signs.
- Lack of attention to the dog's need is the most common reason for poor housetraining or other nonmarking elimination problems in dogs.
- Fecal marking and increased urgency (e.g., sporadic diarrhea) can be non-specific signs associated with anxiety disorders rather than primary gastrointestinal disease. Any dog given a diagnosis of inflammatory bowel disease should be fully screened for behavioral problems.

PREVENTION

- Ensure that dogs are not outside only for the purpose of elimination. If this is so, they may delay eliminating outside to have more opportunity to experience outdoor stimuli and may then eliminate indoors.
- Reward dogs for eliminating outside with play, freedom, exercise, praise, interaction with other dogs, and time to smell their canine world.

CLIENT EDUCATION

- Client education is key to preventing and fixing these problems. All veterinary practices should have handouts (see online version of this textbook for Client Education Sheets; also numerous specialized texts and sources) that explain how to housetrain dogs, and a designated staff member should be responsible for explaining and following up on such training with owners.
- Quick screening at each veterinary visit for elimination complaints and other behavioral concerns saves lives. Veterinarians need to know that clients are unlikely to share behavioral information and questions unless prompted to do so.

SUGGESTED READING

Houpt KA: Housesoiling by dogs. In Horwitz D, Mills D, Heath S, editors: BSAVA manual of canine and feline behavioral medicine. British Small Animal Veterinary Association, 2002, pp 90–96.

Overall KL: Canine behavioral disorders. In Morgan RV, Bright RM, Swartout MS, editors: Handbook of small animal practice. Philadelphia, 2003, WB Saunders, pp 1149–1162.

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Inappropriate Elimination, Cat

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

- Situation characterized by the use of inappropriate or undesirable areas (locations or surfaces) for elimination of urine or feces. As used here, this is a diagnosis associated with an anxiety disorder. Otherwise, “inappropriate” elimination is often elimination that is normal for the species but undesirable to clients. Urinary incontinence: passage of urine without awareness, due to a medical problem. Comparatively rare in cats.
- Marking: passage of urine or feces involving social interaction. Very common in cats. Marking with urine may be in the form of spraying.

SYNONYMS

Toileting problems, litter box problems, undesirable litter box use

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Urine spraying: sexually intact animals > neutered animals. Possibly males > females.
- Marking behaviors—which need not involve spraying—may develop at sexual maturity (~6 months) if they pertain to sexual advertisement, or at social maturity (~24–48 months) if they pertain to social organization, relative roles in social relationships, or stress or distress.

GENETICS & BREED PREDISPOSITION

Long-haired cats possibly overrepresented with substrate (surface onto which a cat eliminates) aversions

RISK FACTORS

- Risk factors for elimination preferences and aversions include:
  - Dirty litter and/or litter boxes
  - Litter boxes that are too small and discourage active digging and exploration
  - Litter boxes that are too high for cats to enter readily
  - Styles (covered) and placement (in closets) that allow the cat using the litter box to be trapped by a child, another cat, a dog
  - Placement of boxes in locations cats cannot reach because of pain (arthritis), access (doors closed), or social factors (being chased by the new puppy)
  - Entrapment of odors by lids of covered boxes placed in areas without adequate ventilation
  - Illness of any cat in the household that causes changes in bladder and bowel function
- Risk factors for marking are based on social stress and distress. Stressors can include:
  - Addition of another pet
  - Loss of a pet
  - Change in the composition of the human household
  - Change in the “stress” level of the household (e.g., illness, changes in jobs)
  - Visitation by an outside cat
  - Illness or change of relationships between cats in the household (e.g., that concomitant with social maturity)
  - True intercat aggression

GEOGRAPHY AND SEASONALITY

Marking behaviors may intensify in spring, when more animals are let outside, visit indoor animals, and scents aerosolize. Marking increases in frequency (by both female and male, though males may be noticed more readily) when females enter estrus.

ASSOCIATED CONDITIONS & DISORDERS

Coexistent intercat aggression is common; identifying relative victims and aggressors is essential to resolving the social conflict and

fixing the toileting complaints.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Three classes of problems that can all be normal behaviors in free-ranging cats:

- Substrate (texture/surface) preferences or aversions. The amounts of urine or feces are small and distributed over areas associated with social stimuli.
- Location preferences or aversions; as for substrate
- In marking involving sprayed urine (spraying is part of a normal signaling repertoire in cats), the cat treads on its front feet, raises its tail, quivering the tip, and sprays urine vertically. If the cat is not backed against a vertical surface, sprayed urine makes a linear pattern on horizontal surfaces. Non-spraying marking involves elimination of small amounts of urine or feces in areas that have social, not tactile, significance.

HISTORY, CHIEF COMPLAINT

Clients find urine or feces in locations they consider unacceptable.

PHYSICAL EXAM FINDINGS

- Unremarkable
- Findings suggesting lower urinary tract disease, gastrointestinal problems, or other nonbehavioral disorder warrant a diagnostic medical evaluation.

ETIOLOGY AND PATHOPHYSIOLOGY

- Behavior is normal for the species but unacceptable to clients and/or coexists with intercat aggression or other behavioral disorder.
- Association between spraying and crystalluria, or inappropriate urination and defecation with impacted anal sacs, remains speculative.

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

Initially it is important to use history, physical exam, and routine lab tests to differentiate between inappropriate/ undesirable elimination and marking, which are behavioral, and urinary/fecal complaints that are primarily medical. Video recordings of the cat in the home environment can be helpful if the owner is unsure. If inappropriate/undesirable elimination of urine is confirmed, history and owner observation should be used for determining whether marking behaviors or substrate/location preferences/ aversions are involved. These different diagnoses have important management and treatment implications.

DIFFERENTIAL DIAGNOSIS

- Feline lower urinary tract signs/disease
- Bacterial cystitis
- Urethral obstruction
- Diabetes mellitus
- Cognitive dysfunction
- Hyperthyroidism
- Lower motor neuron disease
- Enteritis/colitis
- Parasitemia

INITIAL DATABASE

- Inappropriate urination and/or before initiating medications: CBC, serum biochemistry profile, urinalysis with culture, thyroid profile (if > 6 years old)
- Inappropriate defecation: fecal flotation and direct smear, thyroid profile (if >6 years old)

ADVANCED OR CONFIRMATORY TESTING

To identify the nature of inappropriate elimination and any concurrent issues (e.g., intercat aggression), client observations are essential. Videotaping interactions between cats in a multicat household may be extremely informative, especially if the client is unable to determine which cat is eliminating inappropriately and/or is unable to understand social interactions and dynamics between the cats.

TREATMENT

TREATMENT OVERVIEW

Treatment goals include:

- Appropriate and reliable use of intended substrates and locations for elimination, when the problem is substrate preference/aversion
- Identification and management of concurrent behavioral disorders (e.g., social factors such as intercat aggression) that can contribute to inappropriate elimination

ACUTE AND CHRONIC TREATMENT

- Identify previously preferred substrates and locations, and replicate these.
- Ensure there is at least one more litter box than the number of cats.
- Ensure the litter boxes are at least 1.5 cat body lengths long. This is larger than virtually all commercially available litter boxes for cats, but rigorous research has indicated that this is the size preferred by cats.
- Identify locations where the cat spends the most time, and place boxes accordingly.
- Ensure that clients are complying with an appropriate cleaning regimen:
    - Scoop litter multiple times daily.
    - Totally dump litter, including recyclable multicat litters, two to three times a week, depending on the number of cats using them.
    - Wash, rinse, and dry the litter box at least weekly.
    - Avoid liners and scented litters.
    - Ensure that covered litter boxes have good ventilation if they must be used.
- Use good odor eliminations (e.g., Anti-Icky-Poo [AIP]) on all substrates where urine or feces has been inappropriately deposited.
- Pheromonal analog products have been suggested for use to “calm” animals, but they may make some animals more reactive. Their efficacy is in doubt insofar as most studies are poor and show at best a weak contributory effect. No study on the use of pheromonal analogs shows efficacy to the extent seen when the underlying anxiety is treated with medication.
- Identify potential stressors or conflicts in the household (e.g., intercat aggression) and redress them. The most common of these may be relationships between cats in the household. Inter-cat aggression is a serious concern if:
    - One cat is avoiding one or more other cats.
    - One cat consistently leaves the room or a preferred resting spot when one or more other cats enter.
    - One cat cannot or does not eat or drink in the presence of the others.
    - One cat is always hiding.
    - One cat is hyperreactive to any noise or tactile stimuli.
- If any of the above conditions can be identified, ensure that clients separate afflicted cats when they are not supervised. The more timid cat should have free range; the more aggressive cat should be confined in a space that is not highly contested or desirable (e.g., not the client's bedroom or the kitchen).
- If anxiety and aggression are involved, benzodiazepines (BZDs), tricyclic anti-depressants (TCAs), or selective serotonin reuptake inhibitors (SSRIs) may be useful treatments for the anxious/ aggressive cat.
    - TCAs: amitriptyline or nortriptyline (0.5–1 mg/kg PO q 12–24 h × 30 days minimum); clomipramine (0.5 mg/kg PO q 24 h × minimum 60 days)
    - SSRIs: fluoxetine or paroxetine (0.5 mg/kg PO q 24 h × minimum 60 days)
    - BZDs: diazepam or oxazepam (0.2–0.4 mg/kg PO q 12–24 h × minimum 30 days); alprazolam (0.01–40.025 mg/ kg PO q 12–24 h or as needed q 4–5 h for panic)
    - BZDs are helpful primarily in behavior modification programs involving food reward (e.g., teaching cats that have problems with each other to tolerate each other).
    - TCAs and SSRIs can be extremely useful in helping overcome aversions and addressing anxiety involved in marking behaviors and intercat aggression.
- If the toileting issue is associated with intercat aggression and the victim needs to become more outgoing, the partial serotonin agonist, buspirone (0.5–1 mg/kg PO q 24 h × 60 days minimum) can be a good drug of choice, but it may act in part by rendering the afflicted cat sufficiently confident to engage in social interactions that could result in a true physical fight, which clients need to monitor and address if it occurs.
- If more animals are added to the household, clients should expect social upheaval and be prepared to restart analysis of

interaction and behavior.
- Attention should be paid to the victimized cat before the other cats.
- Litter box hygiene must be meticulous and lifelong.
- Outdoor or visitor cats should be kept to a minimum or excluded.
- Consider allowing the cat to be an indoor/outdoor cat if all else fails.

POSSIBLE COMPLICATIONS

- BZDs: hyperexcitability (rare), severe hepatotoxicity (rare), potential abuse by clients
- Cats treated with monoamine oxidase inhibitors (some flea and tick collars) should not be treated with TCAs or SSRIs.

RECOMMENDED MONITORING

Exam and laboratory tests at least every 6–12 months if taking medications

PROGNOSIS AND OUTCOME

- Without treatment, the prognosis is guarded. Inappropriate elimination is the single most common reason cats in North America are euthanized or relinquished.
- Clients maintain cats in their household for an average of 2 years after a complaint has been identified, but the more obvious inappropriate urination is to the client, the more likely he or she is to be intolerant of it.
- Prognosis is improved by early diagnosis, comprehensive treatment, attentive client monitoring, and open communication between clinician and client.

PEARLS & CONSIDERATIONS

COMMENTS

In the absence of meeting the cat's needs, attempts to constrain the cat to eliminate in places, on substrates, or in modes preferred by the client will likely result in a worsening of the problem.

PREVENTION

- Meeting the cat's needs, whether by providing sweater boxes or canine litter boxes, providing multiple boxes, or grouping cats by temperament, is the single best way to prevent elimination problems.
- Veterinarians should screen for elimination problems as a routine part of every appointment and should encourage clients to call at the first sign of any elimination “accident”. Because elimination is a complex behavior in cats, waiting to discuss the issue may result in the death or relinquishment of the cat.

CLIENT EDUCATION

- Treatment of behavioral conditions is an ongoing process, often for the life of the pet. Relapses may occur with treatment discontinuation or with added stressors.
- Physical illness is also a stressor and may promote a behavioral elimination problem where previously none existed.

SUGGESTED READING

Cameron ME, et al: A study of environmental and behavioral factors that may be associated with feline idiopathic cystitis. J Small Anim Pract 45:144–147, 2004.

Frank D, Beauchamp G, Palestrini C: Systematic review of the use of pheromones for the treatment of undesirable behavior in dogs and cats. J Am Vet Med Assoc 236:1308–1316, 2010.

Wright JC, Amoss RT: Prevalence of house soiling and aggression in kittens during the first year after adoption from a humane society. J Am Vet Med Assoc 224:1790–1795, 2004.

AUTHOR & EDITOR: KAREN L. OVERALL

Immunodeficiency Syndromes, Dog

BASIC INFORMATION

DEFINITION

Primary immunodeficiency syndrome: an inherited defect involving either the humoral (B cell) or cell-mediated (T cell) immune system, a combination of the two, or the phagocytic system

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Signs first manifest around 8-12 weeks of age when the protective effects of maternal antibody are lost.
- No sex predilection except for sex-linked severe combined immunodeficiency syndrome (X-SCID)—males

GENETICS & BREED PREDISPOSITION

- Humoral (B-cell) immunodeficiency disorder:
  - Selective IgA deficiency: German shepherd dog, shar-pei, and beagle
  - Complement deficiency: Brittany spaniel
- Cell-mediated (T-cell) immunodeficiency disorder:
  - Thymic hypoplasia: dwarf weimaraner
- Combined (B-cell and T-cell) immunodeficiency disorder:
  - SCID: Jack Russell terrier
  - X-SCID: bassett hound, Cardigan Welsh corgi
- Functional phagocytic immunodeficiency disorder:
  - Canine leukocyte adhesion disorder (CLAD): Irish setter
  - Weimaraner immunodeficiency syndrome: weimaraner

CONTAGION & ZOONOSIS

Most opportunistic infections that affect immunocompromised individuals are overgrowths or infections with organisms that otherwise are not pathogenic to immunocompetent hosts. However, immunocompromised animals are also more susceptible than normal individuals to infection with organisms that are potentially zoonotic (e.g., dermatophytosis) or contagious to other dogs (e.g., respiratory tract pathogens).

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

Recurrent infections that may or may not respond to appropriate therapy. Type of infection may vary with defect in the immune system.

PHYSICAL EXAM FINDINGS

- Humoral (B-cell) immunodeficiency disorder: physical exam findings are largely unremarkable; however, some patients may present with signs associated with chronic/recurring infections; increased incidence of chronic respiratory, skin, and intestinal infections.
- Cell-mediated (T-cell) immunodeficiency disorder: absence of palpable lymph nodes, tonsils are not visible. Affected dogs typically have signs of growth retardation and unthriftiness as compared to the other puppies within the litter.
- Combined (B-cell and T-cell) immunodeficiency disorder: similar findings as for humoral and cell-mediated immunodeficiency disorder
- Functional phagocytic immunodeficiency disorder: fever, generalized lymphadenopathy, dermatitis, pododermatitis, gingivitis, osteomyelitis; striking absence of pus formation and poor wound healing

ETIOLOGY AND PATHOPHYSIOLOGY

- Humoral (B-cell) immunodeficiency: decreased concentrations or absence of certain immunoglobulins, with increased

susceptibility to bacterial infections
    - IgA deficiency: mode of inheritance is unknown. Epidemiologic studies show that puppies born to dams with IgA deficiency are at increased risk of developing upper respiratory infections as compared to puppies from dams with normal IgA concentrations.
    - Complement deficiency: autosomal recessive mode of inheritance; dogs that are homozygous for the trait have no detectable C3, required for opsonization of bacteria.
- Cell-mediated (T-cell) immunodeficiency: affected animals have either low numbers of or nonfunctional T cells. Findings include a small thymus and lack of lymph nodes, tonsils, and Peyer's patches on postmortem examination. Affected animals are at increased risk for infections with intracellular bacterial, fungal, protozoal, and viral organisms.
- Combined (B-cell and T-cell) immunodeficiency:
    - SCID: autosomal recessive: affected individuals are unable to mount an appropriate antigen-specific immune response, owing to a lack of DNA protein kinase (DNA-PK) activity; DNA-PK is required for lymphocyte precursors to mature.
    - X-SCID: sex-linked mutation in the g chain of the interleukin 2 (IL-2) receptor required for normal B-cell and T-cell function. Affected male puppies are able to synthesize IgM, but IgG concentrations are significantly reduced and IgA is not detectable.
- Functional phagocytic immunodeficiency: affected animals have an increased risk for systemic or superficial infections with pyogenic microorganisms.
    - Weimaraner immunodeficiency syndrome: inherited, exact mechanism unknown; neutrophil dysfunction at the site of the lesion. However, there also appears to be a failure to produce IgA and IgG.
    - CLAD: deficiency of leukocyte surface glycoprotein (B2 integrin) associated with leukocyte adherence and egress into affected tissues; failure to express B2 integrin CD18.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Affected puppies present with varying, often nonspecific clinical signs and commonly with recurrent infections. It is the recurrence of the infections and the poor response to therapy that warrant further investigation of a primary immunodeficiency syndrome.

DIFFERENTIAL DIAGNOSIS

- Humoral immunodeficiency: varies based on presenting complaint.
    - Upper respiratory infection: *Bordetella bronchiseptica*
    - Primary ciliary dyskinesia
    - Otitis
    - Stomatitis
    - Staphylococcal dermatitis
    - Atopic dermatitis
- Cell-mediated immunodeficiency:
    - Fungal (e.g., cryptococcosis, aspergillosis, blastomycosis, dermatophytosis)
    - Protozoal (e.g., toxoplasmosis, giardiasis)
    - Viral infections can be seen after vaccination with modified live virus vaccine
    - Intracellular bacteria (e.g., mycobacterial infections)
- Combined immunodeficiency: affected animals are susceptible to bacterial, viral, fungal, and protozoal agents.
- Functional phagocytic immunodeficiency:
    - Sepsis
    - Bacteremia
    - Pelger-Huët: hyposegmentation of nuclei in granulocytes and monocytes; persistent degenerative left shift without toxic change or any signs of illness (it is only an incidental finding).
    - Other infectious disease that would cause a neutrophilic leukocytosis with a left shift

INITIAL DATABASE

Appropriate diagnostic testing based on clinical presentation:

- Minimum database: CBC, serum biochemistry profile, urinalysis with culture and sensitivity, fecal examination, thoracic radiographs
- Humoral (B-cell) immunodeficiency disorder: minimum database within normal limits
- Cell-mediated (T-cell) immunodeficiency disorder: normal/decreased lymphocyte count
- Combined (B-cell and T-cell) immunodeficiency disorder: normal/decreased lymphocyte count (average 1000/mcL); possibly low total protein due to low globulin levels; agammaglobulinemia (protein electrophoresis)
- Functional phagocytic immunodeficiency disorder: persistent leukocytosis with regenerative left shift; neutrophil count >

200,000/mcL

ADVANCED OR CONFIRMATORY TESTING

- Specific tests performed should be geared toward the clinical presentation and tailored to the suspected immunodeficiency. Commonly considered tests include abdominal ultrasound, transtracheal wash with culture and sensitivity, bone marrow aspirate or core biopsy, lymph node biopsy, lesional biopsy. With CLAD, biopsy of lesion shows bacteria and possibly necrosis but no infiltration of neutrophils.
- Humoral immunodeficiency: serum protein electrophoresis to evaluate immunoglobulin concentrations, serum immunoglobulin quantitation, quantitation of serum C3 for C3 deficiency
- Cell-mediated immunodeficiency: lymphocyte transformation (blastogenesis) evaluates the ability of the T cell to proliferate after stimulation; measurement of growth hormone or insulin-like growth factor 1 if dwarfism is suspected (testing generally available only in research laboratories).
- Functional phagocytic immunodeficiency:
  - Bactericidal assays: measure the ability of neutrophils to kill bacteria.
  - PCR: to identify affected, normal, or carrier animals

TREATMENT

TREATMENT OVERVIEW

A substantial degree of variation in severity may exist for a given immunodeficiency syndrome. Therefore, treatment intensity, treatment success, and prognosis are individually variable and must be determined case by case. Some individuals require minimal or no treatment (e.g., intermittent antimicrobial treatment during clinical exacerbation), whereas in others, euthanasia is the most humane option. Control opportunistic infections with antimicrobials and supportive care; hospitalize when necessary.

ACUTE GENERAL TREATMENT

Supportive care to treat opportunistic infections:

- For example, antibiotics for confirmed bacterial infections. Empirical antibiotics may be used initially, pending culture and sensitivity results. Antibiotic type should be selected based on suspected bacterial population of involved site:
  - Skin: gram-positive bacteria most common; consider cephalosporins (e.g., cephalexin or cefadroxil, 22 mg/kg PO q 8-12 h) or penicillins (e.g., amoxicillin, 22 mg/kg PO q 8 h; or ampicillin, 22 mg/kg IV q 8 h).
  - Oral cavity and respiratory tract:
    - Gram positive cocci: consider cephalosporins, 22 mg/kg PO, IV q 8 h; or trimethoprim-sulfadiazine, 15 mg/kg SQ, IM, IV q 12 h
    - Gram negative rods: trimethoprim-sulfadiazine, 15 mg/kg SQ, IM, IV q 12 h; or enrofloxacin, 5-10 mg/kg IV q 24 h; or gentamicin, 8 mg/kg IV, IM, SQ q 24 h
    - *Bordetella* infection: gentamicin, 9 mg/kg IV, IM, SQ q 24 h; or doxycycline, 5 mg/kg IV, PO q 12 h; or chloramphenicol, 50 mg/kg IV, SQ, PO q 8 h
    - Mixed populations: consider fluoroquinolones (enrofloxacin, 5 mg/kg PO or slow IV q 12 h), or β-lactamase–resistant penicillins (e.g., amoxicillin-clavulanate, 10-20 mg/kg PO q 12 h), or macrolides (e.g., azithromycin, 5-10 mg/kg PO q 24 h × 1-5 days).
- Due to strong possibility of opportunistic fungal, viral, and protozoal infections, empirical antibiotic therapy may be inadequate or may select for resistant strains of bacteria; diagnostic samples for culture should be obtained before initiating antibiotic treatment, and judicious antibiotic use is warranted.
- Nebulization and coupage for bacterial pneumonia (see p. 887 and p. 1310)
- Disinfection of cutaneous wounds with diluted (0.05%) chlorhexidine solution
  - With standard 4% chlorhexidine solution, dilute 1 part chlorhexidine to 80 parts water to obtain 0.05% concentration.
  - The same concentration may be used as an ear wash in opportunistic otitis and as an oral antiseptic rinse in cases of stomatitis.

CHRONIC TREATMENT

- Humoral immunodeficiency:
  - Nonspecific supportive therapy tailored toward treating recurrent microbial infections
- Cell-mediated immunodeficiency:
  - Supportive care with frequent monitoring for opportunistic infections and then proceed with aggressive treatment when warranted.
  - Dwarf weimaraners respond to thymosin fraction 5 therapy (1 mg/kg SQ q 24 h for 7 days).
- Combined (B-cell and T-cell) immunodeficiency:

    - Bone marrow transplantation
- Phagocytic immunodeficiency:
    - Bone marrow transplantation

NUTRITION/DIET

- Caloric requirements of the critically ill patient may be less than those of healthy animal.
- Resting energy requirement: RER = 70 × body weight (kg)$^{0.75}$
- RER approximation - 30 × body weight (kg) + 70
- Parenteral nutrition versus enteral nutrition

DRUG INTERACTIONS AND CONTRAINDICATIONS

- When using chloramphenicol, consider human risks (myelosuppression, aplastic anemia; wear gloves).
- When using aminoglycosides, ensure that patient is well hydrated.

POSSIBLE COMPLICATIONS

- Sepsis
- Recurring and resistant infections

RECOMMENDED MONITORING

Monitoring of appetite, activity, temperature, and CBCs can aid in the early detection of infection.

PROGNOSIS AND OUTCOME

- Humoral immunodeficiency: fair to good
- Cell-mediated immunodeficiency: poor
- Combined (B-cell and T-cell) immunodeficiency: poor. Affected animals usually die between 2 and 4 months of age from systemic bacterial or viral infections.
- Phagocytic immunodeficiency: poor

PEARLS & CONSIDERATIONS

COMMENTS

The diseases listed here are rare but are severe and have a poor/guarded prognosis.

PREVENTION

The most important aspect of controlling the prevalence of the immunodeficiency syndromes that affect dogs of predisposed breeds is by client education and appropriate genetic screening of potential breeding pairs when molecular testing is possible.

TECHNICIAN TIPS

- Wear gloves when handling immunocompromised patients.
- Protect yourself from opportunistic zoonotic infections by wearing protective shielding.
- Use sterile saline when performing nebulization.
- Encourage patient appetite by warming foods (see p. 1377).

CLIENT EDUCATION

It is important to discuss with the client that affected dogs will not be cured, the disease is heritable, and other puppies of the same litter may be affected. Affected puppies are at an extremely high risk for secondary infections and should avoid other ill animals.

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Immunodeficiency Syndromes, Cat

BASIC INFORMATION

DEFINITION

Conditions resulting from a defective immune response. They may be primary, from an inherited defect, or secondary to another disease process or infection. They may be specific, with a defect in either B or T lymphocyte function, or nonspecific, due to a defect in phagocytic cell function or skin or mucosal integrity.

SYNONYMS

Immune or immunologic deficiency

EPIDEMIOLOGY

SPECIES, AGE, SEX

- One rare nonspecific defect is seen in young Persian cats with Chédiak-Higashi disease syndrome.
- All other known specific immunologic defects in cats are acquired and secondary to retroviral (feline leukemia virus [FeLV; see 385], feline immunodeficiency virus [FIV; see 381]) infections. These infections can occur at any age and in either gender, although young cats are most susceptible to FeLV infection.

GENETICS & BREED PREDISPOSITION

Persian cats with a dilute smoke gray coat color and yellow irises may have Chédiak-Higashi syndrome.

RISK FACTORS

- Greater FeLV propagation in crowded multicat households or shelters
- FIV occurs primarily in adult, outdoor, intact male cats.
- Either virus can be spread easily through blood, as in transfusions.

CONTAGION & ZOONOSIS

- FeLV is spread through contact with saliva, respiratory secretions, and milk. Kittens < 4 months old are most at risk from queens or other cats.
- FIV is less contagious and is spread primarily through bite wounds.
- No known zoonotic risk

GEOGRAPHY AND SEASONALITY

Both viruses have worldwide distribution. FIV is more prevalent in countries where cats routinely roam outdoors. Over time, FeLV has decreased in prevalence in countries where testing and vaccination have been used.

ASSOCIATED CONDITIONS & DISORDERS

- Chédiak-Higashi syndrome: slight increased risk for bacterial infections. Bleeding tendencies are also more common with this disease.
- FeLV can cause hematologic neoplasia, myelosuppression, immune-mediated diseases.
- FIV is less pathogenic and more likely associated with stomatitis or neurologic disorders.
- Both FeLV and FIV cause immunodeficiency, which can result in opportunistic infections.
- Almost any infection can occur in cats infected with FeLV or FIV.
    - Examples: bacterial (stomatitis, pyoderma), fungal (dermatophytosis, cryptococcosis), protozoal (toxoplasmosis, cryptosporidiosis), other viral (feline infectious peritonitis, panleukopenia), and hemotropic mycoplasmosis (*Mycoplasma haemofelis* infection, formerly hemobartonellosis)
    - Some infections may be abnormally persistent or recurrent.
    - Some infections also may be secondary to neutropenia (more common with FeLV than FIV).

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

Signs may be vague, such as weight loss and lethargy, or may be referable to the specific infection that occurs. Common clinical signs are salivation or dysphagia from stomatitis, chronic nasal discharge from bacterial or viral rhinitis, or diarrhea from enteritis.

PHYSICAL EXAM FINDINGS

- Stomatitis (lymphocytic-plasmacytic proliferative type): more commonly associated with FIV than FeLV (FIV > FeLV; see 1051)
- Signs of neurologic disorders, especially dementia or twitching: FIV > FeLV
- Gingivitis: FeLV ≈ FIV
- Anemia: FeLV > FIV
- Lymphadenopathy (reactive; may be caused by bartonellosis): FeLV > FIV

ETIOLOGY AND PATHOPHYSIOLOGY

- FeLV/FIV (retroviral)-associated im-mune deficiency
  - The subset of lymphocytes most affected by retroviral infection is the CD4 helper T cell. The ratio of CD4 to CD8 cells is also decreased.
  - Also described with FeLV: secondary decreased ability of B cells to respond to new antigens
  - Thymic atrophy in neonatal kittens can cause “fading kitten syndrome.”
  - FIV is much less pathogenic than is FeLV. Many cats infected with FIV can live for many years without signs of illness (see p. 381 and p. 385).
  - Neither FeLV nor FIV causes cytopathic changes or inflammation in tissues. Thus if a fever is present, a second infectious agent is likely to be the cause.
- Chédiak-Higashi–associated immune deficiency (rare disorder)
  - Abnormal neutrophil granules with abnormal function and survival. Bleeding tendencies are a result of platelet function defects.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

- Proving that an immunodeficiency is present requires specialized testing, not readily available to clinicians (e.g., lymphocyte immunophenotyping, counting of CD4 cells).
- One may assume that cats with retroviral infections may be immunodeficient.

DIFFERENTIAL DIAGNOSIS

- Any unusual, persistent, or recurring infection in any cat might be secondary to a retroviral infection.
- Neutropenia can also be caused by other primary bone marrow disease, drugs, toxins, or may be secondary to an overwhelming infection.

INITIAL DATABASE

- CBC to evaluate for anemia, neutropenia, or thrombocytopenia
  - FeLV/FIV: anemia, neutropenia, or thrombocytopenia. Persistent lymphopenia may occur but is nonspecific.
  - Chédiak-Higashi syndrome produces characteristic large granules in neutrophils.
- Urinalysis to evaluate for proteinuria or infection
- Serum biochemistry profile: usually unremarkable but rarely will reflect visceral organ involvement with opportunistic infections (e.g., pyelonephritis, bacterial translocation via portal circulation). Serum globulin level may be normal or elevated.
- FeLV (antigen) and FIV (antibody) ELISA blood tests are excellent for initial screening.
  - Maternal antibody and vaccination interfere with FIV test but not FeLV.

ADVANCED OR CONFIRMATORY TESTING

- A positive ELISA for either FeLV (antigen) or FIV (antibody) in a cat with signs compatible with an immunodeficiency syndrome is likely to be accurate. A positive test in a healthy cat without known risk factors is more likely to be a false positive and should be confirmed by IFA testing (FeLV) or Western blot (WB; FIV).
- PCR testing for these retroviruses is somewhat variable between labs and is not needed in most situations.

- Specific testing for other infectious diseases as needed (e.g., serologic titers, bacterial culture and sensitivity for purulent/septic processes)
- Bone marrow aspirate and biopsy if cytopenias are present or abnormal cells are circulating
- Testing of CD4 counts not readily available nor prognostic, as not all cats with low counts develop infections.
- When compared to a normal cat, microscopic examination of the shaft of a hair plucked from a cat with Chédiak-Higashi syndrome reveals large, clumped melanin granules.

TREATMENT

TREATMENT OVERVIEW

- FeLV/FIV-associated immunodeficiency:
  - Maintain good nutrition and husbandry, including core vaccinations.
  - Keep infected cats indoors for their own protection as well as to protect other cats.
  - Treat any secondary infections early and aggressively.
- Chédiak-Higashi–associated immunodeficiency:
  - Treat secondary infections as they arise; prophylactic treatment if surgery or trauma (bleeding).

ACUTE GENERAL TREATMENT

- Find and treat any secondary infections as quickly and thoroughly as possible.
- Use supportive care and nutritional support as needed.
- No value in FeLV/FIV vaccines for infected cats

CHRONIC TREATMENT

- No drug has proven efficacy in eliminating feline retroviruses.
- Anecdotal benefit has been reported for oral human α-interferon (IFN), *Propionibacterium acnes*, acemannan, *Staph* protein A, and PIND-ORF, but so far none of these has been shown to be effective either in decreasing viral replication or prolonging survival in limited controlled clinical trials.
- Recently IFN-omega improved clinical signs and 1-year survival in some cats, but another study in FIV infection showed no benefit.
- Azidothymidine (AZT) at a dose of 5 mg/ kg q 12 h SQ caused improvement in clinical signs and immune function in some cats infected with FeLV or FIV. Anemia can result from long-term use of AZT.

BEHAVIOR/EXERCISE

Immunodeficient cats should be kept indoors, away from other cats.

DRUG INTERACTIONS

Avoid corticosteroids or other immunosuppressive drugs unless absolutely needed. They may increase the risk of infections.

POSSIBLE COMPLICATIONS

- Inability to eradicate some infections
- Bone marrow failure, myelodysplasia, or hematopoietic malignancy, especially from FeLV

RECOMMENDED MONITORING

Monitor weight, since weight loss is often an early sign of complications. Also monitor appetite and activity. Once or twice yearly, CBCs might identify a problem, but healthy FeLV-infected cats generally have normal counts except for lymphopenia.

PROGNOSIS AND OUTCOME

- Previous studies showing 50% mortality for FeLV infection in 2 years and 80% in 3 years were done with multicat households where risks of secondary infections were high. For a single indoor cat, the prognosis is guarded but much better than these figures indicate.
- Many FIV-positive cats will survive for many years without developing signs of illness if they are kept indoors.

PEARLS & CONSIDERATIONS

COMMENTS

- Although FeLV and FIV cause immunosuppression, most secondary infections can be treated successfully.
- Keeping these cats indoors and separated from ill or young cats (especially cats with signs of respiratory disease, skin disease, or diarrhea) will protect them from the majority of these infections.

PREVENTION

- FeLV: test kittens at 8 weeks. If negative and from a high-risk environment, repeat in 4 weeks. Isolate FeLV-negative kittens until they are >4 months old and have some natural resistance to FeLV.
- FIV test result can be positive from maternal antibody. Kittens testing positive should be retested after 5 months of age. Young kittens are rarely actually infected with FIV.
- FIV, FeLV: vaccinate only cats at risk (outdoor cats with exposure to other cats or those in multicat households). Neutered male cats are less likely to fight with other cats.

TECHNICIAN TIPS

- Be sure to wash hands thoroughly before and after handling cats carrying retroviruses.
- Most soaps and disinfectants will kill retroviruses, so infected cats may be housed in the same room as other cats so long as cages are cleaned well after they leave.

CLIENT EDUCATION

- Explain the benefits of keeping cats indoors. Never introduce new cats without testing. Indoor cats do not need to be vaccinated against retroviruses.
- For multicat households with endemic FeLV infection, isolate or remove positive cats, vaccinate the rest, and do not bring in new cats. Retest negative cats 3 months later. Repeat until all are negative.
- Spread of virus requires carrier cats, as the virus does not survive outside the cat.

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Idiopathic Tremor Syndrome

BASIC INFORMATION

DEFINITION

- A brain disorder of unknown etiology that causes spontaneous generalized tremors and is responsive to immunosuppressive doses of corticosteroids
- *Tremor* refers to a rhythmic oscillatory involuntary movement in the body.

SYNONYMS

Corticosteroid responsive tremor syndrome; white shaker dog syndrome (a poor term, as approximately half of the dogs with idiopathic tremor syndrome do not have a white coat)

EPIDEMIOLOGY

SPECIES, AGE, SEX

The majority of dogs affected with this syndrome are young (<5 years) and of small breeds (<15 kg).

GENETICS & BREED PREDISPOSITION

White dogs, including the West Highland white terrier and Maltese, are overrepresented, although any breed may be affected.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Owners typically notice an acute onset of a fine, whole-body tremor that often worsens with exercise, stress, and excitement and lessens with rest or sleep.
- The course of the disease is nonprogressive.

PHYSICAL EXAM FINDINGS

- The most notable finding is a fine, whole-body tremor.
- Additional findings may include poor menace responses, head tilt, nystagmus, paresis, tetraparesis, ataxia, seizure activity, and an elevated rectal temperature.

ETIOLOGY AND PATHOPHYSIOLOGY

The exact etiology is unknown but may be the result of an autoimmune-mediated disruption of neurotransmitter metabolism in the central nervous system (CNS), with a decreased conversion of tyrosine to dopamine. Dopamine is an important neurotransmitter for the regulation of movement.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A clinical diagnosis generally is reached based on signalment, history, and clinical signs. Advanced tools such as MRI and CSF analysis are helpful in ruling out other causes of tremors.

DIFFERENTIAL DIAGNOSIS

- Congenital abnormal myelin formation (e.g., hypomyelination, dysmyelination)
- Toxicosis (e.g., penitrem A produced by *Penicillium* in moldy foods, hexachlorophene, and organophosphates)
- Metabolic conditions (e.g., hepatic or uremic encephalopathies)

- Cerebellar disease

INITIAL DATABASE

Basic blood work (CBC, serum chemistry panel) is typically within normal limits.

ADVANCED OR CONFIRMATORY TESTING

- Cerebrospinal fluid analysis is helpful in differentiating idiopathic tremor syndrome from other inflammatory diseases:
  - Results may include minimal to moderate nonsuppurative pleocytosis (lymphocytic, with mean white blood cell count being approximately 16 cells/mcL).
  - This is in contrast to the polymorphonuclear pleocytosis associated with mycotic and bacterial encephalitis and the mixed-cell pleocytosis seen in granulomatous meningoencephalitis and protozoal diseases.
  - The protein concentration is often high in cases of idiopathic tremor syndrome.
- MRI of the brain is typically normal.
- Histopathologic evaluation:
  - Histopathologic lesions are not seen in all dogs with idiopathic tremor syndrome.
  - Abnormalities may include diffuse, mild meningoencephalitis with mild perivascular cuffing and lymphocytic infiltrates throughout the CNS, especially in the cerebellum.

TREATMENT

TREATMENT OVERVIEW

The goal of therapy is to eliminate tremors and is achieved mainly with corticosteroids, though diazepam can also be used. If tremors return when therapy is complete, they are typically mild and associated with excitement.

ACUTE GENERAL TREATMENT

Treatment consists of immunosuppressive doses of corticosteroids (i.e., prednisone, 1–2 mg/kg PO q 12 h). Clinical signs often decrease within the first few days of treatment.

CHRONIC TREATMENT

- Once tremors are fully controlled, the dose of prednisone should be gradually decreased over 1-3 months.
- Occasionally, dogs need to be kept on low doses or alternate-day therapy to control tremors.
- Additional tremor control can be achieved with oral diazepam (0.2 mg/ kg PO q 8 h).

PROGNOSIS AND OUTCOME

Excellent

PEARLS & CONSIDERATIONS

COMMENTS

The synonym *white shaker dog syndrome* is a poor term, as approximately half of the dogs with idiopathic tremor syndrome do not have a white coat.

SUGGESTED READING

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Icterus

BASIC INFORMATION

DEFINITION

Yellow discoloration of the skin and mucous membranes

SYNONYM

Jaundice

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dependent on underlying cause (i.e., hepatobiliary disease, hemolytic anemia). Observed in both dogs and cats of any age.

GENETICS & BREED PREDISPOSITION

For primary liver disease:

- Dogs: Doberman pinschers (inflammatory liver disease), cocker spaniels, Labrador retrievers, Skye terriers
- Cats: Abyssinian (amyloidosis), Asian breeds (feline infectious peritonitis)

For hemolytic anemia: American cocker spaniel, English springer spaniel, Old English sheepdog, Irish setter, poodle

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Hepatobiliary disease:
  - Anorexia, lethargy/weight loss
  - Vomiting/diarrhea
  - Abdominal distension
  - Cranial abdominal pain
  - Polyuria, polydipsia
  - Orange discoloration to the urine
  - Encephalopathy
- Hemolytic anemia:
  - Pallor
  - Anorexia
  - Lethargy, weakness, exercise intolerance
  - Vomiting
  - Orange discoloration to urine
  - Pigmenturia (dark red/brown) if intravascular hemolysis
  - Syncope/collapse

PHYSICAL EXAM FINDINGS

- Yellow discoloration of skin, mucous membranes (gingival, nictitans, sclera, etc.)
- Hepatobiliary disease:
  - Abdominal distention
    - Cranial abdominal organomegaly
    - Ascites
  - Dehydration
  - Halitosis
- Hemolysis:
  - Pale mucous membranes

- Sinus tachycardia, ventricular arrhythmia
- Fever
- Respiratory difficulty if pulmonary thromboembolism (PTE)

ETIOLOGY AND PATHOPHYSIOLOGY

- Prehepatic icterus: increase in production of bilirubin due to presentation of excessive amount of heme (e.g., hemolysis)
- Hepatic icterus: abnormality in hepatic bilirubin uptake, conjugation, or excretion
- Posthepatic icterus: extrahepatic biliary system obstruction (bile duct system, gallbladder)

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

Icterus is the result of either hemolysis or hepatobiliary disease. Therefore, in addition to history and physical exam, a hematocrit and assessment of biochemical liver values in serum are indicated in every icteric patient. Serum bile acid levels are not routinely measured in icteric patients unless a patient has both anemia and biochemical evidence of hepatobiliary disease (normal serum bile acid concentrations are consistent with hemolysis rather than cholestasis).

DIFFERENTIAL DIAGNOSIS

- Hepatobiliary disease:
  - Inflammatory/immune-mediated/ infectious:
    - Idiopathic chronic hepatitis (dogs)
    - Cholangiohepatitis of cats (suppurative/neutrophilic)
    - Cholangiohepatitis of cats (lymphocytic)
    - Secondary to bacterial translocation from the gastrointestinal system
    - Leptospirosis (dogs)
  - Hepatic lipidosis (cats)
  - Neoplastic:
    - Lymphoma, hepatocellular carcinoma, hemangiosarcoma, biliary carcinoma, other
  - Extrahepatic obstruction:
    - Pancreatitis
    - Cholelithiasis (rare in dogs and cats)
    - Bile duct neoplasia
    - Biliary mucocele
    - Inspissated bile syndrome (cats)
  - Cholestatic drug injury:
    - Acetaminophen, azathioprine, diazepam, phenobarbital, sulfonamide, many others
  - Extrahepatic sepsis: coliform septicemia most common resulting in cholestasis:
    - Endotoxin and acute phase reactants interfere with transport of bile acids into canaliculi.
  - Anoxia: can lead to cholestasis
- Hemolytic anemia:
  - Idiopathic immune-mediated hemolytic anemia
  - Associated with other immune disorders:
    - Inflammatory bowel disease
    - Systemic lupus erythematosus
  - Infectious:
    - Ehrlichiosis, Rocky Mountain spotted fever, leptospirosis, babesiosis, hemobartonellosis *(Mycoplasma haemofelis)*
    - Viral: feline leukemia virus
    - Bacterial: any chronic infection
  - Neoplasia: lymphoma, common association; any form of neoplasia
  - Microangiopathic hemolysis: commonly associated with hemangiosarcoma, heartworm, disseminated intravascular coagulation (DIC), vasculitis
  - Drug reaction: postvaccinal, sulfonamides, many others
  - Erythrocyte membrane fragility/oxidative damage:
    - Abyssinian, Somali cats (osmotic fragility)
    - Hypophosphatemia (phosphorus <1.5 mg/dL)
    - Oxidative damage (intoxications):
      - Onions (dogs)
      - Acetaminophen (cats)
      - Zinc

- Red blood cell (RBC) enzyme deficiencies: phosphofructokinase deficiency (English springer spaniel), pyruvate kinase deficiency (Basenji and others), stomatocytosis of malamutes

INITIAL DATABASE

- CBC:
  - Evaluation of plasma in PCV tube is more sensitive for icterus (seen at bilirubin = 1–1.5 mg/dL) than mucous membranes (icterus when bilirubin >2 mg/dL).
- Serum biochemical profile:
  - Alkaline phosphatase is always elevated in cholestatic disease causing icterus.
  - Liver enzymes may be elevated secondary to hypoxemia of severe anemia.
- Urinalysis and culture
- Abdominal radiographs
- Abdominal ultrasound
- Thoracic radiographs

ADVANCED OR CONFIRMATORY TESTING

- Hepatobiliary:
  - Prothrombin time (PT)/activated partial thromboplastin time (APTT)/ platelet count
  - Liver aspirate or biopsy for histopathologic evaluation and culture
  - Amylase/lipase/pancreatic lipase immunoreactivity
  - Infectious disease titers
  - Serial blood cultures, body fluid cultures if suspect sepsis
- Hemolysis:
  - Whole blood smear (spherocytes)
  - Reticulocyte count
  - PT/APTT platelet count to rule out bleeding disorder, disseminated intravascular coagulation (DIC)
  - Antinuclear antibody test
  - Direct Coombs' test (false-negative results common)
  - Slide agglutination test
  - Direct IFA for RBC isotype-specific antibodies (IMHA)
  - Infectious disease titers/PCR (see Etiology and Pathophysiology above).
  - PCR for RBC enzyme deficiencies
  - Arterial blood gas
  - D-dimer (to rule out PTE associated with hemolytic anemia; high sensitivity, low specificity)
  - Bone marrow aspirate (evaluate for erythrophagocytosis, differentiate from myelodysplasia, pure red cell aplasia, lymphoma).
  - Fecal occult blood to differentiate hemolysis from gastrointestinal blood loss

TREATMENT

TREATMENT OVERVIEW

- Hepatobiliary disease:
  - Suppress or eliminate the disease process.
  - Manage the metabolic condition.
- Hemolysis:
  - Treat inciting cause (e.g., drug withdrawal, toxin removal).
  - Suppress immune system if indicated.
  - Treat complications such as PTE, DIC.

GENERAL TREATMENT

Because icterus is a clinical sign, not a disease entity, appropriate management depends on identification and treatment of the underlying cause.

POSSIBLE COMPLICATIONS

- PTE: very common with immune-mediated hemolytic anemia
  - Oxygen/heparinization if PTE suspected
- Persistent/worsening anemia

- RBC transfusion reactions (cross-matching important)
- Hepatic encephalopathy (see p. 501)
- Gastric ulcer (see p. 440)

PROGNOSIS AND OUTCOME

- Varies with the cause of each disease
- Extrahepatic sepsis: mortality rate usually quite high
- Hemolytic anemia:
  - Prognosis good if inciting cause can be removed
  - Idiopathic immune-mediated hemolytic anemia: 40%–70% mortality rate: prognosis worse with intravascular hemolysis

PEARLS & CONSIDERATIONS

COMMENTS

- Bilirubin concentrations are usually above 2 mg/dL to result in clinical icterus.
- The purpose of measuring serum bile acids is to assess liver function. Therefore, bile acids are an unnecessary diagnostic test in an icteric patient with a normal PCV.
- PTE diagnosis is sometimes difficult: low PaO2 on an arterial blood gas that is drawn during oxygen therapy is suggestive. High-velocity tricuspid regurgitation also suggestive if a murmur is present. D-dimer for thrombolysis: high sensitivity but poor specificity (i.e., many false-positive results for unrelated conditions).
- Portosystemic shunts do not cause icterus unless a complicating factor (e.g., other concurrent hepatopathy) also is present.
- Subtle icterus may be difficult to detect (or “icterus” may incorrectly be detected in a normal patient) when the physical examination is performed in a room illuminated with fluorescent tube lighting.
- Ultra low-dose aspirin may become a new therapeutic to replace heparin in the prevention of PTE.
- Hemolytic anemia can be associated with immune-mediated thrombocytopenia (often referred to as Evans syndrome).
- Blood transfusions can suppress the reticulocyte response.

SUGGESTED READING

Piek CJ, et al: Idiopathic immune-mediated hemolytic anemia: treatment outcome and prognostic factors in 149 dogs. J Vet Intern Med 22:366–373, 2008

Webster CRL: History, clinical signs, and physical findings in hepatobiliary disease. In Ettinger SJ, Feldman EC, editors: Textbook of veterinary internal medicine, ed 7, St Louis, 2010, Saunders Elsevier, pp 1612–1626.

AUTHOR: MAUREEN CARROLL

EDITOR: ETIENNE CÔTÉ

Juvenile Polyarteritis

BASIC INFORMATION

DEFINITION

Systemic necrotizing vasculitis most often reported in young beagles. The neurologic aspects of this disorder are discussed in greater detail under Steroid-Responsive Meningitis-Arteritis, .

SYNONYMS

Beagle pain syndrome, canine juvenile polyarteritis syndrome, canine pain syndrome, juvenile polyarteritis, necrotizing vasculitis, steroid-responsive meningitis-arteritis (SRMA)

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Seen most often in young (<12-month-old) beagles; also affects young (8-18 months) dogs of other breeds
- No sex predilection

GENETICS & BREED PREDISPOSITION

- Colonies of research beagles
- Beagle, Bernese mountain dog, boxer overrepresented; may be inherited in the beagle
- Reported in Nova Scotia Duck Toller retriever and occasionally other breeds

RISK FACTORS

Incidence may be higher in the spring.

CONTAGION & ZOONOSIS

Neither contagious nor zoonotic

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Acute form (typical)
- Atypical, protracted form

HISTORY, CHIEF COMPLAINT

- Acute to gradual onset of hunched posture, guarding of the neck, reluctance to move, cervical rigidity
- Paresis may occur.
- Signs may be episodic: persist for 2-7 days and then resolve.
- After several relapses without therapy, patients may develop the protracted form with progressive worsening of neurologic dysfunction.

PHYSICAL EXAM FINDINGS

- Signs of cervical pain and rigidity with an associated hunched posture and unwillingness to move
- Generalized hyperesthesia
- Fever
- Anorexia
- Weakness
- With the atypical/protracted form, patients may have proprioceptive deficits, ataxia, paraparesis, or tetraparesis.
- Cranial nerve deficits rarely reported

- Nonspecific signs such as lethargy, malaise, and depression common

ETIOLOGY AND PATHOPHYSIOLOGY

- Systemic necrotizing vasculitis with severe subarachnoid hemorrhages throughout spinal cord and brainstem
- Intimal thickening and fibrinoid necrosis of the tunica media of small to medium-sized arteries result in occlusion and thrombosis that may cause neural ischemia and pain.
- Vessels of the cervical spinal cord leptomeninges, cranial mediastinum, and coronary arteries may be involved.
- Mechanism is believed to be immune mediated; may be triggered by an environmental factor that has yet to be identified.
- Hereditary component suspected in beagles

DIAGNOSIS

DIAGNOSTIC OVERVIEW

There are many differential diagnoses for a dog presenting with these clinical signs. Initial lab work results are nonspecific; advanced imaging helps rule out other neurologic disorders, and arthrocentesis or a cerebrospinal fluid (CSF) tap confirms the diagnosis.

DIFFERENTIAL DIAGNOSIS

- Bacterial meningitis: rule out with CSF analysis and culture
- Granulomatous and infectious menin-goencephalomyelitis
- Polyarthritis
- Polymyositis
- Discospondylitis: rule out with diagnostic imaging.
- Cervical disk disease, disk herniation: rule out with diagnostic imaging.
- Spinal cord trauma: rule out with diagnostic imaging, history.
- Protozoal infection: rule out with muscle biopsy, serology.

INITIAL DATABASE

- CBC: mild nonregenerative anemia, leukocytosis, neutrophilia
- Serum biochemistry profile: hypoalbuminemia possible
- Urinalysis: proteinuria possible
- Thoracic, abdominal, cervical radiographs: normal findings

ADVANCED OR CONFIRMATORY TESTING

- Synovial fluid analysis: neutrophilic inflammation typical; negative culture
- CSF analysis: characteristic findings include erythrophagocytosis, neutrophilic pleocytosis, increased protein; negative culture. In protracted cases, protein content is either slightly elevated or normal with a mild to moderate mixed pleocytosis.
- Brain MRI, CT: results usually normal
- Systemic and intrathecal immunoglobulin (Ig)A levels elevated in acute and atypical/protracted forms
- Histopathologic evaluation of tissues: severe necrotizing vasculitis, perivasculitis, and thrombosis of small to medium-sized vessels in the leptomeninges of the cervical spinal cord, cranial mediastinum, coronary arteries, and other affected organs

TREATMENT

TREATMENT OVERVIEW

Signs should resolve in 24-48 hours with corticosteroid therapy as remission is induced. To avoid relapse, treatment should not be abruptly stopped or tapered too quickly.

ACUTE GENERAL TREATMENT

- Fluid therapy may be needed if patient is anorexic.
- Restrict activity.
- Prednisone/prednisolone therapy: start at 1-2 mg/kg PO, IM, or SQ q 12 h

CHRONIC TREATMENT

- Taper corticosteroids to the minimum dose that controls clinical signs (usually 0.25-0.5 mg/kg q 48 h) over 6 months.
- Azathioprine (1.5-2 mg/kg PO q 48 h) for patients who do not respond to corticosteroids

POSSIBLE COMPLICATIONS

- Gastrointestinal (GI) upset and GI ulceration/bleeding, polyuria, polydipsia, polyphagia, Cushingoid syndrome as adverse effects of corticosteroid therapy
- Infections possible, secondary to chronic immunosuppression
- Myelotoxicity and hepatic failure are possible adverse effects of azathioprine therapy.

RECOMMENDED MONITORING

- CBC, serum chemistry profile, urinalysis every 4-6 weeks to monitor for inflammation and organ dysfunction.
- Monitor for neck pain (sign of possible recurrence) and GI bleeding.
- Repeat CSF tap every 4-6 weeks at the beginning of therapy to help guide corticosteroid therapy. Once CSF is normal and clinical signs remain absent, weaning can commence.

PROGNOSIS AND OUTCOME

- Good prognosis for acute cases if treated promptly and intensively
- Disease can spontaneously resolve when patient is 12 to 18 months old.
- Prognosis more guarded with protracted cases, owing to frequent relapses
- Some patients do not respond to further therapy after relapses.
- Some patients need continuous therapy to control clinical signs.

PEARLS & CONSIDERATIONS

COMMENTS

- Early diagnosis and aggressive treatment result in the best outcome.
- Adverse effects of corticosteroid therapy may be unacceptable to some clients. Azathioprine should be used for its steroid-sparing effects in these cases.

TECHNICIAN TIPS

- No neck leads
- These pets often are painful, so be cognizant of pain management.

CLIENT EDUCATION

Although patients usually respond to therapy for the acute form, relapses can be common, and some patients require long-term or indefinite treatment to control clinical signs.

SUGGESTED READING

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Tipold A: Juvenile polyarteritis (beagle pain syndrome). In Tilley LP, editor: The 5-minute veterinary consultant canine and feline, ed 2, Philadelphia, 2000, Lippincott, Williams & Wilkins, p 877.

Tipold A: Steroid-responsive meningitis-arteri-tis in dogs. In Bonagura JD, editor: Kirk's current veterinary therapy XIII. Philadelphia, 2000, WB Saunders, pp 978–981.

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Juvenile Cellulitis

BASIC INFORMATION

DEFINITION

An uncommon vesiculopustular to granulomatous skin disease primarily affecting dogs < 4 months old. The pinnae, face, and submandibular lymph nodes are typically involved.

SYNONYMS

Juvenile sterile pyogranulomatous dermatitis and lymphadenitis, puppy strangles, juvenile pyoderma

EPIDEMIOLOGY

SPECIES, AGE, SEX

Young puppies of either sex between 3 weeks and 4 months old are typically affected, although confirmed cases in young adults have been rarely reported. One or more puppies in the same litter may be affected.

GENETICS & BREED PREDISPOSITION

Many breeds, including mixed breeds, may develop this disease, but some breeds appear predisposed (e.g., golden retrievers, dachshunds). A hereditary component is proposed. The exact mode of inheritance has not been established.

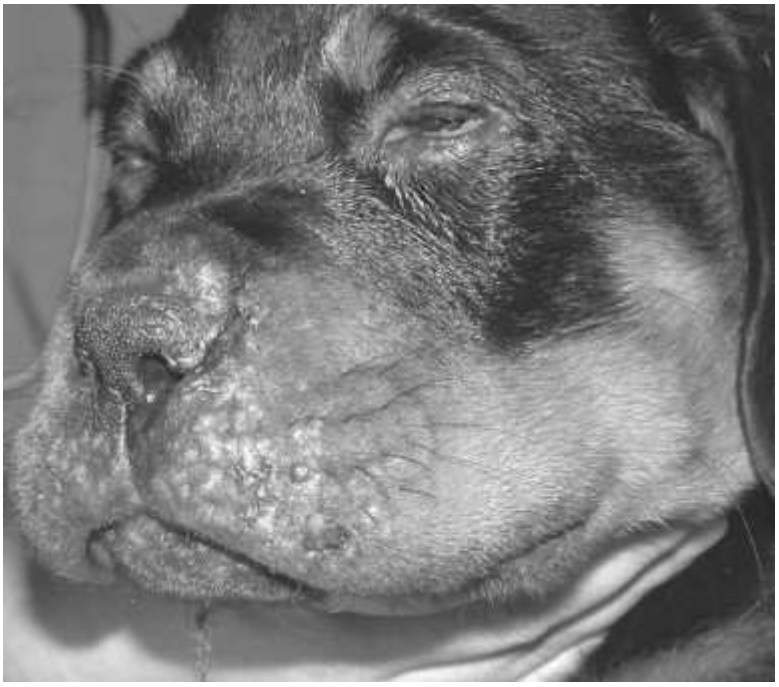
CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

Early in the course of the disease, an affected puppy develops an acutely swollen face, in particular the muzzle, lips, and eyelids. Marked submandibular lymphadenopathy is usually present even in the absence of cutaneous lesions.

PHYSICAL EXAM FINDINGS

- Acute swelling of face noted initially.
- Within 24-48 hours, vesicles and pustules appear around mouth, eyes, and muzzle. Lesions rapidly develop into a serous to purulent exudative dermatitis with or without fistulation.
- Serous to purulent bilateral otitis externa with edematous pinnae is common.
- Marked regional (submandibular and prescapular) to diffuse lymphadenopathy is common. Submandibular lymphadenopathy may occur as only clinical abnormality.
- Fistulation of affected lymph nodes is variable.
- Affected skin is frequently painful but rarely pruritic.
- Rarely, sterile subcutaneous nodules with or without fistulation develop on the trunk, preputial, or perineal regions.
- Approximately 50% of puppies are lethargic. Anorexia, pyrexia, and lameness (sterile suppurative arthritis) are inconsistent findings.



JUVENILE CELLULITIS Typical lesions in a 9-week-old rottweiler with edematous eyelids and papules, pustules, and swelling of the muzzle.

(Courtesy Dr. J. Wellington.)

ETIOLOGY AND PATHOPHYSIOLOGY

- The etiology and pathogenesis of juvenile cellulitis are unproven; immune dysfunction is suspected.
- Bacterial invasion is not considered to be the primary cause. Any evidence of infection usually reflects secondary pyoderma.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is based almost entirely on signalment, history, and physical exam, with cytologic examination of smears for support and skin scrapings to rule out demodicosis. Juvenile cellulitis should be suspected when a puppy presents with an acutely swollen face, especially the eyelids, lips, and muzzle, edematous pinnae, and submandibular lymphadenopathy. The rapid development of papules, pustules, and serous crusts on the facial and pinnal lesions further supports the diagnosis.

DIFFERENTIAL DIAGNOSIS

- Angioedema: vaccine reaction or insect bite reaction
- Deep pyoderma/muzzle folliculitis
- Demodicosis
- Drug eruption (cutaneous drug reaction)

INITIAL DATABASE

- Impression cytologic analysis of pustule: numerous neutrophils and macrophages (pyogranulomatous inflammation) without bacteria
- Skin scrapings: negative for *Demodex* mites

ADVANCED OR CONFIRMATORY TESTING

These additional diagnostic tests may be performed but are rarely required:

- Anaerobic or aerobic bacterial culture and sensitivity: usually sterile
- Skin biopsy: multiple discrete or confluent granulomas and pyogranulomas composed of nodular clusters of large epithelioid

macrophages with variably sized neutrophilic centers
- Lymph node aspirate: pyogranulomatous lymphadenitis

TREATMENT

TREATMENT OVERVIEW

Early and intensive immunosuppressive systemic therapy with predniso(lo)ne or dexamethasone is indicated to prevent secondary scarring. Concurrent systemic antibiotics are recommended if secondary pyoderma is found cytologically or marked fistulation is present.

ACUTE GENERAL TREATMENT

- Prednisone or prednisolone (2 mg/kg PO q 24 h, or total dose can be divided q 12 h) until lesions resolve (approximately 1-4 weeks), then reduce to 2 mg/kg PO q 48 h for 2 weeks, then taper off prednisone over the next 2-3 weeks.
- Some dogs respond better to dexamethasone (0.2 mg/kg PO q 24 h). Gradually taper dosage (similar to prednisone).
- Bactericidal antibiotics for 3-4 weeks required if cytologic or clinical evidence of secondary pyoderma present.
- Warm water soaks to remove crusts and exudates; topical astringents (e.g., 2% aluminum acetate [Burow's solution] q 12 h) can be attempted.

PROGNOSIS AND OUTCOME

Prognosis is good. Scarring may be extensive in severe cases.

PEARLS & CONSIDERATIONS

COMMENTS

- Taper corticosteroids gradually (over a few weeks) to reduce the risk of relapse.
- Adult dogs and dogs with panniculitis (subcutaneous nodules) require a longer treatment interval.
- If relapse occurs, restart immunosuppressive dosage of corticosteroid immediately.
- Avoid routine vaccinations during therapy.

SUGGESTED READING

Medleau L: Small animal dermatology: a color atlas and therapeutic guide, ed 2, St Louis, 2006, Saunders Elsevier.

AUTHOR: JOCELYN WELLINGTON

EDITOR: MANON PARADIS

Keratoconjunctivitis Sicca

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

A common inflammatory condition of the cornea and conjunctiva secondary to a deficiency in the aqueous portion of the tear film

SYNONYMS

KCS, dry eye, quantitative tear film abnormality, xerophthalmia

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Common in dogs; rare in cats
- Age of onset variable depending on underlying cause
- Increased predisposition reported for both castrated male and spayed female dogs and female West Highland white terrier

GENETICS & BREED PREDISPOSITION

Predisposed breeds (dogs): English bulldog, West Highland white terrier, Lhasa Apso, pug, American cocker spaniel, Pekingese, Yorkshire terrier, shih tzu, miniature schnauzer, Boston terrier, dachshund, Chihuahua, German shepherd, Doberman pinscher

RISK FACTORS

- Medications, metabolic disorders, and infectious diseases (see Etiology and Pathophysiology below)
- Removal of gland of the third eyelid
- Systemic immune-mediated disease (e.g., systemic lupus erythematosus [see p. 1070])

CONTAGION & ZOONOSIS

Infectious causes (e.g., canine distemper; feline herpesvirus 1 [FHV-1]) are contagious.

ASSOCIATED CONDITIONS & DISORDERS

Conjunctivitis and ulcerative and nonulcerative keratitis

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- “Red” eye (p. 967)
- Ocular pain
- Mucoid to mucopurulent ocular discharge

PHYSICAL EXAM FINDINGS

- Systemic: generally unremarkable
- Ophthalmic:
  - Mucoid to mucopurulent ocular discharge
  - Conjunctival hyperemia and chemosis
  - Blepharospasm
  - Protrusion of the third eyelid
  - Dry/lackluster corneal appearance
  - Signs of keratitis with chronicity:
    - Corneal vascularization (see p. 254)
    - Corneal pigmentation (see p. 246)

        - Corneal ulceration (see p. 250)
    - Blepharitis
    - Periocular dermatitis secondary to exudates and/or self-trauma
    - Vision impairment with chronic disease
- Cats often show fewer clinical signs than dogs.

ETIOLOGY AND PATHOPHYSIOLOGY

- Immune-mediated adenitis: most common (dogs)
- Congenital: lacrimal gland hypoplasia or aplasia
- Drug-induced: general or topical anesthesia and atropine (transient KCS)
- Drug toxicity: some systemic medications (e.g., sulfonamide therapy; phenazopyridine; 5-aminosalicylic acid; etodolac) may cause transient or permanent KCS.
- Iatrogenic: removal of the gland of the third eyelid increases risk of developing KCS, especially in predisposed breeds.
- Infectious disease (e.g., canine distemper [see p. 317], FHV-1 [see p. 524])
- Metabolic disease (e.g., hypothyroidism [see p. 588], hyperadrenocorticism [see p. 548], diabetes mellitus [see p. 297])
- Neurogenic: may occur with facial nerve paralysis and denervation of parasympathetic fibers innervating the gland, or following ocular proptosis (see p. 918)
- Chronic blepharoconjunctivitis due to obstruction of lacrimal ductules secondary to chemosis or ascending infection into lacrimal gland
- Chronic conjunctivitis (e.g., FHV-1; see p. 524)
- Irradiation: when primary beam near or on periocular region

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on the presence of conjunctivitis or ulcerative and/or nonulcerative keratitis; the confirmatory test of choice is the Schirmer tear test (STT).

DIFFERENTIAL DIAGNOSIS

- Dogs, other causes of keratoconjunctivitis:
    - Conjunctivitis (see p. 239)
    - Corneal vascularization (see p. 254) or pigmentation (see p. 246)
    - Corneal exposure (e.g., lagophthalmos); common cause of misdiagnosis of “KCS”
    - Corneal ulceration (see p. 250)
    - Blepharitis
- Cats, other causes of keratoconjunctivitis:
    - FHV-1 conjunctivitis/keratitis
    - Proliferative (eosinophilic) keratoconjunctivitis

INITIAL DATABASE

Complete ophthalmic examination, including:

- Schirmer tear test (STT)
    - Normal: ≥15 mm/min in dogs; variable in cats
    - Early or subclinical KCS: 11-14 mm/ min
    - Mild to moderate KCS: 6-10 mm/ min
    - Severe KCS: ≤5 mm/min
- Fluorescein dye application: secondary corneal ulceration is common.
- Intraocular pressure (IOP): normal IOP values; normal IOPs range from 15-25 mm Hg (dogs and cats).

ADVANCED OR CONFIRMATORY TESTING

- Other quantitative test:
    - Phenol red-thread tear test:
        - Dogs: normal 34.15 ± 4.45 mm/15 sec
        - Cats: normal 23.04 ± 2.23 mm/15 sec

TREATMENT

TREATMENT OVERVIEW

Treatment goals are to stimulate tear production, stabilize the tear film, and eliminate ocular pain by controlling ocular inflammation (conjunctivitis and nonulcerative keratitis), secondary bacterial infections, and corneal ulceration (see p. 250) if present.

ACUTE GENERAL TREATMENT

- Lacrimostimulants:
  - Cyclosporine-A (CsA) 0.2% ointment or 0.5%-2% solution q 8-12 h.
- Lacrimomimetics (tear substitutes and stabilizers) q 4-6 h (e.g., hyaluronic acid 0.4%)
- Antimicrobials if secondary bacterial conjunctivitis and/or corneal ulceration:
  - Topical broad-spectrum antibiotic (e.g., bacitracin-neomycin-polymyxin antibiotic solution q 6-8 h)
- Antiinflammatories if severe conjunctivitis and/or corneal vascularization/ pigmentation:
  - Dexamethasone, 0.1% solution q 6-8 h if corneal ulceration is absent

CHRONIC TREATMENT

Lacrimostimulants:

- CsA 0.2% ointment or 0.5%-2% solution q 8-24 h (typically q 12 h)
  - For STT values that remain 10 mm/ min after 3-4 weeks of treatment, CsA may be increased to q 8 h.
  - CsA should not be decreased until STT values are ≥20 mm/min.
  - CsA may be decreased to q 24 h if favorable response occurs.
- Tacrolimus 0.02%-0.03% ointment or aqueous suspension q 12 h
  - Used if no response to CsA after 3-6 weeks of treatment
  - Studies evaluating long-term safety have not been performed.
- Some ophthalmologists advocate increasing the concentration of the lacrimostimulant if there is no response (i.e., 0.2% CsA ointment to 2% CsA solution).
- Pilocarpine: 1 drop 2% pilocarpine/10 kg body weight on food q 12 h, gradually increasing by 1-drop increments until increased tearing or systemic side effects (e.g., vomiting, diarrhea, anorexia, salivation, bradycardia); primarily effective in neurogenic KCS
- Consider parotid duct transposition if no response to lacrimostimulants.

POSSIBLE COMPLICATIONS

- Corneal ulceration
- Vision impairment from progressive corneal vascularization/pigmentation (uncontrolled KCS)

RECOMMENDED MONITORING

- Variable depending on underlying cause
- Complete ophthalmic examination with STT and corneal fluorescein staining performed every 3-4 weeks initially
- Rechecks performed every 4-6 weeks until KCS controlled, then every 3-4 months

PROGNOSIS AND OUTCOME

Variable depending on underlying cause

PEARLS & CONSIDERATIONS

COMMENTS

- Immune-mediated KCS usually requires lifelong treatment.
- Some forms of KCS may require transient treatment until tear production returns (e.g., topical atropine, topical or general anesthesia).
- May take weeks to months of therapy before determining if favorable response to lacrimostimulants

PREVENTION

Breeds predisposed to KCS: avoid breeding affected or closely related dogs.

CLIENT EDUCATION

Immune-mediated KCS is a chronic disorder that is manageable but not curable; usually requires lifelong treatment.

SUGGESTED READING

Sanchez RF, Innocent G, Mould J, et al: Canine keratoconjunctivitis sicca: disease trends in a review of 229 cases. J Small Anim Pract 48:211, 2007.

AUTHOR: PHILLIP A. MOORE

EDITOR: CHERYL L. CULLEN

Lymphoma, Gastrointestinal

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Gastrointestinal (GI) lymphomas (LSA) are malignant tumors of lymphoid cell origin that can arise at any location within the gastrointestinal tract, including the stomach, small intestine, colon and rectum. Lesions may be of B-, T-, or large granular lymphocyte subtype, a distinction that is important prognostically.

SYNONYMS

Alimentary lymphoma, alimentary lymphosarcoma, gut-associated lymphoid tissue (GALT) lymphoma, large granular lymphocyte lymphoma, mucosal associated lymphoid tissue (MALT) lymphoma, neoplasm of globule leukocytes

EPIDEMIOLOGY

SPECIES, AGE, SEX: GI LSA is the second most common form of lymphoid malignancy in dogs (after multicentric lymphoma), accounting for 5%-7% of all LSA.

- Dogs with gastrointestinal lymphosarcoma are middle-aged to older (mean 7.7 years in one study).
- In the cat, the alimentary form of LSA is currently the most prevalent anatomic form, since feline leukemia virus (FeLV) infection as a cause of mediastinal and multicentric LSA in young cats has been largely curtailed by FeLV vaccination and management strategies.
    - Cats with GI LSA are typically older (7-10 years), although the disorder can occur in much older and also younger cats.
- No sex predisposition is noted in dogs or cats.

GENETICS & BREED PREDISPOSITION

- Dog breeds predisposed include boxers, shar-peis, golden retrievers, springer spaniels, Doberman pinschers, Labrador retrievers, and German shepherds.

RISK FACTORS: Etiology of most cases of alimentary LSA is unknown.

- Chronic inflammatory bowel disease is a predisposing factor.
- Epidemiologic studies implicate exposure to phenoxy herbicides (2,4-D) and environmental cigarette smoke in lymphoma genesis.
- *Helicobacter pylori* infection is implicated in human GI LSA, but that association has not been established in veterinary medicine.
- Underlying immune disorders may predispose.

CONTAGION AND ZOONOSIS: No infectious or zoonotic cause is known in dogs. In cats, retroviral infection with FeLV and/or FIV is rarely found associated with GI lymphoma genesis.

ASSOCIATED CONDITIONS & DISORDERS

- Anemia and panhypoproteinemia may occur secondary to chronic GI blood loss.
- Hypercalcemia may be associated with canine GI LSA but is rare in cats.
- LSA metastatic to the liver may be associated with elevated liver enzymes and biliary obstructive disorders.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Lymphoma of the gastrointestinal tract may be of B-, T-, or large granular lymphocyte (LGL) type. LGL lymphomas are typically of T-cell origin, although they can represent a null cell phenotype of natural killer (NK) cells.
- Lesions may be focal masses or diffusely infiltrative throughout the gut.
- Lesions may be submucosal, epitheliotropic, or transmural.

- GI LSA may be a low-grade disease of cellular accumulation due to impaired apoptosis, as in human MALT lymphoma, or may be high-grade with rapid cell replication.

HISTORY, CHIEF COMPLAINT: GI LSA is associated with gastrointestinal signs including:

- Evidence of malassimilation such as weight loss
- Anorexia
- Vomiting and diarrhea
- Melena, hematemesis, hematochezia

PHYSICAL EXAM FINDINGS

- On physical exam, these animals typically are thin and ill-kempt, especially cats.
- Signs of anemia (lethargy or weakness, hyperpnea, tachycardia) or hypercalcemia (muscle tremors) may be evident.
- Palpable abdominal masses and intraabdominal lymphadenomegaly may be noted.
- Hepatosplenomegaly may be present.
- In cases of diffuse intestinal infiltration, turgid, thickened intestinal walls may be palpated.
- Physical examination may be within normal limits.

ETIOLOGY AND PATHOPHYSIOLOGY

Most lymphomas are thought to arise secondary to abnormal somatic cell DNA recombination events, which may be random or may be induced by retroviral infection, environmental carcinogen exposure, or chronic infection/inflammation that increases lymphoid cell population expansion.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected in a patient with persistent vomiting, diarrhea, systemic signs such as weight loss, or some combination thereof. Increased suspicion arises when abdominal ultrasound reveals thickening of the gastric or intestinal wall. Confirmation requires a biopsy; endoscopic samples are less invasive but may be insufficient; full-thickness samples are the gold standard but require laparoscopy or laparotomy. Interpretation of histologic features in some cases is difficult and may require advanced staining or other techniques, with some samples remaining permanently ambiguous.

DIFFERENTIAL DIAGNOSIS

Depending on the form and location of the LSA lesion(s):

- Inflammatory bowel disease
- Chronic endoparasitism
- GI foreign body or intussusception
- Chronic pancreatitis (especially cats)
- Other causes of liver disease such as hepatitis, cholangiohepatitis, toxic hepatopathy, or feline hepatic lipidosis
- Benign GI disease such as gastric ulcer, polyp, or adenoma
- Other GI tumors including mast cell disease, adenocarcinoma, and mesenchymal tumors
- Granulomatous bowel disease secondary to bacterial (i.e., mycobacterium) or fungal infection (i.e., histoplasmosis)

INITIAL DATABASE

- Minimum database: CBC, serum chemistry panel, urinalysis, fecal examination for parasites, *Giardia* antigen test, thyroid assay in cats, FeLV/feline immunodeficiency virus (FIV) testing in cats
- Evaluation for chronic pancreatic or GI disease (trypsinlike immunoreactivity [TLI], cobalamin/folate, or pancreatic lipase immunoreactivity [PLI])
- Three-view thoracic radiographs
- Abdominal ultrasonography with guided fine-needle aspiration cytologic analysis
    - Normal thickness (dog, cat) <5 mm
    - Any layer may be thickened, thickening may be focal or diffuse (diffuse more common), and mesenteric lymph node enlargement is common but not specific to lymphoma. Intestinal mural layering is commonly preserved.

ADVANCED OR CONFIRMATORY TESTING

- Endoscopy for biopsy of gastric, duodenal, or colorectal lesions
- Diagnosis is made histologically on endoscopic or full-thickness surgical biopsies of affected tissues (gut, lymph nodes, etc.).
- Tumor staging for extent of systemic involvement:
  - Radiographs and ultrasound as described previously
  - Bone marrow evaluation for staging and/or as indicated by cytopenias
  - Peripheral node aspiration or biopsy for staging and/or as indicated for lymphadenomegaly
- Immunohistochemical phenotyping for B-, T-, or LGL subtypes:
  - CD3 for T-cell subset
  - CD79a or CD20 for B-cell disease
  - CD3 and CD57 for LGL subtype
  - PCR for monoclonality by B-cell (IG gene rearrangement) or T-cell (T-cell receptor gene rearrangement) clonal expansion rather than polyclonal lesions seen in lymphoplasmacytic enteritis

TREATMENT

TREATMENT OVERVIEW

- Focal GI LSA lesions can be surgically cured by excision with complete margins, when neoplastic cells have not yet disseminated.
- It is extremely unlikely that dogs and cats with diffuse, nodal, or visceral organ involvement will be cured.
- For most cases, the goal is to prolong life with good quality while avoiding adverse effects to therapy.

ACUTE GENERAL TREATMENT

General supportive care includes:

- Rehydration and restoring electrolyte homeostasis
- Managing anemia with transfusions and hematinics as indicated by clinical condition
- Antibiotic and emergency management for peritonitis
- Analgesic management as indicated for pain in obstructive lesions or peritonitis
- Promotility agents are contraindicated in obstructive disease.
- Management of hypercalcemia of malignancy by IV fluid and furosemide (1-2 mg/kg IV or PO q 12-24 h) diuresis, possibly calcitonin (4-8 IU/kg IV, IM, or SQ q 12 h) acutely. Management of hypercalcemia by treating the underlying malignancy should be started (corticosteroids, chemotherapy) only *after* the cytologic or histopathologic diagnosis of GI LSA is established, as treatment with corticosteroids or other lympholytic agents can compromise detection of lymphoma lesions.

CHRONIC TREATMENT

- Curative therapy for focal GI LSA lesions is through complete surgical excision.
- Because of the high likelihood of systemic or local spread, these animals are followed with a course of lymphoma chemotherapy.
- Low-intensity radiation therapy may be palliative for refractory GI LSA.
- Chemotherapy is generally the treatment of choice for GI LSA.
- A number of chemotherapy protocols (see pp. 674 and 673) have been used to treat GI LSA, which include:
  - For high-grade disease, the University of Madison-Wisconsin protocol involves:
    - Rotating sequential treatment with vincristine, L-asparaginase, prednisone, cyclophosphamide, doxorubicin over 25 weeks
    - A concurrent combination form of this multidrug protocol called COPLA is less dose intense, and thus has lower adverse effects for metabolically compromised patients.
    - CHOP therapy (cyclophosphamide, doxorubicin, vincristine, prednisone) may also be effective.
    - Single-agent doxorubicin, mitoxantrone, ifosfamide, or CCNU and combination therapy with doxorubicin/dacarbazine have been used as rescue agents for refractory or relapsed disease, with limited success.
  - For low-grade disease, treatment with milder chemotherapy protocols may be helpful in prolonging life with good quality. Low-grade protocols include:
    - Chlorambucil and prednisolone
    - COP (cyclophosphamide, vincristine, and prednisone)

POSSIBLE COMPLICATIONS

- Surgical wound dehiscence with secondary peritonitis, pneumoperitoneum
- Chemotherapy-induced leukopenia might predispose to infection.

- Chemotherapy-induced thrombocytopenia might increase tumor hemorrhage.
- Chemotherapy might result in perforation of transmural lesions.

RECOMMENDED MONITORING

- Ultrasonography is most sensitive for detecting intraabdominal metastasis or recurrence and may identify small amounts of peritoneal fluid as the first manifestation of peritonitis in cases of bowel rupture.
- Periodic restaging (physical examination monthly, laboratory evaluation, thoracic radiographs, abdominal ultrasound examination every other month) for patients in complete remission after surgical excision or completion of dose-intense therapy with CHOP or University of Wisconsin, Madison protocol.

PROGNOSIS AND OUTCOME

- GI LSA is a serious, life-threatening illness, but because of the widely differing biological behaviors of various subtypes, predicting therapeutic response and duration of survival is difficult for individual cases.
- In general, low-grade disease is indolent and associated with longer survival than high-grade disease, depending on extent of disease at the time of diagnosis.
- T-cell phenotype is generally less responsive and associated with shorter survival duration than B-cell disease. Historically, median survivals for extra-nodal T-cell lymphomas were typically 6 months or less.
- Treatment efficacy remains variable, with reports of median remission times of 3 months or 12 months, depending on the study. Failure to achieve remission, and diarrhea at presentation, appear to be negative prognostic indicators.
- Anatomic location may have prognostic significance in dogs: colonic lymphoma is associated with a better prognosis than gastric or jejunal lymphoma.
- Cats with low-grade GI LSA requiring minimal therapy may survive for years.

PEARLS & CONSIDERATIONS

COMMENTS

- Full-thickness surgical biopsies may be necessary to establish a diagnosis of small-intestinal LSA, as endoscopic access is limited to the duodenum or ileum. Fine-needle aspiration cytology of intestinal wall is possible, but low-grade LSA is difficult to differentiate from reactive lymphocyte expansion.
- In general, the underlying cause of refractory diarrhea should be pursued aggressively, as GI LSA is an important differential diagnosis.
- Treatment with corticosteroids may impede the accurate diagnosis of LSA, as lymphoblasts will be rapidly lysed.

PREVENTION

- Aggressive management of lymphoplasmacytic enteritis is recommended, as some of these inflammatory bowel disease patients will progress to develop GI LSA.
- Managing endoparasitism and food allergies is theoretically important, but proof of benefit has not been established.
- Limiting exposure to lawn and agricultural chemicals and second-hand smoke is likely beneficial, but beyond these theoretical benefits, no specific preventive measures are known.

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Lymphoma, Dog (Multicentric)

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Well-recognized systemic malignant neoplasm of lymphoid origin

SYNONYMS

Lymphosarcoma, malignant lymphoma. non-Hodgkin's lymphoma (human)

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Lymphoma is the most common hematopoietic malignancy in dogs, with a reported incidence of 24-114 cases per 100,000 dogs.
- Affected dogs are typically middle-aged to older, although lymphoma may develop at any age.
- No gender predisposition

GENETICS & BREED PREDISPOSITION

- Several breeds are reported to be at increased risk, including golden retrievers, boxers, Rottweilers, Scottish terriers, basset hounds, cocker spaniels, German shepherds, Airedales, bulldogs, and poodles, and certain breeds (e.g., boxers) may be more likely to develop T-cell lymphoma.
- Genetic predisposition reported for a pedigree of bull mastiffs and for a family of rottweilers and otter hounds

RISK FACTORS

- Reported association between herbicide use, particularly 2,4-D, and lymphoma, although a subsequent study failed to confirm this relationship.
- Reported positive association with electromagnetic radiation exposure
- Residing in industrial areas and use of chemicals by the owners, specifically paints or solvents, are reported to increase risk of lymphoma in dogs by 8.5- and 4.6-fold, respectively.

ASSOCIATED CONDITIONS & DISORDERS: Hypercalcemia secondary to elaboration of parathormonerelated protein (PTH-rP) by tumor cells.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Histologic grade:
  - High-grade, or lymphoblastic, lymphoma: most common; rapid onset and progression; affected cells are large and blastic in appearance.
  - Low-grade, or lymphocytic, lymphoma: rare; chronic insidious onset; affected cells are well differentiated and similar in appearance to small lymphocytes.
- Stage: see table

HISTORY, CHIEF COMPLAINT

- Most typical presentation is generalized lymphadenopathy
- Owners usually report rapid increases in lymph node size over days to a few short weeks.
- Lymph nodes are generally nonpainful and dogs usually appear otherwise healthy in the early stages of disease.
- Some patients present for evaluation of nonspecific signs such as anorexia, weight loss, vomiting, diarrhea, dyspnea, and fever.

PHYSICAL EXAM FINDINGS

- Marked generalized lymphadenopathy is the most common physical exam finding, although occasionally dogs will present with only single lymph node or regional lymph node enlargement or single organ (e.g., spleen, GI, thymus) involvement with or without regional lymph node enlargement.
- Hepatosplenomegaly may be noted in dogs with visceral involvement.
- Other physical exam findings, including dyspnea, fever, and neurologic signs, may be reflective of other organ involvement.

ETIOLOGY AND PATHOPHYSIOLOGY

- Rapid onset and disease progression
- If untreated, most dogs succumb to disease within 1 to 2 months.

Lymphoma Staging

Stage	Characteristics
I	Single lymph node
II	Multiple regional lymph nodes
III	Generalized lymphadenopathy
IV	Hepatic and/or splenic involvement (± stages I-III)
V	Involvement of bone marrow, blood, and/or any nonlymphoid organ (±stages I-IV)
Substage a	No overt clinical signs of disease
Substage b	Overt clinical signs of disease are present.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on the presence of marked generalized lymphadenopathy with minimal to no associated clinical signs in an otherwise healthy middle-aged to older dog; confirmation begins with aspiration cytologic analysis of an affected lymph node.

DIFFERENTIAL DIAGNOSIS

- Infectious diseases (e.g., Rocky Mountain spotted fever, ehrlichiosis, leptospirosis, bartonellosis)
- Sepsis
- Pyoderma causing lymphadenopathy
- Other neoplasms (e.g., leukemia, disseminated histiocytocytic sarcoma)

INITIAL DATABASE

- CBC: to identify anemia, thrombocytopenia (due to lymphoblast infiltration in the marrow or secondary to immune-mediated destruction), neutropenia, or the presence of circulating lymphoblasts (= leukemia)
- Serum biochemistry panel: to identify paraneoplastic hypercalcemia; to identify liver or renal value abnormalities which suggest organ involvement and may alter ability to metabolize chemotherapeutic agents
- Urinalysis ± urine culture and sensitivity: to identify urinary tract infections as may be present secondary to immunocompromise; to identify isosthenuria which, if associated with azotemia, suggests kidney disease (e.g., hypercalcemia-induced)
- Lymph node (or affected organ) aspiration cytology: may provide a definitive diagnosis of lymphoma

ADVANCED OR CONFIRMATORY TESTING

- If lymphoma is identified cytologically, the following tests are indicated as part of routine staging in all cases of lymphoma, prior to initiation of chemotherapy:
  - Lymph node biopsy: for definitive diagnosis, histologic grading, and possibly for immunophenotyping
  - Thoracic radiographs: to identify lymphadenopathy, cranial mediastinal mass, pulmonary involvement
  - Abdominal ultrasound exam: to identify changes consistent with hepatic or splenic involvement, lymphadenopathy, or other sites of lymphoma
  - Bone marrow aspiration cytology: to identify marrow involvement and/or develop better understanding of etiology of

any cytopenias
    - Phenotyping (flow cytometry, immunocytochemistry, immunohistochemistry, PCR): to determine B-cell versus T-cell origin (prognosis worse with T-cell)
- If financial restrictions prohibit these tests, one may elect to omit certain tests (e.g., if CBC results are unremarkable, one may elect not to perform a bone marrow aspirate), as long as the client understands that sites of disease may be missed, and staging will be less certain.

TREATMENT 

TREATMENT OVERVIEW

Treatment involves the administration of chemotherapy to promote rapid and complete remission (CR) of the cancer while maintaining an excellent quality of life for the patient. Special drug-handling requirements and potentially severe or life-threatening adverse patient effects exist with many of chemotherapeutics; these concerns and rapid evolution of protocols warrant consultation with/ referral to an oncologist.

ACUTE AND CHRONIC TREATMENT

- Reports on single-agent chemotherapy including prednisone, L-asparaginase, cyclophosphamide, and doxorubicin describe response rates ranging from 20%-80%, with remission durations of approximately 1-6 months. While prednisone may be used as a single agent, its use prior to the initiation of other chemotherapy should be avoided, since this may decrease response rate and duration to other agents.
    - Prednisone: (30-40 mg/m^2 PO q 24 h, usually for 2 weeks, then continued at 20-40 mg/m^2 q24-48 h as long as a clinical response is seen); approximately 50% of dogs achieve a complete or partial remission for duration of 2-3 months
    - Doxorubicin: (30 mg/m^2 IV q 21 days as long as a clinical response is seen and to a recommended maximum cumulative dosage of 180 mg/ m^2) 50%-75% complete remission rate for 4-6 months
- Improved remission rates and duration are achieved with combination chemotherapy. Numerous protocols are reported with variations in scheduling, drug dosages, and dose intensity, although most utilize induction followed by maintenance chemotherapy. The most commonly used agents in these protocols include prednisone, L-asparaginase, vincristine, cyclophosphamide, and doxorubicin, although recent studies suggest that while associated with low risk of complications, the inclusion of L-asparaginase in the initial protocol does not significantly impact outcome. Complete response rates range from approximately 65%-90%, with remission durations of approximately 6-11 months (see p. 674). Options may include one of the following:
    - COP (see p. 674): 70%-75% complete remission rate for median duration of 3-6 months; *or*
    - CHOP (see pp. 673, 674): 80% complete remission rate for a median duration of 9-10 months; *or*
    - AMC protocol: 77% complete remission rate for median duration of 9 months; *or*
    - UMW protocol (see online chapter: Lymphoma Chemotherapy Treatment Tables, Dog): 84% complete remission rate for median duration of 8 months; *or*
    - ACOPA1: 76% complete remission rate for median duration of 11 months; *or*
    - ACOPA2: 65% complete remission rate for median duration of 9 months; *or*
    - VELCAP-L (see online chapter: Lymphoma Chemotherapy Treatment Tables, Dog): 69% complete remission rate for median duration of 13 months
- Recent studies suggest that discontinuous chemotherapy protocols provide remission duration that is comparable to more traditional protocols relying on induction followed by maintenance chemotherapy.
    - VELCAP-S (see online chapter: Lymphoma Chemotherapy Treatment Tables, Dog): 68% complete remission rate for median duration of 10 months
    - Modified UMW protocol: 92% complete remission rate for duration of 9 months
    - 12-week combination chemotherapy protocol: 76% complete remission rate for median duration of 8 months
    - Chemotherapy remains standard therapy; however, its use in combination with other treatment modalities, such as radiation therapy or bone marrow transplantation, may improve remission duration. Early results suggest that half-body radiation therapy (HBRT) after induction chemotherapy is well tolerated and may increase remission duration compared to conventional protocols utilizing chemotherapy alone, although a more recent study with a shorter induction chemotherapy phase failed to confirm this. Bone marrow transplantation (BMT) after induction chemotherapy may also improve outcome and approximately 25%-30% of treated dogs become long-term survivors with remission durations of 7-22 months.
    - NCACTP protocol (11-week combination chemotherapy followed by HBRT)): 78% complete remission rate for median duration of 16 months
    - 8-week combination chemotherapy followed by HBRT: *66%* complete remission rate for median duration of 8 months
- Low-grade lymphoma: given the chronic indolent course of low-grade lymphoma, oral chemotherapy consisting of chlorambucil (6-8 mg/m^2 PO q 48 h as long as clinical response is seen) and prednisone (20-40 mg/m^2 PO q 24-48 h as long as clinical response is seen) may be more appropriate than intensive injectable chemotherapy for this group of dogs.

- When a patient relapses and no longer responds to front-line chemotherapy, rescue chemotherapy can be considered. Complete response rates for relapsed lymphoma are generally lower, ranging from approximately 30%-50%, with remission durations of approximately 2-4 months (see p. 674). Options may include one of the following:
  - MOPP (Mustargen, vincristine, procarbazine, prednisone): 31% complete remission rate and 34% partial remission rate for median duration of 2 months; *or*
  - MPP (Mustargen, procarbazine, prednisone): 17% complete remission rate and 17% partial remission rate for median duration of 7.9 and 1.8 months, respectively; *or*
  - DMAC (dexamethasone, melphalan, actinomycin-D, cytosine arabinoside): 44% complete remission rate and 28% partial remission rate for median duration of 4 and 2 months, respectively; *or*
  - Doxorubicin/DTIC: 35%-80% complete remission rate for median duration of 3 months; *or*
  - L-asparaginase/CCNU/prednisone: 52% complete remission rate and 35% partial remission rate for 4 and 1.4 months, respectively; *or*
  - CCNU: 25% complete and partial remission rate for median duration of 3 months

NUTRITION/DIET

Dogs with lymphoma have alterations in carbohydrate, protein, and lipid metabolism and may benefit from a low-carbohydrate/moderate-quantity high-quality protein diet. Supplementation with poly-unsaturated fatty acids may also be of benefit.

Body Weight–to–Body Surface Area (BSA) Correlation for Dogs

Weight, kg *(lb)*	BSA (m^2)
0.5 *(1)*	0.06
1 *(2)*	0.1
2 *(4.5)*	0.15
3 *(6.5)*	0.2
4 *(9)*	0.25
5 *(11)*	0.29
6 *(13)*	0.33
7 *(15.5)*	0.36
8 *(17.5)*	0.40
9 *(20)*	0.43
10 *(22)*	0.46
11 *(24.5)*	0.49
12 *(26.5)*	0.52
13 *(28.5)*	0.55
14 *(31)*	0.58
15 *(33)*	0.6
16 *(35)*	0.63
17 *(37.5)*	0.66
18 *(39.5)*	0.69
19 *(42)*	0.71
20 *(44)*	0.74
21 *(46)*	0.76
22 *(48.5)*	0.78
23 *(50.5)*	0.81
24 *(53)*	0.83
25 *(55)*	0.85
26 *(57)*	0.88
27 *(59.5)*	0.9
28 *(61.5)*	0.92
29 *(64)*	0.94
30 *(66)*	0.96
31 *(68)*	0.99
32 *(70.5)*	1.01
33 *(72.5)*	1.03
34 *(75)*	1.05
35 *(77)*	1.07
36 *(79)*	1.09
37 *(81.5)*	1.11
38 *(83.5)*	1.13
39 *(86)*	1.15
40 *(88)*	1.17
41 *(90)*	1.19
42 *(92.5)*	1.21
43 *(94.5)*	1.23
44 *(97)*	1.25
45 *(99)*	1.26
46 *(101)*	1.28
47 *(103.5)*	1.3
48 *(105.5)*	1.32
49 *(108)*	1.34
50 *(110)*	1.36
51 *(112)*	1.39
52 *(114.5)*	1.41
53 *(116.5)*	1.43
54 *(119)*	1.44
55 *(121)*	1.46
56 *(123)*	1.48
57 *(125.5)*	1.5
58 *(127.5)*	1.51
59 *(130)*	1.53
60 *(132)*	1.55
61 *(134)*	1.57
62 *(136.5)*	1.58
63 *(138.5)*	1.6
64 *(141)*	1.62
65 *(143)*	1.64
66 *(145)*	1.65
67 *(147.5)*	1.67
68 *(149.5)*	1.68
69 *(152)*	1.7
70 *(154)*	1.72
71 *(156)*	1.74
72 *(158.5)*	1.75
73 *(160.5)*	1.77
74 *(163)*	1.78
75 *(165)*	1.8
76 *(167)*	1.81
77 *(169.5)*	1.83
78 *(171.5)*	1.84
79 *(174)*	1.86
80 *(176.5)*	1.88

POSSIBLE COMPLICATIONS OF TREATMENT

- Systemic chemotherapy targets rapidly dividing cells. Due to their rapid and often abnormal division and defective repair mechanisms, tumor cells can be destroyed by chemotherapy.
- Some normal tissues have a high rate of cell turnover (gastrointestinal mucosa, bone marrow, hair) and may be sensitive to chemotherapy, although unlike cancer cells, these normal tissues are able to repair chemotherapy-induced damage. Potential side effects of chemotherapy include gastrointestinal upset 2-4 days following treatment, myelosuppression 7-10 days after treatment, and hair loss in breeds with continuously growing haircoats (e.g., poodle, Lhasa apso, Old English sheepdog, many terrier breeds; see pp. 188 and p. 706).
- All chemotherapeutic agents are potentially toxic, most are mutagenic or teratogenic, and at least some are proven

carcinogens. Safe handling requires the use of a vertical flow hood and closed-system drug transfer device.

RECOMMENDED MONITORING

- Regular monitoring of remission status
  - CR: disappearance of all clinical evidence of cancer
  - PR: decrease in volume of cancer by ≥50% without decrease to completely normal size
  - Stable disease (SD): decrease in volume of cancer by <50% or increase in volume of cancer by <25%
  - Progressive disease (PD): increase in cancer volume by ≥25% or appearance of new lesions
- CBC (including differential) monitoring after administration of chemotherapy

PROGNOSIS AND OUTCOME

Several prognostic factors have been identified that may help predict an individual's response to treatment:

- Gender (females better than males)
- Weight (small dogs better than large dogs, although possibly influenced by dosing regimen)
- Histologic grade (high-grade lymphoma has a better complete remission rate than low-grade, although low-grade is often associated with comparable survival times with less intensive chemotherapy due to its chronic indolent nature).
- Stage and substage (I, II, or III better than IV or V; *a* better than *b)*
- Phenotype (B-cell better than T-cell)
- Hypercalcemia (a negative prognostic indicator, likely because of its association with T-cell phenotype)
- Presence of a mediastinal mass (a negative prognostic indicator, likely because of its association with T-cell phenotype)
- Administration of prior prednisone (negative prognostic indicator, possibly because of induction of multidrug resistance or masking of higher-stage disease)
- Other factors conferring a more negative prognosis: AgNOR staining, chromosomal aberrations, older age, anorexia, anemia, fever, dyspnea, thrombocytopenia, hypoalbuminemia, and chronic inflammatory disease

PEARLS & CONSIDERATIONS

COMMENTS

- Lymphoma is a common canine malignancy.
- The majority of dogs with lymphoma achieve complete remission when treated with chemotherapy, and treatment can be very rewarding for both the pet owner and veterinarian.
- A variety of prognostic factors have been identified that may help predict an individual's response to treatment and guide the decision whether or not to pursue treatment.
- An understanding of the relative efficacy and potential toxicoses of the various protocols aids in determining the best treatment protocol for an individual animal.
- Differentiation of cell type (phenotype) is mainly prognostic. B-cell lymphoma carries a more favorable prognosis than T-cell lymphoma (“B is better”), and B-cell lymphoma makes up the majority of cases of lymphoma in dogs.

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Lymphoma, Central Nervous System

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Lymphoma is a systemic malignant neoplasm of lymphoid origin. Central nervous system (CNS) lymphoma can be primary, occurring only within the CNS; or secondary, as part of multicentric disease.

SYNONYMS

Lymphosarcoma, malignant lymphoma, non-Hodgkin's lymphoma (human)

EPIDEMIOLOGY

SPECIES, AGE, SEX

- In dogs, lymphoma is the most common hematopoietic malignancy, but involvement of the CNS is uncommon. There is no breed, age, or gender predilection.
  - Lymphoma accounts for <5% of all primary CNS tumors and <10% of all CNS tumors (primary and secondary) in dogs.
- In cats, lymphoma is the most common hematopoietic malignancy, and CNS involvement is reported in 5%-10% of affected cats.
  - Lymphoma accounts for about 15% of all brain tumors and 50% of all nonosseous tumors affecting the spinal cord in cats.
  - There is no breed or gender predilection. Cats of any age can be affected; those infected with FeLV tend to be <5 years old.

RISK FACTORS

- Feline leukemia virus (FeLV)
  - The relative risk of lymphoma in FeLV-seropositive cats is 60 times that of FeLV-seronegative cats.
  - Initial studies indicated that 90% of cats with spinal lymphoma are FeLV seropositive, but as the overall incidence of FeLV-associated lymphoma has decreased (see p. 669) more recent studies report only 55% testing positive.
  - Less than 20% of cats with brain involvement are FeLV seropositive.
- Feline immunodeficiency virus (FIV)
  - The relative risk of lymphoma in cats infected with FIV is five times that of noninfected cats.
  - FIV has been reported in association with CNS lymphoma, but many cats are not tested, and the true contribution of FIV is not known.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- CNS lymphoma can be primary or secondary (see Definition).
  - In dogs, CNS lymphoma is primary in 20% of affected patients and secondary in 80%.
    - Common sites affected concurrently include lymph nodes, liver, spleen, and bone marrow.
    - Up to half of dogs with secondary CNS lymphoma do not have neurologic signs at initial diagnosis; neurologic signs instead develop when the cancer relapses.
  - In cats, up to 30% of brain lymphomas are primary, but only 15% of spinal lymphomas are primary.
    - When CNS lymphoma is secondary, common sites affected concurrently include the kidneys, bone marrow (with or without circulating lymphoblasts), liver, spleen, and mesenteric lymph nodes.
    - Most cats present with neurologic signs at initial diagnosis, but up to 50% of cats with renal lymphoma relapse with CNS involvement.
- CNS lymphoma can be categorized based on anatomic site.
  - Intracranial disease usually affects the forebrain (cerebrum and diencephalon), but cerebellar and brain-stem involvement has been reported as well. Lesions can be focal, multi-focal, or diffuse. Infiltration of the meninges can occur with or without parenchymal involvement.
  - Involvement of cranial nerves III-VIII has been reported, with V and VII being the most common. Tumors may extend along the floor of the cranial fossa to involve multiple nerves and compress the adjacent brain.

- Spinal involvement historically has been characterized by focal extradural masses, but more recent studies have shown most lesions to contain both extradural and intradural components. Additionally, up to half of affected cats will have lesions involving multiple sections of the spinal cord. Concurrent brain and spinal involvement also has been reported.
- Brachial plexus involvement may occur in both dogs and cats. Lesions may extend through the subarachnoid space and invade the spinal cord.

HISTORY, CHIEF COMPLAINT

- Most patients present with neurologic abnormalities that are acute in onset and rapidly progressive.
  - The specific neurologic abnormalities depend on the site(s) of involvement (see Physical Exam Findings below).
- Patients with secondary CNS lymphoma might have other clinical signs referable to the extraneural sites affected.

PHYSICAL EXAM FINDINGS

- Forebrain lesions are associated with seizures, mentation or behavior changes, blindness, conscious proprioceptive deficits with a normal gait, circling, and occasionally neck pain.
- Brainstem lesions are associated with gait and proprioceptive abnormalities, vestibular changes, and occasionally mentation changes (stupor or coma).
- The clinical signs associated with cranial nerve deficits depend on the specific nerve(s) affected.
- Depending on the segments involved, spinal cord lesions can result in upper motor neuron signs (stiff ataxic gait, proprioceptive deficits, spastic paresis/ paralysis, hyperreflexia) and/or lower motor neuron signs (short-strided gait, flaccid paresis/paralysis, hyporeflexia). Signs can be bilateral but usually are asymmetric.
- Brachial plexus tumors present with unilateral sensory and motor deficits based on the specific nerve roots affected.

ETIOLOGY AND PATHOPHYSIOLOGY

Etiology is unknown.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on signalment, history, neurologic abnormalities, and MRI imaging. Definitive diagnosis occasionally can be obtained from CSF analysis but usually requires cytology or preferably histopathology of a CNS lesion or, in patients with secondary CNS lymphoma, an extraneural lesion.

DIFFERENTIAL DIAGNOSIS

- Intracranial lesions: other primary brain tumors (meningioma, glioma, ependymoma, choroid plexus tumor), toxoplasmosis, neosporosis, meningoencephalitis of unknown etiology (including granulomatous meningoencephalitis), ischemic encephalopathy, feline infectious peritonitis
- Spinal lesions: intervertebral disk disease, diskospondylitis, abscess, fibro-cartilaginous emboli, infarction, spinal tumors (meningioma, glioma, nephroblastoma), vertebral tumors (osteosarcoma, chondrosarcoma, myeloma), feline infectious peritonitis virus
- Peripheral nerve lesions: peripheral nerve sheath tumor, trauma, avulsion of the brachial plexus or lumbosacral plexus, trigeminal neuritis (dogs)

INITIAL DATABASE

- Complete neurologic examination
- CBC, serum chemistry panel, urinalysis
- FeLV/FIV serology (cats)
- Thoracic radiographs, abdominal ultrasound, bone marrow aspiration: screening for evidence of lymphoma in other organ systems might allow a diagnosis to be reached rapidly and less invasively.

ADVANCED OR CONFIRMATORY TESTING

- MRI is the imaging modality of choice for CNS lesions.
  - Intracranial lesions can be intraaxial or extraaxial. Spinal lesions can appear extradural, intradural but extramedullary, or occasionally intramedullary.
  - Lesions typically are hyperintense on T2-weighted images and hypointense to isointense on T1-weighted images.

Contrast enhancement is strong but often patchy.
- CT or CT/myelogram (for spinal lesions) can be considered if MRI is not available.
- Radiography:
  - Skull radiographs are not routinely recommended.
  - Plain vertebral radiographs usually are normal, but purely lytic lesions occasionally are seen. Additionally, radiographs can be helpful for ruling out osseous tumors.
  - Myelography accurately identifies mass lesions and can help determine extradural, intradural, or intramedullary involvement.
- Cerebrospinal fluid (CSF) analysis:
  - CSF consistently has an elevated protein count.
  - Nucleated cell count can be normal or increased. A mixed-cell pleocytosis is most common.
    - Neoplastic lymphoblasts are identified in <50% of affected patients.
- To reach a definitive diagnosis, histopathologic or cytologic analysis is required. For CNS lesions, this usually requires surgery or specialized equipment (fluoroscopy, stereotactic biopsy [see p. 1214]). Whenever possible, obtaining samples from other affected organs is preferable.

TREATMENT

TREATMENT OVERVIEW

Optimum treatment regimens are not yet known. Definitive treatment centers around systemic chemotherapy, but drug selection is controversial owing to concerns about the blood-brain barrier. Additionally, surgery and radiation therapy play more prominent roles to help rapidly resolve neurologic abnormalities.

ACUTE GENERAL TREATMENT

- The majority of CNS lymphomas are secondary, and systemic chemotherapy remains the mainstay of therapy.
  - The protocols most commonly used to treat lymphoma include the drugs L-asparaginase, vincristine, cyclophosphamide, doxorubicin, and prednisone. (Several protocols exist; see pp. 673 and 674 for dosages.)
  - For tumors infiltrating the brain or spinal cord parenchyma, the ability of drugs to penetrate the blood-brain barrier is of concern. Inclusion of CCNU, cytosine arabinoside, and/ or procarbazine—drugs that cross this barrier and achieve therapeutic levels within the CNS—is reasonable but controversial.
    - Tumor microvasculature likely has greater permeability than the normal blood-brain barrier.
    - These drugs only have modest activity against other more common forms of lymphoma.
  - Consultation with an oncologist for the most current treatment recommendations is indicated.
  - Single-agent prednisone may be used as a palliative treatment.
- Radiation therapy used in combination with chemotherapy may improve outcome by rapidly shrinking compressive tumors.
  - Radiation treatment fields may be focal but more commonly include the entire brain and spinal cord.
- Surgery is indicated only when a biopsy is needed to confirm the diagnosis of lymphoma, or when rapid decompression of the brain or spinal cord is needed and radiation therapy is unavailable.

PROGNOSIS AND OUTCOME

- There is little information regarding the prognosis for dogs with CNS lymphoma. Treatment outcomes have been reported for very few dogs, and the protocols used were less aggressive than those currently recommended.
  - When treated with systemic chemotherapy, with or without radiation therapy, dogs have had reported survival times ranging from 1-3 months.
  - In the author's experience, when dogs present with CNS signs at the time of initial diagnosis, survival times of up to 1 year or more are possible. In contrast, when dogs first present with CNS signs at the time of relapse, prognosis is very guarded, and survival times are almost uniformly <l-2 months.
- Several recent studies that included cats with various forms of lymphoma (including CNS involvement) have not shown anatomic location to be a prognostic factor (see p. 669).
  - Earlier studies looking specifically at cats with brain lymphoma reported survival times of up to 7 months. Cats treated with both radiation therapy and chemotherapy tended to have a better outcome.
  - Earlier studies looking specifically at cats with spinal lymphoma reported remission rates of only 50% and median response durations of only 3-5 months. However, treatment protocols were not as aggressive as those currently recommended. Additionally, a higher percentage of the cats in those studies were FeLV seropositive compared to what is seen today.

PEARLS & CONSIDERATIONS

COMMENTS

If a cat tests positive for FeLV or FIV, the owner should be educated about these diseases, and all other cats in the household should be tested.

SUGGESTED READING

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Lymphoma, Cat (Multicentric)

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

A systemic malignant neoplasm of lymphoid origin

SYNONYMS

Lymphosarcoma, malignant lymphoma, non-Hodgkin's lymphoma (human)

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Lymphoma is the most common hematopoietic malignancy in the cat.
- Disease forms/anatomic presentation has changed over the past 25 years, coincident with decreases in feline leukemia virus (FeLV) infection rates and FeLV-associated types of lymphoma.
- May develop at any age
- Siamese cats may be at increased risk for developing certain forms of lymphoma.

RISK FACTORS

- FeLV, and possibly feline immunodeficiency virus, infection are risk factors for the development of lymphoma.
  - FeLV status influences age and anatomic location at which lymphoma develops.
- Household exposure to environmental tobacco smoke (i.e., “second-hand smoke”) increases the risk.
  - In one study, cats exposed to tobacco smoke had a 2.4-fold increased risk of lymphoma.
  - Risk increased with duration of exposure, years of exposure, and number of smokers in the house.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Histologic grade:
  - High-grade, or lymphoblastic, lymphoma: most common; rapid onset and progression; affected cells are large and similar in appearance to lymphoblasts.
  - Low-grade, or lymphocytic, lymphoma: most often reported with gastrointestinal (GI) lymphoma; chronic insidious onset; affected cells are well differentiated and similar in appearance to small lymphocytes.
- Anatomic distribution:
  - Multicentric: typically lymph node, spleen, or liver involvement; presenting signs and physical exam findings vary with organ(s) affected.
  - Alimentary (GI) (see p. 678): older cats; majority are FeLV negative; presenting signs include anorexia, weight loss, vomiting, diarrhea; physical examination may reveal palpable abdominal mass.
  - Mediastinal: young cats; most are FeLV infected; thymus, mediastinal and sternal lymph nodes may be involved; presenting signs include dyspnea, tachypnea; physical exam may reveal a noncompressible anterior mediastinum and also be suggestive of pleural effusion.
  - Renal: presenting sign is acute renal failure which may completely resolve with chemotherapy; physical exam reveals marked bilateral renomegaly; high rate of central nervous system relapse.
  - Spinal: affected cats are often FeLV infected; presenting sign is hind limb paraparesis; many will have malignant lymphoblasts concurrently in bone marrow (see pp. 671 and 1037).
  - Nasal: unique form of lymphoma, as it is often localized and may be treated best with radiation therapy.

HISTORY, CHIEF COMPLAINT

- Highly variable presentation (see Disease Forms/Subtypes above)
- Generalized peripheral lymphadenopathy, as is common in dogs with lymphoma, is rare in cats with lymphoma.

PHYSICAL EXAM FINDINGS: Physical exam findings vary and are reflective of organs involved (see Disease Forms/Subtypes

above).

ETIOLOGY AND PATHOPHYSIOLOGY

- Rapid onset and disease progression over days to weeks
- Low-grade lymphoma, as reported with alimentary disease, may have chronic history.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on the detection of a mass lesion in an affected organ or site with associated clinical signs; confirmation generally begins with aspiration cytology of the mass or site.

DIFFERENTIAL DIAGNOSIS

- Other neoplasms (e.g., leukemia, mast cell tumor)
- Multicentric: other neoplasms (e.g., mast cell tumor), cholangitis-cholangiohepatitis and other hepatopathies, pancreatitis
- Mediastinal: other neoplasms (e.g., thymoma, mesothelioma), heart disease, pyothorax, feline infectious peritonitis, diaphragmatic hernia
- Renal: acute renal failure, other renal failure, poly cystic kidney disease
- Nasal: other neoplasms (e.g., adenocarcinoma), rhinitis, inflammatory polyps, cryptococcosis

INITIAL DATABASE

- CBC: to identify anemia, thrombocytopenia and/or neutropenia due to lymphoblast infiltration in the marrow or secondary to immune-mediated destruction; to identify the presence of circulating lymphoblasts
- Serum biochemistry panel: to identify liver or renal abnormalities that may develop secondary to organ involvement and may alter ability to metabolize or eliminate chemotherapeutic drugs
- Urinalysis ± urine culture: to further evaluate renal function and to identify any occult urinary tract infection before chemotherapy
- FeLV serology: FeLV antigenemia is associated with certain forms of lymphoma and may be prognostic (see Prognosis and Outcome below).
- Aspiration cytologic evaluation of affected organ(s) or site(s): to identify lymphoblasts

ADVANCED OR CONFIRMATORY TESTING

- If lymphoma is identified cytologically, the following tests are indicated as part of routing staging, prior to initiation of chemotherapy:
    - Biopsy of affected organ(s): for definitive diagnosis and histologic grading
    - Thoracic radiographs: to identify lymphadenopathy, mediastinal mass, pleural effusion, pulmonary involvement
    - Abdominal ultrasound examination: to identify changes consistent with hepatic, splenic, renal, or gastrointestinal involvement, lymphadenopathy, or other sites of lymphoma
    - Bone marrow aspiration cytology: to identify marrow involvement and/or develop better understanding of etiology of any cytopenias
    - Phenotyping (flow cytometry, immunocytochemistry, immunohistochemistry, PCR): to determine B- versus T-cell origin
- If financial restrictions prohibit these tests, one may elect to omit certain tests (e.g., if CBC results are unremarkable, one may elect not to perform a bone marrow aspirate), as long as the client understands that sites of disease may be missed, and staging and follow-up monitoring will be less certain.

TREATMENT

TREATMENT OVERVIEW

Treatment involves the administration of chemotherapy to achieve complete remission (CR) while maintaining a good quality of life for the patient. Special drug-handling requirements and potentially severe or life-threatening adverse patient effects exist with many chemotherapeutics; these concerns and rapid evolution of protocols warrant consultation with/referral to an oncologist.

Body Weight–to–Body Surface Area (BSA) Correlation for Cats

Weight, kg (*lb*)	BSA (m^2)
2 *(4.5)*	0.159
2.5 *(5.5)*	0.184
3 *(6.5)*	0.208
3.5 *(7.75)*	0.231
4 *(8.75)*	0.252
4.5 *(10)*	0.273
5 *(11)*	0.292
5.5 *(12.25)*	0.311
6 *(13.25)*	0.33
6.5 *(14.25)*	0.348
7 *(15.5)*	0.366
7.5 *(16.5)*	0.383
8 *(17.5)*	0.4
8.5 *(18.75)*	0.416
9 *(19.75)*	0.432
9.5 *(21)*	0.449
10 *(22)*	0.464

ACUTE AND CHRONIC TREATMENT

- Reports on single-agent chemotherapy, including prednisone, doxorubicin, and mitoxantrone describe response rates ranging from 9%-40% with remission durations ranging from 3-12 months. Prednisone may be used as a single agent, but its use before the initiation of other chemotherapy should be avoided, as this may decrease rate and duration of response to other agents.
  - Prednisone/prednisolone (20-40 mg/ m^2 PO q 24-48 h as long as a clinical response is seen): mean survival of 1 month with spinal lymphoma
  - Doxorubicin (25 mg/m^2 or 1 mg/kg IV q 21 days as long as a clinical response is seen, provided there is no evidence of renal toxicosis and to a recommended maximum cumulative dosage of 180-240 mg/m^2): 26% complete remission rate for median duration of 3 months
- Improved remission rates and duration are achieved with combination chemotherapy. Numerous protocols are reported with variations in scheduling, drug dosages, and dose intensity, although most utilize induction followed by maintenance chemotherapy. The most commonly used agents in these protocols include prednisone, L-asparaginase, vincristine, cyclophosphamide, and doxorubicin (see p. 673). Complete response rates range from approximately 50%-75%, with remission durations of approximately 5-9 months. Options may include one of the following:
  - Cyclophosphamide, vincristine (Oncovin), prednisone (COP; see p. 673): approximately 50% complete remission rate for median duration of 3-8 months; *or*
  - Combination (cyclophosphamide, vincristine, prednisone, L-asparaginase, doxorubicin; see p. 673): approximately 75% complete remission rate for median duration of 7-9 months; *or*
  - COP induction + doxorubicin maintenance: 47% complete remission rate for median duration of 9 months; *or*
  - Combination (cyclophosphamide, vincristine, prednisone, L-asparaginase, doxorubicin, methotrexate [see online chapter: Lymphoma Chemotherapy Treatment Tables, Cat]): 38%-74% complete remission rate for median duration of 9-22 months
- When a patient relapses and no longer responds to frontline chemotherapy, rescue chemotherapy can be considered, with protocols such as MOPP (rnechlorethamine, vincristine, procarbazine, and prednisolone) or CCNU (50-60 mg/m^2 PO every

3-6 weeks, with dosing interval based on weekly CBC monitoring and individual patient's neutrophil nadir)

- Chemotherapy remains standard therapy; however, its use in combination with other treatment modalities, such as radiation therapy, may improve outcome. Studies are underway to evaluate the normal tissue tolerance and potential benefit of radiation therapy after a short course of induction chemotherapy in cats with lymphoma.
- Given the chronic indolent course of low-grade lymphoma, oral chemotherapy consisting of chlorambucil and prednisone may be more appropriate than intensive injectable chemotherapy for this group of cats.
    - Chlorambucil (6-8 mg/m^2 PO q 48 h as long as a clinical response is seen) and prednisone (20-40 mg/m^2 PO q 24-48 h as long as a clinical response is seen): 56%-69% complete remission rate for median duration of 21-30 months in cats with low-grade alimentary lymphoma.
- Radiation therapy may be considered for nasal lymphoma.
    - Disease-free intervals of 6-69 months are reported after radiation therapy.
    - It has been suggested that radiation therapy, chemotherapy, or a combination of both modalities yield comparable survival times.

POSSIBLE COMPLICATIONS

- Systemic chemotherapy targets rapidly dividing cells. Due to their rapid and often abnormal division and defective repair mechanisms, tumor cells can be destroyed by chemotherapy.
- Some normal tissues have a high rate of cell turnover (gastrointestinal mucosa, bone marrow, hair) and may be sensitive to chemotherapy, although unlike cancer cells, these normal tissues are able to repair chemotherapy induced damage. Potential side effects of chemotherapy include gastrointestinal upset 2-4 days after treatment, myelosuppression 7-10 days after treatment, and loss of whiskers (see p. 188).
- All chemotherapeutic agents are potentially toxic, most are mutagenic or teratogenic, and at least some are proven carcinogens. Safe handling requires the use of a vertical flow hood and closed-system drug transfer device.

RECOMMENDED MONITORING

- Regular monitoring of remission status
    - Complete remission: disappearance of all clinical evidence of cancer
    - Partial remission: decrease in volume of cancer by ≥50% without decrease to completely normal size
    - Stable disease: decrease in volume of cancer by <50% or increase in volume of cancer by <25%.
    - Progressive disease: increase in cancer volume by ≥25% or appearance of new lesions
- CBC (including differential) monitoring if administration of chemotherapy

PROGNOSIS AND OUTCOME

Several prognostic factors may help predict an individual's response to treatment:

- Stage
- Substage (*a* is better than *b)*
- Anatomic site of disease (mediastinal lymphoma may have a higher complete remission rate than other anatomic sites; nasal lymphoma has among the longest survival times).
- Histologic grade (low-grade lymphoma is often associated with longer remission and survival times with less intensive chemotherapy due to its chronic indolent nature).
- FeLV status; FeLV status does not appear to influence rates of response to chemotherapy, but FeLV-positive cats have significantly shorter remission and survival times, possibly due in part to concurrent FeLV-related diseases.

PEARLS & CONSIDERATIONS

COMMENTS

- Lymphoma is a common feline malignancy.
- The majority of cats achieve complete or partial remission when treated with chemotherapy, and treatment can be rewarding for both the pet owner and veterinarian.
- A variety of prognostic factors have been identified that may help predict an individual's response to treatment and guide the decision whether or not to pursue treatment.
- An understanding of the relative efficacy and potential toxicoses of the various protocols aids in determining the best treatment protocol for an individual patient.

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Lymphoma Chemotherapy Treatment Tables, Cat

Client Education Sheet Available on Website

CBC: to identify cytopenias that could contraindicate treatment. CTX: cyclophosphamide, 200–250 mg/m^2 IV or PO single weekly dose. VCR: vincristine, 0.5 mg/m^2 IV. PRED: prednisoloe, 5–10 mg PO q 24 h continuously.*COP,* Cyclophosphamide, vincristine (Oncovin), and prednisolone.*Continue with 3-week treatment cycle as long as complete remission persists or for 1 year from start of protocol.

COP Protocol for Cats

Week	1	2	3	4	5	6	7	8	9	10*
CBC	•	•	•	•			•			•
CTX	•			•			•			•
VCR	•	•	•	•			•			•
PRED	•	•	•	•	•	•	•	•	•	•

CBC: to identify cytopenias that could contraindicate treatment. PRED: prednisolone, 5–10 mg PO q 24 h continuously weeks 1–8, then tapered and discontinued. L-ASP: L-asparaginase, 400 IU/kg SQ or IM. VCR: vincristine, 0.5 mg/m^2 IV. CTX: cyclophosphamide, 200 mg/m^2 IV. DOX: doxorubicin, 20–25 mg/m^2 IV. Weeks 1–9 are induction chemotherapy, and weeks 11–25 are maintenance chemotherapy. The maintenance chemotherapy given weeks 11–17 is repeated weeks 19–25, after which treatment is stopped.Body surface area (m^2): see Lymphoma, Cat (Multicentric), table (p. 669).*CHOP,* Cyclophosphamide, hydroxydaunorubicin (doxorubicin), vincristine (Oncovin), and prednisolone.

CHOP Protocol for Cats

Week	1	2	3	4	5	6	7	8	9	11	13	15	17
CBC	•	•	•	•	•	•	•	•	•	•	•	•	•
PRED	•	•	•	•	•	•	•	•					
l-ASP	•												
VCR	•		•			•		•		•		•	
CTX		•					•				•		
DOX				•					•				•

CBC Monitoring Guidelines: Cats

Dosage Reduction:

If neutrophils <1000 cells/mcL on any CBC → decrease dosage of causative agent by 25% for future treatments, begin empirical prophylactic antibiotics (e.g., amoxicillin-clavulanate 11-22 mg/kg PO q 12 h), and consider additional supportive care and diagnostic testing if cat is overtly ill.

If platelets <50,000 cells/mcL on any CBC → decrease dosage of causative agent by 25% for future treatments.

Treatment Delay:

If neutrophils <2000 cells/mcL on day treatment is due → postpone treatment, recheck CBC in 3-7 days, and resume treatment when neutrophil count is >2000 cells/mcL.

If platelets <50,000 cells/mcL on day treatment is due → postpone treatment, recheck CBC in 3-7 days, and resume treatment when platelet count is >50,000 cells/mcL.

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Lymphoma Chemotherapy Treatment Tables, Dog

Client Education Sheet Available on Website

COP Protocol for Dogs

Week	1	2	3	4	5	6	7	8	9	10*
CBC	•	•	•	•			•			•
CTX	•			•			•			•
VCR	•	•	•	•			•			•
PRED	•	•	•	•	•	•	•	•	•	•

CBC: to identify cytopenias that could contraindicate treatment. CTX: cyclophosphamide, 200–250 mg/m^2 IV or PO single weekly dose (give furosemide, 2 mg/kg SQ or PO with cyclophosphamide; if cystitis occurs, substitute cyclophosphamide with chlorambucil at 1.4 mg/kg PO q 3 weeks [same interval as intended for cyclophos-phamide]). VCR: vincristine, 0.7 mg/m^2 IV. PRED: prednisone, 30 mg/m^2 PO q 24 h for 7 days, then 30 mg/m^2 PO q 48 h continuously.*COP,* Cyclophosphamide, vincristine (Oncovin), and prednisone.*Continue with 3-week treatment cycle as long as complete remission persists or for 1 year from start of protocol.

CHOP Protocol for Dogs

Week	1	2	3	4	5	6	7	8	9	11	13	15	17
CBC	•	•	•	•	•	•	•	•	•	•	•	•	•
PRED	•	•	•	•									
L-ASP	•												
VCR	•		•			•		•		•		•	
CTX		•					•				•		
DOX				•					•				•

CBC: to identify cytopenias that could contraindicate treatment. PRED: prednisone, 2 mg/kg PO q 24 h for 7 days (week 1), then 1.5 mg/kg PO q 24 h for 7 days (week 2), then 1 mg/kg PO q 24 h for 7 days (week 3), then 0.5 mg/kg PO q 24 h for 7 days (week 4). l-ASP: l-asparaginase, 400 IU/kg SQ or IM, to a maximum dose of 10,000 IU per administration. VCR: vincristine, 0.5–0.7 mg/m^2 IV. CTX: cyclophosphamide, 200 mg/m^2 IV single weekly dose (give furosemide, 2 mg/kg IV or PO with cyclophosphamide; if cystitis occurs, stop cyclophosphamide and begin chlorambucil at 1.4 mg/kg PO at the same interval as intended for cyclophosphamide). DOX: doxorubicin, 30 mg/m^2 IV for dogs weighing >15 kg or 1 mg/kg IV for dogs <15 kg. Weeks 1–9 are induction chemotherapy, and weeks 11–25 are maintenance chemotherapy. The maintenance chemotherapy given weeks 11–17 is repeated weeks 19–25, after which treatment is stopped.*CHOP,* Cyclophosphamide, hydroxydaunorubicin (doxorubicin), vincristine (Oncovin), and prednisone.

CBC Monitoring Guidelines: Dogs

Dosage Reduction:

If neutrophils <1000 cells/mcL on any CBC γ decrease dosage of causative agent by 25% for future treatments, begin empirical prophylactic antibiotics (e.g., amoxicillin-clavulanate 11-22 mg/kg PO q 12 h for 7 days), and consider additional supportive care and diagnostic testing if animal is overtly ill.

If platelets <50,000 cells/mcL on any CBC γ decrease dosage of causative agent by 25% for future treatments.

Treatment Delay:

If neutrophils <2000 cells/mcL on day treatment is due γ postpone treatment, recheck CBC in 3-7 days, and resume treatment when neutrophil count is >2000 cells/mcL.

If platelets <50,000 cells/mcL on day treatment is due γ postpone treatment, recheck CBC in 3-7 days, and resume treatment when platelet count is >50,000 cells/mcL.

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Lymphedema

BASIC INFORMATION

DEFINITION

Lymphedema is a swelling of protein-rich interstitial fluid caused by impaired lymphatic function. The condition can be localized, regional, or widespread. Lymphedema is classified as primary (developmental) or secondary in origin.

SYNONYMS

While not specific for lymphedema, other terms for edematous states include anasarca, pitting edema, subcutaneous edema (see p. 333), and ventral edema.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs or cats. Primary lymphedema: puppies and young dogs. Secondary lymphedema: any age.

GENETICS & BREED PREDISPOSITION: Has been observed in English bulldogs, Labrador retrievers, and others. Idiopathic lymphedema may be more common in giant breeds such as Irish wolfhounds.

RISK FACTORS: Primary lymphedema is developmental in origin; diseases that obstruct, invade, inflame, or destroy normal lymphatic drainage predispose to secondary lymphedema. Lymphatic filariasis associated with infection by *Brugia pahangi* could be a consideration for lymphedema in tropical environments.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Localized involving a limb, intermandibular space, or ventral thorax
- Bilateral pelvic or forelimb lymphedema
- Generalized lymphedema (that may include pleural or peritoneal effusions)

HISTORY, CHIEF COMPLAINT

- In developmental lymphedema, the typical presentation is nonpainful, bilateral, pitting edema of the pelvic limbs. Generalized fluid retention is rare.
- In secondary lymphedema, there is nonpainful or painful swelling of the limb(s), ventral thorax, or intermandibular space.
- In generalized cases, respiratory distress may be related to pleural effusion.

PHYSICAL EXAM FINDINGS

- Nonpainful or painful swelling(s). In primary lymphedema, pain typically indicates secondary infection.
- Regional lymph nodes may be underdeveloped or enlarged.
- Isolated swellings with pain or inflammation suggest associated cellulitis, trauma, or neoplasia.
- Intermandibular edema with normal jugular venous pressure is suggestive of lymphatic obstruction; with jugular venous distension, vena caval thrombosis or compression is more likely.
- Chronic lymphedema or that associated with lymphangitis may produce firm, nonpitting swellings, skin ulceration, or oozing of serum across the skin.
- Lymphedema related to lymphangiosarcoma can be associated with ecchymotic hemorrhage.

ETIOLOGY AND PATHOPHYSIOLOGY

- Lymph is produced by ultrafiltration of capillary blood and normally returns to the bloodstream across the venous end of capillaries and via lymphatic channels and lymph nodes. Lymph traverses the thoracic or lymphatic ducts to reach the systemic venous circulation.
- Malformation of the lymphatic system, lymphangitis, widespread obstruction to lymph drainage, or infiltration of regional lymph nodes can cause accumulation of high-molecular-weight protein and edema. Interstitial or subcutaneous protein and fluid accumulation can initiate an inflammatory reaction and fibrosis.
- Progressive accumulation of lymphatic fluid leads to palpable swelling and impairs oxygen delivery, wound healing, and local

resistance to infection.
- Gravitational forces and the tightness of the skin influence the accumulation of tissue lymph.
- Lymphedema may be variable, pitting, nonpitting, or fibrotic in character. These are well-recognized stages of lymphedema in human patients and also may be observed in dogs or cats with chronic lymphatic disease.
- Strictly speaking, lymphedema stems from impaired lymphatic drainage. Subcutaneous edema also can be caused by reduced capillary oncotic pressure (hypoalbuminemia), increased vascular permeability, or elevated capillary hydrostatic pressure from venous obstruction, arteriovenous (AV) fistula, or right-sided congestive heart failure.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on nonpainful regional pitting edema and exclusion of other potential causes.

DIFFERENTIAL DIAGNOSIS

Lymphedema must be distinguished from other causes of tissue swelling, including:

- Overinfusion of intravenous crystalloid fluids; migration of subcutaneous fluids
- AV fistula
- Venous obstruction or thrombophlebitis
- Hypoproteinemia
- Localized infection
- Vasculitis
- Insect bites
- Localized or generalized allergic reactions
- Postinfarction edema
- Right-sided congestive heart failure
- Cellulitis, abscess, or localized infection
- Infectious or immune-mediated skin disorders with secondary edema
- Chylous effusion
- Localized neoplasm
- Lymphatic tumors: lymphangioma and lymphangiosarcoma

INITIAL DATABASE

- Careful inspection of regional systemic veins
- Auscultation over swellings for the bruit (continuous murmur) of an AV fistula
- Rectal examination to identify caudal abdominal or pelvic mass lesions
- CBC, serum biochemical panel, and urinalysis
- Chest radiographs: evaluate for heart disease, mediastinal mass, and pleural effusion
- Abdominal radiographs or ultrasonography: identify iliac lymphadenopathy, or pelvic mass lesion, or hepatosplenomegaly
- Cytologic examination of regional lymph nodes or tissue fluid
- Biopsy of affected tissues to rule out lymphangiosarcoma

ADVANCED OR CONFIRMATORY TESTING

- Culture and sensitivity (in cases of lymphangitis)
- Duplex Doppler ultrasonography to identify venous obstruction or AV fistula
- Serologic tests or PCR for tickborne infections, including *Bartonella* spp.
- Fluid and serum triglyceride concentrations when there is pleural or peritoneal effusion; elevated fluid triglycerides suggest a diagnosis of chylous effusion.
- Lymphoscintigraphy or lymphangiography: these advanced radiologic methods may demonstrate normal or abnormal lymphatic drainage.
- The patent blue violet dye test has been used to diagnose congenital lymphedema in dogs and cats.
- Computed tomography to identify regional mass lesions

TREATMENT

TREATMENT OVERVIEW

- Correct the underlying disorder if possible; for example, treat a malignancy with chemotherapy.
- Prevent or treat infections.
- Protect swollen tissues from injury; consider lightly compressive bandages.
- Improve macrophage function to reduce protein-rich edema.
- Treat associated pain.

ACUTE GENERAL TREATMENT

- Antibiotic treatment of infections
- Pain management for tense lymphedema or infection

CHRONIC TREATMENT

- Soft compression bandages (may not be well tolerated; discontinue if uncomfortable)
- Controlled exercise to enhance venous return.
- Long-term use of benzopyrones, such as rutin, to enhance macrophage function and proteolysis
- Advanced surgical techniques are of uncertain value: consult with a surgical specialist.

POSSIBLE COMPLICATIONS

Recurrent infection is likely even in cases of resolved primary lymphedema.

RECOMMENDED MONITORING

- Limb size, firmness, and associated pain
- Use of affected limbs
- Changes in subcutaneous swellings

PROGNOSIS AND OUTCOME

- Spontaneous resolution or marked improvement in some dogs with primary lymphedema
- Death or euthanasia related to complications of lymphedema
- Spontaneous death in puppies with generalized anasarca

PEARLS & CONSIDERATIONS

COMMENTS

- In primary lymphedema, the swelling is typically caudal and bilateral; regional lymph nodes are smaller or absent (whereas in healthy puppies superficial lymph nodes are prominent).
- A subtle pleural effusion in a dog with limb edema is suggestive of a more generalized lymphatic disorder (or severe hypoalbuminemia).
- Lymphangioma and lymphangiosarcoma can results in severe lymphedema unresponsive to treatment.
- When pelvic limb edema is caused by right heart failure, also expect ascites.
- Consultation with a radiologist may be informative regarding advanced imaging methods.

CLIENT EDUCATION

- Observe the swelling for discharge, odor, or inability to use a limb.
- Constitutional signs (anorexia, lethargy, fever) should prompt reevaluation.

SUGGESTED READING

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Lymphangiectasia/Protein-Losing Enteropathy

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

- Intestinal lymphangiectasia: abnormality of the intestinal lacteals (lymphatics); commonly results in protein-losing enteropathy
- Protein-losing enteropathy (PLE): gastrointestinal (GI) disease or dysfunction, causing loss of protein into the GI tract; results in hypoalbuminemia +/− hypoglobulinemia
    - Intestinal protein loss can occur with both acute and chronic GI diseases.
    - The term *PLE* is usually reserved for patients with chronic disorders.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs are affected more commonly than cats.
- Can occur at any age
    - Breed-associated disorders are usually reported in young or middle-aged dogs.

GENETICS & BREED PREDISPOSITION

- Basenji: predisposed to immunoproliferative enteropathy
- Norwegian Lundehund: predisposed to intestinal lymphangiectasia
- Soft-coated wheaten terrier: predisposed to PLE with protein-losing nephropathy
- Yorkshire terrier: predisposed to intestinal lymphangiectasia +/− concurrent inflammatory bowel disease
- German shepherd dog, rottweiler, Chinese shar-pei: all appear predisposed to PLE.

RISK FACTORS: Dependent on underlying cause of PLE

CONTAGION & ZOONOSIS: Infectious causes are uncommon in patients with chronic PLE, although salmonellosis should be considered in febrile or immunocompromised patients. Fungal infections of the GI tract (e.g., *Histoplasma capsulatum)* may result in PLE, but affected animals are not directly contagious.

ASSOCIATED CONDITIONS & DISORDERS

- Inflammatory bowel disease (IBD)
- Lymphatic compromise/dysfunction:
    - Confined to the GI tract (i.e., intestinal lymphangiectasia)
    - Generalized
- Adverse food reactions (e.g., gluten-sensitive enteropathy)
- GI infection (e.g., histoplasmosis, salmonellosis, hookworms)
- Intestinal neoplasia (e.g., lymphoma, adenocarcinoma)
- Mechanical enteropathy (e.g., chronic foreign body, chronic intussusception)
- GI ulceration (e.g., NSAID-induced, hookworm infection)
- Venous hypertension:
    - Portal vein thrombosis or hypertension
    - Severe right-sided cardiac compromise
- Patients with PLE may present with complications from hypoproteinemia rather than overt GI disease:
    - Ascites, pleural effusion, pitting edema
    - Thromboembolic disease

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Patients may show no overt clinical signs; hypoalbuminemia may be an incidental finding.
- Weight loss commonly occurs and may be the only clinical sign.
- Intermittent vomiting

- Chronic small bowel diarrhea may or may not be present.
- Abdominal distension may be noted if ascites is present.
- Respiratory distress may occur with pleural effusion or pulmonary thromboembolism.
- Thromboembolic complications may cause central neurologic signs or limb dysfunction.

PHYSICAL EXAM FINDINGS

- Weight loss, emaciation
- Thickened intestinal loops may be noted on abdominal palpation.
- Ascites (generally noted if serum albumin <1.5 g/dL)
- Peripheral edema (may be present if serum albumin <1.5 g/dL)
- Dyspnea or tachypnea with pleural effusion and/or pulmonary thromboembolism
- Soft stool may be noted on rectal examination.

ETIOLOGY AND PATHOPHYSIOLOGY

- Hypoalbuminemia occurs when the loss of protein from the GI tract exceeds albumin synthesis by the liver.
- Several mechanisms (either alone or in combination) contribute to intestinal protein loss:
  - Abnormalities of the intestinal lymphatics cause leakage of lymph across the intestinal mucosa.
  - Increased intestinal permeability permits protein loss across the mucosa.
  - Intestinal mucosal erosion and ulceration results in protein loss into the GI lumen.
  - Elevated venous pressures result in protein leakage into the intestine.
- Hypoalbuminemia results in decreased oncotic pressure and leakage of fluid into interstitial spaces, causing peripheral edema, ascites, and/or pleural effusion.
- Loss of anticoagulant proteins, including antithrombin III, results in a prothrombotic state and predisposes patients to thromboembolic disease.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Preliminary diagnostics are used for confirming intestinal protein loss in a hypoalbuminemic patient. More advanced diagnostic testing then defines the cause of GI dysfunction and provides a targeted treatment plan.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis for hypoalbuminemia:

- Protein-losing nephropathy (PLN):
  - Glomerulonephritis
  - Glomerular amyloidosis
- Liver disease resulting in decreased albumin synthesis
- Other causes of albumin loss from the vascular space:
  - Peritonitis, pleuritis, vasculitis
  - Severe dermal burns or exudative dermatitis
- Protein malnutrition

INITIAL DATABASE

- Serum biochemistry profile:
  - Hypoalbuminemia is the hallmark of all PLEs.
  - Globulins are often decreased, resulting in panhypoproteinemia, but this finding is variable
    - Inflammatory GI diseases may cause serum globulins to increase.
  - Hypocholesterolemia is commonly noted in patients with PLE.
  - Hypocalcemia (both ionized and total) and hypomagnesemia also are common findings in patients with lymphangiectasia.
  - Liver enzymes may be slightly elevated with various GI diseases:
    - Serum bile acids are required to rule out hepatic insufficiency as cause of hypoalbuminemia.
- CBC:
  - Lymphopenia is commonly noted in dogs with lymphangiectasia.
  - Anemia may be noted; may indicate:
    - GI hemorrhage (anemia may be regenerative with acute blood loss or microcytic with chronic blood loss).

        - Chronic inflammatory disease may result in a nonregenerative anemia.
- Urinalysis:
    - Required to rule out proteinuria as cause of hypoalbuminemia.
    - Urine protein/creatinine ratio will help determine significance of any proteinuria:
        - Hypoalbuminemia due to PLN is associated with protein/creatinine ratios >5.
- Abdominal radiographs:
- May be unremarkable or demonstrate loss of serosal detail secondary to ascites
    - Underlying cause, such as an abdominal mass or foreign body, may be apparent.
- Thoracic radiographs:
    - May be unremarkable or reveal pleural effusion due to hypoalbuminemia.
    - Changes related to underlying etiology, such as pericardial disease or fungal disease, may be seen.
- Abdominal ultrasound:
    - Ascites may be noted if serum albumin <1.5 g/dL.
    - Intestinal walls may be thickened, +/− loss of normal layering.
    - Focal intestinal lesions may be noted in areas inaccessible via endoscopy.
    - Lymphadenopathy is commonly detected; suggests inflammatory, fungal, or neoplastic disease.
- Fluid analysis of ascites or pleural effusion: consistent with pure transudate
- Fecal evaluation (centrifuged flotation and saline preparation): for parasite and pathogen detection

ADVANCED OR CONFIRMATORY TESTING

- Canine fecal (α1-proteinase inhibitor can be assayed to confirm the presence of PLE:
    - (α1-proteinase inhibitor is a protein similar in size to albumin.
    - It is resistant to digestion by endogenous and bacterial proteinases.
    - It can therefore be measured in the feces to confirm PLE.
    - Three voided fecal samples are collected into calibrated tubes (available from the GI Lab, Texas A&M University; http://www.cvm.tamu.edu/gilab/assays/index.shtml).
    - Primary use is confirming PLE in the presence of coexisting PLN or liver disease.
- Rectal scrapings can be examined cytologically for histoplasmosis or lymphoma (see p. 1334).
- Serum folate and cobalamin concentrations should be measured:
    - Low folate suggests proximal intestinal disease.
    - Low cobalamin suggests distal small-intestinal disease or changes in GI microflora.
- Intestinal biopsies are necessary to establish a specific diagnosis in patients with PLE:
    - Tissue specimens may be collected via endoscopy, laparoscopy, or laparotomy.
    - General anesthesia carries substantial risk in severely hypoalbuminemic patients:
        - Fluid and electrolyte imbalances should be addressed first.
    - Endoscopy is minimally invasive and allows evaluation of intestinal mucosa for ulceration or dilated lacteals:
        - Tissue samples may be collected from stomach, duodenum, ileum, and colon.
        - Samples are not full thickness, so deeper lesions may be missed.
        - Feeding a small amount of corn oil 2 hours prior to induction may increase the visibility of dilated lacteals.
    - Exploratory laparotomy allows visualization of the entire abdomen and serosal surface of intestine:
        - Full-thickness biopsies may be diagnostically superior.
        - Risk of infection or dehiscence, especially with hypoalbuminemic state

TREATMENT

TREATMENT OVERVIEW

The long-term therapeutic goal is to increase serum albumin concentrations. However, some patients need immediate intervention to:

- Remove or control third-space fluid accumulation
- Provide nutritional support
- Prevent thromboembolic complications
- Address electrolyte imbalances (e.g., hypocalcemia and hypomagnesemia)

ACUTE GENERAL TREATMENT

- Fluid therapy should be planned carefully, as PLE patients have challenging colloid issues and may have an increased total body fluid volume at presentation. Injudicious fluid therapy may cause acute decompensation.
    - Synthetic colloids (e.g., hetastarch, dextran), improve oncotic pressure and limit peripheral edema and ascites.
        - Starting doses should be low (e.g., 5 mL/kg/d), as acute volume overload and pulmonary edema have been noted in dogs with severe PLE due to depletion of colloids in the interstitial space.

  - Fresh frozen plasma provides modest colloidal support; also supplies natural anticoagulant proteins such as antithrombin III.
  - Crystalloid support is rarely necessary in dogs with chronic PLE unless persistent vomiting or profuse diarrhea are reported; must be given with colloid support to minimize extravascular fluid accumulation.
  - Electrolyte disorders such as low potassium, ionized calcium, and magnesium should be addressed; patients with severe hypocalcemia may not improve unless magnesium is also supplemented.
- Abdominocentesis/thoracocentesis:
  - Fluid removal is required for patients with respiratory distress due to cavity effusion(s).
- Total or partial parental nutrition provides interim nutritional support in patients unable to absorb nutrients (see p. 1322).

CHRONIC TREATMENT

- Effective treatment of PLE requires management of the underlying cause; this may not be possible in all patients, particularly those with intestinal lymphangiectasia.
- Immunosuppressive agents should be used in patients with IBD:
  - Corticosteroids are the mainstay of medical therapy (e.g., prednisone, 1-2 mg/kg PO q 12 h, tapering to lowest effective dose after 14 days or when clinical signs are controlled).
  - Additional immunosuppressive agents (e.g., azathioprine, cyclosporine, chlorambucil) may be necessary in refractory patients or when chronic therapy is required.
- Corticosteroids +/− other immunosuppressive agents may be helpful in patients with lymphangiectasia:
  - Are thought to decrease lipogranuloma formation and lymphangitis
  - Inflammation triggered by release of chylomicrons into adjacent tissue exacerbates lymphatic dilation, dysfunction and leakage.
- Antibiotic therapy using metronidazole (10-15 mg/kg PO q 12 h × 4 weeks) may help control secondary bacterial disturbances and provide some antiinflammatory effects.
- Thromboembolism prophylaxis is warranted (e.g., aspirin 0.5 mg/kg PO q 24 h).
- Diuretics are rarely immediately helpful in patients with edema or cavitary effusion, but spironolactone may delay return of fluid (1-2 mg/kg PO q 12 h).

NUTRITION/DIET

- Dietary therapy is essential in dogs with PLE due to IBD, adverse food reactions, or lymphangiectasia.
  - Ultra low-fat, easily digestible diets should be fed to patients with intestinal lymphangiectasia to minimize fat malabsorption and lymph accumulation. Suitable choices would include cottage cheese (1% fat) and cooked white rice or commercially available highly digestible diets containing <3 g/100 kcal metabolizable energy fat.
  - Hypoallergenic or novel antigen diets should be considered in patients with concurrent IBD to decrease the inflammatory response in the intestine.
    - Most prescription diets in this category are not adequately fat restricted for patients with lymphangiectasia; consider a home-cooked diet or one of the commercially available novel antigen diets that are ultra low in fat.
  - Gluten-free diets should be provided if gluten-sensitive enteropathy is suspected.
  - Supplementation with an elemental enteral feeding product may be helpful. Such diets contain free amino acids to facilitate nutrient uptake by a compromised GI tract. Low-fat formulations such as Vivonex T.E.N. are appropriate for dogs with lymphangiectasia.
- Cobalamin supplementation should be provided if serum concentrations are subnormal:
  - Cyanocobalamin must be given parenterally (i.e., by SQ administration).
  - Dose is 0.25-1 mL/patient q 7 d for 6 weeks, then q 4 wk
- Folate supplementation should be provided if serum concentrations are subnormal:
- Dose is 0.5 mg PO q 24 h.
- Vitamin and mineral supplementation may be necessary in dogs with lymphangiectasia, as uptake of fat soluble vitamins is substantially compromised.
  - Vitamins D, E, and K are most likely to be depleted.
  - Calcium and magnesium supplementation may be necessary.

DRUG INTERACTIONS AND CONTRAINDICATIONS

- Immunosuppressive therapy is contraindicated in patients with infectious diseases such as intestinal histoplasmosis.
- Glucocorticoids should be withheld until surgical sites have healed.

POSSIBLE COMPICATIONS

- Azathioprine:
  - May cause substantial compromise in cats and should be avoided in this species
  - May cause myelosuppression or acute hepatopathy in dogs
- Thromboembolic disease:

- Patients may present with lameness, neurologic signs, or respiratory distress secondary to thromboembolic disease.
- Antithrombin III levels may be monitored to assess risk.

- Respiratory distress:
  - Patients may exhibit respiratory distress from severe ascites or pleural effusion, necessitating abdominocentesis or thoracocentesis.
  - Pulmonary thromboembolism associated with the PLE may also result in respiratory distress.

RECOMMENDED MONITORING

- Monitor serum albumin levels.
  - Response to therapy can be monitored objectively if no other disease processes are contributing to hypoalbuminemia.
- Monitor calcium (preferably ionized) and magnesium concentrations.
- Monitor CBC if patients are receiving myelosuppressive agents.
- Monitor body weight and assess at-risk patients regularly for third-space fluid accumulation.

PROGNOSIS AND OUTCOME

Long-term prognosis depends on eventual diagnosis:

- Most patients with PLE secondary to IBD have a guarded to fair prognosis.
- Basenjis with immunoproliferative enteropathy have a guarded to poor prognosis.
- Yorkshire terriers also have a guarded prognosis, as their inflammatory bowel disease or lymphangiectasia is often difficult to control.
- Prognosis for patients with GI fungal infection or neoplasia is guarded to grave.

PEARLS & CONSIDERATIONS

COMMENTS

- Hypoalbuminemia should always be investigated, even if the patient appears otherwise healthy. Early recognition of PLE may improve outcome and prevent life-threatening complications.
- Dietary modifications are an essential part of therapy in many cases.
- Always consider the risk of thromboembolism in patients with PLE.

CLIENT EDUCATION

- Clients should be warned that intestinal lymphangiectasia and IBD are usually lifetime problems and that chronic therapy may be necessary.
- Dietary recommendations must be strictly followed to minimize the chances of relapse.

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Lymphadenopathy

BASIC INFORMATION

DEFINITION

Enlargement of a solitary, a regional group of, or all lymph nodes

SYNONYM

Lymphadenomegaly

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs and cats, any age, either sex

GENETICS & BREED PREDISPOSITION: Dogs; bullmastiff, rottweiler, retrievers, other breeds: lymphoma

RISK FACTORS: Exposure to ticks and other vectors: infectious diseases

CONTAGION & ZOONOSIS: Exercise caution when aspirating lymph nodes, especially in animals with fungal disease (zoonosis via needlestick injury).

GEOGRAPHY AND SEASONALITY: Tick vectors are more prevalent in summer in the tropics. Many infectious agents have specific geographic areas of prevalence.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Solitary/regional versus generalized

HISTORY, CHIEF COMPLAINT

- History: visits to geographic areas where certain infectious diseases are endemic
- Clinical signs generally reflect the underlying disorder and are not directly caused by the lymphadenopathy.
    - Exception: if lymph node enlargement is marked, mechanical obstruction may cause dysphagia, respiratory stridor, regurgitation, cranial vena cava syndrome, swollen limb(s), and dyschezia.

PHYSICAL EXAM FINDINGS

- Evaluate all accessible lymph nodes during physical examination; the following nodes are readily palpable in dogs and cats:
    - Mandibular, prescapular (superficial cervical), axillary, superficial inguinal, and popliteal
    - Node pain, erythema, heat, adherence of node to underlying tissue suggest lymphadenitis.
- Patients with lymphadenopathy may show signs of systemic illness from underlying disease.
    - Signs generally are vague and include general malaise, pyrexia, anorexia, weight loss, lethargy and polyuria/polydipsia; lacking diagnostic specificity.
- Patients with chronic leukemias, postvaccinal lymphadenopathies, and early lymphoma generally show subtle signs or no clinical signs at all.
- Evaluate for overtly apparent inciting causes:
    - Example, lesions of the foot (dermatosis, foreign body, neoplasm) if a single node proximal to a limb is enlarged
      *Nodes that are normally palpable in the healthy dog.

Selected Superficial Lymph Nodes of the Dog and Associated Anatomic Regions of Lymphatic Drainage

Lymph Node (and Alternative Name)	Location	Distribution of Lymphatics Contributing to the Node
Submandibular (mandibular)*	Ventral to the angle of the mandible; subcutaneous and mobile (versus mandibular salivary glands, which are deeper, fixed structures)	Most structures of the head, except for the external ear and some parts of the skin of the dorsal muzzle
Prescapular (superficial cervical)*	Medial and dorsal to the point of the shoulder	Skin of the head, neck, and forelimb
Axillary	Dorsal to deep pectoral muscle and at the dorsal-most aspect of medial forelimb	Thoracic wall, deep structures of the forelimb
Inguinal (superficial inguinal)	Caudoventral abdomen, immediately caudal to the fifth mammary gland	Mammary glands, prepuce, scrotum, vulva, ventral abdominal wall up to the umbilicus
Popliteal*	Caudal surface of stifle (femorotibial joint)	All parts of the hind limb distal to the node
Sublumbar (medial or external iliac)	Trifurcation of aorta (dorsal surface of pelvic canal/abdomen); may be palpable per rectum	Genital system, caudal part of the urinary and digestive systems, pelvis, hind limbs, and dorsal half of the abdomen.

Lymph Node (and Alternative Name)	Location	Distribution of Lymphatics Contributing to the Node

- Fat surrounding lymph nodes is a common impostor for lymphadenopathy; the animal's overall body condition needs to be considered when suspecting lymphadenopathy.

ETIOLOGY AND PATHOPHYSIOLOGY

- Lymph nodes enlarge as a result of proliferation of normal cells within them or to infiltration with either normal or abnormal cells.
- Reactive hyperplasia:
  - Proliferation of lymphocytes and plasma cells in response to antigens arriving through afferent lymphatics
  - Occurs mostly in response to inflammation in the tissues drained by the lymph node
  - After vaccination
  - Immune-mediated diseases
- Lymphadenitis:
  - Migration of inflammatory cells into the node, usually caused by infection (bacterial, rickettsial, fungal, parasitic, viral)
- Neoplasia:
  - Primary: lymphoma
  - Secondary: carcinomas, melanomas, sarcomas, mast cell tumors
- Extramedullary hematopoiesis (rare)
- Vascular changes: edema, congestion (rare)

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Start with a fine-needle aspirate of the lymph node to classify the disease process, then perform a CBC, serum biochemistry profile, and urinalysis together with diagnostic imaging as needed to search for the underlying cause. Lymph node biopsy may be necessary if no etiology is found.

DIFFERENTIAL DIAGNOSIS

- Generalized:
  - Reactive: systemic inflammation (infectious or noninfectious)
  - Lymphoma (most common), systemic mastocytosis, leukemia, multiple myeloma
  - Nonspecific hyperplasia (mainly cats)
  - Rickettsial diseases
  - Parasitic diseases
  - Systemic fungal infections
- Solitary or regional:
  - Superficial:
- Abscessation (lymphadenitis)
- Wounds, tick bites, and other inflammatory causes in the drained region
- Metastatic neoplasia
  - Deep (visceral):
    - Systemic mycoses
    - Metastatic neoplasia

INITIAL DATABASE

- Review history for visits to areas where specific infectious diseases are prevalent.
- CBC:
  - Anemia:
    - Anemia of chronic disease: inflammatory, infectious, or neoplastic disorders
    - Hemolytic anemia: hemoparasitic lymphadenopathies
    - Nonregenerative anemia: chronic ehrlichiosis, feline leukemia (FeLV), feline immunodeficiency virus (FIV), bone marrow neoplasia
  - Circulating blasts: lymphoma, acute leukemia
  - Eosinophilia: allergic, parasitic

  - Neutrophilia: lymphadenitis, lymph node hyperplasia or neoplasia, depending on the degree of systemic involvement
  - Thrombocytopenia: ehrlichiosis, lymphoma
- Serum biochemistry profile:
  - Hypercalcemia: lymphoma, multiple myeloma, anal sac adenocarcinoma if sublumbar nodes are enlarged
  - Hyperglobulinemia: neoplasia, ehrlichiosis, chronic inflammatory diseases
- Imaging: radiographs, CT, and ultrasound to search for neoplasia and determine the extent of lymph node involvement

ADVANCED OR CONFIRMATORY TESTING

- Fine-needle aspiration of lymph nodes allows classification of the disease process and frequently yields etiologic agents in infectious etiologies.
- Excisional lymph node biopsy (usually popliteal node) and histopathologic evaluation sometimes is necessary to confirm the diagnosis, especially in neoplasia and to perform immunophenotyping in lymphoma for prognostication.
- Aspiration and cytologic evaluation of spleen, liver, bone marrow
- Test cats for FeLV, FIV.
- Antibody tests for agents such as *Blastomyces* or *Ehrlichia*

TREATMENT

TREATMENT OVERVIEW

- Generalized lymphadenopathy: treat the underlying condition.
- Single node involvement: treat the process in the area drained by the lymph node.

ACUTE GENERAL TREATMENT

Prompt therapy in cases where lymph nodes obstruct the airway or vessels

CHRONIC TREATMENT

Chemotherapy protocols for lymphoma (see pp. 675, 669, 674, and 673)

POSSIBLE COMPLICATIONS

Acute tumor lysis syndrome (see online chapter: Acute Tumor Lysis Syndrome)

RECOMMENDED MONITORING

Imaging to monitor response to therapy or detect recurrence of neoplasia

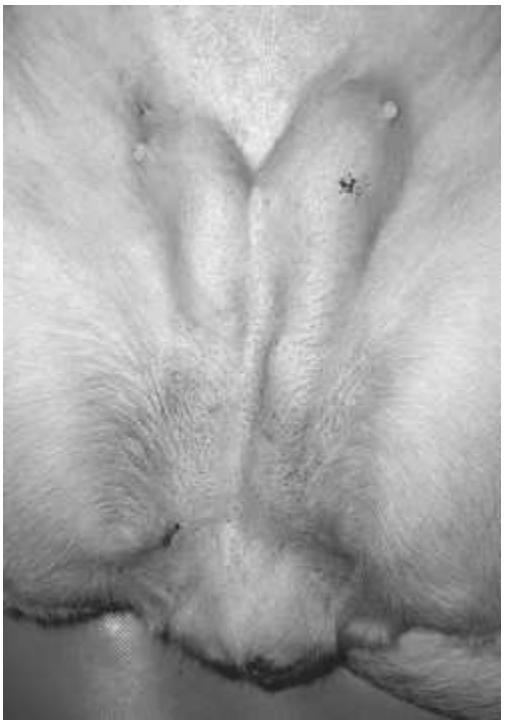
PROGNOSIS AND OUTCOME

Variable, determined by underlying cause

PEARLS & CONSIDERATIONS

COMMENTS

- Most dogs and cats with lymphadenopathy have lymph nodes that are firm, irregular, painless, nonadherent to underlying tissue and not warm to the touch.
- Nodes that are softer, warm, painful, and adherent to underlying tissue denote lymphadenitis.
- Metastatic lesions or lymphoma with extracapsular invasion of nodes are adherent to underlying tissue.
- Marked generalized lymphadenopathy (5 to 10 times enlarged) occurs almost exclusively in dogs with lymphoma or in cats with lymphoma or lymph node hyperplasia.
- Sublumbar lymph nodes can be palpated per rectum in small- and medium-breed dogs.



LYMPHADENOPATHY Caudal ventral abdomen of a female dog; cranial is toward top of image. Marked bilateral superficial inguinal lymph node enlargement is evident, with vulvar inflammation. Caudal fifth (inguinal) mammary glands are normal and not palpable in this dog.

PREVENTION

Tick and flea control

CLIENT EDUCATION

Parasite control and early presentation for veterinary care

SUGGESTED READING

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Lung Parasites

BASIC INFORMATION

DEFINITION

Infestation of major airways or pulmonary alveoli with parasites such as *Oslerus osleri, Paragonimus kellicotti, Eucoleus aerophilus, Filaroides hirthi, Crenosoma vulpis,* or *Aelurostrongylus abstrusus*

SYNONYMS

Lungworms; *O. osleri* formerly was *Filaroides osleri; Eucoleus aerophilus* formerly was *Capillaria aerophila.*

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs and cats:
  - Parasites seen in dogs include O. *osleri, C. aerophila, P. kellicotti, C. vulpis,* and *F. hirthi*.
  - Parasites seen in cats include *P. kellicotti, C. aerophila,* and *A. abstrusus.*
- Clinical signs are most common in younger animals but can be seen in animals of any age.
- No sex predisposition

RISK FACTORS: Dogs clinically affected by *F. hirthi* often have concurrent immune system compromise.

GEOGRAPHY AND SEASONALITY: The fluke *P. kellicotti* is most often found in the southeast, Midwest, and Great Lakes regions, owing to the prevalence of the snail and crayfish intermediate hosts. *Crenosoma vulpis* is highly prevalent in Atlantic Canada (red fox reservoir).

ASSOCIATED CONDITIONS & DISORDERS

- Eosinophilic pneumonia
- Pneumothorax

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Infestation can be an incidental finding.
- Cough
- Wheezes
- Exercise intolerance
  - Respiratory distress may be noted if pneumothorax is present.

PHYSICAL EXAM FINDINGS

- Cough may be elicited on tracheal palpation. However, this sign is nonspecific, and tracheal palpation may also elicit coughing in patients with other tracheal disorders, bronchial disorders, or pulmonary parenchymal diseases.
- Thoracic auscultation is usually unremarkable.
  - Wheezes or crackles can be heard in severely affected animals.

ETIOLOGY AND PATHOPHYSIOLOGY

- *O. osleri:*
  - Obtained via direct transmission (ingestion) of larvae in regurgitated food, feces, or saliva
  - Adults live in carina and mainstem bronchi and cause local nodular inflammation and fibrosis.
- *P. kellicotti:*
  - Obtained via ingestion of crayfish intermediate host or paratenic host such as rodents
  - Adult flukes live in a subpleural cyst that communicates with a bronchus.

        - Rupture of cyst/bulla in patients with *P. kellicotti* can cause pneumothorax.
- *E. aerophilus:*
    - Obtained via direct transmission (ingestion) of eggs in respiratory secretions or feces or by ingestion of earthworm intermediate host
    - Adults live in bronchial mucosa.
- *F. hirthi:*
    - Obtained via ingestion of larvae in feces
    - Adult worms live in lung parenchyma (alveoli and terminal airways).
- *A. abstrusus:*
    - Obtained via ingestion of snail or slug intermediate host or paratenic host such as birds and rodents
    - Adults live in terminal bronchioles, alveolar ducts and alveoli.
- *C. vulpis:*
    - Obtained via ingestion of snail or slug intermediate host
    - Adults live in bronchi.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on age of patient (typically young animals), signs of respiratory disease, possible exposure to paratenic or intermediate host, and compatible radiographic findings; confirmation requires seeing parasite or egg in specialized fecal examination.

DIFFERENTIAL DIAGNOSIS

- Chronic sterile bronchitis
- Infectious tracheobronchitis
- Asthma
- Pulmonary edema
- Bacterial or fungal pneumonia
- Pulmonary metastatic disease
- Pneumothorax
- Eosinophilic bronchopneumopathy (pulmonary infiltrates with eosinophils)

INITIAL DATABASE

- Thoracic radiographic abnormalities reflect the causative organism:
    - *O. osleri:* tracheal and bronchial nodules
    - *P. kellicotti:*
        - Solid or cavitary mass lesion, most commonly in the right caudal lobe
        - Bulla may also be present.
        - Pneumothorax
        - A bronchial or interstitial lung pattern is possible.
    - *C. aerophila:* normal or bronchial to bronchointerstitial pattern
    - *A. abstrusus:* bronchial to diffuse miliary or nodular interstitial pattern most common early; generalized alveolar pattern may be seen in severely affected animals.
    - *F. hirthi:* nodular interstitial pattern or alveolar infiltrates
    - *C. vulpis:* normal to mild to moderate bronchial or interstitial pattern
- No specific changes may be seen on CBC, serum biochemistry panel, or urinalysis.
    - Occasionally, eosinophilia is present, representing nonspecific parasitic infection or inflammation from other

ADVANCED OR CONFIRMATORY TESTING

- Transtracheal or bronchial washes may demonstrate larvae or eggs.
- Bronchoscopy to identify nodules of *O. osleri*
- Fecal examination may show eggs or larvae:
    - Zinc sulfate flotation or Baermann technique is recommended for identification of ova or larvae, respectively, of *O. osleri, A. abstrusus, C. vulpis,* and *F. hirthi.*
    - Fecal flotations can identify *C. aerophila* ova.
    - High-density fecal flotation or fecal sedimentation is preferred for identification of *P. kellicotti* ova.
- Nested PCR has been studied and may prove helpful for diagnosis of *A. abstrusus* in cats.

TREATMENT

TREATMENT OVERVIEW

Treatment consists of administration of parasiticidal drugs to eliminate the parasite infestation, with other medications used as necessary to decrease clinical signs secondary to inflammation.

ACUTE GENERAL TREATMENT

- With severe respiratory signs (rare), oxygen administration may be necessary.
  - Although secondary inflammation is often seen with infection, corticosteroid therapy (antiinflammatory doses) should be reserved for severe cases.
- Thoracocentesis for pneumothorax
- Parasiticidal drugs:
  - Fenbendazole, 50 mg/kg PO q 24 h for 10-14 days (14-21 days for O. *osleri)* can be used for all.
  - Other approaches include:
    - *A. abstrusus*
      - Ivermectin, 0.4 mg/kg SQ once
    - O. *osleri*
      - Ivermectin, 0.4 mg/kg PO, SQ once every 2 weeks for 3 treatments
    - *P. kellicotti*
      - Praziquantel, 25 mg/kg PO q 8 h for 3 days (dog)
      - Praziquantel, 10 mg/kg PO q 24 h for 10 days (cat)
    - *F. hirthi*
      - Albendazole, 25-50 mg/kg PO q 12 h for 5 days, repeat in 3 weeks
    - *C. vulpis*
      - Milbemycin oxime, 0.5 mg/kg PO once

POSSIBLE COMPLICATIONS

Certain breeds of dogs (such as collies) should not be treated with ivermectin without testing for MDR (multiple drug resistance) gene mutations (see p. 706). Albendazole may cause bone marrow toxicity.

RECOMMENDED MONITORING

- Clinical signs
- Thoracic radiographs
- Fecal examinations

PROGNOSIS AND OUTCOME

The prognosis depends on degree of clinical signs and extent of disease; generally good for recovery with appropriate treatment.

PEARLS & CONSIDERATIONS

COMMENTS

Lung parasites should be considered in any young animal presenting for coughing and with radiographic evidence of interstitial or bronchial lung disease.

PREVENTION

Limit exposure to intermediate or paratenic hosts.

TECHNICIAN TIPS

- False-negative results are considered common when examining stools for respiratory parasites.
- Fresh stool samples obtained per rectum are preferred for Baermann testing to limit contamination and confusion caused by soil nematodes.

- MDR testing is easily accomplished by submission of a cheek swab to the Veterinary Clinical Pharmacology Laboratory (for information see this link: http://www.vetmed.wsu.edu/depts-VCPL/).

CLIENT EDUCATION

Reinfection is possible unless pets are limited in opportunities to ingest known paratenic hosts.

SUGGESTED READING

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Traversa D, Guglielmini C: Feline aelurostrongylosis and canine angiostrongylosis: a challenging diagnosis for two emerging verminous pneumonia infections. Vet Parasitol, 157:163–174, 2008.

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Lung Lobe Torsion

BASIC INFORMATION

DEFINITION

A rotation of a lung lobe along its long axis, with twisting of the bronchus and pulmonary vessels at the hilus

EPIDEMIOLOGY

SPECIES, AGE, SEX: Reported in dogs and cats, although rare in cats. Middle-aged dogs are more commonly affected. There is no gender predilection.

GENETICS & BREED PREDISPOSITION

- Dogs with deep, narrow chests have a higher incidence.
  - Afghan hounds are overrepresented.
- Has been reported in small-breed dogs.
  - Pugs are overrepresented in the veterinary literature.

RISK FACTORS: Preexisting conditions leading to atelectasis of lung lobes such as:

- Pleural effusion
- Pneumothorax
- Trauma
- Surgical manipulation

ASSOCIATED CONDITIONS & DISORDERS

- Usually associated with massive pleural effusion
- Associated with chronic respiratory disease, trauma, chylothorax, thoracic surgery, or neoplasia

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- History of pneumothorax, pneumonia, or trauma
- Dyspnea
- Coughing
- Hemoptysis
- Anorexia with weight loss
- Exercise intolerance

PHYSICAL EXAM FINDINGS

- Muffled heart and lung sounds
- Crackles
- Coughing
- Hemoptysis
- Dyspnea

ETIOLOGY AND PATHOPHYSIOLOGY

- Spontaneous lung lobe torsion can occur.
- Any mechanism that increases the mobility of a lung lobe can lead to the development of torsion.
- Torsion of a lung lobe leads to venous congestion from occlusion of twisted pulmonary veins of the affected lobe and lung consolidation.
  - Persistent venous congestion leads to pleural effusion.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis should be considered in any patient, especially canine, with pleural effusion. Suspicion is typically increased by the presence of pleural effusion in an at-risk breed or by abnormalities found on thoracic imaging (plain radiographs, ultrasonography, CT scans) or bronchoscopy.

DIFFERENTIAL DIAGNOSIS

- Other causes of pleural effusion:
  - Hydrothorax
  - Hemothorax
  - Chylothorax
  - Pyothorax
- Pneumonia
- Pulmonary thromboembolism
- Pulmonary contusion
- Pulmonary neoplasia
- Pulmonary atelectasis
- Diaphragmatic hernia

INITIAL DATABASE

- Results of CBC, biochemistry panel, and urinalysis are variable.
  - Stress or inflammatory leukogram is possible.
- Analysis of pleural fluid may reveal a sterile, inflammatory serosanguineous effusion or chyle.
- Thoracic radiographs show pleural effusion and lung consolidation.
  - Large-volume pleural effusions may obscure lung atelectasis. Therefore repeating radiographs after thoracocentesis is important.
- Thoracic ultrasound reveals “hepatization” of the torsed lung lobe, with fluid-filled bronchi having an appearance similar to hepatic vessels and fluid-filled pulmonary parenchyma resembling normal liver.

ADVANCED OR CONFIRMATORY TESTING

Rarely needed or used

- Bronchoscopy may demonstrate an obstructed orifice of the main bronchus supplying the affected lobe.
  - Bronchial mucosa may appear folded and edematous.
- Thoracic CT may demonstrate anatomic alterations of the affected bronchus that suggest lung lobe torsion.
- For some patients, the diagnosis is confirmed at thoracotomy.

TREATMENT

TREATMENT OVERVIEW

- Improve respiratory function and stabilize the patient.
- Lobectomy of the affected lobe

ACUTE GENERAL TREATMENT

- Thoracocentesis (see p. 1338)
- Oxygen by face mask, nasal cannula, or oxygen cage (see p. 1318)
- Fluid therapy as needed based on patient status, physical examination, and laboratory parameters

CHRONIC TREATMENT

- This is a surgical condition; spontaneous resolution is rare.
- Lobectomy of the affected lobe is the treatment of choice.

POSSIBLE COMPLICATIONS

- Torsion of another lung lobe is possible.
- Lung lobe torsion may lead to chylothorax.

RECOMMENDED MONITORING

- Vital signs
- Respiratory pattern
- Resolution of pleural effusion:
- Thoracic radiographs
    - Volume of fluid aspirated from chest tube in the postoperative period; 1 mL/kg/d of fluid production is expected from the presence of the chest tube alone.
- Postoperative pain

PROGNOSIS AND OUTCOME

The prognosis is good if lung lobectomy is performed.

PEARLS & CONSIDERATIONS

COMMENTS

- Any lobe can torse, but the right cranial and middle lung lobes are more frequently affected.
- Air bronchograms can be seen in affected lobes early in the process, but bronchial air is absorbed and replaced by fluid within 2-3 days.
- During lobectomy, clamp the affected pedicle with noncrushing forceps before derotation to help prevent release of toxins into the bloodstream.
- The use of automated stapling devices (TA-30 V3) simplifies the surgery and decreases surgery time.
- Submit excised lung for culture and histologic examination.

TECHNICIAN TIPS

Materials for thoracocentesis to evacuate pleural fluid just after anesthetic induction to better stabilize the patient while prepping for surgery include: 22-gauge over-the-needle catheter or butterfly needle, three-way stop cock, extension set, syringe, and collection bowl.

CLIENT EDUCATION

Animals with concurrent chylothorax may have a poorer prognosis.

SUGGESTED READING

Gelzer AR, et al: Accessory lung lobe torsion and chylothorax in an Afghan hound. J Am Anim Hosp Assoc 33:171, 1997.

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Lumbosacral Stenosis, Degenerative

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

- A variety of pathologic conditions (malformation, growth disturbance, degeneration, compressive myelopathy, inflammation, infection, subluxation, ischemia) of the lumbosacral vertebral segments and related soft tissues
- The most common clinical presentation involves degenerative lumbosacral stenosis.

SYNONYMS

Cauda equina syndrome, lumbosacral spondylopathy, spondylolisthesis

EPIDEMIOLOGY

SPECIES, AGE, SEX: Middle-aged, medium- to large-breed, male dogs overrepresented

GENETICS & BREED PREDISPOSITION: German shepherds are predisposed.

RISK FACTORS: Working dogs at increased risk

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Some or all may be present:

- Lumbosacral pain
- Pelvic limb weakness/dragging
- Exercise intolerance/reluctance to exercise (especially jumping, rising, climbing stairs)
- Unilateral or bilateral pelvic limb lameness
- Paresthesia of the perineum and/or extremities (manifested by licking or chewing)
- Tail paresis/paralysis
- Urinary/fecal incontinence

PHYSICAL EXAM FINDINGS: Some or all may be present:

- Pain on hind limb or tail hyperextension
- Pain when digital pressure is applied to dorsal sacral/caudal lumbar vertebrae, with or without simultaneous lifting of the pubis
- Pain on rectal palpation of L7-S1 disk space
- Abnormal hind limb conscious proprioceptive response (monoparesis or paraparesis)
- Reduced hind limb flexor reflex (especially hock flexion)
- Exaggerated patellar reflex (pseudohyperreflexia)
- Unilateral or bilateral atrophy of sciatic-innervated muscles (hamstring, gastrocnemius, cranial tibial); reduced perineal reflex
- Poor anal and urethral sphincter tone
- Atonic bladder
- Decreased tail sensation

ETIOLOGY AND PATHOPHYSIOLOGY

- Large biomechanical forces are placed on the lumbosacral joint, which acts like a “hinge” between the stiff pelvis and the mobile spine. Presumably, the mechanical stress in the lumbosacral joint leads to early disk degeneration, destabilization of the disk space, and dorsal protrusion of the disk.
- Osteophytes may form adjacent to the unstable disk space and contribute to spinal canal stenosis along with the bulging disk, hyperplastic soft tissues, and sacral subluxation.

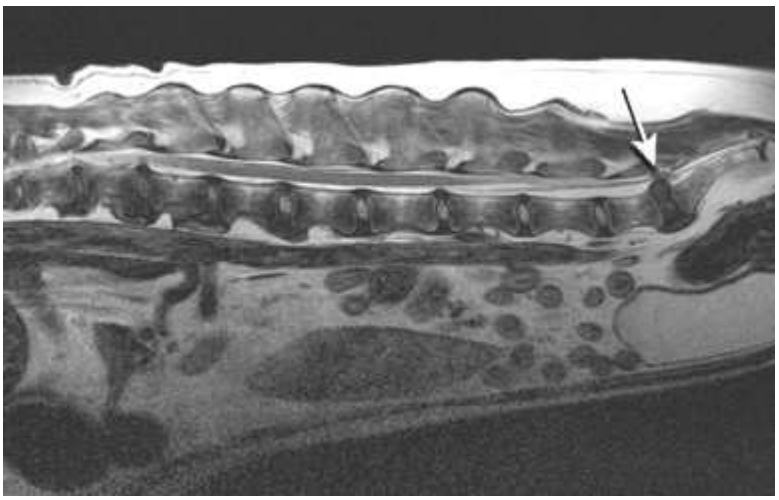
DIAGNOSIS

DIAGNOSTIC OVERVIEW

Lumbosacral stenosis is suspected in dogs with signalment, clinical signs, and radiographic findings consistent with this disease, especially if lower motor neuron signs (dysreflexia) to the hind limbs are noted. However, advanced imaging (MRI, CT, myelography/epidurography) is necessary to confirm diagnosis.

DIFFERENTIAL DIAGNOSIS

- Lumbosacral diskospondylitis
- Spinal cord, spinal nerve, or vertebral neoplasia
- Thoracolumbar disk disease
- Spinal trauma
- Degenerative myelopathy
- Coxofemoral arthritis/hip dysplasia
- Cranial cruciate disease
- Pelvic/sacral fracture(s)
- Fibrotic myopathy (semitendinosus, gracilis muscles)
- Prostatic disease



LUMBOSACRAL STENOSIS, DEGENERATIVE Sagittal T2-weighted MRI of the lumbosacral spine of a mature dog with degenerative lumbosacral stenosis; cranial is to the left. The disk at the LS junction *(arrow)* is protruding into the spinal canal and shows low signal intensity consistent with degeneration.

INITIAL DATABASE

- CBC, serum biochemistry panel, urinalysis (older dogs)
- Survey radiographs (heavy sedation/ general anesthesia) with evacuated colon, to rule out differential diagnoses (trauma, diskospondylitis). Radio-graphic changes associated with degenerative lumbosacral stenosis:
    - L7-S1 disk space narrowing
    - Lumbosacral end-plate sclerosis, spondylosis deformans
    - Ventral sacral subluxation
    - Lumbosacral disk mineralization
    - Note: These changes may also be identified in clinically unaffected dogs and do not predict the development of lumbosacral stenosis.

ADVANCED OR CONFIRMATORY TESTING

- MRI is extremely useful for evaluating disk degeneration or nerve root compression (soft tissue).
- CT gives excellent bone detail and can provide cross-sectional imaging. The soft-tissue imaging is inferior to MRI, however.
- Myelography: useful if the dural sac extends beyond the lumbosacral area. Contrast filling of the epidural space may be inconsistent and hard to interpret.
- Diskography: may demonstrate disk protrusion. Note: a normal disk can be injected with less than 0.2 mL contrast agent, and a degenerated disk can often easily receive 1 to 3 mL.
- Electromyography (EMG) may delineate denervation. Normal EMG does not rule out lumbosacral stenosis.

TREATMENT

TREATMENT OVERVIEW

Surgical treatment is recommended if pain is refractory to medical management and/or if neurologic signs are deteriorating. Goals of treatment are pain relief and return to function, although return to complete normalcy may not be possible.

ACUTE GENERAL TREATMENT

- Conservative management: strict rest (4-6 weeks), then gradually increased activity over 4-6 weeks. Antiinflammatory/analgesic medication to control pain as needed. Consider codeine, 1 mg/kg every 6-12 hours PO or tramadol (1 mg/kg q 4-6 h PO) in combination with a nonsteroidal anti-inflammatory drug.
- Dogs with continuous pain or neurologic dysfunction are surgical candidates. Surgical treatment most frequently consists of spinal canal/ nerve roots decompression through a dorsal laminectomy and (sometimes) foraminotomy.
- Distraction and stabilization of unstable LS space is possible with facet joint transarticular screws in combination with decompression. May decrease the risk of recurrence.

CHRONIC TREATMENT

- Strict confinement necessary for 8-12 weeks after surgery, followed by gradual return to function over 2 months. Early excessive exercise associated with less favorable outcome.
- Sling support may be necessary in the early postoperative period. Urinary bladder management is imperative until there is normal voluntary voiding.

NUTRITION/DIET

Dietary modification to avoid obesity is beneficial.

BEHAVIOR/EXERCISE

High-impact physical activity (jumping, frisbee catching, etc.) should be avoided, whereas consistent low-impact activity (walks, running on soft surfaces, swimming) should be provided.

POSSIBLE COMPLICATIONS

- Laminectomy scarring
- Implant failure

PROGNOSIS AND OUTCOME

- Decompressive surgery provides a good to excellent long-term outcome in 78%-97% of cases.
- Working dogs return to full function in 41%-78% of cases.
- Recurrence rates have been reported as 3% in a population of primarily pet dogs, whereas more active or working dogs show recurrence rates of 18%-54%. A second surgery can be beneficial in cases with recurrent clinical signs.
- Urinary or fecally incontinent dogs have less favorable outcomes.

PEARLS & CONSIDERATIONS

COMMENTS

- Transitional lumbosacral vertebrae and sacral osteochondrosis have been associated with lumbosacral stenosis but can also occur in normal dogs.
- Lumbosacral diskospondylitis can be difficult to distinguish from degenerative lumbosacral stenosis. In cases with osteolytic or severely proliferative changes, urine, blood, and, if surgery is performed, the removed disk should be submitted for bacterial and fungal culture.

SUGGESTED READING

Suwankong N, et al: Review and retrospective analysis of degenerative lumbosacral stenosis in 156 dogs treated by dorsal laminectomy. Vet Comp Orthop Traumatol 3:285, 2008.

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Liposarcoma

BASIC INFORMATION

DEFINITION

An uncommon primary malignant neoplasm of adipocytes. Can occur anywhere in the body but more commonly found in the skin and subcutaneous tissue.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Liposarcomas are uncommon in dogs and rare in cats. They are more common in older dogs (10 years of age average), but can occur at any age. They have been reported at injection sites in cats. No sex predilection has been reported.

GENETICS & BREED PREDISPOSITION: No breed predilection has been reported.

RISK FACTORS: Liposarcomas have been reported in previously irradiated tissues, at the site of a glass foreign body, and at the site of an injected microchip. The limited number of cases suggests that these factors may have a small impact on the risk of developing liposarcoma.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Liposarcomas have different pathologic subtypes, but these have not been shown to have prognostic significance. This tumor type has been reported at injection sites in cats (see 610).

HISTORY, CHIEF COMPLAINT

- Dogs and cats with liposarcoma in the skin and subcutaneous tissue usually present for evaluation of a progressively growing mass noticed by the owner.
- Dogs with abdominal liposarcoma often present for evaluation of signs related to an abdominal mass.

PHYSICAL EXAM FINDINGS

- Liposarcoma in the skin and subcutaneous tissue often presents as a firm, palpable mass.
- Regional lymphadenopathy may be present secondary to inflammation or (rarely) lymph node metastasis.
- Dogs with an abdominal liposarcoma may present with abdominal mass, pain, or enlargement.

ETIOLOGY AND PATHOPHYSIOLOGY

- Liposarcomas are thought to be spontaneously occurring in most cases in dogs. However, there are reports of tumors developing at the site of foreign bodies.
- Pathologic changes caused by liposarcomas depend on the location of the primary tumor and the invasion into and destruction of surrounding normal structures.
- Liposarcomas are not thought to be malignantly transformed lipomas.
- Liposarcomas may grow rapidly.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Definitive diagnosis can only be confirmed via histopathologic analysis, although additional testing such as diagnostic imaging is often helpful in defining the extent of the tumor.

DIFFERENTIAL DIAGNOSIS

- Other skin and subcutaneous tumors:
  - Soft-tissue sarcoma
  - Mast cell tumor

    - Lipoma
    - Others
- Other splenic tumors:
    - Hemangiosarcoma
    - Lymphoma
    - Others

INITIAL DATABASE

- Fine-needle aspirate cytologic analysis may help identify the tumor type before other diagnostics.
- Three-view thoracic radiographs to rule out pulmonary metastases
- Radiographs of the affected area may reveal involvement of underlying bone.
- Fine needle aspirate of draining lymph nodes to help rule out metastasis.

ADVANCED OR CONFIRMATORY TESTING

- CT or MRI may be necessary to delineate the local extent of the tumor and plan for surgery or radiation therapy.
- Biopsy: definitive diagnosis is based on histopathologic examination of tissue. Special stains may be necessary to differentiate liposarcoma from other soft-tissue sarcomas, especially poorly differentiated tumors.

TREATMENT

TREATMENT OVERVIEW

Definitive treatment is based on complete eradication of the primary tumor whenever possible. However, additional treatment such as chemotherapy may be indicated to prevent or delay metastases or in dogs with high-grade tumors or tumors that have already metastasized. Palliative treatment options, such as palliative radiation, may help control pain or discomfort in patients with advanced tumors or in patients where definitive treatment cannot be tolerated.

ACUTE GENERAL TREATMENT

- Aggressive surgical resection, radiation therapy, and/or chemotherapy may be used for treatment of liposarcoma (see 1034).
- Although response of liposarcomas to radiation and chemotherapy has not been determined, these treatments may be useful as adjuvant therapy.

POSSIBLE COMPLICATIONS

Complications of treatment for liposarcomas depend on the types of treatments and the location of the primary tumor.

RECOMMENDED MONITORING

After appropriate local treatment, follow-up examination should be done on a routine basis to monitor for recurrence (every 2-3 months) and metastasis (including thoracic radiographs at 6 months and 1 year). High-grade tumors may require more frequent monitoring for metastases during and after chemotherapy administration.

PROGNOSIS AND OUTCOME

- Early studies reported metastasis to multiple sites (liver, lung, bone). However, in a more recent retrospective study of 56 dogs, very few dogs died as a result of metastasis. Dogs in this study had a median survival of almost 2 years, and dogs that had wide excision of their tumor had a median survival >3 years.
- Surgical excision with a clean histopathologic margin may not be adequate for local tumor control in some dogs with liposarcoma, based on a recurrence rate of 31% for dogs with clean margins and a higher risk of recurrence following reexcision.

PEARLS & CONSIDERATIONS

COMMENTS

Fine-needle aspirates of skin and subcutaneous masses should always be evaluated microscopically. Aspirates of liposarcoma may

give “fatty” appearing fluid, which could falsely be interpreted as indicating lipoma or subcutaneous fat. However, liposarcoma can be readily differentiated from benign tumors of adipocytes such as lipoma or infiltrative lipoma with routine microscopic (cytologic) evaluation of smears.

PREVENTION

The individual case of liposarcoma developing at the site of an implanted microchip does not warrant concern about an increased risk of tumors caused by microchips.

CLIENT EDUCATION

Pet owners can be educated to monitor their pets for masses and have them evaluated in a timely fashion. Early detection may allow for easier treatment via surgery and may help avoid the need for radiation therapy.

SUGGESTED READING

Baez JL, et al: Liposarcoma in dogs: 56 cases (1989-2000). J Am Vet Med Assoc 224:887–891, 2004.

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Lily Toxicosis

BASIC INFORMATION

DEFINITION

Lilies are a family of flowering ornamental plants that are known to cause acute renal failure when ingested by cats. Lily poisoning is a well-recognized and potentially fatal plant toxicosis in cats. In dogs, only mild gastrointestinal upset is expected with lily ingestion.

SYNONYMS

Lilies toxic to cats include daylilies *(Hemerocallis* spp.), Easter lilies *(Lilium longiflorum),* Rubrum or Japanese showy lilies *(L. speciosum, L. landifolium),* Star-gazer lilies *(L. auratum),* and tiger lilies *(L. tigrinum).* There are many new *Lilium* varieties developed each year. All *Lilium* or *Hemerocallis* species should be considered toxic.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Lily toxicosis has only been reported in cats.

GENETICS & BREED PREDISPOSITION: All breeds, ages, and both sexes of cats are susceptible.

RISK FACTORS: Younger cats may be more likely to eat plant material.

GEOGRAPHY AND SEASONALITY

- Easter lilies are most commonly sold in March and April. Other lilies are found year round.
- Lilies grow naturally along the Pacific Coast of the United States. Lilies are frequently cultivated as garden plants or houseplants.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- History of plant ingestion and/or presence of lilies in owner's home. Cats typically present vomiting (plant material may be present in the vomitus), anorexic, and lethargic.
- Signs usually develop within 12 hours after exposure (range: 2 hours to 5 days).
- Polyuria, polydipsia, and acute renal failure develop within 36-72 hours post ingestion.

PHYSICAL EXAM FINDINGS

- Unremarkable if ingestion was recent. Initial signs of vomiting, anorexia, and lethargy may appear to resolve without treatment.
- Signs progressing to oliguria and anuria, dehydration, lethargy, and vomiting. Some cats also show vocalization, adipsia, drooling, tremors, ataxia, weakness, and seizures.
- Evidence of pancreatitis may be present.

ETIOLOGY AND PATHOPHYSIOLOGY

Source:

- Lilies have large, showy, funnel-shaped flowers. The plants grow from bulbs and have erect stems 30-250 cm high. Lilies are frequently included in bouquets and floral arrangements. Daylilies are often grown in gardens.
- Peak incidence during Christmas and Easter holidays, as lilies are popular holiday ornamentals.

Mechanism of Toxicosis:

- Intoxication is via ingestion. A single bite, or even exposure to pollen only, can cause the clinical syndrome.
- Mechanism of action is unknown. Toxin is believed to be a water-soluble fraction. All parts of the plant are considered toxic, including pollen. Flowers contain the highest amount of toxin.

- Affected cats develop acute renal failure due to degeneration and necrosis of the proximal renal tubules. Sloughing of necrotic tubular epithelial cells results in tubular blockage and anuria.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is based on history of vomiting in a cat with either known exposure to lilies or unexplained/unexpected elevations in serum renal values (or both). In absence of history of exposure, other potential causes for acute renal failure must be ruled out, but empirical treatment should be initiated prophylactically during diagnostic testing because of the potentially severe consequences of unchecked toxicosis. There is no specific confirmatory test for in-clinic use.

DIFFERENTIAL DIAGNOSIS

Toxicologic:

- Ethylene glycol
- Nonsteroidal antiinflammatory drugs
- Cholecalciferol or calcipotriene
- Oxalic acid
- Nephrotoxic antibiotics

Nontoxicologic, spontaneous:

- Acute glomerulonephritis (e.g., feline infectious peritonitis, autoimmune disease related)
- Renal thromboembolism
- Acute-on-chronic renal failure (e.g., pyelonephritis, renal lymphoma, polycystic renal disease)

INITIAL DATABASE

- Serum biochemistry panel: azotemia (blood urea nitrogen [BUN] >34 mg/dL; creatinine is often disproportionately elevated), hyperkalemia, and hyperphosphatemia are common. Occasionally, hypercalcemia, elevated pancreatic enzymes.
- Urinalysis: isosthenuria, epithelial granular casts, and glucosuria in the absence of hyperglycemia are typical findings.

ADVANCED OR CONFIRMATORY TESTING

- There is no definitive confirmatory test for lily toxicosis.
- Histologically, the renal lesion generally includes acute necrosis of proximal convoluted tubules. Renal tubular mineralization may be present.
- Pancreatic acinar cells may show degeneration.
- Ultrasound can be used for measuring renal size and cortical thickness and to rule out other causes of acute renal failure.
- Renal biopsy may help determine extent of renal damage and prognosis (rarely done, since history and exclusion of other causes are usually sufficient).

TREATMENT

TREATMENT OVERVIEW

When cats are presented prior to the onset of clinical signs, the aim of treatment is early decontamination (induction of emesis, ideally within 2 hours, and administration of activated charcoal) and to prevent the development of acute renal failure. Such treatment, including therapy aimed at avoiding acute renal failure, is appropriate in all cases including exposures that are suspected but unconfirmed, because unchecked, toxicosis may have devastating and irreversible results

ACUTE GENERAL TREATMENT

- Decontamination of patient (no clinical signs):
  - Emesis: in cats with recent ingestion (within a few hours) and not showing clinical signs, induce vomiting (see p. 1364), and give activated charcoal 1-4 g/kg PO. Protect airway with cuffed endotracheal tube if patient is unconscious.
- Prevent/slow development of renal failure (if cat is suspected or known to have ingested lilies in the preceding 2 days).

Important: Treatment is implemented regardless of whether or not signs are present:
    - Intravenous fluids:
        - Intravenous fluid diuresis for a minimum of 48-72 hours at two to three times maintenance fluids plus volume deficit (adjust based on hydration, fluid volume tolerance, and response to treatment)
        - Cats with normal renal values throughout diuresis may be weaned off fluids after 48 hours.
        - In cats with elevations in renal values, IV fluids should be continued until azotemia resolves. In some cases, this may mean days to weeks of treatment.
    - Monitor urine output in azotemic patients. If oliguria is present (urine production < 0.25 mL/kg/h), furosemide (2.2-4.4 mg/kg IV q 8-12 h) may increase urine output.
    - Treat hyperkalemia if present (see p. 556).
- Supportive care:
    - Persistent nausea: if gastrointestinal obstruction has been ruled out, consider maropitant, 1 mg/kg SQ q 24 h; dolasetron mesylate, 0.6 mg/ kg IV q 24 h; or metoclopramide, 0.1-0.5 mg/kg SQ q 6-12 h.
    - Abdominal pain may be managed with opiates such as butorphanol, 0.1-0.2 mg/kg IV.
    - Peritoneal dialysis (see online chapter: Peritoneal Dialysis) or hemodialysis (see p. 1286) possibly oriented toward renal transplantation if response is positive; can be considered if anuric renal failure develops.
    - Control seizures with diazepam (0.5-2 mg/kg IV PRN).

RECOMMENDED MONITORING

- Serum biochemistry profile baseline, 24, 48, and 72 hours (especially electrolytes and renal values). Recheck BUN and creatinine daily during clinical syndrome or for 72 hours if no abnormalities are seen.
- Urinalysis (baseline, 24, 48, 72 hours): ensure isosthenuria/hyposthenuria as sign of adequate fluid diuresis.
- If azotemia develops, monitor urine output.
- Monitor for fluid overload: respiratory character, onset of gallop sound on cardiac auscultation, central venous pressure if possible.

PROGNOSIS AND OUTCOME

- If treatment is initiated within 18 hours of ingestion, before onset of renal failure, prognosis is good.
- Prognosis after renal failure has developed is guarded to poor.

PEARLS & CONSIDERATIONS

COMMENTS

- Even when vomiting is mild and self-limiting, the presence of plant material in vomitus makes it critical to initiate treatment, including intravenous fluids, to avoid subsequent renal failure.
- Lily toxicosis is high on the differential list for any cat with acute renal failure and an extremely high serum creatinine level.
- Neither lily-of-the-valley *(Convallaria majalis)* nor peace lily *(Spathiphyllum* spp.) belong to the *Lilium* or *Hemerocallis* genera. They are not true lilies and do not cause acute renal damage in cats.

TECHNICIAN TIP

Some florists believe that plucking the stamens out of lily flowers renders them nontoxic, which is wrong. Therefore, presence of any part of the lily plant in vomitus should be considered evidence of possible toxic exposure.

PREVENTION

Do not keep any *Lilium* or *Hemerocallis* species in the cat's environment

CLIENT EDUCATION

Clients should make sure plants are safe before bringing them into a cat's environment.

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Licking and Barbering Behavioral Disorders

BASIC INFORMATION

DEFINITION

Self-directed, repetitive, apparently purposeless behaviors that may derive from otherwise normal processes such as grooming or eating but are abnormal in that they are excessive in duration, frequency, or intensity in the context in which they are performed.

SYNONYMS

Acral lick granuloma (ALG; see p. 22), feline hyperesthesia syndrome, obsessive-compulsive disorders (OCD; see p. 775).

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Age of onset may overlap with social maturity (dogs 12-36 months of age, cats 24-48 months of age).
- Excessive licking has been reported in all ages and sexes.

GENETICS & BREED DISPOSITION

- Some lines of some larger canine breeds may be more predisposed to acral lick granuloma (e.g., Doberman, dalmatian, Labrador retriever, golden retriever).
- Asian breeds of cats such as the Siamese appear to be more predisposed to OCDs such as wool eating.

RISK FACTORS: Pain, stress, or anxiety; injury to area that changes sensory function

GEOGRAPHY AND SEASONALITY: Hot humid weather has been associated with acute moist dermatitis, which in turn has been speculated to be associated with acral lick granulomas.

ASSOCIATED CONDITIONS & DISORDERS: Hypothyroidism in dogs, hyperthyroidism in cats, allergies, bacterial or fungal infections, nerve damage. Coexisting anxiety-related conditions are common.

CLINICAL PRESENTATION

DISEASES FORMS/SUBTYPES

- Feline: hyperesthesia, overgrooming, self-mutilation, and psychogenic alopecia
- Canine: acral lick dermatitis/granuloma (ALD/G)

HISTORY, CHIEF COMPLAINT: Persistent chewing, barbering, plucking, or licking of the skin and hair

PHYSICAL EXAM FINDINGS

- Hair loss and discoloration occur only on the parts of the body that can be reached by the teeth and tongue. In cats, it is especially evident around the sides and rump, back legs, and inguinal region; other areas may have normal hair coat (e.g., head and back of neck). Alopecia is usually patchy and asymmetric. Skin may look normal.
- Feline overgrooming may become true self-mutilation with cutaneous ulceration. Secondary bacterial infections may then occur.
- In dogs, ALG lesions appear as thickened oval plaques, often with secondary bacterial and/or fungal infection.

ETIOLOGY AND PATHOPHYSIOLOGY

- Normal adult cats spend about 30%-50% of their time awake grooming.
- Grooming behaviors such as licking and chewing serve many purposes, including cleaning, removal of parasites, thermoregulation, and potentially, alleviation of stress (e.g., after punishment, intercat aggression).
- Hair can be removed by plucking, barbering, or just by licking and excoriation. The plucked hair has evidence of shearing.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is based on a history of licking, chewing, or barbering excessively that has led to skin lesions that have no physical underlying cause. Trichography is an easy way to confirm that alopecia is due to hair plucking/removal, not hair spontaneously falling out.

DIFFERENTIAL DIAGNOSIS

Pruritic skin disease:

- External parasites
- Bacterial and/or yeast dermatitis
- Food allergy dermatitis
- Endocrine dermatopathies (hair loss symmetric)
- Pain associated with any condition including trauma, infection, anal sac disorders, or feline lower urinary tract signs/disease
- Behavioral response to environmental changes, such as moving, a new baby or spouse, separation from owner, too many cats in the household or area, presence of new cats in the area, changes in the social and physical environment, punishment from the owner, and lack of stimulation

INITIAL DATABASE

- Behavioral history
- CBC, serum biochemistry profile, urinalysis; serum thyroxine level in adults (hyper-/hypothyroidism): to rule out systemic disorders and prior to medication initiation
- Dermatologic examination, including scraping and culture (see p. 1248), to assess causes such as atopy, external parasites, food allergy
- Microscopic examination of plucked hair (trichogram) for evidence of shearing (broken hair shafts). Hair that is lost due to endocrine conditions may have visible telogen bulbs.

TREATMENT

TREATMENT OVERVIEW

Goals of treatment are to minimize or resolve the licking, chewing, or barbering of the hair and skin by removing or minimizing the underlying cause of the anxiety, and to treat any lesions and pruritus.

ACUTE GENERAL TREATMENT

- Treatment of any concurrent or underlying medical problem, such as elimination of fleas, or resolution of food allergy (see pp. 397 , p. 400, p. 402)
- Remove or minimize the cause of the anxiety if possible.
- Provide a regular predictable routine, such as feed and play at a set time each day.

CHRONIC TREATMENT

Treatment involves altering the neurochemical as well as the physical environment.

- Anxiolytic medication has also proved useful in some cases:
  - Tricyclic antidepressants (TCAs):
    - Cats:
      - Amitriptyline (0.5-1 mg kg PO q 12-24 h; average of 5-10 mg/cat PO q 24 h; start at the lowest dose and increase after 10 days if no response): *or*
      - Clomipramine (0.5 mg/kg PO q 24 h); *or*
      - Doxepin (0.5-1 mg/kg PO q 12-24 h)
    - Dogs:
      - Amitriptyline (1-2 mg/kg PO q 12 h); *or*
      - Clomipramine 1-2 mg/kg PO q 12 h for 2 weeks, then 3 mg/kg PO q 12 h; *or*
      - Doxepin 3-5 mg/kg PO q 12-24 h

- Selective serotonin reuptake inhibitors (SSRIs):
  - Cats:
    - Fluoxetine (0.5 mg/ kg PO q 24 h); *or*
    - Paroxetine (2.5 mg/cat PO q 24 h)
  - Dogs:
    - Fluoxetine (1 mg/kg PO q 12-24 h)
- Benzodiazepines such as diazepam (0.2-0.4 mg/kg PO q 12 h, average of 1-2 mg/cat PO q 12 h) or oxazepam (0.2-0.5 mg/kg PO q 12-24 h) are effective in some cats

- Medication may be necessary for a prolonged period (up to 6-12 months) and for some animals treatment may be lifelong.
- When long-term control of signs is successful, gradual withdrawal of medication may be attempted under veterinary supervision.

BEHAVIOR/EXERCISE

- Punishment is not effective in changing behavior. It serves to further increase the anxiety as well as impede learning of nonanxious behavior.
- Increasing physical and mental exercise may help decrease stress. Environmental enrichment may provide additional stimulation.

DRUG INTERACTIONS

TCAs and SSRIs should not be used concurrently with monoamine oxidase (MAO) inhibitors such as those present in medications or some flea and tick collars.

POSSIBLE COMPLICATIONS

May progress or coexist with other anxiety-related disorders such as panic disorders. Referral to a veterinary behaviorist should be considered.

RECOMMENDED MONITORING

- Serum biochemistry profile every 6-12 months or as needed based on clinical signs. Response to treatment should be monitored every 4-6 weeks.
- If long-term medication is needed, repeat blood work is recommended.

PROGNOSIS AND OUTCOME 

Prognosis is variable and depends on owner commitment, success in determining underlying cause, and management of the underlying problem. Early treatment leads to the best prognosis.

PEARLS & CONSIDERATIONS 

COMMENTS

Avoid punishing the behavior; doing so may increase the anxiety and arousal and exacerbate the undesirable behavior.

PREVENTION

Early intervention and redirection of concerning behaviors may be useful for cats and dogs without a genetic predisposition for the development of such conditions. Research has shown that even in cats with familial OCD, the specific behaviors involved do not substantially manifest until some social stressor (e.g., moving house) is involved. Clients who anticipate such stressors should be given guidance on prevention strategies.

TECHNICIAN TIPS

Educating clients about normal versus abnormal grooming behaviors in animals as well as early intervention can be very useful.

CLIENT EDUCATION

Clients should record the occurrence of these behaviors to assist in monitoring and managing triggers. Lifelong management and medication may be necessary.

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Leukemias, Chronic

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

- Chronic leukemias are neoplastic diseases characterized by clonal proliferation of malignant mature hematopoietic cells in the bone marrow and blood. They are categorized as lymphoid or myeloid.
- Chronic lymphocytic leukemia (CLL) involves the proliferation of mature lymphocytes and is clinically indolent, similar to small lymphocytic lymphoma.
- Chronic myeloid (myelogenous) leukemias (CML) involve the proliferation of myeloid cells and include myeloid, monocytic, myelomonocytic, basophilic, mastocytic, megakaryocytic, and erythrocytic leukemias.

EPIDEMIOLOGY

Chronic leukemias are rare in dogs and cats. CMLs are extremely rare.

SPECIES, AGE, SEX: Typically older dogs and cats but can occur at any age

GENETICS & BREED PREDISPOSITION: Mast cell leukemia (MCL): associated with derangement of KIT receptor or its ligand (stem cell factor) in dogs and humans

RISK FACTORS: In contrast to acute lymphocytic leukemia, most cats with CLL are not infected with feline leukemia virus (FeLV) or feline immunodeficiency virus (FIV).

ASSOCIATED CONDITIONS & DISORDERS

- CLL: monoclonal gammopathy, hyperviscosity syndrome
- CML: myelofibrosis
- Chronic basophilic leukemia (CBL) and MCL: hyperhistaminemia resulting in urticarial rashes and gastrointestinal (GI) signs/ulceration
- PV: hyperviscosity syndrome

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Chronic lymphocytic leukemia:
  - T-cell: 70%-90% canine CLL
  - B-Cell: 12%-30% canine CLL
  - Granular lymphocyte CLL (GL CLL; cytotoxic T cells or natural killer cells): 55%-80% of canine CLL; suspected to originate in the spleen
- CML: chronic myeloid leukemias
  - CNL: chronic neutrophilic leukemia
  - CMoL: chronic monocytic leukemia
  - CMML (or CMMoL): chronic myelomonocytic leukemia
  - CEL: chronic eosinophilic leukemia
  - CBL: chronic basophilic leukemia
  - MCL: mast cell leukemia
  - PV: primary erythrocytosis (polycythemia vera)
  - ET: megakaryocytic myelosis (essential thrombocythemia)

HISTORY, CHIEF COMPLAINT

- Insidious onset of increased peripheral blood count of affected cell line noted as incidental finding.
- Initially no clinical signs
- Later, nonspecific signs (lethargy, loss of appetite, weight loss) and signs associated with cytopenias (weakness, hemorrhage, infection)
- PV (rarely CLL) can cause neurologic signs (seizures, behavior changes, blindness, ataxia) due to hyperviscosity. Polyuria/polydipsia also possible.

- CEL in cats usually results in gastrointestinal (GI) signs due to infiltration.
- Some forms of CML frequently cause clinical signs due to production of cytokines or other factors (e.g., CBL, MCL: GI signs due to histamine).

PHYSICAL EXAM FINDINGS

- Initially, normal physical examination
- Hepatomegaly/splenomegaly common as disease progresses
- Lymphadenomegaly frequent in dogs with CLL
- Brick-red mucous membranes and neurologic signs possible with PV
- Palpable GI wall thickening possible with CEL and MCL
- Fundic examination: large, tortuous retinal vessels and retinal hemorrhages possible with PV

ETIOLOGY AND PATHOPHYSIOLOGY

- Chronic leukemias arise from neoplastic transformation of a pluripotent stem cell in the marrow or spleen.
- Progression is insidious, with gradual increases in marrow and peripheral blood cell counts of the leukemic cell type. Bone marrow infiltration may eventually result in myelophthisis (crowding of normal cells, changes in the marrow microenvironment, and secretion of suppressor factors) or myelofibrosis. These conditions result in anemia, neutropenia, and thrombocytopenia.
- Hepatic and splenic infiltration with leukemic cells is gradual, resulting in organomegaly, abdominal distension, and loss of appetite. Organ infiltration and dysfunction are possible in chronic stages or with transformation to acute leukemias.
- Transformation into a blast phase (acute leukemias) may occur in the terminal stages of chronic leukemias.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis of chronic leukemias has traditionally been based on detection of a high count of a cell line on CBC and bone marrow cytologic findings. Recently, flow cytometric immunophenotyping of cells in blood or bone marrow has become readily available for diagnosing leukemias in veterinary patients. This technique is used in combination with cytologic exam and allows more accurate identification of cell type and count, primarily for CLL and acute leukemias.

DIFFERENTIAL DIAGNOSIS

- Based on the type of cell(s) with elevated counts on CBC and bone marrow cytology
- Lymphocytes:
  - CLL
  - Small cell or large granular cell lymphoma
  - Ehrlichiosis
  - Viral infection (feline leukemia virus, feline herpes virus type 1)
  - Chronic antigenic stimulation (e.g., inflammatory bowel disease, cholangiohepatitis)
  - Recent vaccination
  - Stress/epinephrine in cats (redistribution of lymphocytes, typically <20,000 cells/µL)
  - Pure red cell aplasia
  - Immune-mediated hemolytic anemia
  - Hypoadrenocorticism
  - Feline hyperthyroidism
  - Thymoma
- Neutrophils:
  - CML: CNL
  - Infection (bacterial, fungal, protozoal)
  - Inflammation (immune-mediated, tissue trauma, neoplasia)
  - Leukemoid reaction (regenerative bone marrow with IMHA or hemorrhage)
  - Rebound following myelosuppressive drugs or chemical or viral insult to the bone marrow
  - Paraneoplastic syndrome (lymphoma, others)
  - Demargination
- Monocytes:
  - CMoL
  - CMML
  - Chronic infection/inflammation
  - Granulomatous disease
- Eosinophils:

    - CEL
    - Hypereosinophilic syndrome (HES; difficult to distinguish from CEL; CEL may be associated with an increase in blast cells)
    - Parasites (gastrointestinal, dirofilariasis, other)
    - Eosinophilic granuloma complex
    - Mast cell neoplasia
    - Feline asthma
    - Eosinophilic enteritis
    - Allergic diseases
    - Paraneoplastic syndrome
    - Hypoadrenocorticism
- Basophils:
    - CBL
    - Mast cell neoplasia
    - Dirofilariasis
- Mast cells:
    - MCL
    - Systemic mast cell tumor
    - Allergies
    - Dermatitis
    - Parasites
    - Parvoviral infection (dogs)
    - Regenerative anemias
    - Trauma
- Platelets:
    - Essential thrombocytosis
    - Hyperadrenocorticism
    - Iron deficiency
    - Postsplenectomy
    - Chronic inflammatory disorders
    - Acute infection
- Erythrocytes:
    - Relative erythrocytosis:
        - Dehydration
        - Diuretics, cardiac medications
        - Breed variation (sight hounds)
    - Absolute erythrocytosis:
        - PV
        - Chronic hypoxemia (right-to-left cardiac shunts, chronic respiratory disease, high altitude)
        - Paraneoplastic production of erythropoietin (renal tumors, others)
        - Splenic contraction

INITIAL DATABASE

- Laboratory tests:
    - CBC and blood smear reveal a high count of the leukemic cell type. Cell counts can be very high (hundreds of thousands and higher); for PV, PCV typically ranges from 60% to ≥80%. Both mature and immature forms of affected cell line may be present. Cytopenias are not generally observed until leukemic cell counts are very high. Mild anemia is common with CLL and CML. CLL is associated with selective suppression of erythropoiesis.
    - Serum biochemistry profile and urinalysis to evaluate overall health and look for paraneoplastic syndromes
    - FeLV/FIV ELISA for cats; typically will be negative
    - Erythropoietin level should be low with erythrocytosis, if not, supports PV.
- Bone marrow cytology (see p. 1212; if unable to obtain diagnostic sample, core biopsy is indicated):
    - Infiltration of bone marrow with leukemic cell type and its precursors is diagnostic.
- Cytologic evaluation of enlarged peripheral lymph nodes may reveal leukemic cells.
- Imaging for staging and to evaluate overall health and identify concurrent abnormalities:
    - Thoracic radiography
    - Abdominal ultrasonography

ADVANCED OR CONFIRMATORY TESTING

- Chronic leukemias often can be diagnosed by cell morphology. Additional tests improve the accuracy of determining cell type in CLL (flow cytometric immunophenotyping and PCR for antigen receptor rearrangement [PARR]).
- For diagnosing CLL, fresh blood in EDTA should be submitted for flow cytometry or blood or bone marrow smears should be

submitted for PARR. Flow cytometry will provide cell counts and phenotype (B cell or T cell). PARR will confirm clonality and provide phenotype. Submission information: http://www.cvmbs.colostate.edu/mip/people/Faculty/clinimmuno-submit-form.pdf (Colorado State University) and http://www.cvm.ncsu.edu/dphp/labs/documents/ncsu_flow_cytometry_sub_form_052010.pdf (North Carolina State University). At this time, use of these tests for CML is not routine in veterinary medicine.

TREATMENT

TREATMENT OVERVIEW

Goals are to eradicate leukemic cells with chemotherapy and provide symptomatic care as needed.

ACUTE GENERAL TREATMENT

- Supportive care may or may not be necessary with chronic leukemias.
  - Broad-spectrum antibiotic therapy for treating/preventing secondary infections if severe neutropenia (see p. 188). This is uncommon in chronic leukemias. Cats generally do not require prophylactic antibiotic therapy for neutropenia.
  - Intravenous fluid therapy for patients with infection, fever, or decreased appetite
  - Situations that might result in hemorrhage (e.g., jugular vein venipuncture or catheterization) should be avoided if severe thrombocytopenia or hyperviscosity syndrome is present.
  - Transfusions if needed (see p. 1347); this is uncommon.
  - Phlebotomy for PV or plasmapheresis may be considered for hyperviscosity syndrome.
  - Nutritional support for patients with decreased appetite
- Chemotherapeutic agents are used for eradicating leukemia cells. Response is slower and more durable than for acute leukemias. Special handling requirements and potentially severe adverse effects exist for these drugs. Consultation with or referral to a veterinary oncologist is recommended to determine the best protocol.
  - CLL: Treatment recommended if patients have clinical signs, cytopenias, or lymphocyte counts > 60,000/mcL. Treat with prednisone (dogs: 30-40 mg/m^2 PO once daily for 7 days and then every other day; cats: prednisolone, 5-10 mg daily) and chlorambucil (6-8 mg/m^2 PO every other day; cats 2 mg PO every 2nd or 3rd day depending on size). Some protocols add vincristine (0.7 mg/m^2 IV for dogs) during the first 1-4 weeks. When these drugs fail, other drugs for lymphoma may be used.
  - CML: Treatment depends on diagnosis. Because these are exceptionally rare diseases, referral to/consultation with a veterinary oncologist is recommended.
    - PV, CML, and CEL: treated with hydroxyurea (dogs: 30 mg/kg PO once daily for 7-10 days, then 15 mg/kg PO once daily; cats: 125 mg PO q 3-4 days. Dosages are adjusted long term based on response and toxicity.). It is important to know the potential side effects of hydroxyurea before using this drug. PV may be able to be managed with phlebotomy and fluid replacement initially. Busulfan has also been used in the treatment of CML and ET, but a recommended dosage has not been established.
    - Imatinib mesylate is a tyrosine kinase inhibitor used in people with chronic myelogenous leukemia. Use in veterinary patients has been limited by cost and hepatotoxicity in dogs. A receptor tyrosine kinase inhibitor (toceranib) is currently FDA approved for dogs, but at this time it is unknown whether CML in dogs has the same genetic abnormality as the disease in humans, so the role of this drug is not known. Consultation with a veterinary oncologist is recommended.

CHRONIC TREATMENT

Patients responding to treatment typically receive chemotherapy for the rest of their lives or until they develop bone marrow toxicity.

POSSIBLE COMPLICATIONS

- Myelosuppression: neutropenia, thrombocytopenia
- Chronic bone marrow injury
- Hydroxyurea can cause methemoglobinemia in cats. It can also cause anemia and skin/hair/nail changes.
- Gastrointestinal toxicity
- Rare hepatic, renal, pulmonary, or neurologic toxicity

RECOMMENDED MONITORING

- Will depend on diagnosis and how severely patient is affected.
- Physical examinations: weekly or more frequently if needed in induction period. Monthly to every other month once on chronic maintenance therapy.
- CBC: to monitor myelosuppression and remission status. Performed weekly or more frequently if needed during the induction period. Monthly to every other month once on chronic maintenance therapy, must monitor for chronic bone marrow injury and

relapse.
- Serum biochemistry profile, urinalysis (free catch if risk of hemorrhage): 1 month after starting therapy and then q 3-4 months to monitor overall health, paraneoplastic syndromes, and toxicity; more frequently if indicated.

PROGNOSIS AND OUTCOME

In general, the prognosis for chronic leukemias is better than acute leukemias because of the indolent nature of chronic leukemias. Dogs and cats with CLL can enjoy long-term survival. There is less information for CML.

- CLL: progresses slowly; responsive to chemotherapy; survival times of 1-3 years expected for dogs and suspected to be similar for cats. If CLL transforms into lymphoma/acute leukemia (as indicated by recurrence of clinical signs and/or appearance of blast cells on a blood smear), the prognosis is poor.
- CML: depends on type. There is little or no information describing the prognosis for some of these conditions.
    - CML/CBL: some dogs may live 1 year or more with treatment.
    - PV: survival times of >1 to >6 years reported.
    - CEL: in cats, not very responsive to treatment. Survival times of a few months. Unclear if dogs develop CEL, but if they do, it may respond to prednisone.
    - ET: Early attempts at treatment did not yield responses. More recently a dog experienced long-term control (>500 days) with busulfan.

PEARLS & CONSIDERATIONS

COMMENTS

- Chronic leukemias have a slow onset and often progress slowly. Patients are initially clinically normal and then show nonspecific signs.
- Diagnosis is based on identifying proliferating mature hematopoietic cells in blood and bone marrow. Use of flow cytometry for immunophenotyping is becoming more routine.
- Patients with chronic leukemias can enjoy long survival times.

TECHNICIAN TIPS

- Patients with chronic leukemias often undergo chronic chemotherapy.
- Monitoring of CBCs for chronic bone marrow injury and relapse is important.
- Owners should be educated on how to monitor their pet and precautions to protect themselves from chronic exposure to chemotherapy.

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Leukemias, Acute

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

- Acute leukemias are uncommon neoplastic diseases characterized by clonal proliferation of malignant immature progenitor cells in the bone marrow and blood and are broadly categorized as lymphoid or nonlymphoid (myeloid). The specific diagnosis depends on the cell of origin.
- Acute lymphoblastic leukemias (ALL) involve the proliferation of lymphoblasts and prolymphocytes.
- Acute myeloid leukemias (AML), involve the proliferation of myeloid cells and include myeloid, monocytic, megakaryocytic, and erythrocytic leukemias. Historically AML and myelodysplastic syndromes in veterinary patients have been classified according to the Animal Leukemia Study Group modified version of the French-American-British system used in humans.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Young cats and dogs (median 4-5 years) are more commonly affected with acute leukemias. Recent studies indicate older median age at incidence (7-9 years) for dogs with ALL.
- ALL: uncommon. Because it is difficult to distinguish ALL from stage V lymphoma, the percentage of leukemic dogs with ALL is unclear but reported to be 25%-30%. When considering only acute leukemic dogs, 40%-60% have ALL. Golden retrievers are overrepresented in cases of T-cell lymphoproliferative disorders. Specifically considering ALL, purebred dogs, in particular large breeds, predominate; German shepherd dogs and retrievers.
- AML: rare. In studies of leukemic dogs, 15%-40% have AML. Considering acute leukemic dogs only, 40%-60% have AML. The reported frequencies of canine AML types vary; M1 has been cited as most common, but a new study of 33 dogs with AML described 10 cases of M0, 3 M1, 5 M2, 12 M4, 2 M5, and 1 M7 (no M3 or M6). In 99 cats, 21% had M1, M2 was most common at 32%, and M6 was seen in 29%. Less common AMLs were M4 in 5%, M5 in 7%, and AUL in 8%. There is a possible male predilection in dogs and cats but no known breed predispositions.

RISK FACTORS: FeLV infection: 60%-80% of cats with ALL are FeLV positive and ≥90% of cats with AML are FeLV positive. Some patients with myelodysplastic syndromes will progress to AML.

ASSOCIATED CONDITIONS & DISORDERS

- ALL in dogs: paraneoplastic hypercalcemia
- AML in cats: myelofibrosis, hypercalcemia, glomerulonephritis

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Acute lymphoblastic leukemias:
  - B-cell origin: most common type in dogs
  - T-cell origin: most common type in cats
- Acute myeloid leukemias (classified based on bone marrow nucleated cell population):
  - Acute undifferentiated leukemia (AUL): ≥30% of bone marrow nucleated cells are blasts of uncertain lineage.
  - Myeloblastic leukemia without maturation (M1): ≥30% of marrow nucleated cells are myeloblasts; <10% of nonerythroid cells are maturing granulocytes.
  - Myeloblastic leukemia with maturation (M2): ≥30% of marrow nucleated cells are myeloblasts; >10% of nonerythroid cells are maturing granulocytes.
  - Promyelocytic leukemia (M3): ≥30% of marrow nucleated cells are myeloblasts; >10% of nonerythroid cells are maturing granulocytes, predominantly atypical promyelocytes. Has not been reported in animals.
  - Acute myelomonocytic leukemia (M4): ≥30% of marrow nucleated cells are myeloblasts and monoblasts; differentiated granulocytes and monocytes each represent >20% of nonerythroid cells.
  - Monoblastic/monocytic leukemia (M5): ≥30% of marrow nucleated cells are monoblasts or promonocytes.
  - Erythroleukemia (M6): ≥50% of marrow nucleated cells are erythroid precursors, and ≥30% of nonerythroid cells are myeloblasts and monoblasts, or ≥30% of bone marrow nucleated cells are rubriblasts, myeloblasts, and monoblasts.
  - Erythremic myelosis (M6-Er): ≥50% of marrow nucleated cells are erythroid precursors; ≥30% are erythroblasts.

- Megakaryoblastic leukemia (M7): ≥30% of marrow nucleated cells are megakaryoblasts.

HISTORY, CHIEF COMPLAINT

- Acute onset of nonspecific signs such as lethargy, weakness, loss of appetite, and weight loss
- Hemorrhage (e.g., epistaxis or petechiae) may be noted.
- Lameness due to bone pain is possible.

PHYSICAL EXAM FINDINGS

- Lethargy, weakness, pallor, weight loss, and dehydration are common.
- Fever due to secondary infection
- Tachypnea/dyspnea and tachycardia may be noted secondary to anemia.
- Hepatomegaly and splenomegaly are common.
- Lymphadenomegaly is often mild.
- Evidence of hemorrhage secondary to thrombocytopenia (petechiae, ecchymoses, epistaxis, intestinal bleeding)
- Ocular lesions (hyphema, uveitis, chorioretinitis, retinal detachment, chemosis, and conjunctivitis)

ETIOLOGY AND PATHOPHYSIOLOGY

- Acute leukemias are primary diseases of the bone marrow. As leukemic cells infiltrate the marrow, they crowd normal cells, change the marrow microenvironment, and secrete suppressor factors (myelophthisis). Consequently, normal hematopoiesis decreases, causing anemia, neutropenia, and thrombocytopenia. Cytopenias may result in weakness, secondary infections, and hemorrhage.
- Hepatic and splenic infiltration with leukemic cells is common, resulting in organomegaly, abdominal distention, and contributing to loss of appetite. Other sites may be involved, including lymph nodes, nervous system, kidneys, and gastrointestinal tract. Organ infiltration causes signs referable to failure of affected organs or nonspecific signs such as malaise and gastrointestinal disturbances.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is made by identification of abnormal numbers of blast cells on peripheral blood or bone marrow smears. Morphologic differentiation of acute leukemias and stage V lymphoma is limited. Recently, flow cytometric immunophenotyping (FCI) and PCR for antigen receptor rearrangements (PARR) have become routinely available for definitive diagnosis and classification of acute leukemias.

DIFFERENTIAL DIAGNOSIS

- Stage V lymphoma
- Ehrlichiosis

INITIAL DATABASE

- Laboratory tests:
  - CBC and peripheral blood smear may reveal a leukocytosis with circulating blasts and cytopenias of other cells. Nonregenerative anemia and thrombocytopenia are common (nearly 100% and 90% of canine patients, respectively) and may be severe. Neutropenia occurs in 60%-80% of dogs and neutrophilia in 10%-20%. Aleukemic or subleukemic patients have normal or low white blood cell counts with no or some circulating blasts, respectively.
  - Serum chemistry profile and urinalysis evaluate overall health and identify paraneoplastic syndromes.
  - FeLV/feline immunodeficiency virus ELISA test for all cats. Consider PCR test for FeLV using bone marrow (submit marrow sample in EDTA).
  - Rickettsial titers are indicated if in endemic area, history of tick exposure, or other compatible features.
- Bone marrow cytologic analysis (if unable to obtain a diagnostic sample, a core biopsy is indicated):
  - If the blast cell count is ≥30% of all nucleated cells in the bone marrow, a diagnosis of acute leukemia can be made.
  - Fine-needle aspiration and cytology of enlarged peripheral lymph nodes or organs frequently reveals infiltration with blasts.
- Imaging is performed to stage patients with leukemias and evaluate overall health:
  - Thoracic radiography
  - Abdominal ultrasonography

ADVANCED OR CONFIRMATORY TESTING

- Flow cytometric immunophenotyping is now routine for determining the cell lineage of acute leukemias. Morphologic appearance is not as accurate in distinguishing ALL from AML. Fresh blood in EDTA should be submitted for flow cytometry if there is a high number of circulating blasts; blood or bone marrow smears should be submitted for PARR in cases with rare abnormal cells. Flow cytometry provides cell counts, identification, and classification of leukemias. PARR identifies and confirms clonality of abnormal cells. Information for submission of samples for flow cytometry or PARR to the Colorado State University Veterinary Diagnostic Laboratory can be found at http://www.cvmbs.colostate.edu/mip/people/Faculty/clinimmuno-submit-form.pdf and for the North Carolina State University College of Veterinary Medicine Clinical Immunology Lab can be found at http://www.cvm.ncsu.edu/dphp/labs/documents/ncsu_flow_cytometry_sub_form_052010.pdf
- Cytochemical, immunocytochemical, or immunohistochemical staining are used by some centers to distinguish lymphoid from nonlymphoid leukemias and allow classification of AMLs.
- Acute leukemias are currently being examined for molecular abnormalities that might be prognostic or serve as targets for novel therapies. Mutations in RAS, FLT3, and C-KIT have been identified.

TREATMENT

TREATMENT OVERVIEW

Goals are to eradicate leukemic cells with chemotherapy and support the patient with transfusions and other measures until normal hematopoiesis resumes. Patients with ALL can respond to chemotherapy for short periods of time. AML are less responsive.

ACUTE GENERAL TREATMENT

- Intensive supportive care is important in patients with acute leukemias:
  - Broad-spectrum antibiotic therapy for treating/preventing secondary infections (see p. 188)
  - Intravenous fluid therapy for patients with infection, fever, or decreased appetite
  - Situations that might result in hemorrhage (e.g., jugular vein venipuncture or catheterization) should be avoided if severe thrombocytopenia is present.
  - Transfusions as needed (see p. 1347)
  - Nutritional support for patients with decreased appetite
- Chemotherapeutic agents are used for eradicating leukemia cells (induce remission). Clinically significant myelosuppression is expected because of myelophthisis. Hospitalization for supportive care during the induction period is indicated. Special handling requirements and potentially severe or life-threatening adverse patient effects exist with these chemotherapeutic drugs; these concerns and rapid evolution of protocols warrant consultation with/referral to an oncologist.
  - ALL: treatment is generally with standard chemotherapy protocols for lymphoma (see p. 674). Agents include prednisone, vincristine, cyclophosphamide, doxorubicin, and L-asparaginase.
  - AML: Chemotherapy protocols generally include cytosine arabinoside and doxorubicin. Agents such as 6-thioguanine, mitoxantrone, cyclophosphamide, busulfan, melphalan, vincristine, vinblastine, prednisone, and L-asparaginase have also been used. To date, results with chemotherapy have been disappointing.
  - Future treatments may include targeted therapies and bone marrow transplant.

CHRONIC TREATMENT

Patients responding to treatment will likely receive chemotherapy for the rest of their lives.

POSSIBLE COMPLICATIONS

- Myelosuppression:
  - Neutropenia: sepsis
  - Thrombocytopenia: hemorrhage
  - Anemia requiring transfusion
- Gastrointestinal toxicity: vomiting, diarrhea, lethargy, loss of appetite

RECOMMENDED MONITORING

- Physical examinations and CBC: weekly to every other week, more frequently if needed during the induction period; to monitor remission status and myelosuppression due to therapy
- Serum chemistry profile: every 2 months to monitor renal and liver status, electrolytes, and critical parameters; more frequently if indicated

PROGNOSIS AND OUTCOME

In general, the prognosis for acute leukemias is poor. Because many patients are euthanized at diagnosis and acute leukemias are relatively uncommon, there is limited information available regarding treatment outcomes. Most patients are clinically ill at presentation and if left untreated or given supportive care only, survival times are generally less than 2 to 4 weeks.

- CD34 expression: a stem cell marker; in dogs, expression of this antigen supports a diagnosis of acute leukemia and is associated with poor prognosis (median survival 16 days, range 3-128).
- ALL: for cats, a remission rate of 65% for a median of 7 months has been reported. Information about prognosis in dogs is confounded by the difficulty distinguishing ALL from stage V lymphoma; 30%-50% respond to chemotherapy for an average survival of 2-4 months. In dogs with CD8+ (cytotoxic T cell) lymphocytosis, higher cell counts are associated with poorer prognosis. The median survival for dogs with large cell CD21+ (B cell) lymphocytosis is 129 days. Note that this study of lymphocytosis included dogs with stage V lymphoma, CLL, and ALL. If chemotherapy is not an option, prednisone may be palliative.
- AML: A few cases surviving 3-4 months have been reported. Treatments attempted to date have done little to alter the course of AML, and prognosis is grave for cats and dogs.

PEARLS & CONSIDERATIONS

COMMENTS

- Cytologic examination of a blood smear is imperative for all patients with leukocytosis or significant cytopenias.
- Patients with acute leukemias present with an acute onset of nonspecific signs. Cytologic evaluation of peripheral blood and bone marrow smears will generally provide a diagnosis, but special diagnostics are needed to differentiate ALL, AML, and stage V lymphomas. Flow cytometry is recommended.
- Because acute leukemias progress rapidly, consultation with an oncologist should be pursued quickly, and emergency referral should be considered for sick patients.
- Owners should be advised of the poor prognosis and the potential for complications with treatment of acute leukemias. Supportive care may help reduce complications with treatment.
- Better characterization of acute leukemias and development of novel treatments targeting the molecular abnormalities that cause them will improve the treatment and prognosis of dogs and cats with acute leukemias in the future.

TECHNICIAN TIPS

- Patients with acute leukemias are often sick and pancytopenic. Hospitalization for supportive care and monitoring will be required at treatment induction. Precautions should be taken to avoid exposure to infectious diseases and hemorrhage during phlebotomy or treatment.
- Owners should be educated on how to monitor their pet and precautions to protect themselves from exposure to chemotherapy.

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Lethargy

BASIC INFORMATION

DEFINITION

Inert or apathetic state; lack of interest and/or energy; morbid drowsiness

SYNONYM

Listlessness

EPIDEMIOLOGY

SPECIES, AGE, SEX: Any patient

ASSOCIATED CONDITIONS & DISORDERS: Any disease process affecting any organ system, if sufficiently severe (systemic and/or direct intracranial involvement), can cause lethargy.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- The owner presents the pet because of a period of decreased activity, depressed mentation, and/or associated loss of appetite.
- A detailed history includes information as to the pet's water intake, presence or absence of vomiting/diarrhea, and whether the pet is eating. Additional useful information includes the pet's exercise level in the preceding days, whether other pets are affected, current medication history, and vaccination and de worming status.

PHYSICAL EXAMINATION

- Temperature, pulse, and respiratory rate: comparison to normal to look for early signs of shock.
- Examination of the mouth for severe dental disease and mucous membrane color. Capillary refill time to assess peripheral perfusion.
- Palpation of all lymph nodes for enlargement, suggesting hyperplasia (e.g., inflammation) or infiltration (e.g., neoplastic).
- Chest auscultation must include listening to 3 to 5 breath sounds in each of a few quadrants of the chest as well as heart auscultation. Evaluate the pulse while auscultating the heart.
- Abdominal palpation must be methodical. It focuses on quadrants within the abdomen, involving specific palpation of individual organs. The examination includes palpating the small intestine a second time for a foreign body/mass or for fluid accumulation.
- Rectal examination: to check for perianal masses, to assess the prostate, and to collect feces for a fecal flotation.
- Manipulation of the neck for pain and palpation of the whole spine. Simultaneous palpation of the abdomen is important, as pressure on hyperpathic points in the spine always causes abdominal tensing.
- Manipulation of all joints

ETIOLOGY AND PATHOPHYSIOLOGY

- Direct central nervous system (CNS) insult (inflammatory, vascular, neoplastic, other)
- More commonly, lethargy is the result of systemic disturbances with CNS effects, such as:
    - Inflammation: cytokine effects
    - Vascular: decreased perfusion
    - Metabolic: hypoglycemia, electrolyte disturbance, acid-base imbalance
    - Environmental: hyperthermia/hypothermia
    - Many others

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Lethargy is one of the most common yet least specific chief complaints in small-animal practice. A useful approach to diagnosis is to use the history to differentiate between medical and social/ behavioral causes; to also use the history to identify other concurrent clinical signs with an onset that coincides more or less with that of the lethargy (guiding testing towards a particular body system); and to identify abnormalities on the physical exam that can focus diagnostic efforts. In most cases, routine blood tests and urinalysis are justified as screening tools.

DIFFERENTIAL DIAGNOSIS

Any disease process (metabolic, infectious, neoplastic, traumatic, vascular, degenerative)

INITIAL DATABASE

Minimum database on each case:

- Return to/repeat the physical exam (most important diagnostic test in these cases)
- Urinalysis
- Blood smear: evidence of infection versus inflammation; platelet count
- Fecal flotation

ADVANCED OR CONFIRMATORY TESTING

- CBC, serum biochemistry profile, urinalysis
- The minimum database and physical exam orient the selection of additional tests. The more tests are performed, however, the greater the likelihood of a false-positive result.
- Thoracic radiographs (two views)
- Abdominal ultrasound and/or radiographs

TREATMENT 

TREATMENT OVERVIEW

- Treatment for confirmed disease processes
- Antibiotics are reserved for confirmed or highly suspected bacterial disease.
- Withholding of glucocorticoids unless their need has been proven. Glucocorticoids complicate many further diagnostics and can cause clinical deterioration if used inappropriately.

ACUTE AND CHRONIC TREATMENT

- If no trigger is found after the history, physical exam, and initial database, and the pet is not very ill, outpatient empirical treatment can be acceptable (e.g., in patients with gastrointestinal signs, using intestinal formula diet and asking owner to watch and return if pet is no better).
- Antibiotics are only considered if the blood smear/CBC shows signs of infection or if there is fever *with a second sign of infection* (e.g., blood in the feces).
- Specific aspects of treatment are guided by results of the minimum database and advanced testing:
    - Fluids if dehydrated
    - Analgesics if needed

POSSIBLE COMPLICATIONS

Lack of communication. It is essential to explain to the owner that an underlying trigger exists and must be found to provide optimal treatment.

PROGNOSIS AND OUTCOME 

Highly variable, depending on the underlying cause of lethargy

PEARLS & CONSIDERATIONS 

COMMENTS

- First do no harm; treatment is centered on identified triggers and underlying causes.
- More than 35% of sick pets presented to veterinary clinics have acute gastrointestinal upsets.
- Confident presentation of information is essential. Otherwise, owners can mistakenly sense uncertainty rather than a logical stepwise approach to a biological system.

SUGGESTED READING

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Leptospirosis

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

A bacterial disease affecting humans and animals, caused by pathogenic subtypes (serovars) of the aerobic gram-negative filamentous spirochetes, *Leptospira interrogans* and *L. kirschneri*

SYNONYMS

Weil's disease, Stuttgart disease, fall fever

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs: 4-7-year-old males more commonly affected
- Younger dogs are more susceptible to severe disease
- Cats: not clinically affected nor renal carriers; do seroconvert with exposure

GENETICS & BREED PREDISPOSITION: More common in hounds, working dogs, and herding breeds (likely greater exposure risk)

RISK FACTORS

- Suburban or rural environment
- Outdoor exercise areas/activities
- Exposure to wildlife or livestock (maintenance hosts)
- Exposure to moist environments/ standing water or to raw sewage
- Flooding
- Human risk factors: direct contact with domestic animals, environmental exposure (e.g., fisheries, rice fields, water sports), exposure to wild rodents (urban areas of poor sanitation)

CONTAGION & ZOONOSIS

- Readily contagious and zoonotic, typically via exposure to infected urine. When handling patients suspected of having leptospirosis, veterinary personnel and laypersons must use gloves and personal protective equipment to avoid exposure to urine and fomites.
- Leptospirosis is the most widespread zoonosis worldwide, accounting for up to 30% of human cases of acute renal failure in developing countries. Most human infections are asymptomatic or associated with mild, self-limiting flulike symptoms.

GEOGRAPHY AND SEASONALITY

- Worldwide distribution but predominant serovar(s) responsible for disease vary by region. In North America, serovars grippotyphosa, pomona, and bratislava are most common (historically, serovars canicola and icterohaemorrhagiae prior to vaccines targeting them).
- Previously considered a rural disease, leptospirosis is now also urban (rodents) and suburban (wildlife).
- The organisms survive in warm, moist environments, especially water but also mud and soil.
- The incidence of disease is highest in warmer months.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- There are at least 8 serovars (*L. interrogans:* autumnalis, bataviae, bratislava, canicola, hardjo, icterohaemorrhagiae, pomona; *L. kirschneri:* grippotyphosa) infectious to dogs and cats, causing variable degrees of renal and liver disease in dogs.
- Most infections are asymptomatic.
- Clinical disease: peracute (rare; sudden death from massive leptospiremia), acute, subacute (common), or chronic (common)

forms
- Some reported variation in tissue tropism and disease severity depending on the infecting serovar and the age and immune status of the host

HISTORY, CHIEF COMPLAINT

- Acute form: younger animals; lethargy, anorexia, shivering, muscle tenderness, vomiting
- Subacute form: lethargy, anorexia, vomiting, polydipsia/polyuria, reluctance to move, lumbar pain, icterus, hemorrhage
- Chronic form: +/− polyuria/polydipsia, icterus, inappetence

PHYSICAL EXAM FINDINGS

- General:
  - Anorexia
  - Lethargy
  - Fever
  - Dehydration +/− progression to hypovolemic shock
  - Injected mucous membranes
  - Conjunctivitis, uveitis
  - Petechial and ecchymotic hemorrhages
  - Nasal discharge
  - Increased lung sounds
  - +/− Abdominal pain, myalgia
- Additional findings vary based on tissue tropism and severity of injury:
  - Most cases show hypovolemia.
  - Manifestations of renal disease are very common.
  - Liver involvement is common; overt signs of liver failure (icterus, hepatic encephalopathy) may be present.
  - Vomiting is common.
  - Diarrhea is very common in experimentally infected puppies, less common in naturally occurring infections (but more common than in other causes of renal failure).
  - Pulmonary disease (labored breathing, cough) is much less common.

ETIOLOGY AND PATHOPHYSIOLOGY

- Leptospires enter the body by penetrating intact mucous membranes or bruised, abraded, or water-softened skin.
- Leptospiremia (7-10 days) causes dissemination to kidney, liver, spleen, central nervous system, eyes, and genital tract.
- Leptospires can express hemolysin and other factors which cause endothelial damage and vasculitis.
- Renal tubular epithelial-cell colonization occurs in most infected dogs, causing shedding for months to years post infection if not appropriately treated.
- Hepatic disease may result from toxin-induced injury and may be severe; some cases present with acute hepatic dysfunction as the predominant feature. Leptospirosis has been implicated as a cause of chronic hepatitis (serovar grippotyphosa).

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

Unexplained fever or signs of renal and/ or hepatic insufficiency should prompt consideration of leptospirosis. Diagnosis is multimodal: a serum titer alone is rarely sufficient, and a combination of history (exposure, clinical signs), physical examination, routine blood test results, serologic titers, and organism demonstration (via PCR) all contribute to confirming or refuting the clinical diagnosis.

DIFFERENTIAL DIAGNOSIS

- Other causes of acute renal failure (e.g., toxin, pyelonephritis, heat stroke, shock; see p. 31)
- Other causes of vasculitis (e.g., sepsis, rickettsial disease, pancreatitis)
- Other causes of hepatic injury (e.g., bacterial cholangiohepatitis, toxin, sepsis, idiopathic chronic hepatitis)

INITIAL DATABASE

- CBC:
  - Often inflammatory leukogram, with or without a left shift
  - +/− Variable degree of anemia

- +/− Thrombocytopenia; a third of cases, mild to moderate (90,000-150,000/mm^3), especially if vasculitis or disseminated intravascular coagulation (DIC)
- Serum biochemistry profile:
  - Azotemia and hyperphosphatemia are common.
  - Electrolyte disturbances: hyponatremia, hypochloremia, and hypokalemia
  - Metabolic acidosis
  - +/− Hypoalbuminemia in cases with vasculitis or severe liver dysfunction
  - Liver parameters: increased alanine aminotransferase (ALT), alkaline phosphatase (ALP), and bilirubin usually peak at 6-8 days after the onset of disease.
- Urinalysis:
  - Glucosuria, proteinuria, granular casts, pyuria, and hematuria may be present.
  - Variable specific gravity
- Thoracic radiographs: interstitial, nodular, or patchy alveolar infiltrates with pulmonary involvement or vasculitis
- Abdominal radiography and ultrasonography: +/— enlargement of liver, spleen, kidneys; renal “medullary rim sign” (hyperechoic concentric ring); perinephric effusion

ADVANCED OR CONFIRMATORY TESTING

- Microscopic agglutination test (MAT):
  - In animals with compatible clinical signs, the following results are considered diagnostic:
    - Titer > 1:800 in unvaccinated animal
    - Titer > 1:3200 in vaccinated (previous 3-4 months) animal
    - Paired titers 2-4 weeks apart with fourfold increase from first to second titer. Cross-reactivity among serovars is common, and highest serovar's titer often is not the causative serovar.
- ELISA: used as field tests for human infections
- PCR assays: sensitive and specific; may be positive in early infection before rise in specific antibody detected by MAT or ELISA is present. Current techniques distinguish pathogenic organisms but not serovars.
- Darkfield microscopy: examination of fresh urine for leptospires; low sensitivity (intermittent shedding means frequent false-negative results) and not routinely used
- Bacterial culture: leptospires are difficult to grow in culture; frequent false-negative results; does allow identification of infecting serovar (important epidemiologically)
- Fluorescent antibody techniques: fluid and tissue samples; not widely used
- Histopathologic assessment: lesions nonspecific (lymphoplasmacytic tubulointerstitial nephritis); organisms may be identified using special stains.

TREATMENT

TREATMENT OVERVIEW

Treatment goals are to treat bacteremia/leptospiremia, maintain renal perfusion and urine output to minimize renal injury, eliminate bacteria to prevent disease progression and shedding to environment, and treat associated conditions (renal failure, hepatic insufficiency, DIC, uveitis).

ACUTE GENERAL TREATMENT

- Penicillins: antimicrobial of choice for bacteremic phase (crystalline [transparent] formulations for IV use)
  - Penicillin sodium, 20,000 IU/kg IV q 4 h; *or*
  - Ampicillin, 22 mg/kg IV or PO q 8 h; *or*
  - Amoxicillin, 22 mg/kg IV or PO q 8 h
- Intravenous fluid therapy to replace deficits (vomiting, polyuria, decreased intake) and initial management of renal injury: target is rapid rehydration without volume overload (see p. 31)
- Adjunctive management of organ dysfunction and other consequences of infection as indicated for individual case (see Acute Renal Failure, p. 31; Acute Liver Injury, ; Disseminated Intravascular Coagulation p. 315; Vasculitis ; Sepsis p. 1014)

CHRONIC TREATMENT

Doxycycline, 5 mg/kg PO q 12 h for 2 weeks to eliminate leptospires from tissues, eliminate renal shedding

RECOMMENDED MONITORING

- Serum electrolyte levels, renal and hepatic parameters: to assess response to treatment or disease progression and to tailor therapy

- Hypertension may occur, requiring modification of treatment (see p. 1068).
- Urine output monitoring is essential in patients with acute renal failure.
- Monitor for development of complications (DIC, respiratory failure).

PROGNOSIS AND OUTCOME

- Survival rates for patients with clinical leptospirosis: 70%-85%
- Patients with acute renal failure are frequently oliguric to anuric and may require dialysis.
- Survivors may have persisting/chronic kidney (common) or liver dysfunction.

PEARLS & CONSIDERATIONS

COMMENTS

- Leptospirosis should be considered as a differential in any case of acute renal failure, fever of unknown origin, vasculitis, and/or acute or chronic liver disease in a dog.
- Due to the zoonotic potential of *Leptospira* pathogens, extreme caution should be used when handling suspected leptospirosis cases (dogs with acute febrile disease, especially with evidence of acute renal or liver disease).
- Human physicians are often unfamiliar with leptospirosis and its zoonotic potential.
- Intensive early therapy is important both for the patient's benefit and to reduce the risk of transmission to humans and other animals (empirical penicillin therapy in leptospirosis suspects while awaiting confirmatory test results).
- Serovars icterohaemorrhagiae and pomona: liver disease > renal disease. Serovars canicola and grippotyphosa: renal disease > liver disease.
- Leptospirosis is a reportable disease in many U.S. states; contact regional authorities.

PREVENTION

- Vaccination: whole-cell killed bacterin and subunit vaccines exist; vary in duration of immunity (6-13 months) and which serovars are included; prevent clinical disease and development of carrier state; most protect against icterohaemorrhagiae and canicola, newer vaccines include pomona and grippotyphosa.
- Vaccine protection is serovar specific: no cross-protection against nonvaccine serovars.
- Adverse reactions have been reported with disproportionate frequency with whole-cell leptospirosis vaccines; patients with a history of intolerance should either not receive the vaccine or be premedicated with antihistamines (e.g., diphenhydramine, 2 mg/ kg IM) and glucocorticoids (e.g., dexamethasone, 0.2 mg/kg IM) 15-30 minutes before vaccination
- Rodent control, avoidance of contact with reservoir hosts, and proper sanitation/drainage are also important.

TECHNICIAN TIPS

- Leptospirosis can be transmitted from infected animals to humans. To prevent exposure of people and other animals to the disease, strict protective measures should be used in handling animals, their bedding, and all laboratory samples. Use of hoses to clean cages of infected animals may result in generation of aerosols that can spread the organisms to people and other animals, and seed building surfaces with bacteria. Goggles, masks, and gloves should be worn to prevent exposure via mucous membranes (eyes, nose, mouth) and skin.
- Leptospirosis patients or suspects should be isolated from other patients and their movement restricted (patient remains in assigned cage unless absolutely necessary). If moved, patients should be transported by gurney or portable carrier that can be thoroughly disinfected.

CLIENT EDUCATION

- Leptospirosis can be transmitted to people, principally through direct or indirect contact with urine.
- Owners should be advised to contact their family physician for recommendations following exposure to an infected pet.
- The Centers for Disease Control and Prevention (CDC) maintains an informational page for lay persons, “Leptospirosis and Your Pet” at: www.cdc.gov/ncidod/dbmd/diseaseinfo/leptospirosis_g_pet.htm.
- Dogs should be supervised to prevent direct exposure to wildlife and should not be allowed to play in/drink from pools of stagnant water.

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Lens Luxation

BASIC INFORMATION

DEFINITION

Complete dislocation of the lens anteriorly (into the anterior chamber) or posteriorly (into the posterior segment/ vitreous) from its normal position. Occurs as a result of abnormal development or degeneration (*primary:* usually bilateral inherited condition in dogs) or rupture or degeneration (*secondary:* acquired) of the lens zonules (fibers from the ciliary body that hold the lens in place).

SYNONYM

Lens subluxation: partial dislocation of the lens

EPIDEMIOLOGY

SPECIES, AGE, SEX

- *Primary:* occurs most commonly in middle-aged dogs, especially terrier breeds
- *Secondary:* dogs and cats; any age

GENETICS & BREED PREDISPOSITION

- *Primary:* terrier breeds predisposed; typically between 3 and 7 years old
- German shepherd, border collie, and some spaniels may also be predisposed.

RISK FACTORS: See Etiology and Pathophysiology below.

ASSOCIATED CONDITIONS & DISORDERS

- Anterior uveitis
- Cataract
- Corneal endothelial-associated edema (anterior luxation)
- Glaucoma
- Vitreous degeneration
- Intraocular neoplasia
- Retinal detachment

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Signs of ocular pain in cases of anterior lens luxation including tearing, redness, and squinting/blepharospasm. The cornea may be cloudy from edema.
- Vision change noted by the owner, depending on the visual status of the contralateral eye.

PHYSICAL EXAM FINDINGS

- Systemic: generally unremarkable
- Ophthalmic:
  - Anterior chamber depth abnormal: shallow with anterior luxation; deep with posterior luxation
  - Iridodonesis (trembling of the iris)
  - Phacodonesis (trembling of the lens)
  - Aphakic crescent (portion of pupil no longer containing the lens)
  - Vitreous presentation in the anterior chamber (appears as fine white cotton strands)
  - Retina visualized without an ophthalmoscope (i.e., with penlight or transilluminator)
  - Focal or diffuse corneal edema from mechanical damage to corneal endothelium with anterior luxation.
  - Glaucoma (see p. 448) can result in secondary lens luxation by buphthalmos; conversely, primary lens luxation can also result in secondary glaucoma.

- Cataract: with chronic lens luxation
- Blindness from cataract, glaucoma, retinal detachment

ETIOLOGY AND PATHOPHYSIOLOGY

- *Primary* lens luxation occurs as a result of an autosomal recessive inherited, progressive defect in the lens zonules.
- *Secondary* lens luxation occurs as a result of degeneration and/or stretching of the lens zonules; causes include:
  - Chronic anterior uveitis (see p. 1151)
  - Glaucoma with associated buphthalmos (see p. 448)
  - Intraocular neoplasia (see p. 620)
  - Hypermature cataract (see p. 181)
  - Severe ocular trauma (results in other significant ocular damage; see p. 248)
  - Age-related (older dogs/cats)

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Suspected on physical examination subsequent to owner presentation for reduced vision or observed ocular abnormality. A complete ophthalmic examination is indicated to confirm and characterize the luxation and identify predisposing causes that can be treated.

DIFFERENTIAL DIAGNOSIS

- Glaucoma (see p. 448)
- Anterior uveitis (see p. 1151)

INITIAL DATABASE

Ophthalmic examination (see p. 1313):

- Menace response and pupillary light reflexes
- Intraocular pressure (IOP); normal = 10-18 mm Hg with TonoPen
- Penlight or slit-beam examination to determine if the lens luxation is primary or secondary, evaluate depth of anterior chamber, and assess cornea, lens, and vitreous for opacities
- Direct or indirect ophthalmoscopy to evaluate the posterior segment for retinal detachment (see p. 985), and optic nerve and retinal degeneration (see p. 983)

ADVANCED OR CONFIRMATORY TESTING

Ocular ultrasound if opacities of the lens or transmitting media prevent complete examination

TREATMENT

TREATMENT OVERVIEW

Therapeutic goals are to remove anterior lens luxation or lens subluxation early to avoid secondary complications, and to remove posterior lens luxation *or* prevent lens from entering anterior chamber by constriction of the pupil.

ACUTE GENERAL TREATMENT

Primary:

- Acute anterior lens luxation is considered an emergency.
- Determine IOP; treat if pressure elevated (see p. 448).
- Prompt referral of acute anterior lens luxation to a veterinary ophthalmologist for surgical lens removal (lensectomy):
  - Intracapsular lens extraction (entire lens removed) ± intraocular lens sutured in place to restore emmetropia (normal vision, neither far- or near-sighted; without an intraocular lens implant, animals are 14 diopters hyperopic [far-sighted] with abnormal vision).
  - If lens only subluxated, phacoemulsification (ultrasonic fragmentation of the lens) may be attempted. A capsular tension ring may be placed to stabilize the subluxation and a foldable acrylic intraocular lens (IOL) placed.

- If referral is not possible and the lens is luxated anteriorly, consider pupil dilation and intravenous mannitol to shrink the vitreous and shift the lens into the vitreous (seep. 448).
- If lens luxation is posterior, consider use of a miotic (e.g., prostaglandin analog; see p. 448) to constrict the pupil and thus restrict lens movement; consider referral for surgery.

Secondary: treat underlying cause.

CHRONIC TREATMENT

See Cataracts, p. 181

POSSIBLE COMPLICATIONS

See Cataracts, p. 181

RECOMMENDED MONITORING

- See Cataracts, p. 181
- Contralateral eye should be monitored for lens position and anterior chamber vitreous presentation in predisposed breeds with unilateral lens luxation. If lens instability is noted, phacoemulsification should be considered prior to complete luxation.

PROGNOSIS AND OUTCOME 

- Variable depending on underlying cause, duration and extent of the lens displacement, and location of the lens (anterior versus posterior).
- Most common complications are glaucoma and retinal detachment; in some reports, complication rate may be as high as 50%.
- Early surgical intervention while the lens is subluxated will increase success. The use of a capsular tension ring and foldable acrylic IOL may allow restoration of normal vision, with reduced complications and risk of luxation.

PEARLS & CONSIDERATIONS 

COMMENTS

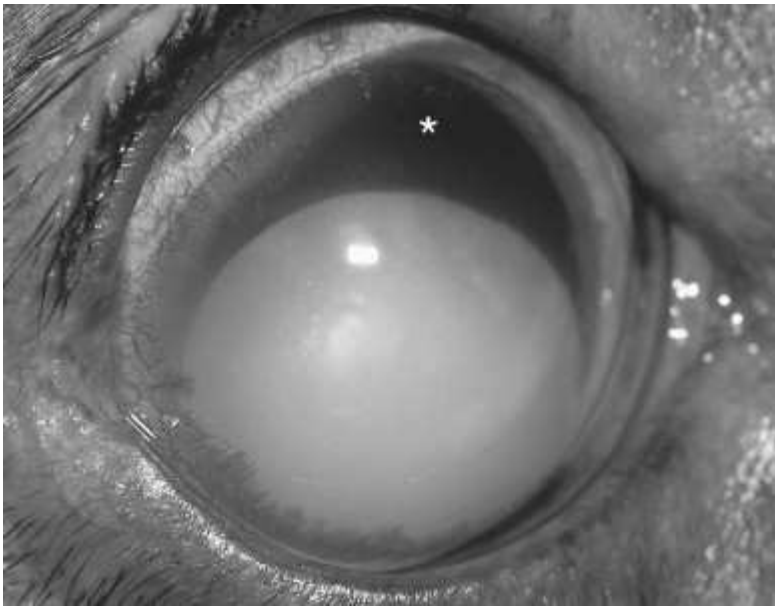
Terriers affected with lens luxation, regardless of severity, should not be used for breeding.

PREVENTION

- Dilated ophthalmic examination of all individuals of predisposed breeds, to detect early phacodonesis and anterior vitreous presentation (presence of vitreous rostral to the lens)
- Genetic testing of terriers to be used for breeding
- Complete dilated examination of the contralateral eye, especially in breeds with primary lens luxation
- Avoid head-shaking behaviors such as toys or rough playing in animals with phacodonesis or primary lens luxation in one eye.

CLIENT EDUCATION

- Breed predisposition and predilection for bilateral involvement in terriers
- With or without surgical intervention, affected eyes are at increased risk for retinal detachment and glaucoma.
- Genetic testing is available to distinguish affected, carrier and normal dogs. Homozygus affected dogs will luxate their lenses between 4-8 years of age.
- Animals that undergo surgical removal of the lens and do not receive an IOL implant have vision that, in human equivalence, is worse than 20/400 and corresponds to being “legally blind.”



LENS LUXATION Canine eye with anterior lens luxation. There is corneal edema, conjunctival hyperemia, deep corneal vascularization, an aphakic crescent (*), and the lens is cataractous.

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Leishmaniasis

BASIC INFORMATION

DEFINITION

Leishmaniasis is a vector-borne zoonotic disease that is endemic in the Mediterranean region and South America (70 countries worldwide) and has recently been found in dogs in the United States.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs, cats, foxes, jackals, humans in endemic areas

GENETICS & BREED PREDISPOSITION: Boxers; most dogs with leishmaniasis in the United States have been foxhounds.

RISK FACTORS: Dogs that have travelled to endemic areas (Middle East, southern Europe, Central and South America), foxhounds, outdoor dogs living in areas where sandflies are endemic

CONTAGION & ZOONOSIS: Dogs are an important reservoir for human disease. In people, the disease occurs most commonly in infants, children, and immuno-suppressed or malnourished individuals.

GEOGRAPHY AND SEASONALITY: Disease is limited to temperate, warm, humid areas where vector sandflies are present. The sandfly vectors in the Old World (Middle East, southern Europe) are *Phlebotomus* spp. and in the New World (Central and South America), *Lutzomyia* spp.

ASSOCIATED CONDITIONS & DISORDERS

- Skin lesions: alopecia; exfoliative dermatitis, ulceration of face, pinnae, or limbs
- Glomerulonephritis
- Ocular lesions: keratoconjunctivitis, uveitis
- Lymphadenopathy
- Epistaxis
- Abnormal growth and elongation of nails (onychogryposis)

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: One or more of the following: chronic weight loss, exercise intolerance, lymphadenopathy, skin lesions, eye lesions/vision loss, lameness, epistaxis

PHYSICAL EXAM FINDINGS

- Lymphadenopathy
- Splenomegaly
- Ulcerative skin lesions of pinnae, face, and limbs
- Ocular discharge
- Miosis, photophobia secondary to uveitis

ETIOLOGY AND PATHOPHYSIOLOGY

- *Leishmania infantum* is the cause of human and canine visceral leishmaniasis in Europe, the Middle East, Africa, Asia, China, and the Americas. It is synonymous with *L. chagasi* found in Latin America.
- The parasite's life cycle is diphasic (vector and host phases). Promastigotes develop in the gut of the sandfly and migrate to the proboscis. They are transmitted to the mammal host during a blood meal and are phagocytized by macrophages. Inside the macrophage, they become amastigotes and multiply by binary fission until the macrophage ruptures, and the amastigotes are then disseminated to other macrophages and throughout the body.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Highly sensitive and specific diagnostic serologic and molecular techniques to detect *Leishmania* infection are now widely available in commercial laboratories. Quantitative serologic and molecular (PCR) techniques are the assays of choice. These should be used wisely and take into consideration that in endemic areas, a large part of the canine population may be infected subclinically and could present for veterinary care for unrelated reasons. Diagnostic testing is usually performed to confirm disease in dogs with suspected clinical signs, to monitor response to treatment, or to evaluate possible infection in apparently healthy blood donors, imported dogs, or dogs who have traveled to endemic areas.

DIFFERENTIAL DIAGNOSIS

- Tickborne diseases: borreliosis, ehrlichiosis
- Leptospirosis
- Dirofilariasis
- Pyoderma
- Immune-mediated skin diseases, vasculitis, glomerulonephritis
- Demodicosis
- Lymphoma
- Malnutrition, poor husbandry

INITIAL DATABASE

- CBC: may show leukopenia or leukocytosis, nonregenerative anemia, thrombocytopenia
- Serum chemistry profile: hyperglobulinemia, hypoalbuminemia ± azotemia
- Cytologic evaluation of lymph node, skin, splenic, and bone marrow aspirates may reveal amastigote forms of *Leishmania.*
- Urinalysis: may reveal isosthenuria and proteinuria secondary to immunoproliferative glomerulonephritis
    - Urine protein/creatinine ratio may be elevated (>0.5).

ADVANCED OR CONFIRMATORY TESTING

- Histopathologic evaluation and immunohistochemical staining of skin biopsies may reveal organisms.
- Serologic tests: indirect immunofluorescent antibody test (IFAT) titers >1:32 indicate suspected exposure; titers >1:200 are consistent with active infection. Specific quantitative recombinant antigen rK39 ELISA or crude-antigen ELISA may also detect subclinical infection.
- PCR test: most sensitive test (confirmatory test of choice); will also detect subclinically infected dogs.

TREATMENT

TREATMENT OVERVIEW

Current drugs used for treating canine leishmaniasis, including newly developed therapies such as treatment with miltefosine or synergistic combinations of drugs, have limited efficacy and do not clear infection completely in most dogs. Treatment of dogs is usually followed by clinical improvement, but the parasite is rarely eliminated, and treated dogs remain latent carriers that may relapse and continue to harbor a zoonotic infection.

ACUTE GENERAL TREATMENT

- Sodium stibogluconate (Pentostam: available from the Centers for Disease Control and Prevention in Atlanta, GA) 30 mg/kg q 24 h IV or SQ for 3-4 weeks; *or*
- Meglumine antimonite (Glucantime): 100 mg/kg SQ or IV q 24 h for 3-4 weeks
- Allopurinol (20 mg/kg/d PO) for 6-12 months; can be administered in combination with meglumine antimonate at the same doses as above for both drugs
- Miltefosine (2 mg/kg/d PO) for 4 weeks with allopurinol (20 mg/kg/d PO) for 6-12 months

CHRONIC TREATMENT

- Dogs with renal insufficiency and protein-losing nephropathy do not respond well to therapy.
- Euthanasia should be considered in dogs with chronic poorly responsive disease or in households with immunosuppressed persons.

RECOMMENDED MONITORING

Negative PCR or declining titers post treatment. Periodic monitoring of renal parameters every 3 months in dogs with no initial azotemia and more frequently in dogs with azotemia at admission.

PROGNOSIS AND OUTCOME

Prognosis is guarded owing to inability to completely eradicate the organism.

PEARLS & CONSIDERATIONS

PREVENTION

- There is no vaccine available in the United States. A vaccine is marketed in Brazil, and there are progressive experiments on new commercial canine vaccines.
- Insecticidal collars and topical insect repellent may prevent vector transmission.
- If possible, keep pet dogs inside during dawn and dusk, the feeding times of sandflies.

CLIENT EDUCATION

- Leishmaniasis is a zoonotic disease that can be fatal in humans.
- Leishmaniasis does not respond very well to treatment.
- Leishmaniasis is often a chronic infection in dogs that may not manifest for years after the initial exposure.

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Leiomyoma, Leiomyosarcoma

BASIC INFORMATION

DEFINITION

- Leiomyoma: uncommon benign tumor of smooth muscle origin
- Leiomyosarcoma: uncommon malignant tumor of smooth muscle origin
- Either can be found wherever smooth muscle is present. Most common sites: gastrointestinal (GI) tract, spleen, genital tract

SYNONYMS

Smooth muscle tumors

EPIDEMIOLOGY

SPECIES, AGE, SEX: Uncommon in dogs and rare in cats

- Leiomyoma: gastric: mean age 16 years (dogs)
- Leiomyoma: colonic: median age 12 years (dogs)
- Leiomyosarcoma: GI; median age 10.5-12 years (dogs)
- Leiomyo(sarco)ma: genital, urinary tract, or intestinal; female > male

GENETICS & BREED PREDISPOSITION: Leiomyosarcoma more common in large-breed dogs, notably in German shepherds (intestinal).

ASSOCIATED CONDITIONS & DISORDERS: Paraneoplastic syndromes:

- Hypoglycemia
- Nephrogenic diabetes insipidus (one dog with intestinal leiomyosarcoma)
- Polycythemia due to elevated plasma erythropoietin levels (one dog with cecal leiomyosarcoma)

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- GI leiomyoma:
  - Incidental finding during endoscopy or necropsy. Occasionally, tenesmus or dyschezia if rectal; vomiting or regurgitation if gastroesophageal.
- GI leiomyosarcoma:
  - Signs referable to the GI tract, including chronic vomiting, weight loss, melena, hematemesis, gastric dilation, or regurgitation
- Peripheral leiomyosarcoma: progressively enlarging mass noticed by the owner
- Rarely, animals with leiomyosarcoma first present with signs related to paraneoplastic hypoglycemia.

PHYSICAL EXAM FINDINGS

- Abdominal mass possible with any visceral leiomyo(sarco)ma
- Signs of peritonitis possible as a result of intestinal rupture, especially with cecal leiomyosarcoma
- Abdominal pain, distended loops of bowel, and/or mass palpable per rectum in some cases
- Weakness or collapse due to gastric hemorrhage
- Subcutaneous mass with peripheral leiomyosarcoma
- Physical exam may be unremarkable, especially with leiomyoma.

ETIOLOGY AND PATHOPHYSIOLOGY

- Both leiomyomas and leiomyosarcomas have been associated with paraneoplastic hypoglycemia. Potential mechanisms: excessive glucose metabolism by the tumor, diminished hepatic gluconeogenic capacity due to hepatic damage by the tumor, associated peritonitis, or due to production of insulin-like growth factors by the tumor. Those tumors associated with

production of insulin-like growth factors have been associated with long-term disease-free intervals or cure as a result of resection of the tumor.
- Although not confirmed, leiomyosarcomas in the female urogenital organs are thought to develop secondary to hormonal stimulation.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on gastrointestinal signs in an older dog, typically with a mass visible on abdominal ultrasound; confirmation is obtained via histopathologic and immunohistochemical evaluation.

DIFFERENTIAL DIAGNOSIS

- GI: foreign body, enteritis causing ileus, other GI neoplasm, GI granuloma (fungal, other), GI inflammation/infiltration (inflammatory bowel disease), renal disease, hepatic disease
- Other sites: other neoplasms (benign or malignant), abscess, granuloma, hematoma

INITIAL DATABASE

- CBC: 63% of dogs are anemic.
- Serum biochemistry panel: 50% are hypoglycemic
- Three-view thoracic radiographs: usually within normal limits
- Abdominal radiographs: may reveal GI mass, evidence of lymphadenopathy, changes consistent with peritonitis, or no abnormalities
- Abdominal ultrasound: 66% have evidence of an abdominal mass. Lymphadenopathy may also be noted.
- Fine-needle aspirate cytologic evaluation, if possible, may help identify the tumor type before invasive diagnostic testing (biopsy).

ADVANCED OR CONFIRMATORY TESTING

- GI contrast radiography (e.g., barium series), endoscopy, or CT may confirm gastroesophageal or intestinal obstruction and/or mass.
- The gold standard for diagnosis is biopsy with histopathologic evaluation, preferably surgically (rather than endoscopically) to resect the entire neoplasm if possible. Histopathologic grade may be prognostic.
- Immunohistochemical staining is required to differentiate leiomyosarcomas from gastrointestinal stromal tumors.

TREATMENT

TREATMENT OVERVIEW

Treatment requires stabilizing the patient and attempting wide and complete surgical resection of the entire tumor (if possible).

ACUTE GENERAL TREATMENT

Stabilization of systemic effects: hypoglycemia, anemia (e.g., due to GI hemorrhage), electrolyte and acid-base disturbances (e.g., due to chronic vomiting).

CHRONIC TREATMENT

- Complete surgical resection:
  - Curative of leiomyoma, and leiomyosarcoma in the absence of metastases.
  - If small intestinal, removal of 5 cm of normal bowel on either side of the tumor and resection of the corresponding mesentery are recommended.
  - Even with gross metastatic disease, surgical resection of leiomyosarcomas can afford long-term survival.
  - Mesenteric lymph nodes, liver, and suspected metastatic lesions should be biopsied for staging purposes.
- Dogs with metastasis or a high likelihood of metastasis (based on tumor location; see Prognosis and Outcome below) can be considered candidates for chemotherapy, although no studies have shown promising efficacy of chemotherapy against these tumors.

POSSIBLE COMPLICATIONS

- Variable, depending on the types of treatments and the location of the primary tumor
- A 50% rate of localized peritonitis associated with tumor rupture has been reported.

RECOMMENDED MONITORING

- According to clinical signs
- Exam and three-view thoracic radiographs and abdominal ultrasound q 3 mon for postoperative GI leiomyosarcoma patients. Exact frequency based on clinical signs and tumor location (see Prognosis and Outcome below).

PROGNOSIS AND OUTCOME

Prognosis depends on the location of the tumor:

- Dogs with hepatic leiomyosarcoma frequently develop metastases and have a grave prognosis.
- Dogs with gastric or intestinal leiomyosarcomas may have metastatic rates >54%, but many can have a good prognosis, even with confirmed metastasis (e.g., median survival 21.7 months for those surviving the perioperative period, including dogs with metastatic disease); 1-year survival rate 75%, 2-year survival rate 66%, and 3-year survival rate 60%.
- Dogs with cecal leiomyosarcomas may have a lower metastatic rate (10%) and better overall prognosis. Most dogs with successful resection of the cecal tumor eventually die of causes unrelated to the tumor.
- Colorectal leiomyomas: mean survival 31.6 months

PEARLS & CONSIDERATIONS

COMMENTS

- Leiomyosarcomas most commonly occur in the cecum and jejunum. They are the second most common intestinal tumor in dogs.
- Even with metastatic disease, including gross hepatic and mesenteric involvement apparent at laparotomy, GI leiomyosarcoma is associated with a fair life expectancy (mean: 2 years) postoperatively.
- Some gastrointestinal leiomyosarcomas (GILMS) have been reclassified as gastrointestinal stromal tumors (GIST) via immunohistochemical techniques (they express c-kit, CD-117 positive; true GILMS do not). GIST are derived from interstitial cells of Cajal, which are the pacemaker cells of the gastrointestinal tract (regulate motility and peristalsis). One study indicated that in dogs, it may be that GILMS and GIST behave differently (GILMS more commonly located in the stomach and small intestine; GIST more commonly located in the cecum and large intestine). GIST were also thought to be more locally invasive and more likely to result in perioperative death as a result of gastrointestinal wall perforation and sepsis. Another study found no clinical importance of reclassification, but did note that future treatments may be dictated by this division.

CLIENT EDUCATION

If leiomyosarcoma: monitor for signs indicating recurrence or abdominal metastasis (e.g., vomiting, diarrhea, abdominal distention, and abdominal pain).

SUGGESTED READING

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Left Bundle Branch Block

BASIC INFORMATION

DEFINITION

An intracardiac conduction disturbance sometimes associated with left ventricular enlargement. There is failure of normal (rapid) conduction from the bundle of His through the left bundle branch to the Purkinje fibers in the left ventricle. Conduction to the left ventricle still occurs but is very slow because it must travel from muscle cell to muscle cell. This results in a marked delay in conduction to the left ventricle, and the QRS complex becomes wider on the electrocardiogram (ECG).

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs and cats of either sex and any age

RISK FACTORS: Left ventricular enlargement, particularly left ventricular dilation

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Intermittence: in some cases, left bundle branch block (LBBB) may occur only when the heart rate surpasses a certain individual threshold (heart rate dependent).
- Left anterior fascicular block:
  - Historically, it was believed the left bundle branched into anterior and posterior fascicles as it does in humans, and that left anterior fascicular block was implicated in causing a marked left axis deviation on the surface ECG, with only slight prolongation of left ventricular depolarization.
  - However, the left bundle does not branch into two distinct fascicles in dogs and cats, making this extrapolation inaccurate.
  - Still, a marked left axis deviation in cats, which has been called *left anterior fascicular block* by some, has often been observed both in cats with hypertrophic cardiac disease and in normal cats.
  - Thus, it is important to recognize this pattern of left axis deviation (tall R wave in leads I and aVL, S wave present in leads II, III, and aVF), although the name left anterior fascicular block is inappropriate.

HISTORY, CHIEF COMPLAINT: Reflective of the underlying structural heart disease. Chief complaints range in severity from none (uncommon; LBBB is an infrequent incidental finding on ECG) to decompensated states of heart disease, such as congestive heart failure (dyspnea, lethargy, abdominal distension possible) or syncope.

PHYSICAL EXAM FINDINGS

- Typically LBBB is clinically silent. However, in some individuals, split heart sounds may be present due to prolonged left ventricular ejection time and delayed closure of the mitral valve (causing a split first heart sound).
- LBBB does not alter the rhythm of the heartbeat or the pulse.
- Findings relating to underlying structural heart disease (heart murmur, arrhythmia, gallop sound, dyspnea) are common.

ETIOLOGY AND PATHOPHYSIOLOGY

LBBB usually indicates significant underlying cardiac disease such as:

- Cardiomyopathy
- Congenital heart disease, in particular subaortic stenosis
- Cardiac ischemia
- Certain drug toxicoses (doxorubicin)

DIAGNOSIS

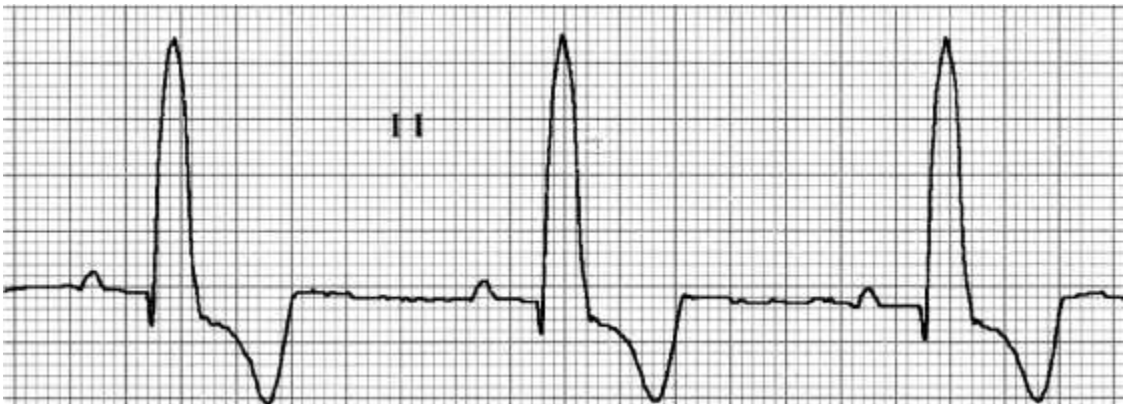
DIAGNOSTIC OVERVIEW

The diagnosis is made entirely on the electrocardiogram: LBBB is suspected when QRS duration is longer than normal (canine: >0.07 sec; feline: >0.06 sec), wide and positive R waves are present in leads I, II, III, aVF and the left precordial leads, and the rhythm appears to be supraventricular in origin.

DIFFERENTIAL DIAGNOSIS

Wide QRS complex(es) on ECG:

- Left ventricular hypertrophy
- Ventricular ectopy (premature ventricular complexes, ventricular tachycardia)
- Ventricular escape rhythm
- ± Motion artifact



LEFT BUNDLE BRANCH BLOCK Lead II ECG from a dog showing normal sinus rhythm with left bundle branch block. The QRS duration is 0.1 sec (normal £0.07). The heart rate is 90 beats/min. 50 mm/sec, 1 cm =1 mV.

INITIAL DATABASE

Electrocardiography is the definitive diagnostic test. Electrocardiographic characteristics of LBBB:

- Prolonged QRS complex duration (canine >0.07 sec, feline >0.06 sec)
- Wide and positive QRS complexes in leads I, II, III, aVF, and left precordial leads (CV6LL [V2] and CV6LU [V4])
- Negative QRS complexes in leads aVR and CV5RL (rV2)

ADVANCED OR CONFIRMATORY TESTING

- Thoracic radiographs to evaluate for left ventricular enlargement
- Echocardiogram to assess heart structure and function

TREATMENT

TREATMENT OVERVIEW

No treatment is necessary for LBBB. LBBB does not result in any hemodynamic sequelae by itself and therefore does not require specific treatment. However, LBBB is often associated with underlying structural heart disease. Treatment of this underlying condition is indicated if present.

POSSIBLE COMPLICATIONS

Complete block of both the right and left bundle branches produces complete (third-degree) atrioventricular block

PEARLS & CONSIDERATIONS

COMMENTS

- The bizarre QRS morphology seen with bundle branch block can be confused with premature ventricular complexes or

ventricular tachycardia (ventricular ectopy).
    - If P waves are present and the PR interval is consistent for every heartbeat, the complex is likely coming from a supraventricular site (and the bizarre QRS morphology is due to bundle branch block rather than ventricular ectopy). However sometimes P waves are buried and not visible, although the rhythm is supraventricular in origin (particularly with tachycardias).
    - Because most dogs with heart rates <140 beats/min have sinus arrhythmia and some degree of irregularity to the heart rhythm, examining the regularity of rhythm can be a helpful clue. A regularly irregular (cyclically varying) rhythm with QRS complexes that are all wide, bizarre, but identical to each other, suggests respiratory sinus arrhythmia with bundle branch block. By contrast, when ventricular ectopy such as ventricular tachycardia produces wide, bizarre QRS complexes that are all of the same shape, the rhythm is often regular (same R-R interval).
- In human patients with heart failure, the presence of a LBBB indicates significant dyssynchrony of ventricular contraction. Cardiac resynchronization, by means of biventricular pacing, results in clinical benefits. This therapy may be used in veterinary patients in the future.

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Lead Toxicosis

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Syndrome secondary to exposure to injurious amounts of lead. Exposure is usually by ingestion, and clinical signs predominantly manifest as neurologic or (less commonly) acute gastrointestinal (GI) changes.

SYNONYMS

Plumbism; lead poisoning

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Cats are at increased risk because of grooming habits in areas contaminated with lead-laden particles (e.g., during home remodeling with exposure to flakes of lead-based paint).
- Immature animals can absorb more lead from the GI tract than adults.
- Lead crosses the blood-brain barrier more readily in immature animals than in adults.
- Juvenile dogs are more likely to be involved, owing to their tendency to lick, mouth, and chew objects that may contain lead or be painted with lead-based paint.

RISK FACTORS

- Lead absorption can be greater in animals deficient in calcium, zinc, iron, or vitamin D.
- Animals living in homes containing paint formulated before 1977 may be at increased risk of exposure, especially during times of home remodeling/renovations.

CONTAGION & ZOONOSIS: Common source lead exposure can occur in animals and humans. The owners of animals with lead intoxication should be made aware of the possible risks of human lead toxicosis, especially to infants and young children who may chew on or swallow lead objects (e.g., curtain weights, fishing weights, older painted toys).

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Acute toxicosis occurs after a single toxic dose of lead.
- Chronic toxicosis, which is more common, occurs after repeated exposures over time, leading to accumulation of lead in the body.

HISTORY, CHIEF COMPLAINT

- Observed or suspected exposure to lead-containing products
- Recent remodeling in older residences or agricultural outbuildings increases suspicion.
- Acute toxicosis: acute onset of anorexia and neurologic signs
- Chronic toxicosis: insidious onset of vomiting, diarrhea, anorexia, abdominal discomfort, regurgitation (uncommon; due to megaesophagus) in cats but not dogs, lethargy, weight loss, anemia, behavior changes and/or intermittent seizures

PHYSICAL EXAM FINDINGS

- Acute toxicosis:
  - Lethargy
  - Anorexia
  - Aberrant behavior
  - Ataxia
  - Tremors
  - Seizures

- Chronic toxicosis:
  - Weight loss
  - Anorexia
  - Lethargy
  - Vomiting
  - Diarrhea
  - Aberrant behavior
  - Intermittent seizures
  - Pallor (anemia)

ETIOLOGY AND PATHOPHYSIOLOGY

- Inhibition of enzymes associated with heme production results in microcytic, hypochromic, regenerative anemia with presence of nucleated red blood cells (RBCs) and possibly basophilic stippling.
- Competition with calcium ions results in storage of lead in bones, alteration of nerve and muscle transmission, and displacement of calcium from calcium-binding proteins.
- Inhibition of membrane-associated enzymes (e.g., sodium/potassium pumps) can result in increased RBC fragility and renal tubular epithelial injury.
- Lead may interfere with γ-aminobutyric acid (GABA) production or activity in the central nervous system (CNS) and lead to loss of inhibitory impulses, resulting in seizures.

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

History and physical exam are often nonspecific (e.g., suggestive of gastroenteritis). Suspect lead toxicosis if there are concurrent GI and neurologic signs, if there is a history suggestive of lead in the pet's environment (old house, recent renovation remodeling), or with incidentally identified red blood cell abnormalities or metallic foreign bodies in the GI tract on radiographs. The confirmatory test of choice (indicated in all suspect cases) is lead concentration in whole blood.

DIFFERENTIAL DIAGNOSIS

- Sterile encephalitides (e.g., granulomatous encephalitis)
- Viral encephalitides (canine distemper, rabies)
- *Toxoplasma* encephalitis
- Hepatic encephalopathy
- Idiopathic epilepsy
- Brain neoplasm

INITIAL DATABASE

- CBC (hematologic abnormalities more common in chronic toxicosis):
  - Nucleated RBC (nRBC) counts of 5-40 nRBC/100 white blood cells (WBCs) consistent with lead toxicity:
    - If >40 nRBC/100 WBCs, rule out myeloproliferative disorders.
    - nRBCs present in approximately 54% of dogs with lead intoxication
  - Microcytic, hypochromic, regenerative anemias uncommon; anemia present in approximately 8% of dogs with lead intoxication
  - Basophilic stippling in dogs can be suggestive of lead toxicosis:
    - Differentiate from RBC parasites (e.g., *Babesia*).
    - Not a consistent finding; present in approximately 25% of dogs with lead intoxication
  - ±Anisocytosis, poikilocytosis, polychromasia, echinocytosis, target cells
  - ±Mature leukocytosis
- Serum bile acids (paired samples: after 12-hour fast [preprandial] and 2 hours postprandial) to help rule out hepatic encephalopathy due to portosystemic shunting unrelated to load toxicosis.
- Radiography:
  - Radiopaque material/objects in GI tract or joint space:
    - Absence does not rule out lead toxicosis.
    - Presence of metallic material in GI tract noted in approximately 20% of dogs with lead intoxication
  - “Lead lines” in epiphyses possible but not common
- Serum chemistry profile, urinalysis:
  - No specific abnormalities expected

ADVANCED OR CONFIRMATORY TESTING

- Neurologic examination (see p. 1311):
  - Mental dullness, depression are most common changes
  - Asymmetric (lateralizing) neurologic deficits are inconsistent with lead intoxication and should suggest other diagnoses.
- Blood lead level (BLL): whole blood (acceptable anticoagulants are heparin [green-top tube] or EDTA [purple-top tube]).
  - Levels >0.35-0.4 ppm (35-40 meg/ dL) are suggestive of lead toxicosis.
    - With appropriate clinical signs, BLL > 35 mcg/dL is diagnostic of lead toxicosis.
  - BLL between 0.1 and 0.35 ppm (10-35 mcg/dL) suggests significant exposure and with appropriate clinical signs is suggestive of lead toxicosis.
  - Normal background BLL usually <0.1 ppm (<10 mcg/dL)
  - BLL is not reflective of total body burden; may not correlate to severity of clinical signs.
  - In chronic toxicoses, BLL may not be appreciably high because of distribution of lead into body compartments (e.g., bone).

TREATMENT

TREATMENT OVERVIEW

Treatment goals are to stabilize the patient and manage severe clinical signs (seizures) or blood abnormalities (anemia) if present, followed by removal of lead objects from the GI tract (if applicable) and chelation therapy for as long as needed to achieve nontoxic whole blood lead levels.

ACUTE GENERAL TREATMENT

- Manage seizures:
  - Diazepam, 0.5-2 mg/kg IV to effect
  - If seizures intractable with diazepam alone: phenobarbital, 2-10 mg/kg IV to effect
  - Consider IV diazepam constant rate infusion (0.1-0.5 mg/kg in 5% dextrose [D5W] at maintenance rate, titrated to effect) for acute, persistently refractory seizures.
  - Pentobarbital (3-15 mg/kg IV to effect), propofol (0.1-0.6 mg/kg/ min), or gas anesthesia are additional treatment considerations for persistently refractory seizures not responding to the treatments listed previously.
- Correct fluid and electrolyte abnormalities as needed.
- Remove macroscopic lead from GI tract. It is essential to accomplish this before chelation.
  - Chelators (except succimer) will enhance absorption of lead from the GI tract.
  - Emesis, gastrostomy, cathartics, enemas, whole bowel irrigation may be used for removing lead from GI tract.
    - Activated charcoal does not adsorb lead well and is not helpful.
    - Magnesium sulfate (125-250 mg/ kg PO) may precipitate lead in GI tract and thus reduce its systemic absorption as well as promote diarrhea (purgative).
- Chelation:
  - Most lead chelators are nephrotoxic.
    - Monitor serum renal values and maintain adequate hydration.
  - Monitor progress of chelation therapy by monitoring BLL; decline is first expected around 5 days after initiating chelation.
  - If signs persist and levels have not decreased after several days of chelation therapy, patient reassessment is necessary to be sure reexposure is not occurring (e.g., through environment, or GI lead foreign body).
  - Succimer (meso-2,3-dimercaptosuccinic acid [DMSA]): treatment of choice in most cases
    - Least nephrotoxic chelator
    - Can be administered orally or rectally
    - Less likely to bind essential minerals
    - Does not increase absorption of lead from GI tract
    - Dogs: 10 mg/kg PO or per rectum q 8 h for 10 days
  - Calcium disodium ethylenediaminetetraacetic acid (Ca EDTA): mostly replaced by succimer, except in patients with intractable vomiting or other situations in which parenteral treatment is preferred.
    - Dogs: 25 mg/kg SQ q 6 h, diluted in 5% dextrose, for 2 to 5 days
    - A 5-day rest is recommended if additional doses needed.
    - Cats: 27.5 mg/kg in 15 mL of 5% dextrose SQ q 6 h for 5 days
  - Dimercaprol (British anti-Lewisite [BAL]): mainly of historic interest; replaced by others (above)
    - Adsorbs lead from RBCs
    - Increases urinary and biliary excretion
    - Painful on injection
    - Nephrotoxic; also contraindicated in hepatic dysfunction

        - Administer 3-6 mg/kg IM q 6-8 h for 2 days.
    - Penicillamine: mainly of historic interest; replaced by others already listed
        - Nephrotoxic; maintain adequate hydration
        - Binds essential minerals (copper, iron zinc)
        - May cause vomiting (premedicate with maropitant 1 mg/kg q 24 h, SQ or 2 mg/kg PO q 24 h)
        - Dogs: 8-35 mg/kg PO q 6-8 h for 1-2 weeks
- Supportive care:
    - Maintain hydration and nutrition.
    - Manage GI signs.
- Prevent reexposure:
    - Identify and remove lead source from environment.

CHRONIC TREATMENT

- Management of CNS signs if persistent (e.g., seizures)
- Management of renal injury if present

NUTRITION/DIET

- NPO if there is excessive vomiting
- A bland diet may be indicated until resolution of signs if there is evidence of diarrhea.

BEHAVIOR/EXERCISE

Clients need to be informed of aberrant behavior some pets with high BLL show during toxicosis (and persistence during early stages of treatment).

POSSIBLE COMPLICATIONS

Severe neurologic injury may be permanent.

RECOMMENDED MONITORING

- CBC
- Packed cell volume
- Hydration
- Renal values
- BLL; generally, one round of chelation therapy is given, followed by reassessment:
    - If lead levels are still elevated *and* clinical signs are still present, consider second round of chelation therapy.
    - If lead levels are still elevated but patient is clinically normal, monitor without repeating chelation.

PROGNOSIS AND OUTCOME

- Animals with mild to moderate signs have favorable prognosis with treatment.
- BLL may rebound within 2 weeks of cessation of chelation owing to redistribution of lead from body stores (e.g., bone). If clinical signs recur at that time, then redosing with chelator is recommended; if no signs occur, monitoring lead levels q 14 days is acceptable to verify that levels are continuing to fall.

PEARLS & CONSIDERATIONS

COMMENTS

- Lead embedded in soft tissues is not a significant source of lead toxicosis.
- Lead in joint spaces or areas of active inflammation may undergo systemic absorption.
- Lead stored in bones may be mobilized during times of increased bone resorption (e.g., lactation, fractures) and can result in delayed toxicosis.
- If chelator therapy is not working, either the lead toxicosis is not being addressed or (more likely) the patient is continuing to be exposed to the source of lead.

PREVENTION

Remove lead objects and lead-based paint from pet's environment.

TECHNICIAN TIPS

If the patient is vomiting, note whether foreign material is in the vomitus (possibly eliminating the need for endoscopic/surgical removal of lead foreign body from the GI tract). All solid lead must be removed from the GI tract prior to chelation therapy or else chelation can extract lead from the foreign body, perpetuating toxicosis.

CLIENT EDUCATION

Keep pets out of areas where home renovation/remodeling is occurring.

SUGGESTED READING

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Laryngeal Trauma

BASIC INFORMATION

DEFINITION

Trauma resulting in disruption of or damage to laryngeal structures (thyroid, cricoid, and arytenoid cartilages) and surrounding soft tissues

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs and cats; no age or sex predilection. Cats may be more predisposed to iatrogenic laryngeal trauma from orotracheal intubation.

RISK FACTORS

- Animals that are outside unsupervised have increased risk for all types of trauma.
- Anesthesia with intubation
- Long-term intubation for positive pressure ventilation
- Bronchoscopy

ASSOCIATED CONDITIONS & DISORDERS

- Polytrauma: head trauma, respiratory compromise, cardiovascular shock
- Laryngeal laceration can result in subcutaneous emphysema, pneumomediastinum, and potentially, pneumothorax and pneumoretroperitoneum.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Acute onset of dyspnea with upper airway stridor
- Possible: history of witnessed trauma (e.g., bite wounds, penetrating missile, choking), recent prolonged intubation, or difficult intubation or bronchoscopy
- The patient can have a change of voice and/or dysphagia

PHYSICAL EXAM FINDINGS

- Tachypnea, dyspnea
- Upper airway noise (stridor), usually more prominent on inspiration but can be both inspiratory and expiratory
- Mucous membranes: pallor or cyanosis possible
- Thoracic auscultation: referred upper airway noise; harsh lung sounds, crackles (with either noncardiogenic pulmonary edema or aspiration pneumonia)
- Subcutaneous emphysema may be present in cervical region with penetrating wounds such as bite, gunshot, or arrow wounds or with laryngeal fracture and laceration.
- Hyperthermia (dogs: inability to pant)

ETIOLOGY AND PATHOPHYSIOLOGY

- Rough or difficult intubation or prolonged intubation can cause trauma to the mucosa, arytenoids, and vocal folds, resulting in hyperemia or edema, ulceration, and granulation tissue formation.
- Bite wounds or projectile missiles can cause penetrating or crush injury to the cartilages or recurrent laryngeal nerves.
- Airway lumen diameter can be drastically reduced if cartilages are crushed (e.g., choke chains) or with swelling/ hemorrhage of surrounding soft tissues (e.g., stick foreign bodies).
- Decreased ventilation from airway compromise: hypoxemia ± hypercarbia.
- Worsened hypoxemia (from ventilation/perfusion mismatch) if blood is aspirated into lungs or with noncardiogenic pulmonary edema from airway obstruction.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on respiratory distress with upper airway noise in a patient with a history of recent trauma to the cervical region or anesthesia with intubation. Confirmation of the diagnosis is made with cervical radiographs, laryngoscopy, and/or tracheoscopy.

DIFFERENTIAL DIAGNOSIS

- Foreign body in airway
- Insect sting/bite or other allergic reaction
- Trauma to caudal pharynx or trachea
- Laryngeal paralysis
- Laryngeal/pharyngeal mass (neoplasm, granuloma)
- Pharyngeal mucocele

INITIAL DATABASE

- CBC, serum biochemistry profile, urinalysis: usually unremarkable
- Pulse oximetry/arterial blood gas analysis:
  - Hypoxemia is common.
  - Hypercarbia if severe airway obstruction is present
- Cervical radiographs:
  - Look for fractures, dislocations, or asymmetry in hyoid apparatus.
  - Subcutaneous emphysema
- Thoracic radiographs:
  - Pneumomediastinum, pneumothorax
  - Concurrent thoracic trauma (e.g., rib fractures)
  - Look for noncardiogenic pulmonary edema secondary to airway obstruction.
- Laryngoscopy under general anesthesia (can be performed after tracheostomy if patient does not have a patent airway, allowing for stabilization of patient first):
  - Evaluate symmetry and function of laryngeal structures.
  - Look for hematomas, exposed cartilage, foreign body, or flaps of laryngeal mucosa.

ADVANCED OR CONFIRMATORY TESTING

- Tracheoscopy/bronchoscopy (can be performed after tracheostomy, if needed):
  - Evaluate larynx beyond the arytenoids.
  - Examine lower airways for evidence of trauma or foreign body.
- Esophagoscopy: rule out concurrent esophageal injury.
- CT may be useful in evaluating the hyoid apparatus for fractures or dislocations.

TREATMENT

TREATMENT OVERVIEW

Treatment should first consist of ensuring a patent airway and providing oxygen supplementation as needed to stabilize the patient, followed by surgical repair if needed. Initial stabilization may require an emergency tracheostomy if the patient cannot be intubated with an orotracheal tube.

ACUTE GENERAL TREATMENT

- Oxygen supplementation (see p. 1318)
- Intubation if needed (see p. 1292)
- Emergency tracheostomy (see p. 1344) if unable to pass endotracheal tube
- Treat cardiovascular compromise (IV catheter, fluids) and other life-threatening injuries if present.
- Surgical exploration and repair or permanent tracheostomy if indicated. Approach: midline ventral thyrotomy or through thyroid cartilage fracture:
  - Mucosal flaps: trim, appose edges.

- Reduce and immobilize cartilage fractures to prevent stenosis.
- Intraluminal stents can be used for preventing adhesions, collapse, and other complications.
- Mitomycin C applied topically has been reported to reduce granulation tissue and stenosis after surgical repair of laryngeal trauma.
- Unilateral arytenoid lateralization (tieback) if traumatic laryngeal paralysis without fractures or if arytenoid avulsion

- Postoperative care:
  - Antibiotics after obtaining cultures from contaminated wounds; continue 3-4 weeks in the postoperative period. Empirical selections while awaiting culture results could include:
    - Ampicillin, 22 mg/kg IV q 8 h, and enrofloxacin 10 mg/kg slow IV or PO q 24 h in dogs (5 mg/ kg q 24 h in cats)
    - Clindamycin, 10 mg/kg IV or PO q 8 h, and either amoxicillin/clavulanic acid 15 mg/kg PO q 12 h or enrofloxacin, as listed above
  - Corticosteroids (dexamethasone sodium phosphate, 0.1-0.2 mg/kg IV) at time of surgery to reduce inflammation; may repeat at a dose of 0.05-0.1 mg/kg IV q 12-24 h for first 24-48 hours.

CHRONIC TREATMENT

- Intraluminal stents will require second surgery 3-4 weeks later to remove stent.
- Permanent tracheostomy may be required if severe damage to larynx has occurred.

POSSIBLE COMPLICATIONS

- Respiratory arrest if complete obstruction
- Stenosis or stricture over the ensuing 1-2 weeks, resulting in secondary airway compromise
- Obstruction of temporary or permanent tracheostomy site with mucus
- Laryngeal paralysis
- Infection

RECOMMENDED MONITORING

- Vital signs and frequent auscultation during initial admission and in the perioperative period
- Tracheostomy care
- Pulse oximetry and/or arterial blood gas analysis
- Respiratory rate and effort, respiratory noise, and exercise tolerance, during and after the recovery stage

PROGNOSIS AND OUTCOME

- Depends on severity of trauma, concurrent injuries, and time to diagnosis and treatment
- If severe laryngeal trauma is present and veterinary care can be quickly obtained, permanent tracheostomy can allow for fair to good prognosis (with the exception of cats and very small dogs, where stoma obstruction with mucus may be recurrent and severe).

PEARLS & CONSIDERATIONS

COMMENTS

- Early temporary tracheostomy: stabilizes patient and allows imaging including laryngoscopy, endoscopic examination, radiographs, and CT.
- Surgical exploration/repair must occur early, optimally within 24 hours after injury.
- Surgical exploration is necessary if:
  - Airway obstruction is severe enough to require temporary tracheostomy
  - There is emphysema in the cervical region and/or pneumomediastinum
  - There is exposed cartilage within the lumen of the larynx
  - The laryngeal cartilage is fractured

PREVENTION

- Selection of appropriate endotracheal tube size and endoscope size along with use of lubrication will prevent iatrogenic trauma.
- Direct visualization of the larynx for intubation can also reduce risk of iatrogenic trauma.
- Long-term intubation for positive pressure ventilation can be maintained by temporary tracheostomy to prevent laryngeal

damage.

TECHNICIAN TIPS

Careful monitoring of these patients is necessary; they can develop acute airway obstruction. Any increased respiratory rate/effort or increase/change in respiratory sounds may indicate impending crisis. If possible, these patients are better monitored when not in an oxygen cage so any airway noises caused by acute obstruction can be heard.

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Laryngeal Paralysis

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Lack of abduction of arytenoid cartilages and vocal folds secondary to dysfunction of either the cricoarytenoideus dorsalis muscle or the recurrent laryngeal nerve. Common in old, large-breed dogs but rare in cats.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Male dogs: affected 2 to 4 times more often than females; no gender predilection in cats
- Congenital form: animals <1 year old
- Acquired form: middle-aged/older dogs (mean: 9-10 years of age)

GENETICS & BREED PREDISPOSITION

- Commonly reported in Labrador retrievers, other large/giant breeds. No breed predilection in cats.
- Inherited (autosomal dominant): Bouviers des Flandres
- X-linked recessive inherited polyneuropathy: Leonberger dogs
- Congenital and most likely hereditary: bull terriers, dalmatians, rottweilers, Siberian huskies, white-coated German shepherd dogs, Pyrenean mountain dogs

RISK FACTORS

- Damage to the recurrent laryngeal nerve (blunt trauma, thoracic or cervical surgery)
- Any condition resulting in polyneuropathy or polymyopathy:
    - Myasthenia gravis
    - Immune mediated
    - Diabetes mellitus
    - Hypothyroidism
        - Cause/effect relationship not established

GEOGRAPHY AND SEASONALITY: Hot weather (panting) may increase severity of clinical signs.

ASSOCIATED CONDITIONS & DISORDERS

- An elongated soft palate may develop with chronic increased inspiratory effort.
- Weakness and muscle wasting may be present in chronically affected dogs.
- Dysphagia or megaesophagus possible in dogs with polymyopathy or polyneuropathy.
- Aspiration pneumonia can develop secondary to dysphagia or esophageal or laryngeal dysfunction.
- Noncardiogenic pulmonary edema/ acute respiratory distress syndrome with vigorous inspiration against upper airway obstruction

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Unilateral:
    - Clinical signs mild or absent except in performance animals
- Bilateral:
    - Clinical signs apparent in most animals

HISTORY, CHIEF COMPLAINT

- Early:
    - Inspiratory stridor; very common

- Exercise intolerance with associated respiratory noise and/or breathlessness; very common
- Coughing, gagging when eating
- Voice change

- With progression:
  - Dyspnea
  - Tachypnea
  - Signs exacerbated with exercise, stress, hot weather, obesity
  - +/− Regurgitation if associated esophageal dysmotility
- Severely affected animals may show:
  - Dyspnea at rest
  - Cyanosis
  - Collapse
  - Death

PHYSICAL EXAM FINDINGS

- Unremarkable in early stages
- With disease progression, one may see:
  - Increased inspiratory effort, inspiratory stridor
    - These hallmark signs often are characterized by open-mouth, gasping respirations (in contrast to reverse sneezing) and improvement or total resolution at rest compared to during exertion.
  - Increased upper airway sounds (referred on thoracic auscultation)
  - Coughing or gagging
    - Laryngeal compression may induce coughing/gagging or increased respiratory sounds.
  - Weakness
  - Muscle atrophy, neurologic deficits if peripheral neuropathy/myopathy is present
  - +/− Crackles from pneumonia or pulmonary edema
  - Severe hyperthermia +/− signs of heatstroke (petechial hemorrhages, mucous membrane hyperemia, abnormal mentation) in severely dyspneic animals

ETIOLOGY AND PATHOPHYSIOLOGY

- Causes:
  - Nucleus ambiguus or axonal degeneration (congenital forms)
  - Idiopathic: most common cause of acquired. Suspected to be a result of underlying generalized peripheral neuropathy.
  - Intrathoracic, peritracheal, or laryngeal masses or foreign bodies (rare)
  - Other acquired causes include trauma to recurrent laryngeal nerve, polymyopathy, polyneuropathy, myasthenia gravis.
- Whatever the cause, recurrent laryngeal nerve dysfunction results in loss of function to all intrinsic muscles of the larynx except the cricothyroideus, causing inability to abduct arytenoids during inspiration (loss of cricoarytenoideus dorsalis muscle function) or actively adduct arytenoids (close the rima glottidis) during swallowing.
  - With increased inspiratory pressure, arytenoids are drawn inward, collapsing the airway during inhalation (paradoxical movement).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Definitive diagnosis is usually based on lack of active laryngeal movement, +/− presence of paradoxical movement, on oral examination under light anesthesia. Intravenous doxapram will stimulate respiration in animals that have inhibition of respiration or reduced inspiratory motion because of sedative and anesthetic administration. Laboratory evaluations, thoracic radiographs, and complete neurologic exam should be performed to assess the animal for signs of concurrent disease (e.g., polyneuropathy/myopathy, pneumonia, hypothyroidism).

DIFFERENTIAL DIAGNOSIS

- Elongated soft palate
- Collapsing trachea
- Laryngeal collapse
- Reverse sneezing
- Laryngeal mass or other laryngeal or proximal tracheal obstruction

INITIAL DATABASE

- Results of a CBC, biochemistry panel, and urinalysis are usually unremarkable except when systemic disease, dehydration, or heat stroke is present.
- Thoracic radiographs:
  - Usually normal or age-related interstitial changes
  - +/− Aspiration pneumonia
  - +/− Megaesophagus in animals with polyneuropathy/polymyopathy
- Low total thyroxine (T4) or free T4 with normal/increased thyroid-stimulating hormone: hypothyroidism
- Pulse oximetry in dyspneic or cyanotic dogs; normal dogs have oxygen saturation ≥95%

ADVANCED OR CONFIRMATORY TESTING

- Definitive diagnosis with laryngoscopy (see p. 1295):
  - May be performed without sedation/anesthesia during dyspneic crisis
  - Otherwise, light anesthetic plane (propofol 2-6 mg/kg IV to effect] or acepromazine/butorphanol/isoflurane
  - If no motion, administer doxapram HCl (1 mg/kg IV):
    - If laryngeal paralysis is present, arytenoid and vocal fold motion will be absent or paradoxical (inward collapse on inhalation, blown open on exhalation).
- In patients with polymyopathy or polyneuropathy, electromyography or nerve conduction velocities may be abnormal (see online chapter: Electromyography and Nerve Conduction Velocity).
- Patients may have antibodies to acetylcholine receptors if myasthenia gravis is present.
- May visualize lack of arytenoid movement on cervical ultrasound or trans-nasal laryngoscopy
- Esophageal dilation or lack of peristalsis on fluoroscopic contrast esophagram if concurrent esophageal motility disorder. Esophagrams not routinely recommended because of risk of aspiration.
- Coagulation panels may be abnormal in animals with hyperthermia or signs of heatstroke.

TREATMENT

TREATMENT OVERVIEW

Mildly affected animals may respond to sedation and oxygen administration during acute exacerbations of clinical signs and may remain stable with limited exercise or stress. Severely affected animals are most commonly treated with unilateral arytenoid lateralization to maintain a patent airway; however, this procedure will increase the risk of aspiration pneumonia.

ACUTE GENERAL TREATMENT

- Oxygen
  - Provide flow by oxygen (mask or nasal catheter) if Spo2 < 95%.
    - Perform immediate tracheostomy (see p. 1344), intubation, and light anesthesia or unilateral arytenoid lateralization if Spo2 cannot be maintained ≥95% on oxygen.
- Reduce laryngeal edema (prednisolone, 0.5-1 mg/kg IV; dexamethasone, 0.1-0.2 mg/kg IV; or furosemide, 2.2-4.4 mg/kg IV)
- Sedation (acepromazine, 0.005-0.02 mg/kg with butorphanol, 0.2-0.4 mg/kg IV q 2-4 h as needed) in stressed animals
- Cool hyperthermic patients
- For dogs with prolonged prothrombin time (PT) and partial thromboplastin time (PTT) secondary to heat stroke, administer fresh frozen plasma

CHRONIC TREATMENT

- Nonsurgical: rarely sufficient long-term without surgery:
  - Weight loss
  - Exercise restriction
  - Stress reduction
  - Treatment of underlying diseases
- Surgical:
  - Unilateral arytenoid lateralization recommended because higher complication rates are seen with other surgical options (permanent tracheostomy, vocal fold excision, partial laryngectomy, castellated laryngofissure, muscle-nerve pedicle transposition)
    - Unilateral arytenoid lateralization is considered a referral procedure.
    - Lateralization should be accomplished with low tension sutures to prevent excessive abduction of arytenoid.
  - Palate resection in dogs with concurrent elongated soft palate
  - Dogs with laryngeal muscle fibrosis and arytenoid cartilage fusion from trauma may require permanent tracheostomy.

POSSIBLE COMPLICATIONS

- Aspiration pneumonia reported in 8% to 33% of dogs after unilateral arytenoid lateralization
- Coughing/gagging in 16% after unilateral arytenoid lateralization
- Dyspnea may recur if suture breaks after unilateral arytenoid lateralization.
- Respiratory distress requiring temporary tracheostomy; postoperative megaesophagus; concurrent respiratory tract, esophageal, neurologic, or neoplastic disease
- Bilateral arytenoid lateralization associated with increase risk of postoperative complications and death

RECOMMENDED MONITORING

- Monitor for respiratory distress 12-24 hours after surgery.
- Avoid morphine or heavy sedation postoperatively (may increase risk of aspiration during recovery)
- Restrict exercise and reduce barking for 1-2 months after surgery.
- Reevaluate laryngeal function and repeat chest films as needed if clinical signs recur.

PROGNOSIS AND OUTCOME 

- Reduction of respiratory signs and improved exercise tolerance in 90% of dogs after unilateral arytenoid lateralization
- Poor with progressive polyneuropathy (rottweiler, dalmatian, others)
- Poor in dogs <10 kg that have undergone unilateral arytenoid lateralization
- Mortality rate 14%; higher complications noted in older animals or those with concurrent respiratory, esophageal, or neurologic disease

PEARLS & CONSIDERATIONS 

COMMENTS

- Videoendoscopy improves visualization during laryngeal exam.
- Laryngeal function is inhibited in normal dogs with some anesthetic combinations (acepromazine/thiopental, acepromazine/propofol, ketamine/ diazepam).
- Nonsurgical management is recommended in mildly affected dogs because of high postoperative complication rates associated with surgical treatments.
- Metoclopramide at the time of surgery reduces the risk of perioperative aspiration pneumonia.

PREVENTION

There is no means of preventing the development of this disease. Affected animals, especially those reflecting predisposed breeds, should not be bred.

TECHNICIAN TIPS

- To assist during oral examination, position the dog in sternal recumbency and hold the upper jaw with a piece of rolled gauze.
- The examiner should pull the tongue down with a gauze sponge and use a videoendoscope or laryngoscope to visualize the larynx. Note each inhalation for the examiner so that normal opening of the cartilages during inspiration can be differentiated from abnormal, paradoxical movement (abnormal: inward motion on inhalation, passive outward motion on exhalation).

CLIENT EDUCATION

- Dogs with polyneuropathy/polymyopathy have increased risk of postoperative complications.
- Upper airway noise, change in/loss of bark, and coughing often persist after surgery.
- There is a lifelong risk of aspiration pneumonia after surgery.
- Some dogs do better when fed dry food from floor level; try different food consistencies, bowl positions, and feeding strategies to reduce postoperative coughing and gagging and slow down food intake.

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Laryngeal Masses

BASIC INFORMATION

DEFINITION

Proliferation of laryngeal tissues due to benign or malignant processes

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Laryngeal masses are rare in dogs and cats but occur most often in middle-aged to older animals.
- Benign lesions may be seen in younger animals.
- There is a higher incidence of laryngeal tumors in male dogs and cats.

ASSOCIATED CONDITIONS & DISORDERS: Laryngeal masses can lead to acute or chronic upper airway obstruction.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Benign or malignant masses

HISTORY, CHIEF COMPLAINT

- Acute or progressive history of inspiratory stridor
- Voice change
- Dyspnea
- Cough
- Exercise intolerance
- Gagging and/or dysphagia
- Ptyalism
- Cyanosis
- Collapse
- Mass in the neck

PHYSICAL EXAM FINDINGS

- May be normal, with mass as an incidental finding at time of endotracheal intubation
- Inspiratory dyspnea, with gasping if severe
- Inspiratory stridor
- Palpable mass in the ventral laryngeal area in some
- Coughing and/or gagging due to laryngeal compression
- Weakness

ETIOLOGY AND PATHOPHYSIOLOGY

- Laryngeal tumors cause luminal obstruction by external compression or internal obstruction.
- Primary:
  - Benign:
    - Oncocytoma
    - Laryngeal cyst
    - Laryngeal polyp
    - Rhabdomyoma
    - Lipoma
  - Malignant:
    - Squamous cell carcinoma (most common)
    - Mast cell tumor
    - Fibrosarcoma
    - Rhabdomyosarcoma

        - Lymphoma
        - Osteosarcoma
        - Melanoma
        - Mixed cell tumor
- Metastatic:
    - Lymphoma
    - Plasma cell tumor
    - Thyroid neoplasia

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis often hinges on direct observation of the larynx in an anesthetized or heavily sedated patient with stridor or voice changes.

DIFFERENTIAL DIAGNOSIS

- Laryngeal paralysis (dogs > cats)
- Laryngeal collapse
- Elongated soft palate (dogs, especially brachycephalic)
- Nasopharyngeal polyp (cats)
- Pharyngeal or laryngeal foreign body
- Granulomatous masses

INITIAL DATABASE

- Results of a CBC, biochemistry panel, and urinalysis are usually unremarkable.
- Cervical radiographs may show a soft-tissue opacity in the area of the larynx, leading to laryngeal distortion or decreased laryngeal luminal space. The normal larynx of dogs, especially if mineralized, should not be confused with an abnormality (foreign body or other on a lateral cervical radiograph).
- Ultrasonography may allow identification of laryngeal masses because of the distortion of normal structural/anatomic relationships. It may also allow for fine-needle aspirates to be taken.
- Thoracic radiographs may have evidence of metastasis or aspiration pneumonia.

ADVANCED OR CONFIRMATORY TESTING

- Note: Patients with large laryngeal masses may be at the cusp of respiratory collapse despite showing only moderate dyspnea (inspiratory).
    - These patients may be unable to recover from anesthesia without respiratory distress/suffocation. Therefore, *before* sedation/anesthesia for evaluation of the upper airway in patients suspected of having airway obstruction:
        - An appropriate-sized endotracheal tube must be available.
        - A tracheostomy kit should be available.
        - Hair should be clipped from the ventral neck (preparation for tracheostomy if needed).
        - A contingency plan should be discussed with the owner if the mass is nonresectable (e.g., recover with tracheostomy versus euthanize on the table).
- Laryngoscopy with animal under general anesthesia to directly visualize the mass
- Tissue biopsy specimen can be obtained by open surgical technique or endoscopically.
    - Masses may also be aspirated for cytologic analysis.
    - A misleading cytologic or histologic diagnosis of lymphoid hyperplasia may be initially obtained by needle cytology or pinch biopsies in patients with primary laryngeal neoplasia.
- Ultrasound may help visualize the mass and aid fine-needle aspiration.
- CT or MRI can better show the extent of the mass and possible involvement of other regional structures.

TREATMENT

TREATMENT OVERVIEW

- Remove/reduce laryngeal luminal obstruction.
- Treatment depends on the extent of the lesion and type of mass.

ACUTE GENERAL TREATMENT

Stabilize the patient:

- Oxygen by face mask, oxygen cage, or nasal cannula if needed (see p. 1319)
- Tracheostomy if in severe distress from near complete obstruction (see p. 1344)

CHRONIC TREATMENT

- Small, benign lesions may be surgically excised by submucosal resection or partial laryngectomy.
- Laryngeal lymphoma is amenable to treatment with chemotherapy.
- Large invasive lesions or malignant tumors are best removed surgically by total laryngectomy combined with a permanent tracheostomy.
    - Permanent tracheostomy can palliate signs of respiratory distress in nonresectable cases or cases managed conservatively. Rarely successful in small individuals (cats, small dogs), because tracheal lumen becomes recurrently obstructed with secretions.
- Certain tumors may be better treated with radiation therapy. Consultation with an oncologist can be beneficial.

POSSIBLE COMPLICATIONS

- Postoperative swelling
- Dysphagia and/or gagging
- Pharyngeal dehiscence
- Laryngeal stenosis/webbing
- Hypoparathyroidism/hypothyroidism (if removed during laryngectomy)
- Tumor recurrence or metastasis
- Obstruction or self-trauma of tracheostoma

RECOMMENDED MONITORING

- Monitor closely for upper airway obstruction secondary to postoperative pharyngeal swelling.
- Withhold water and food for at least 24-48 hours in the postoperative period.
- Exercise should be restricted for 2-4 weeks.
- Routine laryngoscopic reevaluation is recommended to identify tumor recurrence or laryngeal stenosis.
- Periodic physical and radiographic evaluation is recommended to check for recurrence or metastasis.

PROGNOSIS AND OUTCOME

- The prognosis is good for benign lesions if complete resection is possible.
- Prognosis for malignant laryngeal tumors is guarded:
    - Advanced disease is often present at the time of diagnosis.
    - May not be surgically resectable

PEARLS & CONSIDERATIONS

COMMENTS

- A CO2 laser works well for surgical dissection and results in less inflammation and hemorrhage.
    - When using a laser, make sure the endotracheal tube is protected from the laser beam.
- Some patients may benefit from placement of a feeding tube for postoperative nutritional support (see p. 1267 -1273).

PREVENTION

There is no means of preventing the development of laryngeal masses.

TECHNICIAN TIPS

When preparing for examinations of animals with laryngeal disease, handy items to have nearby include a laryngoscope, tongue depressor (to move the soft palate), an extra endotracheal tube (in case a first becomes occluded with blood and mucus), long cup biopsy forceps, formalin, 22- or 23-gauge needles of varying lengths (1-inch, l 1/2-inch, spinal needles) and 6- or 12-mL syringes and

microscope slides (for aspiration cytology), and cotton-tip swabs (or alternatively, gauze sponges and forceps or suction) for clearing mucus or blood.

CLIENT EDUCATION

Vocalization is lost after total laryngectomy.

SUGGESTED READING

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Saik JE, et al: Canine and feline laryngeal neoplasia: a 10-year survey. J Am Anim Hosp Assoc 22:359, 1986.

Withrow SJ: Cancer of the larynx and trachea. In Withrow SJ, Vail DM, editors: Withrow and MacEwen's small animal clinical oncology, ed 4, St Louis, 2007, Elsevier, pp 515–517.

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Lameness

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Alteration of gait caused by structural or functional abnormality in one or more limbs

SYNONYMS

“Favoring leg,” limping

EPIDEMIOLOGY

RISK FACTORS

- Obesity
- Overnutrition during growth
- Trauma
- Genetics

ASSOCIATED CONDITIONS & DISORDERS

- Neurologic disorders
- Metabolic disorders
- Neoplasia
- Certain infectious diseases

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Lameness is most often secondary to pain. However, lameness also commonly occurs secondary to neurologic, mechanical, metabolic, or endocrine dysfunction.

HISTORY, CHIEF COMPLAINT: Thorough history is critical:

- Determine which limb is affected
- Abnormal gait or limping observed by owner
- Difficulty rising
- Improves or worsens with exercise
- Holding leg up (in contrast to neurologic deficit)
- Shifting leg lameness
- Acute or gradual onset
- Progression over time

PHYSICAL EXAM FINDINGS

- Complete general physical looking for any evidence of systemic abnormalities (e.g., fever)
- Complete orthopedic and neurologic examinations (see p. 1315and p. 1311).Orthopedic examination must include assessment of:
  - Abnormal posture
  - Joint effusion
  - Bone, joint pain, or muscle pain
  - Muscle atrophy
  - Thickening or bony prominences at or near joints
  - Crepitus
  - Abnormal range of motion in joints
- Observation at a walk and trot for gait abnormalities to help localize the limb that is affected:
  - Failing to bear full weight on limb
  - Short stride
  - Head bob (“down on sound”: head moves down when patient bears weight on normal limb then up with weightbearing

on affected limb to decrease weight on affected limb) with forelimb lameness
    - Toeing in or out
    - Dragging feet or scuffing nails
    - Bunny hopping (hindlimb weakness)
    - Stumbling
    - Ataxia
    - Hypermetria
- When both hind limbs are affected, weight may be shifted onto forelimbs, resulting in arched posture and abduction of the elbows.

ETIOLOGY AND PATHOPHYSIOLOGY

- Lameness secondary to pain from the musculoskeletal system: pain causes decreased weight bearing of the affected limb and shortness of stride. Severe acute pain may cause non-weight bearing on affected limb.
- Mechanical lameness: may be caused by abnormal length or angulation of bones, joints, ligaments, or tendons.
- Endocrine-related lameness: hyperadrenocorticism may cause myopathy, and diabetes mellitus may cause peripheral neuropathy.
- Neurologic disorders may cause ataxia, paresis, or pain manifesting as lameness.

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

Accurate diagnosis of lameness combines a thorough history, clinical exam, and consideration of signalment of the patient. An orthopedic exam (see p. 1315) is indicated in every case, and additional tests such as radiographs are selected based on abnormalities identified in the exam and medical history.

DIFFERENTIAL DIAGNOSIS

- Immature (<12 months) dogs and cats:
    - Forelimb:
        - Trauma (soft tissue, bone, joint)*
        - Osteochondritis dissecans (OCD) of the shoulder
        - OCD of the elbow
        - Ununited anconeal process (UAP; component of “elbow dysplasia”)
        - Fragmented medial coronoid process (FMCP; component of “elbow dysplasia”)
        - Elbow incongruity
        - Avulsion of flexor muscles
        - Premature growth plate closure
        - Retained cartilage core
        - Panosteitis
        - Hypertrophic osteodystrophy (HOD)
        - Infection (local or systemic)*
        - Nutritional imbalance*
        - Congenital abnormalities* (i.e., radial agenesis, congenital elbow luxation)
        - Atlantoaxial instability
    - Hind limb:
        - Trauma*
        - Hip dysplasia
        - OCD stifle
        - OCD hock
        - Patellar luxation*
        - Avulsion of long digital extensor
        - Aseptic necrosis of femoral head
        - Panosteitis
        - HOD
        - Infection (local or systemic)*
        - Nutritional imbalance resulting in overnutrition felt to be a factor in many developmental orthopedic diseases and dysplasias, or under-nutrition [nutritional secondary hyperparathyroidism/rickets] and development of pathologic fractures.*

        - Congenital abnormalities* (tibial agenesis in cats)
- Mature (>12 months) dogs and cats*:
    - Forelimb:
        - Trauma*
        - Elbow luxation
        - Shoulder luxation
        - Degenerative joint disease*
        - Bicipital tenosynovitis
        - Contracture of infraspinatus or supraspinatus
        - Mineralization of supraspinatus tendon
        - Elbow incongruity
        - Cervical disk disease*
        - Brachial plexus injury*
        - Inflammatory joint disease*
        - Polyneuritis
        - Polymyositis
        - Infection (local or systemic)*
        - Neoplasia of bone or soft tissue*
    - Hind limb:
        - Trauma*
        - Hip luxation*
        - Stifle luxation*
        - Patellar luxation*
        - Superficial digital flexor luxation
        - Hip dysplasia
        - Degenerative joint disease*
        - Cruciate ligament disease*
        - Avulsion of long digital extensor tendon
        - Panosteitis
        - Iliopsoas muscle injury
        - Thoracolumbar disk disease
        - Lumbosacral disease
        - Inflammatory joint disease*
        - Achilles tendon injury*
        - Polyneuritis
        - Polymyositis
        - Hypertrophic osteoarthropathy
        - Aortic thromboembolism*
        - Infection (local or systemic)*
        - Neoplasia of bone or soft tissue*

*Consider differential diagnosis in cats.

INITIAL DATABASE

- Complete orthopedic and neurologic examination
- Radiographs of affected limb(s)

ADVANCED OR CONFIRMATORY TESTING

- CBC
- Serum biochemistry panel
- Urinalysis
- Arthrocentesis (see p. 1199)
    - Can aid in distinguishing degenerative joint disease from infectious, inflammatory, or immune-mediated joint disease
    - Culture and sensitivity: joint fluid should be cultured in blood culture medium for highest yield
- Immunologic testing: rheumatoid factor, antinuclear antibody test
- Serologic evaluation for infectious disease (Lyme disease, Rocky Mountain spotted fever, ehrlichiosis)
- Ultrasound of tendons or muscles

- CT, MRI: CT is most useful for bones and joints, whereas MRI is most useful for soft tissue and spinal disease.
- Arthroscopy: can be used for both diagnostic and therapeutic purposes
- Arthrotomy
- Soft-tissue or bone biopsy
- Force plate and gait analysis
- Nuclear scintigraphy: used for localizing disease such as a difficult-to-diagnose lameness or metastatic tumors
- Electromyography (EMG) (see online chapter: Electromyography and Nerve Conduction Velocity): useful for evaluating neuromuscular conditions
- Muscle or nerve biopsy (see p. 1305)

TREATMENT

TREATMENT OVERVIEW

Treatment of lameness requires a multi-modal approach to alleviate pain and treat the underlying disorder causing the lameness.

ACUTE GENERAL TREATMENT

Lameness is a clinical sign, not a specific disease. Therefore treatment is based on determining the underlying cause.

CHRONIC TREATMENT

- Depends on underlying cause
- Adjunctive/supportive treatment:
  - Weight loss if indicated
  - Glycosaminoglycan administered intramuscularly or intraarticularly
  - Nonsteroidal antiinflammatory drugs (NSAIDs) such as meloxicam, deracoxib, firocoxib, etodolac, or carprofen
  - Amantadine as an *N*-methyl-d-aspartate (NMDA) receptor antagonist or other agents such as tramadol or gabapentin can be used as adjunctive medications for pain management.
  - Intraarticular corticosteroids can be administered for severe arthritis unresponsive to other therapies but carry risk of introducing infection and/or cartilage damage.
  - Stem cell therapy derived from autogenous adipose tissue has recently been described and become available.

NUTRITION/DIET

Nutritional and dietary therapeutics include eicosapentaenoic acid (EPA)-rich diets and nutraceuticals such as chondroitin and glucosamine.

BEHAVIOR/EXERCISE

Behavioral and physical activity recommendations include moderation of physical activity, physical rehabilitation (see p. 1329), stretching, and eliminating environmental risks such as slippery walking surfaces, stairs, and need for jumping.

DRUG INTERACTIONS

Glucocorticoids potentiate the gastrointestinal ulcerogenic effects of NSAIDs; this combination is contraindicated.

POSSIBLE COMPLICATIONS

NSAIDs may be associated with gastrointestinal irritation in some patients. They should also be used cautiously in animals with preexisting renal disease.

RECOMMENDED MONITORING

Repeat examination if response to therapy is not appropriate or if lameness progresses

PROGNOSIS AND OUTCOME

Highly variable, depending on underlying cause of lameness. For example, most cases of panosteitis in growing dogs resolve spontaneously over time (prognosis excellent), whereas lameness due to osteosarcoma of a long bone has a poor long-term prognosis.

PEARLS & CONSIDERATIONS

COMMENTS

Attention to signalment, history, and thorough examination are essential for generating “short list” of differential diagnoses.

PREVENTION

Weight management has been proven to reduce the incidence and severity of osteoarthritis and clinical signs in patients with orthopedic disease.

SUGGESTED READING

Hulse DA, Johnson AL: Orthopedic examination. In Small animal surgery, St Louis, 1997, Mosby, pp 719–729.

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EDITOR: ETIENNE CÔTÉ

Lactation Disorders

BASIC INFORMATION

DEFINITION

Partial or complete failure to produce or secrete milk to meet puppies' demands. They include agalactia (complete failure to produce milk), hypogalactia (partial failure), and galactostasis (accumulation of milk within the mammary gland due to failure of ejection [let-down] from the gland). Primary agalactia is extremely rare, but a delay in milk let-down is more frequent.

SYNONYMS

Agalactia or agalactosis; hypogalactia or hypolactation

EPIDEMIOLOGY

SPECIES, AGE, SEX: Postpartum female dogs, young bitches seem more prone. These disorders have not been described in cats.

GENETICS & BREED PREDISPOSITION: Any breed potentially can be affected. A genetic component may be present with agalactia.

RISK FACTORS: Inadequate nutrition, stress, anxiety, premature delivery or caesarean section, progesterone therapy, and systemic illness may trigger hypogalactia or poor milk let-down with galactostasis.

ASSOCIATED CONDITIONS & DISORDERS: Lactation disorders can coexist with other puerperal diseases, such as mastitis, metritis, and endotoxemia.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: History reveals the previous occurrence of (premature) parturition or caesarean section. Inadequate neonate weight gain, and crying and restless puppies are frequent complaints due to insufficient lactation. Few puppies nursing or abrupt weaning may precede galactostasis.

PHYSICAL EXAM FINDINGS

- Hypogalactia and agalactia: mammary development and milk appearance at nipple squeezing are scarce or absent.
- Galactostasis: engorged, firm and painful mammary glands, which may be associated with nipple anatomic abnormalities.

ETIOLOGY AND PATHOPHYSIOLOGY

- Normal milk production is the consequence of an endocrine cascade of estrogens, progesterone, and prolactin as well as other ancillary hormones. Idiopathic primary agalactia may represent a disruption of the pituitary/ ovarian/mammary gland axis of unknown etiology.
- Failure of milk let-down (secondary agalactia) can be due to stress, anxiety, premature delivery, progesterone therapy, or systemic illness.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Crying puppies and a dam that is reluctant to nurse are suggestive of either primary or secondary agalactia. Consideration of environment where lactation is occurring and physical examination of the mammary glands help differentiate the two causes.

DIFFERENTIAL DIAGNOSIS

- Mastitis
- Mammary tumors
- Pseudocyesis

- Care should be taken, as mastitis and mammary tumors can coexist with lactation disorders.

INITIAL DATABASE

- History and physical findings (as already described)
- CBC is normal if no concurrent inflammatory illness is present.

ADVANCED OR CONFIRMATORY TESTING

- Diagnosis is confirmed by exclusion of other diseases. Occult primary illness may require serum biochemistry profile, vaginal discharge examination, and ultrasound of the uterus.
- Cytologic evaluation of milk reveals cell counts > 3000 cells/μL with macrophages and neutrophils when inflammation (see p. 254) is present.

TREATMENT

TREATMENT OVERVIEW

Agalactia treatment mainly consists of the administration of galactagogues (prolactin increasing drugs). Failure of milk letdown requires treatment of primary cause (see Mammary Disorders, Non-Neoplastic, p. 688; Pyometra, ; Sepsis,p. 954 .) Conversely, galactostasis could be treated with prolactin-decreasing drugs (dopamine agonists or antiserotonergics) if there are no puppies to nurse.

ACUTE GENERAL TREATMENT

Primary agalactia has no effective treatment, so puppies frequently need to be hand reared. Hypogalactia or secondary agalactia can be treated with:

- Metoclopramide, 0.1-0.2 mg/kg SQ q 6-8 h
- Domperidone, 2.2 mg/kg PO q 12 h for 4-6 days, is a safer choice than metoclopramide, as it does not cross the blood-brain barrier and therefore has no central side effects.
- Failure of milk let-down can be treated with nasal oxytocin spray 10 minutes before lactation q 8 h.
- Anxious bitches may benefit from mild tranquilization with phenothiazine compounds (e.g., acepromazine, 0.1-0.25 mg/kg PO or 0.05-0.1 mg/kg IM or SQ), which also increase prolactin release.
- In cases of galactostasis, reduction of milk production can be achieved by the administration of cabergoline, 5 mcg/kg PO q 24 h for 5-7 days. Diuretics and analgesics may also be beneficial when there are puppies to nurse and lactation cannot be interrupted.

NUTRITION/DIET

Diminishing food intake (half) and water for 2 or 3 days may contribute to resolving galactostasis.

BEHAVIOR/EXERCISE

- In hypo/agalactia cases, be sure puppies suckle vigorously so that a natural stimulation of the glands occurs.
- Galactostasis may benefit from wrapping mammary area with an elastic bandage to protect from trauma. Any stimulation on the mammary glands (e.g., padding, touching, or milking) should be avoided if lactation is going to be terminated.

DRUG INTERACTIONS

High metoclopramide doses (5 mg/kg) for more than 5 days usually cause behavioral side effects such as excitation and aggression. Domperidone provokes minimal (soft stools) to no side effects.

POSSIBLE COMPLICATIONS

When gross inflammatory changes of the mammary glands accompany the accumulation of milk, mastitis may be present.

PROGNOSIS AND OUTCOME

Primary agalactia has a poor prognosis for lactation, and neonates should be hand reared. Failure in milk let-down and galactostasis

typically respond to treatment or resolve spontaneously.

PEARLS & CONSIDERATIONS

COMMENTS

Lactation disorders do not pose a risk for the female's life, although they may cause considerable neonatal losses.

PREVENTION

- Provide gradual increase of food intake during the second half of pregnancy, and 125%-159% maintenance requirements after whelping.
- Be sure mammary development is adequate before caesarean section, and slowly and calmly introduce (preferably by the owner) the puppies to the dam after surgery.
- Gradual weaning prevents galactostasis.
- Considering the possible genetic component of primary agalactia, breeding affected bitches should be weighed against the potential of perpetuating the problem.

CLIENT EDUCATION

Teach clients to recognize lactation disorders early so puppies can be saved.

SUGGESTED READING

Anderson PO, ValdÉs V: A critical review ofpharmaceutical galactagogues. BreastfeedMed 2:229, 2007.

Davidson A: Frustrating case presentations in canine theriogenology. Vet Clin North Am Small Anim Pract 31:411, 2001.

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EDITOR: MICHELLE KUTZLER

Myocarditis

BASIC INFORMATION

DEFINITION

Inflammation of the heart muscle, typically associated with myocytolysis. Myocarditis is a poorly understood group of diseases that can result from a collection of diseases of infectious, chemical, or physical etiologies.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Myocarditis occurs rarely and is recognized more often in dogs than cats. No age predilection (exception: puppies—parvoviral myocarditis between 3 and 8 weeks of age).

RISK FACTORS: Myocarditis can result from an extension of infectious endocarditis; therefore preexisting heart disease, persistent bacteremia, or immune compromise can be considered risk factors. Dogs and cats that roam are at risk for traumatic myocarditis.

GEOGRAPHY AND SEASONALITY: Chagas myocarditis *(Trypanosoma cruzi):* southern United States, Latin America. Lyme myocarditis *(Borrelia burgdorferi):* more common in the northeastern United States.

ASSOCIATED CONDITIONS & DISORDERS: Myocarditis often results in or coexists with cardiac arrhythmias (especially ventricular tachyarrhythmias but occasionally atrial tachyarrhythmias or atrioventricular [AV] block). Myocarditis due to a chronic process, especially persistent infection, may lead to dilated cardiomyopathy.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Based on recent discoveries, viral myocarditis has three distinct phases of disease:

- Phase 1: acute myocarditis associated with acute viremia, myocyte necrosis, and macrophage activation
- Phase 2: subacute myocarditis associated with viral clearing and overzealous immune response by cell-mediated and humoral immunity and cytokine activation
- Phase 3: chronic myocarditis, or dilated cardiomyopathy, associated with fibrosis, cardiac dilation, and heart failure

HISTORY, CHIEF COMPLAINT: Presenting complaint can be vague or specific to the cardiovascular system and may include:

- Anorexia
- Lethargy/exercise intolerance
- Cough/dyspnea
- Syncope
- Sudden death
- With traumatic myocarditis, a history of the animal's having been hit by a car is common.

PHYSICAL EXAM FINDINGS: Possible findings include:

- Fever
- Murmur
- Lymphadenopathy
- Skeletal muscle weakness
- Signs of congestive heart failure (CHF; usually phase 3 myocarditis): cough, dyspnea, abnormal breath sounds, weak pulses, pale mucous membranes, ascites, weakness, hepatosplenomegaly, jugular venous distension
- Arrhythmias: bradyarrhythmia (e.g., AV block) and tachyarrhythmias (ventricular ectopy)
- With traumatic myocarditis, evidence of blunt chest trauma or generalized signs of trauma may be present.

ETIOLOGY AND PATHOPHYSIOLOGY

- Bacterial:
  - *Bacillus piliformis, Citrobacter koseri;* streptococcal, staphylococcal, *Bartonella, Brucella, Leptospira,* and *Salmonella* spp.
- Spirochete:
  - *Borrelia burgdorferi*

- Protozoan:
  - *Trypanosoma cruzi, Toxoplasma gondii, Neospora caninum, Babesia* spp.
- Viral:
  - Parvovirus; panleukopenia (cats)
- Other:
  - Doxorubicin chemotherapy, catecholamines, lead, arsenic, stinging insect and snake venom, hyperthermia, radiation therapy, blunt or penetrating trauma

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is usually suspected based on the presence of complex arrhythmias in an atypical breed for heart disease; a recent history of febrile illness, trauma or toxin exposure further heightens suspicion. For suspected neonatal parvoviral myocarditis, a history of the dam having had parvoviral enteritis during gestation is suggestive. Definitive diagnosis requires histopathologic examination of a myocardial biopsy, which is not clinically practical; therefore, the clinical diagnosis is presumptive and treatment is initiated without biopsy confirmation in virtually all cases.

DIFFERENTIAL DIAGNOSIS

- Infectious endocarditis
- Idiopathic dilated cardiomyopathy
- Sepsis

INITIAL DATABASE

- CBC, serum biochemistry profile, urinalysis: inflammatory leukogram possible
- Blood cultures: for diagnosis of bacterial etiology
- Cardiac troponin I or other biomarker of cardiac necrosis: serum troponin levels usually are markedly elevated.
- Thoracic radiographs: may show signs of pulmonary edema and cardiomegaly (phase 3 myocarditis)
- Electrocardiogram (ECG): to identify bradyarrhythmias or tachyarrhythmias
- Echocardiogram: may show cardiac dilation and diminished myocardial function (phase 3 myocarditis)
- Infectious disease serologic tests: *Toxoplasma, Neospora, Bartonella;* based on geographic location, *Babesia,* Lyme, Chagas, and fungal titers may be indicated.

ADVANCED OR CONFIRMATORY TESTING

- Endomyocardial biopsy and histopathologic evaluation:
  - Considered the diagnostic gold standard
  - Rarely performed, owing to invasive nature
  - Classic findings include lymphocyte infiltrates with myocyte necrosis (Dallas criteria). Parvovirus inclusion bodies within cardiomyocytes are also possible.
- In acute viremia, parvovirus isolation may be attempted.
- MRI is an emerging modality, and early studies show high diagnostic accuracy for myocarditis.

TREATMENT

TREATMENT OVERVIEW

Treatment mainly consists of medications to control arrhythmias and CHF if present. If a bacterial or protozoal etiology is suspected, then antimicrobial treatment is recommended.

- Supportive care is the first line of therapy.
- Treatment of hemodynamically significant arrhythmias
- Pacemaker implantation for complete AV block
- Treatment of heart failure with diuretics and vasodilators. Support of cardiac output with positive inotropes may be necessary.
- Treatment with an antimicrobial agent if a bacterial or protozoan etiology is suspected

ACUTE AND CHRONIC TREATMENT

- If severe ventricular arrhythmias: see p. 1600 .
- If high-grade second-degree or third-degree AV block: see p. 117 .
- If CHF (e.g., pulmonary edema, pleural effusion, ascites): see p. 468 and p. 470.
- Antimicrobial therapy:
    - See specific infectious disease topics for recommendations.

POSSIBLE COMPLICATIONS

- Chronic CHF
- Dilated cardiomyopathy
- Complete AV block

RECOMMENDED MONITORING

- Acute monitoring:
    - Continuous ECG
    - Frequent blood pressure measurement: invasive or noninvasive
    - Dyspnea watch and respiratory rate
- Chronic monitoring:
    - Periodic ECG or Holter monitor
    - Echocardiogram
    - Thoracic radiograph
    - Renal and electrolyte parameters if receiving diuretics
    - Convalescent serologic titers for suspected infectious diseases

PROGNOSIS AND OUTCOME

Because myocarditis is an elusive diagnosis and uncommon disease, good information regarding prognosis and outcome is not known. The possibility of lethal arrhythmia and/or progression to dilated cardiomyopathy and CHF warrant an initial guarded prognosis. In humans, fulminant viral myocarditis is interestingly associated with better long-term prognosis than the more chronic clinical presentations if the initial phase is survived.

PEARLS & CONSIDERATIONS

COMMENTS

In the author's clinical experience, myocarditis is strongly suspected when a dog presents with clinical signs attributable to a sudden onset of complex ventricular arrhythmias or complete AV block with no clear underlying etiology.

SUGGESTED READING

Meurs KM: Primary myocardial disease in the dog. In Ettinger SJ, Feldman EC, editors: Textbook of veterinary internal medicine. St Louis, 2005, Elsevier Saunders, pp 1077–1082.

AUTHOR: TERESA DEFRANCESCO

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Myiasis

Additional Images Available on Website

BASIC INFORMATION

DEFINITION

An infestation of living animals with the *larvae* (maggots) of dipteran (two-winged) flies. They may cause cutaneous, nasal, or other tissue lesions.

SYNONYM

Maggot infestation

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs and cats may be affected. Most of these larvae are relatively species specific. However, small animals may serve as aberrant hosts when housed near primary hosts. Overall, myiasis occurs without any predilections in age or sex.

RISK FACTORS: Wounded, soiled, debilitated, or weak animals living in temperate wet regions known to harbor flies causing myiasis may be predisposed. Some dipteran larvae can penetrate normal skin.

CONTAGION & ZOONOSIS

- Emerging adult flies are a potential public health risk, since they serve as fomites for bacteria found in animal waste.
- People with open wounds could be at risk for myiasis.
- Other implications: accidental reintroduction of screwworm *(Cochliomyia hominivorax),* which is currently eradicated from the United States, presents an ongoing threat because of the aggressiveness of infestations: superficial wounds are a point of entry for screwworm larvae, which voraciously feed on living flesh and have fatally infected or "have completely eaten away the facial bones" of unconscious human victims (Bowman). Veterinarians have played a key role in screwworm prevention through identification of larvae.

GEOGRAPHY AND SEASONALITY: Myiasis has a worldwide distribution; however, larvae-specific infestations do occur in some countries. In the Northern Hemisphere, myiasis occurs during the summer months in temperate moist areas.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: A foul, putrid-smelling animal may be the only reason an owner seeks veterinary care, although occasionally malodor may be absent or unnoticed. Other owners are well aware that maggots are taking residence in their animal's skin. Occasionally, owners will present an animal because of incontinence, debilitation, paresis, or skinfold dermatitis in which invading maggots are an incidental finding.

PHYSICAL EXAM FINDINGS

- Maggot infestation typically occurs in moist locations such as those around the eyes, nose, mouth, genitalia, anus, or adjacent to wounded skin. Irregularly ulcerated to crateriform lesions are characteristic.
- Several lesions may coalesce to form large soft-tissue defects.
- Tracts dissecting through nearby soft-tissue structures may cause fistulation.
- Parasitized skin may present as a focal fistulated subcutaneous nodule.
- Aberrant larval migration can cause signs specific to other tissues.
- Findings associated with incontinence or debilitation (e.g., musculoskeletal, neurologic, or internal disease) might be identified in select cases. Severely infested animals may be in shock.

ETIOLOGY AND PATHOPHYSIOLOGY

- Eggs are laid on the moist skin of debilitated or wounded animals. Emerging larvae (maggots) secrete proteolytic enzymes that liquefy cutaneous tissue, creating full-thickness skin defects within hours. Occasionally the initial larval infestation will favor the "strike" of other myiasis-causing flies, resulting in disease propagation.
- Many dipteran flies (e.g., house, stable, horn, and black flies) are capable of infesting the skin of animals with the above risk factors. These flies cause the typical myiases seen in routine small animal practice.
- Blowflies (common in large animals), screwworm flies (reportable in many parts of the world), and flesh flies rarely infest the

skin of small animals. However, their presence is alarming because of contagion implications.
- Although more common in rabbits and rodents, *Cuterebra* flies can cause myiasis in companion animals.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is confirmed based on the observation of maggots in the skin and surrounding soft tissue.

DIFFERENTIAL DIAGNOSIS

Direct visualization of maggots in representative cutaneous lesions excludes other differential diagnoses. Specific species identification is not usually required to treat most cases of myiasis.

INITIAL DATABASE

- Direct visualization of maggots
- Cytologic evaluation of wounded and infested skin to identify secondary bacterial infection

ADVANCED OR CONFIRMATORY TESTING

- Other diagnostic tests are at the discretion of the clinician, but in most patients a CBC, biochemistry profile, and urinalysis will be beneficial to exclude concurrent and predisposing conditions.
- Bacterial culture and susceptibility testing for lesions failing to heal rapidly or in septicemic animals
- Examination of the spiracle and stigmal plates on the maggot can aid in species identification (see online version of the present chapter).
- Larvae can be kept until developing adult flies emerge. Flies of severe concern include blowflies, characterized as having a metallic blue or green sheen on the body, and screwworm flies, which have orange-brown eyes and are bluish green with longitudinal stripes along their thorax. The economic importance of eradication of these flies warrants contacting a regional veterinary office for precautionary identification and confirmation if a suspicion of screwworm myiasis exists (see online version of the present chapter).

TREATMENT

TREATMENT OVERVIEW

The goals are to remove and kill maggots, manage the wound(s), and identify and treat underlying predisposing conditions.

ACUTE GENERAL TREATMENT

- Stabilize patient if needed (e.g., fluid therapy if hypotensive).
- Clip, clean, and surgically débride lesions (general anesthesia required).
- Mechanically remove larvae.
- Apply a non-alcohol-based pyrethrin or pyrethroid (dogs but not cats) spray on lesions to kill maggots.
- Systemically administered avermectins (ivermectin, 0.2-0.4 mg/kg PO or SQ, may repeat in 7-14 days) for nonherding dog breeds (negative for heart-worms) can be used for killing maggots. Caution: susceptible individuals or breeds (see p. 625 and 706).
- Although not approved for myiasis, topical spot-on application of selamectin (Revolution) or imidacloprid + moxidectin (Advantage Multi or Advocate) per label directions may help kill maggots. In the United States, these drugs are labeled U.S. Food and Drug Administration, not Environmental Protection Agency.
- Anecdotally, oral nitenpyram (Capstar) at routine doses may kill maggots.
- Wound care (e.g., wet-to-dry bandages to help débride wound)
- House animal in fly-free area (e.g., indoors, screened-in patio).
- Empirical antibiotic therapy for secondary bacterial infection (e.g., cephalexin, 22-30 mg/kg PO q 8-12 h; or clavulanic acid-potentiated amoxicillin, 12.5-20 mg/kg PO q 12 h for 21-30+ days)

PROGNOSIS AND OUTCOME

Guarded to good, based on the severity of the infestation and underlying predisposing conditions

PEARLS & CONSIDERATIONS

COMMENTS

- Myiasis is a disease of neglect.
- Depending on the country, some types of myiases are reportable.
- Avoid crushing or cutting maggots in vivo, as remaining body parts may cause allergic reactions.
- Some of the newer topical spot-on flea and tick preventatives, when used according to label directions, may also prevent or reduce the severity of myiasis.

TECHNICIAN TIPS

In warm weather, maggots are one of the reasons hygiene (avoidance of fecal staining or urinary scalding of the skin and haircoat) is so important, especially in recumbent patients.

CLIENT EDUCATION

Basic hygiene care and early intervention when a pet is debilitated for any reason are essential for preventing myiasis.

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Myelodysplasia

BASIC INFORMATION

DEFINITION

- Myelodysplasia (MDS) describes a group of bone marrow disorders characterized by peripheral blood cytopenias and a hypercellular to hypocellular bone marrow containing less than 30% blast cells. MDS is often considered a precursor of acute myeloid leukemia (AML) in which the bone marrow blast population exceeds 30%.
- Morphologic signs of abnormal maturation (dysplasia) are present in the erythroid, myeloid, and/or megakaryocytic cells.

SYNONYMS

Ineffective hematopoiesis, refractory cytopenias, preleukemia, smoldering acute leukemia

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs and cats. MDS is becoming less common in cats as the incidence of feline leukemia virus (FeLV) infection decreases.

RISK FACTORS

- Feline leukemia infection
- Some drugs (chloramphenicol, cephalosporins, melphalan, cyclophosphamide, estrogen, and vincristine) have been associated with MDS in animals.
- Vitamin B^{12}/folate deficiency
- Lead toxicity
- Exposure to radiation
- Immune-mediated diseases targeting the bone marrow
- Chronic exposure to alkylating chemotherapy drugs

CONTAGION & ZOONOSIS: FeLV: contagious between cats

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Myelodysplasia may be primary or secondary. MDS is classified into three subtypes, based on cytologic examination of bone marrow. This classification system does not provide specific prognostic information at this time.

- MDS-ER (erythroid predominant): M: E ratio <1, blasts <30% of nucleated bone marrow cells
- MDS-RC (refractory cytopenia): M: E ratio >1, nonerythroid blasts <6% of nucleated bone marrow cells
- MDS-EB (excess blasts): M:E ratio >1, nonerythroid blasts 6%-29% of nucleated bone marrow cells

HISTORY, CHIEF COMPLAINT

- Rapid onset of nonspecific clinical signs related to anemia, including weakness, lethargy, tachypnea, and appetite changes (ranging from anorexia to pica)
- Recurrent/chronic infections if leukopenia or abnormal leukocyte function occur
- Bruising/bleeding secondary to thrombocytopenia or platelet function disorders
- It is important to determine the recent history of drugs administered to the patient.

PHYSICAL EXAM FINDINGS

- Weakness, tachycardia, heart murmurs, and pale mucous membranes may indicate anemia.
- Fever due to secondary infections
- Epistaxis or petechiae due to thrombocytopenia or abnormal platelet/megakaryocyte maturation
- Hepatomegaly and splenomegaly are common in cats and may be noted in dogs.
- Pleural effusion has been reported in cats, possibly leading to muffled heart and lung sounds.

ETIOLOGY AND PATHOPHYSIOLOGY

- MDS may be primary (presumably due to mutations in hematopoietic progenitor cells) or secondary (associated with FeLV infection, drug therapy, or disorders such as lymphoma, myelofibrosis, or immune-mediated anemia/thrombocytopenia).
- A variety of chromosomal abnormalities and mutations in oncogenes and tumor suppressor genes has been identified in humans with MDS, but it is not yet known whether these are present in veterinary patients.
- MDS-associated clonal proliferation, apoptosis, and ineffective hematopoiesis can result in lethal cytopenias, or MDS may progress to acute leukemia.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

History and physical exam findings are nonspecific, but CBC usually reveals at least one abnormality that is repeatable. The diagnosis is obtained on bone marrow examination performed because of persistent peripheral blood cell abnormalities without identifiable cause. Additional tests for identifying underlying causes (e.g., titers for rickettsial diseases) are selected based on history, exam, and results of diagnostic tests to date.

DIFFERENTIAL DIAGNOSIS

- Acute leukemia
- Drug-induced bone marrow dyscrasia
- Hyperplasia of recovering bone marrow
- Nonregenerative anemia: anemia of chronic/inflammatory disease, anemia of renal disease, iron-deficiency anemia, aplastic anemia, drug- or toxin-induced anemia
- Neutropenia: tissue demand, endotoxemia/sepsis, immune-mediated destruction, inherited/genetic leukocyte maturation/function abnormalities
- Thrombocytopenia: drug therapy, immune-mediated destruction
- Rickettsial *(Ehrlichia* and *Anaplasma* spp., Rocky Mountain spotted fever) organism-induced bone marrow dyscrasias
- Congenital conditions associated with dysplastic features:
    - Miniature and toy poodles: familial nonanemic macrocytosis with dysplastic changes in erythroid precursors
    - English springer spaniels: congenital dyserythropoiesis, polymyopathy, and cardiac disease
    - Giant schnauzers: congenital malabsorption of vitamin B^{12} and myelodysplasia
    - Cavalier King Charles spaniels: idiopathic subclinical thrombocytopenia and dysplastic changes in megakaryocytes and platelets (macroplatelets)

INITIAL DATABASE

- CBC and blood smear review: cytopenias and dysplastic blood cell morphology. Blood smear must be reviewed by a clinical pathologist for accurate assessment.
    - Nonregenerative anemia: often with many nucleated red blood cells present. Thrombocytopenia and/or leukopenia also are often present.
    - Leukocyte abnormalities: ringed nuclei, micronuclei, nuclear fragments, abnormal cytoplasmic granulation, or maturation arrest
    - Giant platelets and dwarf megakaryocytes
- Bone marrow evaluation (biopsy may be preferred over aspirate in establishing most accurate detail of bone marrow cellularity and marrow architecture). See p. 1212.
    - Examination of bone marrow is necessary to confirm MDS and identify the subtype.
    - Diagnosis of MDS requires that fewer than 30% of the marrow nucleated cells are blast cells (if >30% blasts are present, the diagnosis is acute leukemia, and the associated prognosis is usually worse).
    - Asynchrony of nuclear and/or cytoplasmic maturation of affected cell lines
    - Bizarre nuclear morphologies resembling bowling pins, doughnuts, or abnormally small nuclei
- Serum biochemistry profile and urinalysis to evaluate overall health
- All cats with MDS should be tested for FeLV and feline immunodeficiency virus (FIV).

ADVANCED OR CONFIRMATORY TESTING

- Cytochemical stains, immunohistochemical stains, and/or flow cytometry may be useful to rule out myeloid and lymphoid malignancies.
- *Ehrlichia* and *Anaplasma* spp. titers may aid diagnosis of rickettsial disease.
- Serum iron, zinc, lead, and vitamin B^{12}/folate levels
- Coombs' test may be needed to rule out immune-mediated disease.

TREATMENT

TREATMENT OVERVIEW

Initial therapy consists of supporting the patient (if needed) until cytopenias resolve. Overall goals are to restore normal hematopoiesis, treat underlying cause (if appropriate), and eradicate dysplastic blast cells or neoplastic cells as possible.

ACUTE GENERAL TREATMENT

- Discontinue all drug therapies, especially agents known to be associated with MDS.
- Intensive supportive care may be warranted for patients with severe cytopenias.
  - Transfusions (see p. 1347)
  - Antibiotics as indicated for treating/preventing secondary infections:
    - For prophylaxis, a common choice is sulfadiazine-trimethoprim, 15 mg/kg PO q 12 h for dogs. Cats do not usually need prophylactic antibiotics.
    - If fever or overt infection is present, intravenous broad-spectrum antibiotics based on culture and sensitivity (preferred, if available) or empirical use of clinician's preferred combination are indicated. Example: a combination of either a cephalosporin (e.g., cefazolin, 22 mg/kg IV q 8 h slow bolus) or a penicillin (e.g., ampicillin, 22 mg/kg IV q 8 h slow bolus) together with either an aminoglycoside (e.g., amikacin, 20 mg/kg IV q 24 h [only in hydrated patient without renal dysfunction; can cause renal injury]) or a fluoroquinolone (e.g., enrofloxacin, 5 mg/kg diluted 1:1 in sterile water and given as a slow IV bolus q 12 h [dogs]; 5 mg/kg q 24 h in cats).
  - Intravenous fluids for patients with infection, fever, dehydration, or decreased appetite
  - Avoid jugular venipuncture or catheterization if severe thrombocytopenia is present.
  - Nutritional support
- Recombinant granulocyte colony stimulating factor (G-CSF; 5 mcg/kg SQ once daily), recombinant human erythropoietin (rh-Epo; Epogen [100 IU/kg SQ q 48-72 h until hematocrit rises, then q 7 days or as needed to maintain low-normal hematocrit; anecdotally, darbepoetin (Aranesp) 0.45 mcg/kg SQ once weekly at first, then q 2-3 weeks adjusted for maintenance, may be less antigenic]) and potentially granulocyte stimulating factor (G-CSF; filgrastim; Neupogen [5 mcg/kg SQ once daily until neutrophil count normalizes]) and/or thrombopoietin (currently experimental) may also have a role in treating refractory cytopenias. However, some recombinant human cytokines may cause dogs and cats to form cross-reactive neutralizing antibodies to the recombinant products and their own cytokines, especially with chronic or repeated use.
- Immunosuppressive doses of prednisone (2 mg/kg PO q 24 h) have been effective for some dogs and cats with refractory cytopenias.
- Low-dose cytosine arabinoside (LD-AraC, 0.7-1.4 mg/kg SQ q 24 h) has been attempted as a differentiation agent in the management of MDS in nine cats. One complete response was described. LD-AraC administered to a dog with MDS-Er at 10 mg/m^2 SQ q 12 h for 3 weeks was ineffective.

CHRONIC TREATMENT

- Patients responding to treatment will likely require lifelong therapy and chronic monitoring of disease progression to leukemic state.
  - Supportive therapy as indicated (antibiotic therapy, transfusions, hematopoietic cytokines as needed)
  - Hematopoietic cytokines should be reduced/discontinued once cell counts are improved, to reduce the risk of production of cross-reactive antibodies that could affect the patient's own erythropoietin, G-CSF, GM-CSF, or thrombopoietin.
- Patients with concurrent MDS secondary to drug administration should never receive that drug again.

POSSIBLE COMPLICATIONS

Chronic administration of rh-Epo can result in the production of antibodies that cross-react with feline or canine erythropoietin and cause severe nonregenerative anemia. Chronic or repeated administration of G-CSF can result in production of antibodies to innate leukocyte-stimulating cytokines and cause life-threatening leukopenias.

RECOMMENDED MONITORING

- Physical examinations and CBC: weekly to every 2 weeks, more frequently during initial therapy. Blood smear review to monitor cytopenias, blasts and other abnormal cell morphology, and possible adverse effects of treatment. If lasting response to therapy is noted, interval may be extended to monthly.
- Serum biochemistry profile: every 2 months to monitor overall health. More frequently if indicated.

PROGNOSIS AND OUTCOME

- In general, the prognosis for most animals with MDS is poor, with survival times ranging from a few days to a few months.
  - Primary MDS is considered to be a preneoplastic condition, progressing to acute leukemia in 40%-60% of cases. Animals may live a year or more but eventually succumb to acute leukemia or bone marrow failure.
  - The prognosis for animals with secondary MDS depends on successful resolution of the underlying disease condition or withdrawal of offending drugs.
- Cats with refractory anemia can enjoy long survival times; however, cats with other types of MDS are typically euthanized due to cytopenias or may develop AML within weeks to months.
- The prognosis for cats with concurrent MDS and FeLV infection is especially grave; most do not survive 1 week after diagnosis.
- Dogs with MDS-RC may have a better prognosis than those with MDS-EB. In one small study, dogs with refractory anemia lived longer (>6 months) than dogs with other MDS (mean, 2 weeks).
- In general, patients with high blast counts and/or poor clinical condition are likely to have a worse prognosis.

PEARLS & CONSIDERATIONS

COMMENTS

- Management of MDS is focused on identifying and treating underlying diseases (especially immune-mediated hemolytic anemia and lymphoma in dogs) and supportive care of secondary cytopenias.
- Myelodysplastic syndromes are uncommon diseases, and it can be challenging to accurately diagnose them. When MDS is suspected based on clinical signs and evidence of hematologic abnormalities, bone marrow evaluation is required for definitive diagnosis.
- When considering these conditions, consultations with a veterinary clinical pathologist and a veterinary oncologist are highly recommended.
- Chemotherapy has not been shown to be beneficial for control of MDS or to prevent progression to leukemia.
- Although the overall prognosis for patients with MDS is poor, there is substantial interindividual variability; some patients can respond well to therapy and enjoy longer survival times.

PREVENTION

All cats should be tested for feline retro-viruses (FeLV; also FIV if >6 months old) as kittens.

CLIENT EDUCATION

- Retrovirus-negative cats should be kept inside to prevent them from becoming exposed to cats harboring FeLV or FIV.
- There is a high risk of progression of primary MDS to acute leukemia.

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Mycoplasma/Ureaplasma Infections

BASIC INFORMATION

DEFINITION

Relatively uncommon opportunistic infections with small microorganisms of the class Mollicutes, which live on respiratory and urogenital mucosal membranes in many species. Hemotropic feline mycoplasmosis (formerly hemobartonellosis) is discussed separately on p. 499)

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs and cats each have a multitude of species, primarily *M. canis* and *M. felis/M. gatae*, respectively.

RISK FACTORS

- Immune suppression
- Underlying disease:
  - General: viral infection, neoplasia, diabetes mellitus
  - Urinary: uroliths, neoplasia, changes in urine concentration or content
  - Pulmonary: aspiration due to laryngeal or esophageal dysfunction; parenchymal disease (lung parasites, viral infection, neoplasia)

CONTAGION & ZOONOSIS: Considered part of the normal flora of upper respiratory, ocular, and urogenital mucosal membranes. There are extremely rare reports of immunocompromised humans with mycoplasmal infections acquired from domestic animals (anthroponosis).

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Ocular: mucoid ocular discharge, excessive tearing, or squinting
- Respiratory: mucoid nasal discharge, sneezing, cough, tachypnea, lethargy, anorexia
- Urogenital: dysuria, stranguria, inappropriate elimination, infertility
- Subcutaneous abscesses: lethargy, anorexia, fluctuant subcutaneous swellings, or nonhealing open sores
- Joint disease (rare): intermittent lameness, unwillingness to move, lethargy, anorexia, swollen joints

PHYSICAL EXAM FINDINGS

- Mucoid to crusting ocular discharge, epiphora, blepharospasm, hyperemic conjunctiva, chemosis
- Tachypnea or dyspnea, increased airway sounds/wheezes upon auscultation, easily induced cough, nasal discharge, upper respiratory stertor
- Signs of pain on bladder palpation
- Subcutaneous abscesses
- Painful or swollen joints

ETIOLOGY AND PATHOPHYSIOLOGY

- *Mycoplasma*/*Ureaplasma* spp. are bacteria that live as normal flora in the upper respiratory tract and distal urethra and cause opportunistic infections in susceptible individuals.
  - Isolation of these bacteria alone is not evidence of infection; concurrent clinical signs and response to treatment must be observed to confirm the diagnosis.
- Pulmonary mycoplasmal infections are presumed to occur secondary to transfer of organisms from upper respiratory tract to the lungs. Often occurs as part of multiorganism pneumonia but can be sole causative agent.
- *Mycoplasma* or *Ureaplasma* spp. should not be found in the healthy urinary bladder. Urinary tract infections occur as a result of ascending opportunistic infections. Often found with mixed populations of bacteria.
- *Mycoplasma/Ureaplasma* spp. are not known to play a causative role in idiopathic feline lower urinary tract signs/disease.
- *M. felis* has been associated with conjunctivitis, rhinosinusitis, pneumonia, chronic bronchial disease, and arthritis in cats. Synovitis/arthritis is extremely rare and typically associated with immunosuppression.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis should be suspected in a patient in whom an infection (typically respiratory or urinary tract) persists despite appropriate sensitivity-based antibiotic treatment and control of known predisposing causes. Definitive diagnosis requires identification of *Mycoplasma/Ureaplasma* in diseased organ systems. Isolation of the organism without clinical signs of infection simply confirms its status as normal flora.

DIFFERENTIAL DIAGNOSIS

- Urinary tract: bacterial or fungal infection, uroliths, urinary tract neoplasia
- Respiratory: bacterial or viral pneumonia, asthma or allergic lung disease lung lobe torsion, foreign body, neoplasia
- Ocular infections in cats: feline herpesvirus 1, *Chlamydophila felis*, corneal ulcer, trauma, or foreign body

INITIAL DATABASE

- CBC: leukocytosis, neutrophilia, left shift possible
- Serum biochemistry profile: typically unremarkable
- Urinalysis:
  - Inflammatory sediment possible
  - *Mycoplasma/Ureaplasma* cannot be seen on sediment exam.
  - Cystocentesis essential, as voided or catheterized urine likely contains normal commensal *Mycoplasma/Ureaplasma* from the distal urethra.
- Urine culture: growth of *Mycoplasma* or *Ureaplasma* spp.
- Thoracic radiographs: alveolar pattern or areas of consolidation, consistent with pneumonia. Bronchial or interstitial pattern also possible, especially in cats.
- Arthrocentesis: thin, cloudy synov-ial fluid with many nondegenerate neutrophils

ADVANCED OR CONFIRMATORY TESTING

- Mycoplasmas cannot be seen with normal stains.
- Culture is the best method for identifying these organisms. Special handling and culture medium are required; contact laboratory prior to sample acquisition.
- Commercially available PCR testing for *M. felis* and *M. canis* is a useful adjunct to culture. Advantages include fast turnaround time, high sensitivity and specificity, and less stringent sample-handling requirements.
- Pulmonary infections should be identified via culture of bronchial wash, since finding *Mycoplasma* in orotracheal/transtracheal washes may be incidental. Pure *Mycoplasma* culture more likely indicates true pathogenicity; oropharyngeal contamination typically shows mixed infection with *Mycoplasma* and aerobic bacteria.

TREATMENT

TREATMENT OVERVIEW

Mycoplasmal/ureaplasmal organisms are very susceptible to appropriate antimicrobials, but opportunistic infection will recur if underlying predisposing factors are not addressed. Therefore, diagnosis and treatment of the causative disease is imperative.

ACUTE GENERAL TREATMENT

- Urogenital: fluid therapy for dehydrated animals, opioid or nonsteroidal antiinflammatories for pain, spasm
- Respiratory: oxygen therapy, nebulization, and coupage for severe pneumonia
- Ocular
  - Topical ophthalmic tetracycline
  - Topical ophthalmic pain medications
  - Systemic antibiotic therapy and pain control are often necessary in addition to topical treatment.

CHRONIC TREATMENT

Systemic antibiotic therapy: options include one of the following:

- Fluoroquinolones: enrofloxacin, 10-20 mg/kg (dogs), 5 mg/kg (cats) PO, SQ or slow IV q 24 h
- Doxycycline, 10 mg/kg PO q 12 h; or tetracycline, 20-30 mg/kg PO q 8 h (lower dose for cats)
- Macrolides: azithromycin, 5-10 mg/kg PO q 24 h; or erythromycin 10-20 mg/kg PO q 8 h
- Treatment duration may vary, typically 14-28 days. Treat for 1-2 weeks after resolution of radiographic pneumonia or negative culture.
- Because they lack cell walls, mycoplasmas are resistant to beta-lactam antibiotics (penicillins, cephalosporins). Failure to respond to these antibiotics should suggest possible mycoplasmal infection.

DRUG INTERACTIONS

- Macrolides and tetracyclines can cause gastrointestinal side effects such as vomiting, diarrhea, and anorexia; more common with erythromycin.
- Enrofloxacin and other fluoroquinolones can cause blindness in cats at high doses.
- Doxycycline has been reported to cause esophagitis and esophageal strictures in cats and possibly dogs. To prevent this complication, owners need to follow oral doxycycline administration with a small amount of butter, soft margarine, or water to ensure passage into the stomach.

RECOMMENDED MONITORING

- Pneumonia: serial radiographs, bronchial lavage cytologic examination, and culture
- Urinary: serial cystocentesis urinalysis and culture
- Ocular: recheck ocular exams and fluorescein staining

PROGNOSIS AND OUTCOME

Mycoplasma/Ureaplasma spp. are usually quite susceptible to appropriate antibiotic therapy. Prognosis is good with antibiotics and management of underlying disease or concurrent bacterial infection.

PEARLS & CONSIDERATIONS

COMMENTS

These organisms are often found in cultures of normal respiratory or urinary tracts and may be commensals that were inadvertently sampled. A search for other pathogens or underlying disease that have caused enhanced susceptibility to these organisms is essential.

TECHNICIAN TIPS

Gentle removal of oculonasal secretions with a warm moist cloth will improve patient comfort and prevent facial dermatitis. Keeping the nares clear and warming food to enhance smell can also keep patients eating better.

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Mycobacterial Diseases

BASIC INFORMATION

DEFINITION

Infection by any species of *Mycobacterium*

SYNONYMS

Atypical mycobacteriosis, feline leprosy, leproid granuloma syndrome, rapidly growing mycobacterial (RGM) panniculitis

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Tuberculous and leproid forms are very rare.
- Opportunistic infections are uncommon in cats, rare in dogs.

GENETICS & BREED PREDISPOSITION: Miniature schnauzers, basset hounds, Siamese cats may be overrepresented with systemic forms.

RISK FACTORS: Traumatic injuries often precede opportunistic infection.

CONTAGION & ZOONOSIS

- Zoonotic risk is present with all mycobacterial infections, especially among immunosuppressed people.
- Tuberculous forms are a constant human health threat (especially exudates from cutaneous lesions). Gloves, mask, and eye protection are necessary during wound debridement and patient care.
- Anthroponosis (reverse zoonosis) is a common source of infection in animals.
- Common-source exposure is more likely than contagion in leproid and opportunistic forms; however, appropriate caution should be used in handling infected animals and their secretions, exudates, and tissues.
- Urine and feces do not pose a significant zoonotic risk to most immunocompetent people.
- *Mycobacterium tuberculosis* infection (tuberculosis) is a reportable disease from the time of clinical suspicion or diagnosis.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Three clinical forms are commonly recognized:

- Tuberculous forms (very rare), characterized by skin and internal organ granulomata
- Leproid forms (very rare), consisting of regionalized cutaneous nodules
- Opportunistic forms (most prevalent), characterized by spreading, nonhealing subcutaneous lesions

HISTORY, CHIEF COMPLAINT

- Tuberculous forms often are subclinical, or cause skin lesions, weight loss, lethargy, coughing.
- Leproid forms are seen in young cats, with fleshy nodules on the face and forelimbs.
- Opportunistic infections produce nonhealing exudative wound(s). Often there is an associated history of partial response to prior antibiotic therapy but persistence of the lesions to some degree.

PHYSICAL EXAM FINDINGS

- Tuberculous: systemic signs reflecting the location of visceral granulomata, with/without cutaneous lesions. Involvement of the lungs, spleen, and/or liver is common. In the tuberculous form (very rare) in cats, the gastrointestinal tract may contain granulomata. Mediastinal or mesenteric lymphadenopathy may be noted on imaging.
- Leproid: multiple nonpainful, nonpruritic, fleshy cutaneous nodules, with/without ulceration. Usually, patients are otherwise well.
- Opportunistic: intermittent serous/serosanguineous discharge from spreading skin lesions at sites of prior trauma, especially the inguinal fat pad in cats.

ETIOLOGY AND PATHOPHYSIOLOGY

- Mycobacteria are a large group of acid-fast, aerobic bacilli, with widely varying pathogenicity.
- Tuberculous species (e.g., *M. tuberculosis, M. bovis)* are facultative intracellular parasites, and none has the dog or cat as the reservoir host.
- Leproid species *(M. leprae, M. lepraemurium)* are obligate intracellular parasites transmitted to cats from rodents.
- Opportunistic species (e.g., *M. avium* complex, *M. smegmatis, M. fortuitum,* etc.) are saprophytes, primarily acquired from water and wet soil across damaged or abraded skin.
- Immune response is insufficient to clear infection but may confine bacteria within granulomata.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The most common form encountered is the opportunistic skin infection, which is suspected when a ventral abdominal, inguinal, or other wound fails to respond to appropriate cleaning, débridement and antibiotic therapy. Cytologic examination of smears or biopsy obtained from a closed, intact portion of the involved skin is the most valuable diagnostic tool.

DIFFERENTIAL DIAGNOSIS

- Bacterial folliculitis
- Mycotic infections
- Sterile nodular panniculitis
- Cutaneous or pulmonary neoplasia
- Foreign-body reactions
- Drug eruption

INITIAL DATABASE

- CBC/serum biochemistry profile/urinalysis
  - Hypercalcemia of chronic granulomatous disease is possible, and it should not mislead the clinician into a diagnosis of neoplasia.
- Cytologic evaluation or biopsy of skin lesions reveals an acid-fast bacillus.
- Thoracic and abdominal radiographs reveal granulomata in systemic forms.

ADVANCED OR CONFIRMATORY TESTING

- Species identification, including antibiotic sensitivity testing, is essential.
- A specialized lab is required (e.g., the National Jewish Center for Immunology and Respiratory Medicine in Denver, Colorado [www.njc.org]).

TREATMENT

TREATMENT OVERVIEW

- Tuberculous: significant human health threat; treatment may not be recommended.
- Leproid: usually curable with aggressive surgical excision
- Opportunistic: often curable with long-term treatment
  - Treatment of opportunistic forms depends upon aggressive complete resection and guided antibiotic therapy for at least 3 months.

ACUTE GENERAL TREATMENT

- Surgical excision of leproid granulomata is the treatment of choice.
- Wide surgical debulking of large opportunistic lesions is the first step in long-term management.
- Submit surgical biopsies for species identification.

CHRONIC TREATMENT

- Consultation with an internist specializing in infectious diseases is advised for drug recommendations; antibiotic resistance is prevalent, and protocols are evolving rapidly.
- Treatment for tuberculous forms may not be recommended; if treatment is undertaken, combination antibiotic therapy must be administered for a minimum of 6-12 months.
- Medical therapy for leproid infections is only indicated if complete surgical excision is not possible.
- Treatment of opportunistic forms, guided by species identification (and sensitivity testing when possible), requires a minimum of 3 months.
- Enrofloxacin, with clarithromycin, gentamicin, or doxycycline, may be acceptable empirical therapy while definitive identification is pending.

POSSIBLE COMPLICATIONS

- Surgical sites prone to dehiscence and recurrence of infection
- Risks of drug resistance, toxicosis, or intolerance with long-term antibiotic use

RECOMMENDED MONITORING

- Reexamination every 2-3 weeks for continued effectiveness of therapy
- Monitor lab work for evidence of drug toxicosis.

PROGNOSIS AND OUTCOME 

- Recurrence or incomplete clearance is likely.
- Leproid forms have the best prognosis.
- With appropriate intensive management, outcome of opportunistic infections can be good.

PEARLS & CONSIDERATIONS 

COMMENTS

- Treatment of tuberculous forms may not be recommended (zoonotic risk).
- Significant commitment of owner time and resources is required for positive outcome.
- Accurate species identification and current antimicrobial therapy recommendations are essential.

PREVENTION

- Vaccination with human or large-animal products is not recommended.
- Limiting rodent exposure reduces risk of leproid forms.
- Opportunistic forms are ubiquitous.

SUGGESTED READING

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Myasthenia Gravis

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Skeletal muscle weakness due to a decrease of acetylcholine receptors at neuromuscular junctions

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Congenital myasthenia gravis is uncommon, and signs occur by 8 weeks of age.
- Acquired myasthenia gravis is fairly common and occurs in adult dogs, with a bimodal age of onset with peaks at 3 and 10 years.
- Acquired myasthenia gravis is uncommon in adult cats.

GENETICS & BREED PREDISPOSITION

- Congenital myasthenia gravis is inherited as an autosomal recessive trait in Jack Russell terriers and smooth fox terriers, and occurs sporadically in other breeds of dog. It is rare in cats.
- Akitas, terriers, German short-haired pointers, and Chihuahuas have the highest relative risks. German shepherds and golden retrievers are also commonly affected.
- Abyssinians and Somalis are at increased risk of feline acquired myasthenia gravis.

RISK FACTORS: Methimazole may increase the risk of acquired myasthenia gravis in cats.

ASSOCIATED CONDITIONS & DISORDERS

- In dogs, associated conditions include hypothyroidism, thymoma and other tumors, hypoadrenocorticism, and thrombocytopenia.
- Thymoma is common in cats with acquired myasthenia gravis.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Acquired: an autoimmune disorder characterized by circulating antibodies against acetylcholine receptors. May occur in generalized, focal, or acute fulminating forms.
- Congenital: an inborn deficiency of muscle acetylcholine receptors

HISTORY, CHIEF COMPLAINT

- Congenital: generalized limb weakness with or without regurgitation/dysphagia, evident by about 8 weeks of age
- Generalized acquired: generalized limb weakness that may be precipitated by exercise, with or without regurgitation/dysphagia
- Focal acquired: dysphagia/regurgitation or facial weakness with no limb weakness
- Acute fulminating acquired: acute generalized limb weakness and dyspnea due to respiratory muscle weakness

PHYSICAL EXAM FINDINGS

- Generalized limb weakness characterized by stiffness, tremor, and short-strided gait that may progress to inability to walk. Weakness may be more severe in the pelvic limbs, is often precipitated by 1 to 2 minutes of exercise, and improves with rest.
- There is no ataxia, and proprioceptive positioning is usually normal when the patient's weight is supported. Muscle atrophy is absent, and tendon reflexes are usually preserved.
- Weak palpebral reflex, especially in cats
- Cats often have neck ventroflexion.
- Abnormal lung sounds and fever possible if concurrent aspiration pneumonia

ETIOLOGY AND PATHOPHYSIOLOGY

- Congenital myasthenia gravis is caused by mutations in genes coding for the acetylcholine receptor.
- Acquired myasthenia gravis is caused by circulating autoantibodies against the acetylcholine receptor. Factors that initiate the immune response are incompletely understood.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected in one of four contexts (see History, above), all characterized by neuromuscular weakness that may (classically) or may not (often) resolve with rest. Measurement of serum antiacetylcholine-receptor antibody levels should be part of any diagnostic evaluation of such neuromuscular weakness in dogs and cats; it is the confirmatory clinical test of choice for myasthenia gravis.

DIFFERENTIAL DIAGNOSIS

- Myopathies: polymyositis, degenerative myopathies
- Tick paralysis
- Acute idiopathic polyradiculoneuritis
- Botulism
- Polyneuropathy
- Metabolic disorders: hypokalemia, hypoglycemia, hypoadrenocorticism, hyperthyroidism in cats
- Orthopedic diseases: polyarthritis

INITIAL DATABASE

- CBC, serum biochemistry profile, urinalysis to rule out metabolic causes
- Thoracic radiographs to screen for megaesophagus, aspiration pneumonia
- Thyroid, adrenal function testing
- Edrophonium response test can help diagnose generalized myasthenia gravis. Administer edrophonium chloride (0.1-0.2 mg/kg IV) during weakness. A positive response is obvious improvement in strength within several minutes and suggests the diagnosis. False-negative results are common, and false-positive results are possible. Potential side effects include dyspnea due to bronchial constriction and secretions; treated with atropine.

ADVANCED OR CONFIRMATORY TESTING

- Acetylcholine receptor antibody test. Serologic evaluation to detect antibodies directed against acetylcholine receptors is the gold standard for diagnosis of acquired myasthenia gravis.
- Electrodiagnostic testing (single-fiber electromyography and repetitive nerve stimulation) is useful in the diagnosis and in excluding other causes (see onine chapter: Electromyography and Nerve Conduction Velocity).
- Definitive diagnosis of congenital myasthenia gravis requires quantification of acetylcholine receptors from muscle biopsy (see p. 1305).

TREATMENT

TREATMENT OVERVIEW

Treatment goals include improving neuromuscular transmission and administering supportive care and immunosuppression (acquired form only).

ACUTE GENERAL TREATMENT

- Anticholinesterase drugs. Pyridostigmine (0.5-3 mg/kg PO q 8-12 h in dogs; 0.25 mg/kg PO q 8-12 h in cats). Titrate dose based on weakness and side effects (hypersalivation, vomiting, diarrhea). If dysphagia/regurgitation precludes oral medication, neostigmine (0.04 mg/kg SQ q 6 h) is an alternative. Human intravenous immunoglobulin can be helpful for shortterm management of acute fulminating myasthenia.
- Aspiration pneumonia is treated with antibiotics, nebulization and coupage, and oxygen if necessary (see p. 1583).
- Endotracheal intubation and ventilatory support may be necessary for the acute fulminating form or for patients with severe aspiration pneumonia.

- Intravenous fluids as needed
- Nutritional support as needed: feedings with the head elevated, or placement of a gastrostomy, nasogastric, or esophagostomy feeding tube (see p. 1267, p. 1269, p. 1270,p. 1273).

CHRONIC TREATMENT

Immunosuppressive therapy (acquired form only) is indicated when there is an inadequate response to anticholinesterase medication. Prednisone is the initial drug of choice (start at 0.5 mg/kg PO q 24 h for 1-2 weeks, then increase to 2-4 mg/kg PO q 24 h if needed; gradual taper if possible based on clinical response). Azathioprine, cyclosporine, or mycophenolate mofetil can be added if there is an inadequate response to prednisone or to allow decreased dose of prednisone in patients with severe side effects caused by prednisone.

DRUG INTERACTIONS

- Avoid drugs that impair neuromuscular transmission, including ampicillin, aminoglycosides, and phenothiazines.
- Organophosphates may increase toxicity of anticholinesterase drugs.
- In cats that develop myasthenia gravis while taking methimazole, the methimazole should be discontinued if possible.

POSSIBLE COMPLICATIONS

Aspiration pneumonia is the most common and serious complication in patients with pharyngeal/esophageal weakness.

RECOMMENDED MONITORING

- Client monitors weakness and dysphagia/regurgitation at home daily.
- Monitor antiacetylcholinesterase receptor antibody titer every 8 weeks in patients with acquired myasthenia gravis, because the disease will spontaneously resolve in many patients, usually by 6 to 18 months.

PROGNOSIS AND OUTCOME

- Prognosis for the acquired form is good for patients without pharyngeal/esophageal weakness. Spontaneous remission occurs in almost 90% of affected dogs.
- Prognosis is guarded in patients with dysphagia/regurgitation, because aspiration pneumonia is a common complication and carries a ≈50% 1-year mortality rate. Spontaneous remission occurs in almost 90% of dogs that survive the acute disease.
- Relapse is rare but can be associated with stress (e.g., surgery) or vaccination.
- The prognosis for the acute fulminating form is poor; most affected dogs die from respiratory failure.

PEARLS & CONSIDERATIONS

COMMENTS

- Early diagnosis and treatment in an attempt to avoid aspiration pneumonia improves the outcome.
- Serologic testing for antibodies to acetylcholine receptors should be evaluated in any adult dog with unexplained megaesophagus or dysphagia.

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Mushroom Toxicosis

BASIC INFORMATION

DEFINITION

Clinical condition resulting from ingestion of any of a variety of toxic mushrooms. Toxic syndrome produced depends on mushroom type and amount ingested:

- Gastrointestinal (GI) irritant mushrooms: large variety of species
- Isoxazole mushrooms: *Amanita gemmata, A. muscaria, A. smithiana, A. strobiliformis,* and *Tricholoma muscarium*
- Muscarinic mushrooms: *Inocybe* spp., *Clitocybe* spp.
- Gyromitrin mushrooms: *Gyromitra* spp., *Helvella crispa, H. lacuose*
- Hallucinogenic mushrooms: *Psilocybe* spp., *Panaeolus* spp.
- Hepatotoxic mushrooms: *Amanita* spp., *Galerina* spp., *Lepiota* spp.
- Nephrotoxic mushrooms: *Cortinarius* spp.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- All mammalian species are susceptible; dogs more likely to ingest compared to cats.
- Cats are particularly sensitive to cardiovascular effects of muscarinic mushrooms.

GEOGRAPHY AND SEASONALITY

- GI irritant mushroom: wide distribution; large range of fruiting seasons
- Isoxazole mushroom: throughout eastern United States and Pacific Northwest; coniferous and deciduous forests; fruits in spring/early summer then again in fall
- Muscarinic mushroom: wide distribution; forests or fields; fruits in fall, early winter in temperate areas, year round in warm, moist climates
- Gyromitrin mushroom: grow throughout North America, primarily found in the spring
- Hallucinogenic mushroom: wide distribution; Pacific Northwest and Gulf Coast; lawns, gardens, roadsides, open woods; cultivated in homes for recreational use
- Hepatotoxic mushroom: wide distribution throughout United States; wide variation in habitats and fruiting seasons
- Nephrotoxic mushroom: abundant in North America, especially Canada. Grow in woods and forests. Uncommon in urban areas.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- GI: acute, self-limiting GI distress
- Isoxazole: acute inebriation followed by coma; generally self-limiting
- Muscarinic: acute muscarinic signs
- Gyromitrin: GI signs followed by neurologic, hepatorenal and/or hemolytic syndromes
- Hallucinogenic: acute central nervous system (CNS) signs; generally self-limiting
- Hepatotoxic: acute GI signs, then liver failure in 24-72 hours
- Nephrotoxic: renal tubular dysfunction

HISTORY, CHIEF COMPLAINT

- History of exposure to a mushroom; presence of mushroom in the vomitus
- GI: vomiting, diarrhea within 4 hours of ingestion
- Isoxazole: vomiting, ataxia, disorientation, sleep/coma within 4 hours of ingestion
- Muscarinic: muscarinic signs (salivation, vomiting, diarrhea, lacrimation, bradycardia) within 4 hours of ingestion
- Gyromitrin: GI signs within 6-8 hours, hepatorenal and hemolytic syndrome 36-48 hours post ingestion
- Hallucinogenic: dysphoria, vocalization within 30 minutes to 2 hours of ingestion
- Hepatotoxic: acute, severe vomiting ± diarrhea within 8-24 hours; apparent recovery then return of GI signs; evidence of

acute liver failure in 24-72 hours; renal failure possible in severe cases
- Nephrotoxic: renal insufficiency/renal azotemia 12 hours to 8 days post exposure

PHYSICAL EXAM FINDINGS

- GI: dehydration possible, but generally unremarkable
- Isoxazole: as described above
- Muscarinic: as described above; wet lung sounds
- Gyromitrin: vomiting, signs of abdominal pain, icterus, hepatomegaly, hemoglobinuria, anemia
- Hallucinogenic: vocalization, agitation
- Hepatotoxic: GI signs, signs of abdominal pain, icterus, hypotension, hepatomegaly, coma
- Nephrotoxic: polyuria, polydipsia, dehydration, vomiting

ETIOLOGY AND PATHOPHYSIOLOGY

- GI: several mechanisms; hypersensitivity, local irritation, induced enzyme deficiencies
- Isoxazole: muscimol mimics γ-amino-butyric acid, causing sedation; ibotenic acid acts on glutamate receptors triggering CNS stimulation; combined effects result in hyperesthesia, sedation, intermittent agitation
- Muscarinic: bind muscarinic acetylcholine receptors in parasympathetic nervous system; prolonged duration due to lack of degradation; does not inhibit acetylcholinesterase
- Gyromitrin: metabolized to monomethylhydrazine, leading to metabolic alterations
- Hallucinogenic: stimulate serotonin and possibly norepinephrine receptors in central and peripheral nervous systems
- Hepatotoxic: interfere with DNA synthesis, protein synthesis, resulting in cellular necrosis
- Nephrotoxic: cortinarin depletes nicotinamide adenine dinucleotide phosphate (NADPH), making cells more susceptible to free radicals and leading to lipid peroxidation (oxidative membrane injury).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

History can be very helpful (observed ingestion of mushrooms, presence of mushrooms in pet's environment); otherwise, the diagnosis is reached when nonspecific disorders (e.g., gastroenteritis, hepatotoxicity, neurologic disturbance, etc.) are combined with direct evidence of exposure, such as mushrooms in vomitus. There is no practical clinical confirmatory test.

DIFFERENTIAL DIAGNOSIS

- GI, isoxazole, muscarinic, hallucinogenic: parvoviral enteritis, foreign body, garbage toxicosis, encephalitis, organophosphate and carbamate pesticide toxicosis, serotonergic drug toxicosis
- Hepatotoxic: other toxicoses (acetaminophen, iron, blue-green algae, *Cycas* spp.)
- Nephrotoxic: ethylene glycol, grapes, raisins, nonsteroidal antiinflammatory drug (NSAID) toxicity

INITIAL DATABASE

- CBC, serum biochemistry profile, urinalysis, venous or arterial blood gas measurement: anemia (with hepatotoxic mushrooms); icterus, significant increase in liver enzymes ± bilirubin; hypoglycemia; acidosis
- Coagulation profile:
    - Coagulopathy possible with severe liver injury
    - Evidence of disseminated intravascular coagulation (hepatotoxic)

ADVANCED OR CONFIRMATORY TESTING

- Radiography: hepatomegaly may be present in cases of hepatotoxic mushroom toxicosis.
- Liver biopsy (hepatotoxic)
- Urine: muscimol can be detected in urine; turnaround time long, little value in acute cases.

TREATMENT

TREATMENT OVERVIEW

Initial treatment requires management of potentially life-threatening abnormalities if present (e.g., seizures, bleeding disorders). In the

absence of these acute abnormalities, treatment goals are centered on prevention and supportive care: induction of vomiting and administration of activated charcoal to minimize absorption, and treatment to prevent acute hepatic injury, excessive muscarinic effects, and complications as they arise.

ACUTE GENERAL TREATMENT

- Manage life-threatening conditions:
  - Control seizures (for isoxazole, hallucinogenic, hepatotoxic).
    - Diazepam (0.5-2 mg/kg IV) for seizures
    - Barbiturates, gas anesthetics if diazepam is ineffective (see p. 501)
  - Atropine for treating excessive bronchial secretions and bradycardia (muscarinic) 0.04 mg/kg (give ¼ of dose IV, remainder IM), titrate up as needed.
- Decontamination of patient (only animals showing no clinical signs):
  - Emesis induction (effective within a few hours; see p. 1364)
  - Gastric lavage (see p. 1281):
    - Consider where emesis is contraindicated (comatose, anesthetized, etc.) or if hepatotoxic mushroom ingestion is suspected.
  - Activated charcoal:
    - 1-4 g/kg or labeled dosage of commercial product given PO, or via stomach tube if patient is unconscious (see p. 1281). Repeat in 8 hours if animal is showing clinical signs of toxicosis, half original dose.
- Manage clinical signs:
  - Antiemetics (for GI irritant mushroom toxicosis):
    - Metoclopramide, 0.2-0.4 mg/kg q 6 h PO, SQ, or IM; or 1-2 mg/kg/d as constant rate IV infusion; *or*
    - Maropitant, 1 mg/kg SQ q 24 h; *or*
    - Dolasetron, 0.6-1 mg/kg IV q 12 h
  - Correct fluid/electrolyte/acid-base abnormalities (GI, hepatotoxic).
  - Blood replacement/clotting factors, vitamin K^1 for coagulopathy (hepatotoxic)
  - Cyproheptadine (for dysphoria or serotonin syndrome-like signs associated with hallucinogenic mushrooms):
    - 1.1 mg/kg PO or pre rectum q 6-8 h PRN
- Prevent/manage liver injury (hepatotoxic mushrooms):
  - *N*-acetylcysteine:
    - 200 mg/kg slow IV loading dose then 10 mg/kg/h IV constant rate infusion (CRI); *or*
    - 280 mg/kg PO loading dose, then 70 mg/kg PO q 6 h for at least 7 doses
  - Crystalline (sodium or potassium) penicillin G (interferes with enterohepatic recirculation of hepatotoxins):
    - 0.5-1 million U/kg/d × 3 days as IV CRI
    - Monitor serum electrolytes as appropriate based on formulation (e.g., sodium, potassium), and adjust therapy if necessary.
    - Do not use procaine penicillin G for intravenous administration (immediately fatal).
  - Silbinin and silymarin (extracts of milk thistle):
    - Veterinary formulation combines silybin and *S*-adenosylmethionine (SAMe) (Denamarin): 1 small/medium/large tablet PO q 24 h for dogs <5.5 kg/6-15.5 kg/16-29.5 kg, respectively.
- Supportive care:
  - Thermoregulation
  - Pain management (options include fentanyl, buprenorphine, tramadol)

CHRONIC TREATMENT

- SAMe:
  - For chronic management of liver injury
  - 18 mg/kg PO q 24 h for 2-3 months

NUTRITION/DIET

For management of chronic hepatopathy (hepatotoxic mushrooms)

- High-quality, low-residue protein, fiber diet (see p. 501)

POSSIBLE COMPLICATIONS

Hepatic insufficiency ± hepatic encephalopathy; chronic kidney disease

RECOMMENDED MONITORING

- Hydration, electrolytes if severe GI signs
- Hepatotoxic and gyromitrin mushrooms:
  - CBC
  - Blood glucose
  - Coagulation parameters
  - Liver enzymes
  - Renal values
- Nephrotoxic mushrooms:
  - Renal values

PROGNOSIS AND OUTCOME

- GI irritant, isoxazole, muscarinic, and hallucinogenic mushrooms: excellent with supportive care
- Hepatotoxic mushrooms: guarded to poor with hepatotoxicity
- Gyromitrin: guarded with hepatotoxicity and hemolysis
- Nephrotoxic: guarded

PEARLS & CONSIDERATIONS

COMMENTS

- Because of difficulty in differentiating between toxic and nontoxic mushrooms, any ingestion of unidentified mushrooms by pets should prompt decontamination procedures (emesis, activated charcoal, etc.).
- Identification of mushrooms is best done by a mycologist; local college biology departments or museums are potentially useful sources of expertise (mycologists). Internet can be used to help narrow down and match the picture of the mushroom involved.

TECHNICIAN TIP

Physical confinement can be important to prevent injury for dysphoric, disoriented animals.

SUGGESTED READING

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Muscular Dystrophy

BASIC INFORMATION

DEFINITION

The muscular dystrophies (MDs) are a heterogeneous group of rare genetic disorders characterized by deficient or abnormal muscle cytoskeletal proteins. Progressive muscular weakness is the clinical feature MDs have in common.

SYNONYMS

There are many forms of muscular dystrophy; the most common terms used in veterinary medicine are Duchenne muscular dystrophy (DMD), or canine X-linked muscular dystrophy (CXMD), golden retriever muscular dystrophy (GRMD); Becker's muscular dystrophy (BMD); and autosomal recessive muscular dystrophy (ARMD) in Labrador retrievers (previously type 2 muscle fiber deficiency). This disorder has also been described as centronuclear-like myopathy.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- The disease is more prevalent in dogs but has been reported sporadically in cats.
- In dogs with DMD, clinical signs typically begin as early as 6 weeks of age and are progressive.
    - Cats frequently do not demonstrate overt clinical signs until they are ≥ years old.
    - The vast majority of affected animals are male.
- In Labradors with ARMD, clinical signs are generally apparent by 12-16 weeks of age. In this form of MD, both males and females may be affected.

GENETICS & BREED PREDISPOSITION

- DMD, an X-linked disorder, is best described in male golden retrievers but has been reported in the male rottweiler, Alaskan malamute, German shorthair pointer, Irish terrier, Samoyed, Groenendaeler shepherd, miniature schnauzer, Brittany spaniel, rat terrier, Pembroke Welsh corgi, Labrador retriever, and in domestic shorthair cats.
- A milder form (BMD) has been described in the Japanese spitz.
- In Labrador retrievers with ARMD, both yellow and black dogs of either sex can be affected.
- Sporadic cases of MD associated with dystrophin defects have been reported in female dogs.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- DMD: affects males mainly. Clinical signs often are severe.
- BMD: milder form
- ARMD: mainly Labrador dogs of either sex

HISTORY, CHIEF COMPLAINT

- Dogs affected with DMD are stunted.
- Dysphagia and difficulty prehending food can be seen as early as 6 weeks of age. Within weeks, muscle stiffness, “bunny-hopping,” exercise intolerance, and muscle atrophy may be observed. Clinical signs typically stabilize by 6-8 months of age. Regurgitation due to megaesophagus and diaphragmatic hypertrophy may lead to the development of cough, dyspnea, and respiratory distress due to aspiration pneumonia. Cardiomyopathy may lead to dyspnea, abdominal distension, and other signs of heart failure.
- ARMD: similar weakness, exercise intolerance, and atrophy may be seen, but dysphagia is rare, and clinical signs typically occur at a slightly later age.
- Cats with MD may show a predominance of muscle hypertrophy and stiffness. Occasionally dysphagia is evident.

PHYSICAL EXAM FINDINGS

- In DMD, no specific neurologic deficits are found. Affected animals have a characteristic gait, displaying elbow abduction,

hock adduction, and lordosis (ventroflexion of the spine). Hypertrophy of specific muscle groups is common, most notably the tongue.
- Dogs affected with ARMD, particularly if clinical signs are severe, will display limb-girdle muscle atrophy, kyphosis (extension/dorsiflexion of the spine), carpal hyperextension, and carpal valgus. In both disorders, myotactic reflexes such as the patellar reflex may be diminished or absent due to severe muscle atrophy.

ETIOLOGY AND PATHOPHYSIOLOGY

- Myofiber cytoskeletal proteins, usually dystrophin, are deficient or absent in DMD.
- Occasionally in DMD, dystrophin-associated or basement membrane proteins are dysfunctional.
- These proteins play a key role in maintaining structural integrity and contractile capability of myofibers. Dystrophin may also play a role in cellular homeostasis.
- The pathophysiologic mechanism of ARMD is unclear but likely related to an abnormally positive resting membrane potential in the myocyte.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is based on persistently elevated CK levels along with signs of neuromuscular weakness in young animals and a high index of suspicion in an at-risk breed.

DIFFERENTIAL DIAGNOSIS

- Polymyositis (autoimmune or infectious)
- Congenital myotonia
- Nemaline rod myopathy
- Polyneuropathy
- Spinal muscular atrophy
- Exercise-induced collapse of Labrador retrievers
- Progressive ossifying fibrodysplasia (cats)

INITIAL DATABASE

- Creatine kinase levels are markedly elevated in DMD as early as 1 week of age. Elevations peak at 6-8 weeks of age and then plateau at approximately 100× normal. Elevations are less dramatic in ARMD and in female dogs with DMD.
- Thoracic radiographs may reveal evidence of megaesophagus ± aspiration pneumonia.

ADVANCED OR CONFIRMATORY TESTING

- Electromyography (see online chapter: Electromyography and Nerve Conduction Velocity) reveals characteristic pseudomyotonic discharges and occasional fibrillation potentials and positive sharp waves. Abnormalities are evident by 10 weeks of age.
- Muscle biopsy in DMD (see p. 1305) typically shows areas of degeneration/mineralization along with areas of regeneration. ARMD is associated with type 2 fiber atrophy.
- Dystrophin deficiency can also be confirmed using immunocytochemistry on biopsy specimens.

TREATMENT

TREATMENT OVERVIEW

- Specific therapies for the muscular dystrophies are lacking. A new genetic technology called “exon-skipping” uses DNA-like molecules to patch the mutant dystrophin gene and has shown great promise for future clinical applications.
- Prevention of aspiration pneumonia

ACUTE AND CHRONIC TREATMENT

- Supportive (e.g., antibiotic therapy and nebulization/coupage for aspiration pneumonia)
- No definitive treatment at present

PROGNOSIS AND OUTCOME

- The prognosis with DMD is guarded to grave, depending on the severity of clinical signs and whether the animal has megaesophagus or congestive heart failure (both negative prognostic indicators).
- Because clinical signs tend to stabilize within the first year of life, some less severely affected animals may make acceptable house pets and may live for several years until they succumb.
- As with DMD, signs of ARMD tend to plateau between 6 and 12 months of age. Typically signs are mild compared with DMD, so affected Labradors may have a normal lifespan.

PEARLS & CONSIDERATIONS

COMMENTS

Breeders should be advised of the heritable nature of these disorders and remove carriers from the gene pool. Genetic counseling should be sought when an affected animal is identified.

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Multiple Organ Dysfunction Syndrome

BASIC INFORMATION

DEFINITION

Failure of two or more organ systems, usually acutely and in association with a systemic illness; commonly represents the end-organ compromise caused by an unchecked systemic inflammatory response syndrome (SIRS)

EPIDEMIOLOGY

SPECIES, AGE, SEX: No predilection for age or sex; dogs appear more commonly affected than cats.

RISK FACTORS: Sepsis, polytrauma (e.g., hit by car), neoplasia

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Multiple organ dysfunction syndrome (MODS) is a subset of critical illness; its expression varies according to the organ systems affected.

HISTORY, CHIEF COMPLAINT: Any critical illness and the associated chief complaint may be associated with the development of MODS.

PHYSICAL EXAM FINDINGS

- Physical exam findings are nonspecific and reflect the organs affected or the primary disease (such as abdominal sepsis).
- Animals are almost invariably collapsed, dull, tachycardic (or possibly bradycardic [cats]), tachypneic, and weak.

ETIOLOGY AND PATHOPHYSIOLOGY

- The organ systems that are commonly affected during MODS are the renal, cardiovascular, nervous, respiratory, gastrointestinal, hepatobiliary, and coagulation systems.
- Acute renal failure is a common feature of MODS in people and has been described in hospitalized dogs with critical illness. In this setting, acute renal failure is characterized by serum creatinine >2-3 mg/dL (>176-264 mmol/L), rising serum creatinine >0.5 mg/dL (>44 mmol/L) in 48 hours, or nonphysiologic oliguria.
- The lungs are a common site of organ dysfunction in MODS, manifesting as acute lung injury (ALI) or acute respiratory distress syndrome (ARDS; see p. 1369). ALI is characterized by a Pao^2:Fio^2 ratio between 300 and 200. ARDS is characterized by the presence of acute respiratory distress, bilateral radiographic pulmonary alveolar infiltrates, decreased pulmonary compliance, the absence of left-sided heart failure (pulmonary capillary wedge pressure <18 mm Hg), and a Pao^2:Fio^2 ratio of less than 200.
- Gastrointestinal (GI) dysfunction is common in dogs with MODS and can present as ileus, gastric ulceration, vomiting, and diarrhea. Secondary sepsis due to bacterial translocation from the GI tract to the circulation is common and potentially life-threatening.
- Neurologic dysfunction can present as peripheral or central disorders. Animals are usually weak, with decreased responsiveness that may progress to stupor or coma.
- Cardiovascular dysfunction may present as decreased cardiac output and hypotension (due to vasodilation, decreased cardiac contractility, etc.), or arrhythmias.
- Hematologic dysfunction produces prolonged coagulation times, decreased fibrinogen concentration, decreased antithrombin concentration, decreased platelet count, and/or clinical evidence of hemorrhage.
- Hepatic dysfunction manifests with progressive increases in alanine aminotransferase, serum alkaline phosphatase activity, and bilirubin concentration. Hepatic failure can lead to profound coagulopathy.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is reached by identifying overt and laboratory evidence of dysfunction of two or more organ systems in an ill patient. The implication of making a diagnosis of MODS is prognostic, since the presence of MODS conveys a worse prognosis.

DIFFERENTIAL DIAGNOSIS

Sepsis or SIRS may occur without the failure of multiple organ systems, in which case MODS is not present.

INITIAL DATABASE

- CBC, serum biochemistry profile, urinalysis, coagulation profile: identification of abnormalities listed previously and abnormalities caused by underlying illness
- Thoracic radiography, pulse oximetry, and arterial blood gas measurement if respiratory dysfunction
- Blood pressure: identify hypotension.
- Electrocardiogram: identify cardiac arrhythmias.
- Neurologic exam: to rule out central and peripheral nerve involvement

TREATMENT

TREATMENT OVERVIEW

Treatment depends on the failing organ system. The overall goals are to stabilize blood pressure and ensure optimal perfusion of the involved organs (correction of dehydration, treatment of hemodynamically significant arrhythmias). This involves aggressive therapy for the underlying cause.

ACUTE GENERAL TREATMENT

- Respiratory failure:
  - Supplemental oxygen and/or positive pressure ventilation
- Cardiovascular dysfunction:
  - Positive inotropic drugs (dobutamine, 5-10 mcg/kg/min) and/or vasopressor drugs (dopamine, 10-20 mcg/kg/min) are used if critically ill, hydrated patients with MODS fail to produce a sufficient arterial blood pressure.
- Coagulopathy:
  - Disseminated intravascular coagulopathy (see p. 1387) is the most commonly seen coagulation dysfunction. Goals are to treat the underlying cause while maintaining an adequate hematocrit to ensure oxygen delivery to tissues (treatment with packed red blood cells) and to replace coagulation factors and endogenous anticoagulants (plasma transfusion).
- Renal dysfunction:
  - Goals are to ensure adequate volume status/hydration and blood pressure and to avoid nephrotoxic medications (see p. 1369).
- Gastrointestinal dysfunction:
  - Gastroprotectants (e.g., famotidine, 0.5-1 mg/kg IV q 12 h; or omeprazole, 0.7 mg/kg PO q 24 h) are administered routinely.
  - Prokinetic drugs (ranitidine, 1-2 mg/kg slow IV; or erythromycin, 0.5-1 mg/kg PO q 8 h; or cisapride, 0.1-1 mg/kg PO q 8-12 h) are considered if ileus is present without obstruction.
  - Start enteral feedings as soon as possible.

PROGNOSIS AND OUTCOME

The presence of MODS conveys a worse prognosis: mortality in dogs with abdominal sepsis is 70% if MODS is present and 25% if it is not.

PEARLS & CONSIDERATIONS

COMMENTS

- MODS should be suspected in any critically ill animal with evidence of organ dysfunction.
- The presence of MODS has prognostic importance (failure of four or more organs is associated with nearly 100% mortality in humans and, by extrapolation, in dogs and cats).
- The onset of MODS is a critical step back in any patient. Critically ill patients should be carefully monitored for the development of signs of failure in a previously unaffected organ, such as new azotemia, icterus, or coagulopathy.
- Rapid appreciation of new-onset abnormalities may permit reversal of organ failure before MODS and subsequently lead to a better prognosis. For example, development of azotemia may respond to a fluid challenge or therapy with mannitol or

dopamine. At the very least, discontinuation of a potentially nephrotoxic agent (e.g., amikacin) in a pet with azotemia is mandatory.

PREVENTION

Rapid identification and correction of sepsis or severe hypovolemia

TECHNICIAN TIPS

Careful monitoring is useful for early detection of MODS. Like many aspects of critical illness, MODS is best prevented rather than treated.

CLIENT EDUCATION

MODS is a severe complication of disease, with guarded to poor outcome.

SUGGESTED READING

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Multiple Myeloma and Plasma Cell Tumors

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

- Multiple myeloma (MM) is a malignant disease of plasma cells derived from one clone in the bone marrow. It is a systemic disease, and multiple bone marrow sites are involved. This disease is characterized by the production of immunoglobulins (Ig) by malignant plasma cells; IgM or IgA in the dog, and IgG in the cat. *Waldenström's macroglobulinemia* refers to the disease in which IgM is the Ig type produced. Major extramedullary involvement (i.e., spleen, liver, skin) at initial presentation is common in cats.
- Plasma cell tumors (PCT) are solitary tumors composed of plasma cells, originating in sites other than the bone marrow (i.e., extramedullary). They can arise from skin, soft tissues, or bone. Serum globulin/Ig levels are often normal in this localized form of disease.

SYNONYM

Plasmacytoma, myeloma-related disorder (MRD)

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Rare in dogs and cats
- Older animals (8-12 years)
- Male predominance in noncutaneous PCT, no sex predilection in MM

GENETICS & BREED PREDISPOSITION

- MM: German shepherd
- PCT: Airedales, cocker spaniels, Kerry blue terriers, Scottish terriers, standard poodles

ASSOCIATED CONDITIONS & DISORDERS: Multiple myeloma:

- Hyperviscosity syndrome
- Bence-Jones proteinuria
- Pathologic fracture
- Bleeding diathesis
- Increased susceptibility to infection; immunosuppression
- Heart failure
- Renal disease
- Visual/ocular disturbances
- Amyloidosis
- Cryoglobulinemia

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Multiple myeloma
- Waldenström's (IgM) macroglobulinemia
- Cutaneous plasma cell tumor
- Extramedullary plasma cell tumor (EMP)
- Solitary osseous plasma cell tumor (SOP)

HISTORY, CHIEF COMPLAINT

- MM:
  - Dogs generally present with lameness or skeletal pain. Bleeding (epistaxis, ecchymoses, mucosal hemorrhage),

polyuria and polydipsia, central nervous system signs (seizures, dementia), and visual disturbances may also occur.
    - Cats tend to present with an insidious onset of nonspecific signs (anorexia, weight loss, lethargy). Other signs similar to those seen in dogs may rarely occur.
- Cutaneous PCT:
    - Raised nodule on the trunk, limbs, head, or in the oral cavity
- EMP:
    - Typically occur in the GI tract and cause signs such as weight loss, anorexia, nausea, vomiting, diarrhea.
- SOP:
    - Occur as a single lesion in bone and can cause bony swellings, lameness, or skeletal pain

PHYSICAL EXAM FINDINGS

- Skeletal pain, fractures
- Weight loss (MM, EMP)
- Lethargy (MM, EMP)
- Visual disturbances (MM)
- Depression, seizures, abnormal reflexes (MM)
- Epistaxis, gingival bleeding, ecchymoses
- Pallor, weak pulses, heart murmur, increased lung sounds (MM)
- Signs of congestive heart failure such as dyspnea (MM)
- Soft-tissue or bony masses
- Abdominal organomegaly

ETIOLOGY AND PATHOPHYSIOLOGY

- Malignant plasma cells produce large amounts of one type of Ig.
- Either the entire immunoglobulin can be produced or just a portion (e.g., light chain). The Ig or portion is referred to as the *M protein,* and the concentration is typically proportional to tumor burden in multiple myeloma. Low levels of M proteins are produced in PCT.
- Isolated lesions in bone or diffuse osteopenias are due to areas of proliferating malignant plasma cells. These areas are weakened, and pathologic fractures are common. Bone lesions are uncommon in cats.
- M protein in the blood increases serum viscosity, which causes hyperviscosity syndrome (HVS). HVS is due to sludging of blood in small vessels, and it causes ineffective oxygen and nutrient delivery. It is more common with IgM MM (Waldenström's), as the IgM molecule is large. HVS manifests as:
    - Bleeding disorder (due to protein coating of platelets, inhibition of platelet and coagulation factor release, and thrombocytopenia due to bone marrow infiltration)
    - Ocular changes
    - Congestive heart failure (due to hypertension, myocardial hypoxia, anemia, and increased workload)
    - Mentation changes and peripheral neuropathy (from M protein destruction of myelin)
- The light chain portion of the Ig is also called the *Bence-Jones protein,* and owing to its small size, it is filtered by the normal glomerulus. These can be detected in the urine of patients with MM with a specific test (but not on a urine dipstick).
- Renal disease develops secondary to Bence-Jones proteinuria, tumor infiltration into kidney, hypercalcemia, amyloidosis, and decreased renal perfusion.
- Hypercalcemia occurs secondary to the release of osteoclast activating factor by neoplastic cells.
- Cytopenias develop secondary to bone marrow infiltration and blood loss due to coagulopathies.
- An increased susceptibility to infection is seen because of the suppression of normal Ig levels, leukopenias, and impaired cell-mediated immunity. Urinary tract infections (UTIs) and pneumonia are the most common manifestations.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Differentials for monoclonal gammopathy: ehrlichiosis, leishmaniasis, feline infectious peritonitis, pyoderma, lymphoma, leukemia, idiopathic (monoclonal gammopathy of unknown significance)

INITIAL DATABASE

- Funduscopic exam: hemorrhage, retinal detachment, dilated/tortuous vessels
- CBC: cytopenias, thrombocytopenia
- Serum biochemistry panel may reveal hypercalcemia, elevated total protein, hyperglobulinemia, azotemia
- Urinalysis: infection possible (immunosuppression)

ADVANCED OR CONFIRMATORY TESTING

- MM:
  - For a diagnosis of MM in dogs, two of the following four criteria are needed: monoclonal gammopathy, lytic bone lesions, plasma cell infiltration of the bone marrow, and Bence-Jones proteinuria.
    - Serum protein electrophoresis: monoclonal gammopathy appears as a spike, typically in the β or γ region.
    - Survey radiographs: multiple areas of bony lysis or diffuse osteopenias are frequently found in the vertebrae, scapulae, and long bones in dogs with MM. Pathologic fractures may also be present. These signs are not typically found in cats. A solitary area of lysis is typically seen with SOPs.
    - Bone marrow aspiration: >10% plasma cells with atypia or >20% plasmacytosis are required for the diagnosis of multiple myeloma. Aspiration of multiple sites may be necessary.
    - Heat precipitation, or electrophoresis of urine: identifies Bence-Jones proteins. They are not detected on urine dipstick.
  - In cats, bony lysis and marked marrow infiltration are uncommon. Organ infiltration (e.g., liver, spleen) by neoplastic plasma cells may be useful in aiding the diagnosis of MM.
  - Serum or urine immunoelectrophoresis: identifies the class of immunoglobulin. (IgG, IgM, IgA). Dogs with multiple myeloma typically produce either IgG or IgM, and cats typically produce IgA.
  - Serum viscosity may be measured in some labs to verify HVS.
- Plasma cell tumor:
  - Tissue biopsy confirmation of cutaneous PCT, EMP, and SOP

TREATMENT

TREATMENT OVERVIEW

Goals of treatment are to reduce myeloma cell burden, relieve bone pain, allow for skeletal healing, and decrease serum viscosity and Ig levels.

ACUTE GENERAL TREATMENT

- Stabilize fractures.
- Surgical excision of plasma cell tumors if possible. Wide surgical margins generally are not necessary, but the margins should be free of both gross and microscopic evidence of neoplasia (i.e., “clean”).
- IV fluids for hydration and diuresis to decrease serum viscosity, azotemia, and hypercalcemia
- Analgesia for bone pain
- Plasmapheresis to decrease serum viscosity and remove Bence-Jones proteins may be available at some institutions. Therapeutic phlebotomy (with donor red cell transfusion) can possibly achieve a similar effect.
- Antibiotic therapy to treat infections (UTI, pneumonia); prophylactic broadspectrum antibiotics may be beneficial. Do not use nephrotoxic or bacteriostatic antibiotics.

CHRONIC TREATMENT

- Chemotherapy: melphalan with prednisone is the mainstay of treatment for MM. Cyclophosphamide can also be given initially in cases of widespread disease or severe hypercalcemia, but the benefit is unclear. Melphalan causes erratic myelosuppression in cats; substituting chlorambucil has been advocated. Chemotherapy can be attempted in cases of cutaneous PCT, EMP, or SOP that are nonresectable or if radiation therapy is not available. However, response information is limited. Other cytotoxic drugs (doxorubicin, vincristine) have been reported to have some activity in the rescue setting for some patients with MM. Consultation with an oncologist for the most current treatment options is recommended.
- Radiation therapy is the treatment of choice for SOP, some incompletely excised PCT, and localized MM bony lesions.
- Surgical excision is curative for most cutaneous PCT.

RECOMMENDED MONITORING

- Monitor CBCs frequently, owing to myelosuppressive effects of melphalan. Doses or schedule may require adjustment based on patient response.
- Monitor serum electrophoresis, as size of monoclonal spike is proportional to tumor burden. Plasma globulin level can also be used for monitoring remission status.
- Monitor for evidence of infection, and treat with antibiotics as needed, owing to immunosuppression.

PROGNOSIS AND OUTCOME

- MM:
  - Dogs: when treated with melphalan/prednisone, response rate is >90%. A good response is defined as 50% reduction of initial M protein level. Long-term prognosis is guarded, as recurrence is inevitable. Median survival time is 540 days with melphalan/prednisone, 220 days for prednisone alone. Negative prognostic factors in dogs include hypercalcemia, Bence-Jones proteinuria, and extensive bony lysis.
  - Cats: prognosis is poor; most responses are partial, and median survival time is 137 days. Degree of differentiation of predicts survival: cats with well-differentiated tumors have a median survival of 254 days, and cats with poorly differentiated tumors have a median survival of 14 days.
- Cutaneous PCT:
  - Benign biological behavior: surgical excision is generally curative.
- Extramedullary plasmacytoma (EMP):
  - EMP at sites other than the oral cavity frequently metastasize, but long-term survival is possible with surgical excision and chemotherapy and/or radiation. Oral plasmacytomas do not metastasize and local control provides long-term control. Median survival of dogs with complete resection was 474 days.
- SOP:
  - Eventually progress to MM, but there may be a long disease-free interval. Radiation therapy may provide control for 1 year or more.

PEARLS & CONSIDERATIONS

COMMENTS

- Perform serum protein electrophoresis on any animal in which MM is suspected, even if globulin and serum viscosity are normal.
- Use size of monoclonal gammopathy to monitor response to treatment.
- Extensive infiltration of plasma cells in sites outside the bone marrow is common during the initial presentation of cats.
- Cats experience more severe myelosuppression from melphalan than dogs.

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Mothball Toxicosis

BASIC INFORMATION

DEFINITION

Adverse reactions, mainly gastrointestinal/hemolytic or gastrointestinal/neurologic, that occur as a result of consuming naphthalene- or paradichlorobenzenecontaining mothballs, respectively

SYNONYMS

Common brand names of mothballs: Enoz Old Fashioned Moth Balls (naphthalene 99.9%), Enoz Para Moth Balls (paradichlorobenzene 99.6%), Garbage Can Deodorizer (paradichlorobenzene 99.75%)

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs of all breeds, ages, and both sexes; dogs more commonly involved than cats
- Young animals may be more sensitive to naphthalene.
- Compared to dogs, cats are considered more sensitive to oxidative hemoglobin damage from naphthalene.

GENETICS & BREED PREDISPOSITION: Animals deficient in glucose-6-phosphate dehydrogenase (dog breeds such as Akitas, Shiba Inus, and Tosas) may be more susceptible to erythrocyte oxidative damage by naphthalene. **RISK FACTORS:** Use of mothballs as repellents

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Naphthalene mothballs
- Paradichlorobenzene mothballs

HISTORY, CHIEF COMPLAINT

- Availability of mothballs in pet's environment
- Acute onset of vomiting, diarrhea, lethargy

PHYSICAL EXAM FINDINGS

- Naphthalene:
  - Listlessness, abdominal pain, inappetence, vomiting, and diarrhea within a few hours after ingestion
  - Mothball scent on the breath
  - Evidence of hemolytic anemia (see p. 71 ; pale mucous membranes, poor capillary refill time, icterus) may not be present until 12-48 hours after ingestion with naphthalene mothballs.
- Paradichlorobenzene:
  - Vomiting, diarrhea, lethargy, tremors, and seizures within a few hours after ingestion

ETIOLOGY AND PATHOPHYSIOLOGY

Source:

- Naphthalene is found in “old-fashioned” mothballs, and in some moth flakes/crystals. A naphthalene mothball weighs 3.6 g. Acute dose causing hemolysis in dogs = 1525 mg/kg, but a minimum lethal dose as low as 400 mg/kg is reported in dogs.
- Paradichlorobenzene mothballs are used as cake deodorizers in diaper and garbage pails and in bathrooms.
- A paradichlorobenzene mothball weighs 5 g. Paradichlorobenzene oral LD^{50} in mouse = 2950 mg/kg, rat = 500 mg/kg.
- Naphthalene-type mothballs are approximately two times more toxic compared to paradichlorobenzene type. Ingestion of one mothball for a medium-sized dog (30 lb [14 kg]) can be a potential toxic hazard.
- According to label claim on some brands, mothballs are occasionally used as animal repellents (rabbits, dogs, cats).

Mechanism of Toxicosis:

- Most cases occur acutely due to accidental ingestion of mothballs.
- Naphthalene:
  - Naphthalene itself does not cause hemolysis; its metabolites (alpha-and beta-naphthoquinones) are responsible for hemolysis. Hemolysis and methemoglobinemia occur secondary to the strong oxidant effect of naphthalene metabolites on red blood cells (RBCs) and the lack of RBC glutathione to prevent these oxidizing effects.
  - Nausea, vomiting, and diarrhea are due to the irritating properties of naphthalene.
- Paradichlorobenzene:
  - Paradichlorobenzene is an organochlorine insecticide. Other members of this class mainly affect the nervous system and cause tremors, salivation, ataxia, and seizures.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A functional diagnosis sufficient to initiate treatment can be made from a known history of exposure or suspected exposure with the presence of one of more of the following: mothball scent on the breath, signs of methemoglobinemia or hemolysis (naphthalene), or tremors and seizures (paradichlorobenzene).

DIFFERENTIAL DIAGNOSIS

- Naphthalene:
  - Other intoxications causing hemolysis (e.g., onions/garlic, zinc, acetaminophen; see p. 71 and p. 1374)
  - Immune-mediated hemolytic anemia
  - Erythrocytic parasites
- Paradichlorobenzene:
  - Other intoxications causing tremors/seizures (organophosphate/carbamate, garbage toxicosis, lead, arsenic)
  - Encephalitis (sterile, infectious)
  - Brain neoplasm
  - Idiopathic epilepsy

INITIAL DATABASE

- Naphthalene:
  - CBC: regenerative anemia due to hemolysis, hemoglobinemia, Heinz bodies (12-48 hours after exposure)
  - Serum biochemical changes: elevation in serum bilirubin, increased liver enzymes, increased blood urea nitrogen (BUN) and creatinine
  - Urinalysis: hemoglobinuria
- Paradichlorobenzene:
  - No significant CBC or serum biochemistry changes may be noted. Rarely, increases in BUN, serum creatinine, and liver enzymes are possible.

ADVANCED OR CONFIRMATORY TESTING

- Naphthalene or its metabolites (1-naphthol or mercapturic acid) can be found in urine, stool, or blood 8-24 hours after ingestion. Body fat or liver can also be used for detecting naphthalene.
- Abdominal radiographs may help differentiate between mothballs and other products which contain paradichlorobenzene (densely radiopaque) from those which contain naphthalene (radiolucent or faintly radiopaque).

TREATMENT

TREATMENT OVERVIEW

In patients with suspected or confirmed ingestion, induction of vomiting and activated charcoal administration are warranted even in the absence of clinical signs. Additional treatment (methemoglobinemia, anemia [naphthalene], control of seizure/tremor [paradichlorobenzene]) is implemented when the specific secondary effects occur.

ACUTE GENERAL TREATMENT

- Decontamination of patient:
  - Induction of vomiting (): useful within 1-2 hours; do not induce if animal is already vomiting; feed the animal first; 3% hydrogen peroxide (0.5-2 mL/kgPO, maximum 45 mL in largest dogs; repeat once after 10-15 minutes if no vomiting); or apomorphine, 0.03 mg/kg IV or 0.04 mg/kg IM; or xylazine (dogs and cats) at 0.5-1 mg/kg IV or IM.
  - Activated charcoal: 2-4 g/kg; mix with 70% sorbitol 1-3 mL/kg and give PO.
- Treat methemoglobinemia:
  - *N*-acetylcysteine (NAC) acts as a precursor to glutathione; may provide some protection to liver and RBCs against oxidative damage; efficacy of NAC in naphthalene toxicosis is not proven; 140 mg/kg PO or slow IV. then 70 mg/kg/dose, q 6 h for up to 7 doses.
  - Similarly, *S*-adenosyl methionine (40 mg/kg PO, then 20 mg/kg PO q 24 h beginning 24 h later) has been used as a glutathione donor in a similar setting of Heinz body hemolytic anemia (acetaminophen toxicosis) in a dog.
  - Ascorbic acid (antioxidant effect) at 20-30 mg/kg PO, IM, or slow IV q 8 h for 2-3 days
- Supportive care:
  - Fluid diuresis
  - Control seizures with diazepam (0.5-2 mg/kg IV PRN) for intoxications involving paradichlorobenzene-type mothballs.
  - Blood transfusion if needed (see p. 1347)
  - 1-2 mEq/kg of sodium bicarbonate added to fluids may help reduce renal damage due to hemoglobinuria (assess and monitor acid-base status first).

POSSIBLE COMPLICATIONS

Rare liver or renal damage with paradichlorobenzene

RECOMMENDED MONITORING

- CBC (methemoglobinemia, Heinz body anemia)
- Serum biochemistry profile (serum bilirubin, renal values, and hepatic enzymes)
- Hematocrit
- Urinalysis

PROGNOSIS AND OUTCOME

- Naphthalene: good prognosis with supportive care; poor prognosis if evidence of severe hemolysis, renal or hepatic damage present
- Paradichlorobenzene: good prognosis with supportive care

PEARLS & CONSIDERATIONS

COMMENTS

- Differentiation of the two types of mothballs is difficult because both are white crystalline solids at room temperature, and both have a similar odor.
- Dissolving a mothball in turpentine for 60 minutes can help differentiate between the two types of mothballs. Paradichlorobenzene is more soluble in turpentine than naphthalene. A paradichlorobenzene mothball usually dissolves within 30-60 minutes compared to about ¼ of a naphthalene mothball.

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Mitral/Tricuspid Regurgitation Due to Myxomatous Valve Disease

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Pathologic degeneration of the atrioventricular (mitral and tricuspid) heart valves, characterized by accumulation of glycosaminoglycans (myxomatous proliferation) and fibrosis of the valve leaflets and tendinous cords. The valvular degeneration leads to valvular regurgitation and eventually to congestive heart failure (CHF). The condition most commonly involves the mitral valve, with or without changes of the tricuspid valve.

SYNONYMS

Acquired mitral or tricuspid regurgitation or insufficiency, chronic degenerative valvular disease, chronic valvular heart disease, chronic valvular fibrosis, endocardiosis, myxomatous degeneration

EPIDEMIOLOGY

SPECIES, AGE, SEX: The most common cardiac disease in dogs. Prevalence is strongly influenced by age; it is uncommon in young individuals but common in old dogs. Males develop the disease at a younger age than females.

GENETICS & BREED PREDISPOSITION: All breeds; most common in small to medium-sized breeds: papillons, poodles, Chihuahuas, dachshunds, and Cavalier King Charles spaniels. The age at which the disease develops is inherited as a poly genetic threshold trait (i.e., multiple genes influence the trait, and a certain threshold has to be reached before the disease develops). Males have a lower threshold than females, leading to a higher disease prevalence at a given age.

ASSOCIATED CONDITIONS & DISORDERS: Myxomatous degeneration of the semilunar valves (very uncommon in dogs and when present, seldom of clinical importance).

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Incidental finding: no clinical signs of disease caused by the valvular regurgitation:
  - Cardiac auscultation (presence of systolic click [early stage] and/or systolic heart murmur)
  - Cardiomegaly on radiographs
  - Electrocardiographic changes: P mitrale and/or P pulmonale, increased R wave amplitude, increased QRS duration
- Valvular regurgitation causing clinical signs of CHF (most commonly left-sided)
- Sudden death may occur but is uncommon, especially in the absence of preceding clinical signs of CHF.

HISTORY, CHIEF COMPLAINT

- Cough (often worse in the morning or evening hours)
- Tachypnea/dyspnea/orthopnea
- Lethargy
- Reduced exercise tolerance
- Syncope
- Anorexia
- Weight loss
- Abdominal enlargement

PHYSICAL EXAM FINDINGS

- Patients without overt clinical signs:
  - Systolic click (early stage)
  - Systolic heart murmur; with progression, the murmur often increases in intensity.
- Patients showing overt clinical signs:
  - Loud heart murmur unless there is significant myocardial failure, which may develop because of concurrent myocardial disease or because of chronic ventricular volume overload
  - Tachycardia and loss of respiratory sinus arrhythmia

- Arrhythmia and pulse deficit may be present, most commonly atrial/supraventricular premature beats or atrial fibrillation.
- Weak femoral pulse
- Prolonged capillary refill time and pale mucous membranes
- Tachypnea/dyspnea/orthopnea
- Respiratory crackles/rales
- Expectation of pink froth: pulmonary edema may be evident in the nostrils and oropharynx in cases with severe CHF.
- Ascites possible with tricuspid valve disease

ETIOLOGY AND PATHOPHYSIOLOGY

- Primary inciting factor for the valvular degeneration is unknown.
- Degeneration begins with subendothelial deposition of mucopolysaccharide and areas of fibrosis, which produces ballooning/thickening of the valve leaflet and tendinous cords.
- With progression, the valve lesions cause insufficient coaptation of the leaflets, leading to regurgitation of blood from the ventricle into the atrium.
- Severity and progression of atrioventricular (AV) valve regurgitation depends on the severity and progression of valve lesions (leaflets and/or tendinous cords).
- Slight to moderate AV valve regurgitation is often completely compensated for years and is not expected to cause clinical signs of disease.
- Compensatory mechanisms include cardiac dilatation and eccentric hypertrophy, increased force of contraction, increased heart rate, increased pulmonary lymphatic drainage (left-sided AV valve regurgitation), fluid retention, and neurohormonal modulation of cardiovascular function.
- With progression, the valvular regurgitation can no longer be compensated, leading to reduced cardiac output and increased venous pressures (leading to pulmonary edema if left-sided CHF and to ascites if right-sided).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on the characteristic left apical location of a systolic heart murmur in an adult dog. Thoracic radiographs are indicated, particularly if cough or dyspnea is present, to differentiate between pulmonary edema and unrelated comorbid conditions such as collapsing trachea and chronic sterile bronchitis, which are common. Echocardiography is the diagnostic test of choice for demonstrating the valve lesion; a high index of suspicion usually exists prior to echocardiography, and it functions as a confirmatory test as well as to identify severity of secondary changes.

DIFFERENTIAL DIAGNOSIS

- Physical:
  - Other causes of heart murmurs:
    - Secondary mitral regurgitation due to dilated or hypertrophic cardiomyopathy
    - Congenital heart disease
    - Vegetative (bacterial) endocarditis
    - Anemia
    - Physiologic flow murmur
  - Other causes of respiratory distress:
    - Primary respiratory disease such as bronchitis, pneumonia, tracheal/bronchial collapse, and neoplasia
    - Pleural diseases with effusion
    - Anemia
    - Metabolic acidosis
    - Other causes of CHF
    - Other (noncardiac) causes of pulmonary edema
  - Other causes of reduced exercise capacity, lethargy, and wasting:
    - Primary diseases of locomotor system, such as chronic degenerative joint diseases, intervertebral disk disease
    - Other systemic or organ-related disease (i.e., renal or hepatic failure, neoplasia, and anemia)
- Radiographic:
  - Cardiac enlargement from other heart disease
  - Increased pulmonary interstitial or alveolar radiopacity due to primary respiratory disease (see Other causes of respiratory distress); expiratory radiographs
  - Normal variation
- Echocardiographic:
  - Valve abnormality: congenital (e.g., AV valve dysplasia) or infectious (endocarditis)

- Increased atrial and ventricular size and secondary regurgitation due to dilated cardiomyopathy or congenital heart disease

INITIAL DATABASE

- Diagnosis of AV valve myxomatous degeneration:
  - Echocardiography: detection of thickened/ballooning AV valve, identification of regurgitant jet (spectral or color-flow Doppler)
- Assessment of disease severity and complications:
  - Auscultation: a low-intensity murmur with or without a systolic click in an otherwise healthy dog usually indicates low disease severity.
  - Echocardiography: atrial and ventricular size, size and velocity of regurgitant jet (reduced velocity indicates high left atrial pressure and severe disease); ventricular motion (fractional shortening) is usually exaggerated in advanced stages, but a normal or reduced motion in the presence of severe regurgitation is indicative of myocardial failure and evidence of complication.
  - Electrocardiogram: presence of tachyarrhythmia such as atrial fibrillation or ventricular ectopy (usually indicates severe disease, presence of complication, or other cardiac disease).
  - Radiography: cardiac size, presence of pulmonary congestion and edema, exclusion of other (noncardiac) causes for clinical signs of disease
  - CBC, serum biochemistry panel, urinalysis: usually unremarkable in less severe cases; cases with CHF may have slightly increased liver enzymes and evidence of prerenal azotemia.

ADVANCED OR CONFIRMATORY TESTING

- Serum cardiac troponin I level: unremarkable in less severe cases, moderate to severe disease is associated with slightly to moderately increased levels, but significant increases indicate complication or presence of other cardiac disease.
- Serum natriuretic peptides (atrial natriuretic peptide [ANP], *N*-terminal pro-brain natriuretic peptide [NT-proBNP]): levels are often unremarkable in less severe cases. Moderate to severe disease is always associated with increased levels, and NT-proBNP levels can help differentiate dyspnea of cardiac origin from noncardiac causes; lack of a cage-side test is limiting.
- Blood culture in case of suspicion of vegetative endocarditis

TREATMENT

TREATMENT OVERVIEW

Goals of treatment:

- Treatment is not indicated in less severe disease without overt clinical signs.
- To alleviate clinical signs and improve quality of life and life expectancy in cases with signs of CHF by evacuating pulmonary edema/ascites and abolishing congestion; improving the hemodynamic situation by controlling heart rate, reducing aortic impedance and with inotropic support; and protecting from detrimental exposure to neurohormones.

ACUTE GENERAL TREATMENT

- For congestive heart failure (see p. 468)
- Provide optimal nursing care, including maintenance of appropriate environmental temperature and humidity, elevation of the head on a pillow and placement of sedated dogs in sternal posture

CHRONIC TREATMENT

- See Heart Failure, Chronic, p. 470
- Exact composition of medical therapy depends on disease severity and clinical signs. Most dogs with CHF require furosemide, which is usually combined with an angiotensin-converting enzyme inhibitor (ACEI) and pimobendan. However, spironolactone has also emerged as adjunct therapy to other heart failure therapy, owing to results from recent clinical trials.
- Furosemide PO. Dose depends on severity of heart failure (CHF) but should be kept as low as possible:
  - Mild to moderate CHF: 1 mg/kg q 1-2 days to 3-4 mg/kg q 8 h
  - Moderate to severe CHF: 2-3 mg/kg q 12 h or higher
- Pimobendan 0.5 mg/kg q 12 h PO
- ACEI (i.e., enalapril, benazepril, ramipril). Dosage and dosage interval dependent on particular ACEI used.
- Spironolactone 2 mg/kg q 12-24 h PO and/or hydrochlorothiazide 2-4 mg/kg q 12 h PO
- Digoxin 0.22 mg/m^2 q 12 h PO, or lower. See p. 675 for body surface area-body weight conversion table.
- Negative inotrope such as betareceptor antagonists or calciumchannel blockers may be required to control ventricular rate in

case of atrial fibrillation, but they should be used with caution because excessive suppression of heart rate is easily achieved, rapidly worsening heart failure. Begin with low dosage (only once CHF is controlled) and titrate up.

NUTRITION/DIET

Maintain adequate calorie intake (approximately 60 kcal/kg body weight) to minimize muscle wasting. Modestly restrict sodium intake, avoid food with high sodium content.

BEHAVIOR/EXERCISE

Allow walks, but avoid strenuous exercise.

DRUG INTERACTIONS

- Furosemide potentiates the effects of an ACEI, spironolactone, or a thiazide.
- Nonsteroidal antiinflammatory drugs should be used with caution in patients receiving furosemide and ACEI.
- The combination of pimobendan and a calcium-channel blocker or a β-receptor antagonist should be avoided.

POSSIBLE COMPLICATIONS

- Dogs initially not showing clinical signs may develop CHF.
- Dogs stabilized by medical therapy may suffer recurrent CHF.
- Dogs with initially left-sided HF may develop biventricular CHF, often due to pulmonary hypertension.
- Development of arrhythmia, most commonly atrial fibrillation
- Rupture of first-order tendinous cord(s), leading to a flail valve leaflet
- Atrial tear leading to acquired atrial septal defect or cardiac tamponade
- Formation of intracardiac thrombus and/or myocardial infarction

RECOMMENDED MONITORING

- Encourage owner to participate in a structured care program to facilitate body weight, appetite, respiratory and heart rate monitoring; provide client support to ensure good medication compliance and dosage adjustments.
- Frequency of reexaminations depends on severity of valvular insufficiency and severity of HF (if present).
- Dogs without signs of CHF:
  - Slight to moderate valvular regurgitation: once every 6 months to once a year
  - Moderate to severe valvular regurgitation may require more frequent monitoring.
- Dogs with signs of CHF:
  - Once acute CHF has been successfully treated, dogs may often be treated at home.
    - Reexamination after 1-2 weeks of therapy (check for signs of CHF, dehydration, electrolyte balance, renal function and presence of any complications)
    - Thereafter once every 3 to 6 months
    - More severe cases may require more frequent monitoring.

PROGNOSIS AND OUTCOME

- Dogs without signs of CHF:
  - Chronic disease progression. Dogs with low disease severity may sustain this compensated state for several years before signs of CHF develop.
  - Risk factors for progression from mild to severe: severity of valve lesions, age, and gender
  - Risk factors for CHF: regurgitant status, left atrial size, natriuretic peptides
- Dogs with CHF (acute or stabilized):
  - Prognosis depends on age, severity of heart failure, presence of complications or other disease (such as kidney disease).
  - Clinical trials indicate a mean survival time from onset of CHF of 8-10 months but may vary from days to years in different dogs.

PEARLS & CONSIDERATIONS

COMMENTS

- If presence of mitral valve regurgitation is equivocal, the murmur or regurgitant jet may become obvious after stressing the dog slightly.
- Loud musical murmurs are unusual. The intensity of this type of murmur is not related to disease severity.
- Dogs with syncope related to intermittent atrial arrhythmia may sometimes be managed by a low dose of digoxin (approximately half recommended dose).
- Syncopal dogs with MR but without clinical signs of CHF should be examined for the presence of pulmonary hypertension.
- Mild pleural and/or pericardial effusion may develop because of CHF. More pronounced accumulation of fluid in these locations raises the suspicion of other causes.

PREVENTION

- Because the susceptibility to myxomatous atrioventricular valve degeneration in dogs is inherited, the disease prevalence in affected breeds should be reduced by breeding measures.
- Currently, no medication or management are known to prevent the disease or stop or slow disease progression.

CLIENT EDUCATION

- The disease and expected progression: low disease severity indicates long period without clinical signs; moderate to severe indicates a shorter period.
- If the client is a breeder, inform him/her about the genetics of the disease and impact of the finding on future breeding.
- Appropriate level of exercise (no restrictions for low disease severity, avoid strenuous exercise in moderate to severe cases).
- Signs of CHF
- How to medicate (if indicated)
- How to monitor resting heart and respiratory rates at home (if indicated)
- Diet (if indicated)

SUGGESTED READING

Atkins C, Bonagura J, Ettinger S, et al: ACVIM consensus statement. Guidelines for the diagnosis and treatment of canine chronic valvular heart disease. J Vet Intern Med 23:1142–1150, 2009.

Olsen LH, Häggström J, Pedersen HD: Acquired valvular heart disease. In Ettinger SJ, Feldman E, editors: Textbook of veterinary internal medicine, ed 7, St Louis, 2010, Elsevier Saunders, pp 1299–1319.

Häggström J, Höglund K, Borgarelli M: An update on treatment and prognostic indicators in canine myxomatous mitral valve disease. J Small Anim Pract 50(suppl. 1): 25–33, 2009.

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Mitral Valve Stenosis

BASIC INFORMATION

DEFINITION

Rare congenital or acquired cardiac disorder characterized by narrowing of the mitral valve orifice. The narrowing is a result of an abnormal mitral valve apparatus; it leads to obstruction of diastolic transmitral inflow and (potentially) left-sided congestive heart failure (CHF).

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs and cats. No reported age or sex predilection.

GENETICS & BREED PREDISPOSITION

- Dogs: bull terrier, Newfoundland (may be predisposed)
- Cats: two Siamese cats reported, but no evidence of breed predisposition

RISK FACTORS

- Predisposed breeds of dogs
- Cardiac valve neoplasia (very rare)

ASSOCIATED CONDITIONS & DISORDERS

- Dogs (concurrent conditions):
  - Mitral valve dysplasia
  - Subaortic stenosis (SAS)
  - Patent ductus arteriosus (PDA)
  - Pulmonic stenosis
- Dogs and cats (associated conditions):
  - Congestive heart failure
  - Pulmonary hypertension
- Cats (concurrent and associated condition): feline aortic thromboembolism

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Valvular mitral stenosis: involves the mitral valve leaflets (dog and cat)
- Supravalvular mitral stenosis: left atrium is divided by a membrane just above the mitral annulus (see online chapter: Cor Triatriatum Sinister and Supravalvular Mitral Stenosis)

HISTORY, CHIEF COMPLAINT

- Exercise intolerance/episodic weakness
- Lethargy
- Cough
- Dyspnea (most common sign in cats)
- Syncope

PHYSICAL EXAM FINDINGS

- Soft (I-III/VI) left apical diastolic murmur (inconsistent)
- Left apical systolic murmur (if mitral regurgitation is present)
- With CHF:
  - Tachycardia
  - Tachypnea

- Pulmonary crackles and wheezes

ETIOLOGY AND PATHOPHYSIOLOGY

- Congenital (possibly heritable in predisposed breeds)
- Acquired:
  - Bacterial endocarditis (controversial)
  - Intracardiac neoplasia (mitral valve chondrosarcoma reported in a dog).
- Pathophysiology:
  - Obstruction of the transmitral diastolic flow (increase in resistance to blood flow between the left atrium and ventricle)
  - Increase in left atrial, pulmonary vein, and pulmonary capillary pressures
  - Pulmonary edema formation
  - Exercise increases left atrial pressure; exercise induced dyspnea/syncope may occur.
  - Pulmonary hypertension may develop due to increased pulmonary capillary pressure.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected in a young patient presenting with left apical diastolic murmur (often very subtle, difficult to hear). Cough, tachypnea, and dyspnea may be present. Left heart enlargement is usually evident on thoracic radiographs, and an echocardiogram is required for confirmation.

DIFFERENTIAL DIAGNOSIS

- Radiographic/electrocardiographic:
  - Left atrial enlargement: other types of cardiac disease (myxomatous mitral valve disease/endocardiosis, mitral valve dysplasia, dilated cardiomyopathy, subaortic stenosis, patent ductus arteriosus, and [in cats] hypertrophic cardiomyopathy)
- Echocardiographic:
  - Myxomatous mitral valve disease/endocardiosis
  - Mitral valve dysplasia
  - Bacterial endocarditis
  - Dilated cardiomyopathy

INITIAL DATABASE

- Thoracic radiographs: left atrial enlargement very common. Signs of pulmonary edema if CHF.
- Electrocardiogram: wide P waves in lead II, supraventricular premature complexes, atrial/supraventricular tachycardia, atrial fibrillation. Increased R wave amplitude in lead II if SAS or PDA is also present.
- Echocardiogram:
  - Two-dimensional mode: left atrial dilation (often severe), thickened mitral valve leaflets or supravalvular membrane (cat), decreased mitral valve leaflet excursion, diastolic doming of the leaflets
  - M-mode: thickened mitral valve leaflets, parallel motion of the leaflets, incomplete leaflet separation in diastole, reduced E-F slope; increased LA: Ao ratio
  - Color-flow Doppler: diastolic aliased or turbulent flow across the mitral valve. Systolic turbulent flow if mitral regurgitation is present.
  - Spectral Doppler: increased early diastolic filling (velocity E wave <1.1 m/s), prolonged pressure half-time (<50 ms), reduced mitral valve area (MVA)

ADVANCED OR CONFIRMATORY TESTING

- Cardiac catheterization: rarely necessary for confirming diagnosis, replaced by echocardiography
  - Angiogram: thickened and restricted MV leaflets, enlarged left atrium, ± mitral regurgitation
  - Pressure measurements: increase in left atrial pressure and pulmonary artery pressure, if pulmonary hypertension or CHF is present
- Transesophageal echocardiography: better visualization of the mitral valve apparatus

TREATMENT

TREATMENT OVERVIEW

Initial control of CHF signs, with therapy to reduce venous congestion (diuretics), inhibit sodium/water retention, counteract vasoconstriction (angiotensin-converting enzyme [ACE] inhibitors, vasodilators), and control supraventricular arrhythmias (digoxin, calcium channel or beta-blockers). Balloon valvuloplasty or mitral valve repair/replacement may be indicated. Consider referral to cardiologist for diagnosis and advice on treatment plan.

ACUTE GENERAL TREATMENT

- Diuretics: indicated if the patient is in congestive heart failure (see p. 468)
- Oxygen therapy/supplementation: for dyspneic patients
- ACE inhibitors: reduce preload and afterload (see p. 470)
- Digoxin, calcium channel blocker or beta-blocker: management of supraventricular arrhythmias (see p. 111)

CHRONIC TREATMENT

- Medical therapy:
  - Diuretics, ACE inhibitors, and antiarrhythmics (see p. 470)
  - In cats, antiplatelet and/or anticoagulant therapy for prevention of atrial thrombus formation (see p. 88). Aspirin, warfarin, unfractionated heparin/low-molecular-weight heparins, clopidogrel.
- Surgical therapy:
  - Open mitral commissurotomy: requires cardiopulmonary bypass (CPB); one encouraging report in the literature.
  - Mitral valve replacement: requires CPB. Postoperative management complications are common.
  - Balloon valvuloplasty: inconsistent results in canine patients; possible damage to the mitral valve apparatus, with worsening of mitral regurgitation.

BEHAVIOR/EXERCISE

Restrict exercise and excitement in patients with collapsing or syncopal episodes.

DRUG INTERACTIONS

- Excessive use of diuretics is contraindicated owing to the decrease in preload, electrolyte disturbances, prerenal/renal azotemia, and increased risk of digitalis toxicity.
- ACE inhibitor: may reduce glomerular filtration rate and cause azotemia; hypotension may occur when used with diuretics; risk of hyperkalemia when K^+ is supplemented or K^+-sparing diuretics are used concurrently.

POSSIBLE COMPLICATIONS

- Recurrence of signs due to progression of CHF
- Systemic thromboembolism (cats)
- Postsurgery: restenosis, coagulation disturbances due to postsurgical management (mitral valve replacement)

RECOMMENDED MONITORING

Recheck examinations should include: thoracic radiographs, serum renal panel including electrolytes, systolic blood pressure measurement, digoxin levels (if applicable), and electrocardiogram.

PROGNOSIS AND OUTCOME

- Long-term prognosis depends on the severity of the stenosis: guarded to poor in severe cases.
- Surgical approach may offer a better outcome in the future.

PEARLS & CONSIDERATIONS

COMMENTS

- A disproportionate number of cases occur in the bull terrier breed.
- Medical management is relatively unrewarding.
- Surgical approach may offer a better long-term prognosis in the future.

PREVENTION

Do not breed affected animals.

TECHNICIAN TIPS

The diastolic murmur/rumble is subtle and requires a quiet environment for auscultation.

CLIENT EDUCATION

- Monitor respiratory rate at rest, exercise tolerance, and appetite.
- Advise client not to breed affected animals.

SUGGESTED READING

Kittleson MD: Cases in small animal cardiovascular medicine. Available at: http://www.vmth.ucdavis.edu/cardio/cases.

Lehmkuhl LB, et al: Mitral stenosis in 15 dogs. J Vet Intern Med 8(1):2–17, 1994.

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Mitral Valve Dysplasia

BASIC INFORMATION

DEFINITION

Common congenital malformation of any component of the mitral valve apparatus (papillary muscles, chordae tendineae, leaflets, annulus), that results in valvular dysfunction

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs and cats. Usually identified early in life.

GENETICS & BREED PREDISPOSITION: Dogs: bull terrier, miniature bull terrier, English bulldog, Great Dane, German shepherd, Newfoundland, and Irish setter are predisposed. Cats: two Siamese cats reported (mitral valve stenosis), but no evidence of breed predisposition.

RISK FACTORS

- Predisposed breeds of dogs

ASSOCIATED CONDITIONS & DISORDERS

- Dogs (concurrent conditions):
  - Mitral valve stenosis (MVS; see online chapter: Mitral Valve Stenosis)
  - Systolic anterior motion of the mitral valve (SAM)
  - Subaortic stenosis (SAS)
  - Patent ductus arteriosus (PDA)
  - Pulmonic stenosis
- Dogs and cats (associated conditions):
  - Congestive heart failure
  - Pulmonary hypertension
- Cats (concurrent and associated condition): feline aortic thromboembolism

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Valvular mitral stenosis (MVS): involves the mitral valve leaflets (dog and cat). See online chapter: Mitral Valve Stenosis.

HISTORY, CHIEF COMPLAINT

- Exercise intolerance/episodic weakness
- Lethargy
- Cough
- Dyspnea (most common sign in cats)
- Syncope

PHYSICAL EXAM FINDINGS

- Left apical systolic murmur (if mitral regurgitation)
- Grade I-VI/VI left apical systolic murmur (inconsistent with MVS)
- With CHF:
  - Tachycardia
  - Tachypnea
  - Pulmonary crackles and wheezes

ETIOLOGY AND PATHOPHYSIOLOGY

- Congenital (possibly heritable in predisposed breeds). Presumed genetic, although specific mutations have not been identified.
- Pathophysiology:
  - Mitral regurgitation (from the left ventricle to the left atrium during systole)
  - Obstruction of the transmitral diastolic flow (increase in resistance to blood flow between the left atrium and ventricle) in MVS
  - Obstruction of the left ventricular outflow tract with systolic anterior motion of the mitral valve (SAM)
  - Increase in left atrial, pulmonary venous, and pulmonary capillary pressures
  - Pulmonary edema formation
  - Exercise increases left atrial pressure; exercise induced dyspnea/syncope may occur.
  - Pulmonary hypertension may develop secondary to increased pulmonary capillary pressure.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected in a young patient presenting with left apical murmur. Cough, tachypnea, and dyspnea may be present. Left heart enlargement is usually evident on thoracic radiographs, and an echocardiogram is required for confirmation.

DIFFERENTIAL DIAGNOSIS

- Radiographic/electrocardiographic:
  - Left atrial enlargement: other types of cardiac disease (myxomatous mitral valve disease/endocardiosis, dilated cardiomyopathy, subaortic stenosis, patent ductus arteriosus, and [in cats] hypertrophic cardiomyopathy)
- Echocardiographic:
  - Myxomatous mitral valve disease/endocardiosis
  - Bacterial endocarditis
  - Intracardiac neoplasia

INITIAL DATABASE

- Thoracic radiographs: left atrial enlargement very common. Signs of pulmonary edema if CHF.
- Electrocardiogram: wide P waves in lead II, supra ventricular premature complexes, atrial/supraventricular tachycardia, atrial fibrillation. Increased R wave amplitude in lead II if SAS or PDA is also present.
- Echocardiogram:
  - Two-dimensional mode: abnormal mitral valve leaflets, abnormal valve motion, mitral regurgitation, left atrial dilation. Supravalvular membrane (cat), decreased mitral valve leaflet excursion and diastolic doming of the leaflets (MVS).
  - M mode: thickened mitral valve leaflets, increased LA: Ao ratio, incomplete leaflet separation in diastole and reduced E-F slope (MVS); SAM.
  - Color-flow Doppler: systolic turbulent flow in the left atrium if mitral regurgitation is present, and in the left ventricular outflow tract with SAM. Diastolic aliased or turbulent flow across the mitral valve (MVS).
  - Spectral Doppler: increased early diastolic filling (velocity E wave >1.1 m/s), prolonged pressure half-time (>50 ms), and reduced mitral valve area (MVS).

ADVANCED OR CONFIRMATORY TESTING

- Cardiac catheterization: rarely necessary for confirming diagnosis but may yield quantitative information and help characterize unusual lesions.
  - Angiogram: mitral regurgitation, thickened and/or restricted MV leaflets, enlarged left atrium
  - Pressure measurements: increase in left atrial pressure and pulmonary artery pressure if pulmonary hypertension or CHF is present
- Transesophageal echocardiography: better visualization of the mitral valve apparatus

TREATMENT

TREATMENT OVERVIEW

Initial control of CHF signs, with therapy to reduce venous congestion (diuretics), inhibit sodium/water retention, counteract vasoconstriction (ACE inhibitors, vasodilators), and control supra ventricular arrhythmias (digoxin, calcium channel or beta-blockers). Consider referral to cardiologist for diagnosis and advice on treatment plan.

ACUTE GENERAL TREATMENT

- Diuretics: indicated if the patient is in congestive heart failure (see p. 468)
- Oxygen therapy/supplementation: for dyspneic patients
- Angiotensin-converting enzyme (ACE) inhibitors: reduce preload and after-load (see p. 470)
- Digoxin, calcium channel blocker or beta-blocker: management of supraventricular arrhythmias (see p. 111)
- For myocardial failure (advanced/end-stage state characterized by left ventricular hypocontractility): inodilators (pimobendan)

CHRONIC TREATMENT

- Medical therapy:
  - Diuretics, ACE inhibitors, inodilators and antiarrhythmics following the acute treatment guidelines ()
  - In cats, antiplatelet and/or anticoagulant therapy for prevention of atrial thrombus formation (see p. 88). Aspirin, worfarin unfractionated heparin/low-molecular-weight heparins, clopidogrel.
- Surgical therapy:
  - Mitral valve replacement or open mitral commissurotomy (MVS): requires cardiopulmonary bypass. Postoperative management complications are common.
  - Balloon valvuloplasty (MVS): inconsistent results in canine patients; possible damage to the mitral valve apparatus with worsening of mitral regurgitation.

BEHAVIOR/EXERCISE

Restrict exercise and excitement in patients with collapsing or syncopal episodes.

DRUG INTERACTIONS

- Excessive use of diuretics is contraindicated owing to the decrease in preload, electrolyte disturbances, prerenal/renal azotemia, and increased risk of digitalis toxicity.
- ACE inhibitors: may reduce glomerular filtration rate and cause azotemia; hypotension may occur when used with diuretics; risk of hyperkalemia when K^+ is supplemented or K^+-sparing diuretics are used concurrently.

POSSIBLE COMPLICATIONS

- Recurrence of signs due to progression of CHF
- Systemic thromboembolism (cats)
- Left atrial rupture (dogs)
- Postsurgery: coagulation disturbances due to postsurgical management (mitral valve replacement), restenosis (MVS)

RECOMMENDED MONITORING

Recheck examinations should include: thoracic radiographs, serum renal panel including electrolytes, systolic blood pressure measurement, digoxin levels (if applicable), and ECG.

PROGNOSIS AND OUTCOME

- Long-term prognosis depends on the severity of the dysplasia: guarded in severe cases.
- Surgical approach may offer a better outcome in the future.

PEARLS & CONSIDERATIONS

COMMENTS

- A disproportionate number of cases occurs in the bull terrier breed.
- Surgical approach may offer a better long-term prognosis in the future.

PREVENTION

Do not breed affected animals.

CLIENT EDUCATION

- Monitor respiratory rate at rest, exercise tolerance, and appetite.
- Advise client not to breed affected animals.

SUGGESTED READING

Kittleson MD, Kienle RD: Congenital abnormalities of the atrioventricular valves. In Kittleson MD, Kienle RD, editors: Small animal cardiovascular medicine. New York, 1998, Mosby, pp 273–281.

AUTHOR: JOAO S. ORVALHO

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Microvascular Dysplasia, Hepatic

BASIC INFORMATION

DEFINITION

A congenital disorder of dogs in which there are histologic hepatic vascular abnormalities presumably causing intrahepatic shunting with no demonstrable macroscopic portosystemic shunt (PSS)

SYNONYMS

Hepatoportal microvascular dysplasia (HMD), MD, MVD, microvascular portal dysplasia, portal vein hypoplasia (with no shunt)

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Primarily dogs; poorly documented in cats
- Typically affects young adult dogs; clinical signs develop at average age 3 years (can be any age), though most dogs show no overt clinical signs. By contrast, dogs with PSS first develop signs at average age 6-18 months.
- Female sex predilection

GENETICS & BREED PREDISPOSITION

- Polygenic mode of inheritance suspected in Cairn terriers
- Cairn terriers and Yorkshire terriers predisposed
- Has been documented in multiple breeds (the vast majority are small dogs)

ASSOCIATED CONDITIONS & DISORDERS: Similar histologic hepatic changes are seen in dogs with PSS

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Most affected dogs show no clinical signs.
- Severely affected dogs present with signs similar to those of dogs with PSS. Signs often wax and wane.
- Clinical signs are typically referable to the central nervous system (CNS), gastrointestinal (GI) system, or urinary tract
- CNS (all secondary to hepatic encephalopathy): lethargy, ataxia, weakness, abnormal behavior, abnormal vocalization, ptyalism (more common in cats), head pressing, bumping into objects because of central blindness, incessant pacing or circling, stupor, seizures, or coma
    - Exacerbation of encephalopathic signs with: high-protein meals, GI bleeding, constipation, azotemia, hypokalemia, metabolic alkalosis, tranquilization, and methionine-containing supplements or medications
- GI: intermittent anorexia, vomiting, diarrhea
- Urinary tract: hematuria, pollakiuria, or dysuria from ammonium urate urolithiasis

PHYSICAL EXAM FINDINGS

- Usually unremarkable
- Small body stature
- Questionably small liver (inability to palpate liver margins)
- CNS signs (see CNS in History, Chief Complaint above)
- Poor haircoat

ETIOLOGY AND PATHOPHYSIOLOGY

- Shunting is hypothesized to occur through microscopic intrahepatic vessels, but this has not been proven.
- Hepatic encephalopathy (HE; see p. 501) and resultant CNS signs occur from toxins and nutrients absorbed from the intestines; thought to bypass metabolism by the liver through microscopic intrahepatic shunting.
- High urinary excretion from elevated blood levels of ammonia and uric acid can occasionally result in development of urate

urolithiasis (renal, ureteral, bladder).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Microvascular dysplasia should be considered when a fasting or postprandial bile acids level is elevated, often with no apparent clinical signs. Histologic characteristics (liver biopsy), together with advanced testing that rules out a macroscopic shunt, are confirmatory.

DIFFERENTIAL DIAGNOSIS

- CNS signs: infectious disease, toxin, other metabolic encephalopathy (hypoglycemia), idiopathic epilepsy, congenital malformations (e.g., hydrocephalus)
- GI signs: parasitism, foreign body, dietary indiscretion, dietary allergy, intestinal inflammation/infiltration
- Urinary tract signs: urinary tract infection, other calculi

INITIAL DATABASE

- CBC is typically normal. Microcytosis, commonly seen in dogs with PSS, rarely occurs in dogs with hepatic microvascular dysplasia. In vitro changes in blood stored in EDTA may mask microcytosis, especially if not analyzed quickly.
- Serum biochemical profile is often normal, but mild elevations in hepatic enzyme activities and mildly low blood urea nitrogen concentration have been noted, as have hyperglobulinemia and hypercholesterolemia.
- Coagulation profile: typically normal
- Urinalysis: usually normal, but ammonium biurate crystalluria, hematuria, or pyuria are possible.
- Abdominal radiographs: usually normal, but occasionally mild microhepatica may be noted.

ADVANCED OR CONFIRMATORY TESTING

- Serum bile acids: Essentially all animals with microvascular dysplasia have elevated postprandial serum bile acid concentrations; fasting/preprandial may be normal. Mean serum bile acid concentrations are lower than in dogs with PSS.
- Plasma protein C concentrations may aid in differentiating between PSS and MD. In one study, a protein C activity of <70% was much more likely to indicate PSS and >70% was more indicative of HMD (though some overlap).
- Liver biopsy:
    - Typically reveals hepatic arteriolar hyperplasia, small portal triads, increased smooth muscle thickness of hepatic venules, and an increase in small vascular structures in the periportal area
    - These findings in association with elevated serum bile acids, in the absence of PSS, are diagnostic for microvascular dysplasia.
    - Certain histologic abnormalities such as portal endothelial cell hyperplasia, Kupffer cell hyperplasia, and portal vein dilation are considered highly suggestive of hepatic microvascular dysplasia, but this theory is not universally accepted.
    - Many pathologists believe the histologic findings in dogs with hepatic microvascular dysplasia are indistinguishable from those of dogs with PSS.
- Abdominal ultrasound: the liver is typically normal in appearance but may be small, and there may be a decreased ease of visualization and number of hepatic vascular structures. No PSS is noted. A portal vein/aortic ratio of >0.8 is strongly indicative of the absence of a PSS.
- Transcolonic or transsplenic portal scintigraphy: distinguishes hepatic microvascular dysplasia from PSS. There is significant hepatic uptake of the radionuclide in the liver with micro vascular dysplasia (<15% shunt fraction).
- Mesenteric or transsplenic portography: negative for shunts in dogs with hepatic microvascular dysplasia where no evidence of extrahepatic shunting is noted. There may also be truncating of the distal hepatic vessels and slow clearance of contrast. This test is typically only available at referral institutions.
- Helical CT angiography: negative for shunting vessels
- Ideally portal scintigraphy or CT angiography could be performed first to rule out the need for the more invasive mesenteric portography.

TREATMENT

TREATMENT OVERVIEW

Reversal of hepatic encephalopathy through reduction in protein intake, prevention of absorption of toxins from the GI tract, and excretion from the kidneys and colon. No treatment is indicated in the absence of clinical signs.

ACUTE AND CHRONIC GENERAL TREATMENT

- As for hepatic encephalopathy (see p. 501) if indicated
- With status epilepticus or seizures: anticonvulsant medications such as IV propofol, low-dose phenobarbital, or oral potassium bromide (via stomach tube if necessary) may be needed in addition to the other medications and dietary therapy listed previously.

NUTRITION/DIET

Restricted protein diets or those formulated for use in hepatic disease should be considered to reduce the overall production of ammonia. Avoid methionine-containing supplements.

DRUG INTERACTIONS

Be careful with drugs requiring hepatic metabolism.

POSSIBLE COMPLICATIONS

Sedative and anesthetic agents should be used with caution.

RECOMMENDED MONITORING

- Due to the typical lack of significant clinicopathologic abnormalities, repeat testing is not indicated.
- Serum bile acid concentrations are typically unchanged with dietary and medical therapy and are not routinely repeated.

PROGNOSIS AND OUTCOME 

- Prognosis is good to excellent in patients that have not shown any signs.
- Prognosis is poor to fair in patients with clinical signs.
- Some patients presenting primarily with gastrointestinal signs may lack adequate response to treatment, although the signs do not typically worsen.
- Rarely, patients will develop noncirrhotic portal hypertension. The prognosis in these patients is poor.

PEARLS & CONSIDERATIONS 

COMMENTS

- Biopsy alone cannot confirm HMD. Macroscopic portosystemic shunts must be ruled out by either transcolonic or transsplenic portal scintigraphy, CT angiography, or mesenteric portography.
- Patients not showing any clinical signs and patients diagnosed at a later age with milder increases in serum bile acid concentrations are more likely to have HMD than PSS.
- Patients with normal CBC and serum biochemistry profiles may be more likely to have HMD than PSS.

PREVENTION

Avoid breeding affected dogs of predisposed breeds.

SUGGESTED READING

Berent AC, Weisse C: Hepatic vascular anomalies. In Ettinger SJ, Feldman EC, editors: Textbook of veterinary internal medicine, ed 7, St Louis, MO, 2010, Saunders Elsevier, pp 1649–1672.

Christiansen JS, et al: Hepatic microvascular dysplasia in dogs: a retrospective study of 24 cases (1987-1995). J Am Anim Hosp Assoc 36:385–389, 2000.

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Metronidazole Toxicosis

BASIC INFORMATION

DEFINITION

Neurologic dysfunction due to administration of high doses of the antibiotic metronidazole

SYNONYM

Flagyl toxicosis

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs and cats of any age and either sex can be affected. **RISK FACTORS:** Toxicosis is usually associated with doses of 60 mg/kg/d or higher for 1 week or longer.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Initial signs in dogs are anorexia and vomiting that progress rapidly to generalized ataxia. Seizures and head tilt are less common.
- Cats suffer a sudden onset of weakness and disorientation, often with seizures

PHYSICAL EXAM FINDINGS

- Affected dogs typically show severe generalized ataxia, depression, and vertical nystagmus that changes in frequency with head position. Postural reactions and spinal reflexes are usually normal.
- Affected cats often show ataxia with postural reaction deficits in all limbs, depression or stupor, seizures, and blindness with intact pupillary light reflexes.

ETIOLOGY AND PATHOPHYSIOLOGY

- The cumulative dose may be important in the mechanism of neurologic dysfunction, although there seems to be substantial individual susceptibility to signs of toxicity.
- Metronidazole is recommended for two different indications in many drug formularies: at an enteric dose for acute gastrointestinal infections and parasitoses (30-65 mg/kg, “divided q 12 h for 5-7 days”) or at doses for anaerobic bacterial infections (15 mg/kg PO q 12 h for days to weeks; lower to 7.5 mg/kg PO q 12 h if hepatic dysfunction).
- Common dosage errors (and therefore risk of toxicosis) appear to be:
  - Prescribing the high enteric dose for >1 week
  - Overlooking the “divided q 12 h” indication and prescribing the high enteric dose q 12 h
  - Failing to reduce the dose in patients with liver disease
  - Failing to accurately divide the 250-mg tablets in cats or very small dogs, where small differences in tablet fractions correspond to relatively large excesses in dose per kg body weight

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is based entirely on medication history and physical signs.

DIFFERENTIAL DIAGNOSIS

- Encephalitis
- Neoplasia

INITIAL DATABASE

Routine laboratory tests are usually normal, but mild elevations in liver enzymes are possible.

ADVANCED OR CONFIRMATORY TESTING

Diagnosis is based on clinical features, history of metronidazole administration, and recovery on stopping the drug.

TREATMENT

TREATMENT OVERVIEW

The goal of treatment is to stop metronidazole administration and provide supportive care until the signs resolve, usually within 3-5 days.

ACUTE GENERAL TREATMENT

- Discontinue the metronidazole.
- Parenteral hydration and nutrition if necessary
- Antiseizure medication such as diazepam as needed
- Oral diazepam administration (0.5 mg/kg q 8 h) may speed recovery from metronidazole toxicosis in dogs, including those that are not showing seizure activity.

RECOMMENDED MONITORING

Clinical response to discontinuation of metronidazole. Deterioration or worsening of clinical signs should prompt evaluation for another diagnosis.

PROGNOSIS AND OUTCOME

The prognosis is excellent with prompt withdrawal of the offending drug. Most patients show improvement within 48 hours, although it may take a week for complete resolution.

PEARLS & CONSIDERATIONS

COMMENTS

- Clinicians should consider metronidazole toxicosis in any patient developing neurologic signs while taking this antibiotic. With prompt recognition and withdrawal of the offending drug, complete recovery is expected.
- In many instances of intestinal parasitosis, metronidazole may not be the best choice of treatment. Alternative medications (e.g., fenbendazole) have shown greater efficacy and far fewer adverse effects in canine *Giardia* infection, for example.

PREVENTION

Avoid doses of metronidazole higher than 30 mg/kg/d. Some published doses are high enough to cause toxicity.

SUGGESTED READING

Caylor KB, Cassimitis MK: Metronidazole neurotoxicosis in two cats. J Am Anim Hosp Assoc 37:258, 2001.

Dow SW, et al: Central nervous system toxicoses associated with metronidazole treatment of dogs: five cases (1984-1987). J Am Vet Med Assoc 195:365, 1989.

Evans J, et al: Diazepam as a treatment for metronidazole toxicosis in dogs: a retrospective study of 21 cases. J Vet Intern Med 17:304, 2003.

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Metaldehyde Toxicosis

BASIC INFORMATION

DEFINITION

An acute toxicosis manifested by rapid onset of clinical signs such as vomiting, anxiety/restlessness, panting, hypersalivation, increasingly vigorous muscle tremors, hyperesthesia, hyperthermia, and seizures. This toxicosis can be rapidly fatal (hours from onset of signs, which begin 30 minutes to 5 hours after ingestion).

SYNONYMS

- Slug or snail bait poisoning
- Ortho Bug-Geta, Corry's Slug and Snail Pellets, Deadline Force II, Dragon Snail and Slug Killer Pellets, Last-Bite Snail and Slug Killer Pellets, Lilly Miller Slug and Snail Bait, Corry's Liquid Slug and Snail Control, Corry's Slug Snail, and Insect Killer are some metaldehyde-containing commercial products.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Toxic to all species
- Poisoning seen mostly in dogs. Bait is more attractive to dogs.
- All breeds, ages, and both sexes susceptible

RISK FACTORS: Animals with preexisting liver or kidney problems may be more sensitive to the toxic effects of metaldehyde.

GEOGRAPHY AND SEASONALITY: Toxicosis can occur anywhere; most common in areas with large populations of snails and slugs (e.g., the North American Pacific Northwest coast [especially California] and East Coast), Hawaii, Caribbean, Upper Midwest region. Less common in drier states.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Witnessed or suspected ingestion or recent use of bait in the pet's environment
- Rapid onset of vomiting, restlessness, muscle tremors and seizures

PHYSICAL EXAM FINDINGS

- Rapid, progressively more frequent (or sustained) muscle fasciculations/tremors are characteristic of metaldehyde intoxication and may progress to extensor rigidity/tetany.
- Secondary hyperthermia, which may be severe (104°F-108°F [40°-42.2°C]), is common. Hyperthermia is not a true fever but rather the result of muscle fasciculations.
- Seizures
- Concurrent nonspecific signs are common:
  - Tachycardia
  - Tachypnea
  - Hypersalivation
  - Vomiting
  - Diarrhea

ETIOLOGY AND PATHOPHYSIOLOGY

- Metaldehyde is a tetramer of acetaldehyde used as a molluscicide.
- Common sources include metaldehyde-containing baits formulated as liquid, granules, powder, or pellets.
- Most poisonings occur in dogs when they consume metaldehyde-containing baits.
- Oral LD^{50} of metaldehyde in dogs in various sources = 100-1000 mg/kg, and in cats = 207 mg/kg.
- Clinical signs of toxicosis can be seen within 30 minutes to 5 hours after ingestion.

- Metaldehyde is rapidly absorbed orally.
  - Acetaldehyde is produced upon exposure to gastric (low) pH.
  - Acetaldehyde is presumed to contribute to acidosis and other central nervous system signs such as seizures.
- Minimum toxic dose of metaldehyde in dogs is not known.
  - Consumption of 1 tablespoon (15 g) of 2% powder or granular bait will provide approximately 300 mg of metaldehyde; possibly a significant hazard for a 10-kg dog (30 mg/kg of metaldehyde). Standard 2% bait = 20 mg metaldehyde/g bait.
- Clinical signs could be due to decreased level of cerebral γ-aminobutyric acid, norepinephrine, and serotonin, which can cause seizures; and increased monoamine oxidase activity, which further decreases serotonin and norepinephrine levels.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is based on some or all of the following elements: geographic location (presence of snails/slugs in region), history of observed or suspected ingestion, and characteristic physical examination findings. No definitive confirmatory clinical test exists. A presumptive diagnosis is generally sufficient to initiate treatment, given the severity of signs in most cases and negative consequences of leaving such signs untreated.

DIFFERENTIAL DIAGNOSIS

- Strychnine toxicosis (see p. 1055)
- Tremorgenic mycotoxins
- Caffeine, nicotine toxicosis
- Permethrin toxicosis in cats
- Organophosphate and carbamate insecticide toxicosis (see p. 792)
- Zinc phosphide intoxication (see p. 1186)
- Garbage toxicosis (see p. 434)
- Primary central nervous system disease (neoplasia, encephalitis, idiopathic epilepsy, tetanus, other)

INITIAL DATABASE

- Acid-base status (acidosis may be present)
- Baseline serum liver enzyme (levels usually normal)
- Creatine phosphokinase (may be elevated due to muscle tremors)
- Baseline body temperature (commonly 104○-108○F [40○-42.2○C])
- Kidney function (myoglobinuria possible due to tremors)

ADVANCED OR CONFIRMATORY TESTING

- Metaldehyde may be detected in stomach contents, vomitus, serum, liver, and urine.
- Acetaldehyde smell (similar to formal dehyde) in the stomach or gastrointestinal tract may help in diagnosis.

TREATMENT

TREATMENT OVERVIEW

Immediate treatment of tremors and seizures when present is a primary goal, in order to curtail the development of severe hyperthermia. Active cooling is also indicated when body temperature >105○F (40.6○C), especially if seizures/muscle tremors are persistent. In patients without clinical signs (mild exposures and/or early presentation), induction of emesis is indicated. Activated charcoal administration is appropriate in essentially all cases, via stomach tube (with airway protection) if the patient is unconscious. Overall goals of treatment are to decontaminate the patient (remove remaining toxin), control tremors and seizures, correct acid-base abnormalities, control hyperthermia, and offer supportive care.

ACUTE GENERAL TREATMENT

- Decontamination of patient:
  - Induction of vomiting (see p. 1364) in patients not showing any clinical signs; useful within 30 minutes of exposure:
    - Hydrogen peroxide, 1 mL/kg PO, repeat once in 10-20 minutes if needed, maximum dose in largest dogs is 45 mL.

        - Apomorphine, 0.04 mg/kg IM or IV, or instill into conjunctival sac part of a crushed tablet dissolved in water.
    - Give activated charcoal after inducing emesis at 1-3 g/kg PO mixed with a cathartic such as magnesium or sodium sulfate, 250 mg/kg; or sorbitol 1-3 mL/kg. Use label dose for commercial preparations; multiple doses may be helpful with large ingestion (Caution: aspiration risk in vomiting patient).
    - Gastric lavage (see p. 1281) if large ingestion in animal showing clinical signs; follow with activated charcoal.
- Control tremors/seizures (see p. 1009):
    - Methocarbamol, 55-220 mg/kg IV; repeat as needed (maximum dose 330 mg/kg/d).
    - Diazepam, 1-2 mg/kg IV; repeat as needed (and/or consider diazepam constant rate infusion).
    - General anesthesia if no response to above measures:
        - Pentobarbital, 10-30 mg/kg IV to effect, repeat as needed; *or*
        - Propofol, up to 5-6 mg/kg slow IV to effect, then constant rate infusion 0.1-0.6 mg/kg/min titrated to effect; *and/or*
        - Isoflurane inhalant anesthesia
- Fluid diuresis for hydration, renal perfusion
- Control hyperthermia (cold bath, fans).
- Control acid-base balance with sodium bicarbonate.

POSSIBLE COMPLICATIONS

- Disseminated intravascular coagulation secondary to prolonged hyperthermia possible
- Acute hepatic failure (see p. 503) in some dogs 2-3 days after exposure can occur (uncommonly) when the patient seems to have recovered; monitor closely.
- Acute renal failure due to myoglobinuria (uncommon)

RECOMMENDED MONITORING

- Body temperature
- Liver enzymes for 3 days (baseline, 24, 48, 72 hours)
- Acid-base status

PROGNOSIS AND OUTCOME

- Good with prompt decontamination of patient and control of tremors and seizures
- Guarded with poorly controlled tremors or seizures or prolonged hyperthermia

PEARLS & CONSIDERATIONS

COMMENTS

- Most commercial baits contain 2%-5% metaldehyde.
- Some formulations may also contain 5% carbaryl (a carbamate insecticide) along with metaldehyde (see p. 792). Toxicity of carbaryl is much less than metaldehyde.
- Read the label carefully. Several recently introduced Slug and Snail Baits contain ferric phosphate 1% as the active ingredient. Ingestion of 1% ferric phosphate-containing slug bait in dogs mostly results in mild to moderate signs of stomach upset (vomiting, diarrhea, anorexia, lethargy).

TECHNICIAN TIPS

- If a client calls with a suspected ingestion of any “bait,” metaldehyde is the most immediately urgent of the common bait poisonings, and the animal should be brought to be examined promptly. The client also should be told to bring the container or product sheet to make it easier to confirm the active component of the ingested bait.

PREVENTION

- Placement of bait in areas inaccessible to animals
- Use of relatively less toxic baits (e.g., iron-based baits) to control slugs and snails

SUGGESTED READING

Puschner B: Metaldehyde. In Peterson ME, Talcott PA, editors: Small animal toxicology, ed 2, St Louis, 2006, Saunders Elsevier, pp. 830–839.

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Mesothelioma

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

A neoplasm of mesodermal origin that may arise from the pleural, pericardial, or peritoneal surfaces. Also reported from scrotum or tunica vaginalis.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs > cats, males are overrepresented. Generally older. GENETICS & BREED PREDISPOSITION: German shepherd dogs (particularly male) are overrepresented. Large-breed dogs are more commonly affected.

RISK FACTORS: Possibly asbestos exposure. The type of cancer caused by chronic asbestos exposure in human beings is mesothelioma, and the same histopathologic findings (ferruginous bodies) have been noted in both canine and human mesothelioma.

ASSOCIATED CONDITIONS & DISORDERS: Pleural, pericardial, and peritoneal effusion with attendant dyspnea, acute cardiac tamponade and right-sided heart failure, or abdominal distension, respectively, are common.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Mesenchymal form: multiple focal nodules of solid or papillary neoplastic growth; historically, more common
- Sclerosing form: characterized by an intense fibroblastic reaction and thick fibrous adhesions involving all abdominal organs but most markedly centered around the stomach and prostate; uncommon in dogs

HISTORY, CHIEF COMPLAINT: Patients most commonly are presented for dyspnea or cough; possibly abdominal distension. This disease should be suspected in any adult patient with a cough that does not respond to standard treatment for nonspecific respiratory problems, or evidence of chronic disease and effusion in any body cavity. Depending on the anatomic location of the malignancy and the subsequent effusion, the patient may present with dyspnea, cough, weight loss, acute cardiac tamponade and right-sided heart failure, or abdominal distension.

PHYSICAL EXAM FINDINGS

- Dyspnea due to pleural effusion in dogs and cats is usually identified by forceful inspiration and prolonged expiration (“holding its breath”).
- In cats, a noncompressible cranial thorax suggests other diagnoses: thymoma, mediastinal lymphoma.
- Tachypnea, open-mouth breathing, cyanosis, muffled heart and lung sounds ventrally with increased bronchovesicular sounds dorsally, poor peripheral pulses, jugular distension, and abdominal distension are possible.
- In a standing patient, thoracic percussion may reveal a “fluid line” (zone of hyporesonance) ventrally.

ETIOLOGY AND PATHOPHYSIOLOGY

Mesothelioma involves a malignant transformation of mesothelial cells that line body cavities. Pleural, pericardial, and peritoneal effusion from mesothelioma are most likely due to increased capillary permeability (parietal foci) secondary to vasculitis.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on chronic recurrent body-cavity effusions with no identified infectious, inflammatory, or other neoplastic cause. This is often a diagnosis of exclusion. Definitive diagnosis requires a biopsy.

DIFFERENTIAL DIAGNOSIS

- Pleural effusion (see p. 882)

- Pericardial effusion (see p. 854)
- Ascites (see p. 93)

INITIAL DATABASE

- The effusion should be sampled and evaluated with fluid analysis and cytological assessment.
- CBC, serum biochemical analysis, and urinalysis: no specific changes
- These tests should be supplemented with fungal, viral, and parasitic (tick and heartworm) serologic evaluations and microbial (fungal and bacterial) culture as clinical suspicion and history warrant.
- Radiographs (especially after removal of as much fluid as possible)
- Ultrasonographic studies (abdomen, heart, and pleural space)

ADVANCED OR CONFIRMATORY TESTING

- Definitive diagnosis requires tissue for histopathology.
- A normal fibronectin level in the effusion could help rule out mesothelioma.

TREATMENT

TREATMENT OVERVIEW

The primary and immediate goal of treatment is the removal of body-cavity fluid that is causing clinical signs.

ACUTE GENERAL TREATMENT

- Stabilization of the patient by relieving the cardiovascular or respiratory embarrassment is paramount.
  - This generally revolves around removal of large-volume effusions and doing so without delay if clinical signs are severe.
- Oxygen therapy is often indicated before centesis or obtaining blood or urine samples if patients are extremely dyspneic or volatile in their behavior, in order to prevent life-threatening cardiovascular or respiratory decompensation (especially cats).

CHRONIC TREATMENT

- For dogs with pericardial mesothelioma, surgical or thoracoscopic pericardectomy (see p. 1340) can palliate clinical signs and reduce tumor burden (disease cytoreduction).
- Periodic thoracocentesis (see p. 1338) or pericardiocentesis (see p. 1325) can be performed when fluid accumulation or symptoms are slow to return (weeks or more).
- The placement of a Pleuralport may aid in treatment. Some clients may be willing to learn proper care and use of such a device for home care.
- Administration of chemotherapy via intracavitary infusion on an every-3-week schedule can be attempted for long-term control.
  - Cisplatin, 50-70 mg/m^2 body surface area, along with saline fluid diuresis; *or*
  - Carboplatin, 250-350 mg/m^2 (has limited penetration); *or*
  - Mitoxantrone, 5-6 mg/m^2
- Potential benefits (unproven on a large scale) must be weighed against the real drawbacks of possible adverse reactions to these agents.
- At this time, only small numbers of patients have been evaluated, so efficacy remains unproven.
- Intravenous chemotherapy with cisplatin, carboplatin, or doxorubicin may have a role in some patients.
- Consultation with an oncologist for the most current treatment recommendations is indicated, but because of the rarity of this disease, multicenter clinical trials will be required to test and develop effective treatments.

POSSIBLE COMPLICATIONS

Pneumothorax, cardiac puncture, hemopericardium, hemothorax, infection

RECOMMENDED MONITORING

- Hourly for critical (ICU) patients: respiratory rates, degree of dyspnea, blood gases
- Daily to weekly for outpatients: respiratory rates, quality of life assessments, repeat thoracic radiographs as warranted or required
- As required per protocol for chemotherapy patients (i.e., CBC), quality of life assessments, repeat thoracic radiographs as

warranted or required

PROGNOSIS AND OUTCOME

- Poor to fair. Survival is dependent on rate of accumulation of the fluid and degree of compensation, which are both variable from patient to patient.
- Many patients are euthanized at the time of diagnosis.
- For those that are treated, the reported survival time varies considerably from weeks to years.
- Some animals may have a dramatic improvement after pericardiocentesis or thoracocentesis and a prolonged (weeks to months) period without clinical signs, whereas others have a reaccumulation of fluid and return of tamponade or dyspnea within hours or days.
- A good quality of life for months to 1-2 years with pericardial or pleural mesothelioma is realistically possible if a good response to the first centesis occurs, and owners are willing to follow up regularly with centesis on an as-needed basis.
- In this author's experience, owners rarely agree to continue with repeat pericardiocentesis after more than 2 or 3 episodes of acute decompensation.

PEARLS & CONSIDERATIONS

COMMENTS

- Thoracocentesis should be considered before blood or urine sample acquisition or radiographic or ultrasonographic studies in patients that are unstable. The removal of even a small amount of fluid may dramatically relieve the respiratory embarrassment and stabilize the patient.
- Although it shares similarities with mesothelioma in terms of distribution (body cavity surfaces), *carcinomatosis* refers to seeding of pleural or peritoneal surfaces with malignant carcinoma cells.
    - Management of dogs and cats with carcinomatosis may include treatment with intracavitary chemo-therapeutics as described for mesothelioma.

TECHNICIAN TIP

The pericardial effusion caused by mesothelioma is usually thick and hemorrhagic (indistinguishable from blood). If blood clots form in the discarded effusion during the pericardiocentesis procedure, this important observation should be brought to the attention of the clinician performing the procedure (catheter may be in the heart).

CLIENT EDUCATION

- Teaching the client to monitor respiratory rate will give both the client and the clinician an objective measure of progression and acuity of decompensation in the patient.
- Pleuralport management for dedicated clients.

SUGGESTED READING

Garrett LD: Mesothelioma. In Withrow SJ, Vail DM, editors: Withrow & MacEwen's small animal clinical oncology, ed 4, St Louis, 2007, Elsevier Saunders, pp 804–808.

Glickman LT, et al: Mesothelioma in pet dogs associated with exposure of their owners to asbestos. Environ Res 32:305, 1983.

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Mesocestoides Infection

BASIC INFORMATION

DEFINITION

Infection with an adult cestode (tapeworm) in the small intestine of mammals (frequently dogs) and birds. The larval or metacestode form of this tapeworm, the tetrathyridium, may infect serous cavities of many animals, particularly canines, causing ascites and pleural effusion.

SYNONYMS

Mesocestoides lineatus, Mesocestoides corti

EPIDEMIOLOGY

SPECIES, AGE, SEX: There is a wide range of intermediate hosts (reptile, avian, amphibian, and mammals), especially carnivores. Domestic and wild canids may serve as definitive hosts and harbor the adult stages of the tapeworm. Cats may also be infected.

RISK FACTORS: Hunting, scavenging carrion, and exposure to wildlife

CONTAGION & ZOONOSIS: Unknown; infections with adult tapeworms have been reported in humans.

GEOGRAPHY AND SEASONALITY: Many parts of the world, including Africa, Asia, and throughout the United States. There is no seasonal association for this cestode/metacestode.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Anorexia, respiratory distress, abdominal distension

PHYSICAL EXAM FINDINGS: Signs of abdominal or pleural effusion (see p. 93and p. 882)

ETIOLOGY AND PATHOPHYSIOLOGY

- Life cycle involves two intermediate hosts.
- First intermediate host unknown but may be a ground-dwelling coprophagous arthropod (oribatid mite, beetle)
- Second intermediate host (reptile, amphibian, bird, rodent, cat) becomes infected by ingestion of the larval forms (cysticercoids) within the first intermediate host. Within this second intermediate host, the cysticercoid develops into a tetrathyridium.
- The tetrathyridium is the second larval stage and often occurs in the peritoneal cavity and musculature of the second intermediate host.
- Dogs and cats (definitive hosts) are presumably infected by ingestion of the tetrathyridia within the second intermediate host (i.e., from capturing infected birds, snakes, and small mammals as prey).
- Dogs often serve as definitive hosts, harboring the adult tapeworms, but may also be infected by the larval stages of the parasite, the tetrathyridia.
- Tetrathyridia develop into adult tapeworms within the intestines and rarely produce clinical disease. Development into adults may take 16-20 days in dogs. In cats, development into adults may take longer.
- Some tetrathyridia migrate through the intestinal wall and continue as tetrathyridia within subcutaneous tissues, liver, lungs, retroperitoneal space, or abdominal and thoracic cavities. These tetrathyridia are capable of asexual multiplication by binary fission; one tetrathyridium splits into two tetrathyridia, two into four, and so on. The tetrathyridia multiply to the point that they completely fill and expand both the peritoneal and pleural cavities.
- Tetrathyridia may incite a nonpurulent granulomatous inflammatory response on serosal surfaces.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A patient with abdominal or pleural effusion whose centesed fluid is grossly milky white should be suspected of having *Mesocestoides* infection, especially if the patient appears less ill than would be expected if the fluid were chylous or septic.

Confirmation is through cytologic examination of aspirated fluid.

DIFFERENTIAL DIAGNOSIS

Abdominal and pleural effusions: congestive heart failure, portal hypertension, liver disease, hemorrhagic effusions, neoplastic effusions, hypoalbuminemia, septic effusions, chylous effusions. The latter two would be most likely to be confounded grossly with *Mesocestoides*-related effusions (color).

INITIAL DATABASE

- Abdominocentesis or thoracocentesis typically reveals a distinctive thick, opaque white fluid, which often contains hundreds to thousands of tetrathyridia.
- Cytologic evaluation of fluid may show a mixed inflammatory exudate ± hemorrhage and necrosis. Calcareous corpuscles (clear to yellow-gold round to oval structures that are remnant tissues of the cestodes) may be present.
- Tetrathyridia are often found on aspiration of cystic lesions.

ADVANCED OR CONFIRMATORY TESTING

Recovery of organism from peritoneal cavity, with identification of cestode DNA via PCR

TREATMENT 

TREATMENT OVERVIEW

The adult stage of this parasite within the canine small intestine can be easily treated. The larval tetrathyridium stage within serous cavities is almost impossible to eliminate, owing to its ability to undergo asexual multiplication, and the goal of ongoing treatment becomes palliation of the infection.

ACUTE AND CHRONIC TREATMENT

- Laparotomy and lavage of peritoneal cavity may be helpful to decrease larval tetrathyridia burdens.
- Anthelmintics:
    - Praziquantel for adult organisms: 5 mg/kg PO q 24 h
    - Fenbendazole for larvae: 100 mg/kg PO q 24 h for 28 days. Off-label use. Side effects (bone marrow, others) possible.

POSSIBLE COMPLICATIONS

Gastrointestinal signs may be seen with antiparasitics.

RECOMMENDED MONITORING

Regular fecal examinations

PROGNOSIS AND OUTCOME 

Guarded for infection with larval tetrathyridia, since infection generally persists

PEARLS & CONSIDERATIONS 

PREVENTION

- Prevent dogs and cats from roaming and ingesting second intermediate hosts such as birds, amphibians, reptiles, and rodents as live prey or carrion.
- Regular anthelminthic therapy

TECHNICIAN TIPS

During microscopic examinations, look for the characteristic ovum on fecal flotation. Following administration of anthelminthics, look

for the characteristic gravid proglottids expelled in the feces of infected dogs. Look for the unique tetrathyridia within serous cavities.

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Mesenteric Volvulus

BASIC INFORMATION

DEFINITION

An uncommon disorder characterized by a twisting of the intestine around the root of the mesentery, a process that potentially can be rapidly fatal

SYNONYMS

Intestinal volvulus, mesenteric torsion

EPIDEMIOLOGY

SPECIES, AGE, SEX: Young adult (>3 years old), male dogs predisposed. Also reported in cats.

GENETICS & BREED PREDISPOSITION: Large-breed dogs, German shepherds, and English pointers

ASSOCIATED CONDITIONS & DISORDERS: Conditions that have been associated with mesenteric volvulus include exocrine pancreatic insufficiency, recent gastrointestinal surgery, gastrointestinal foreign bodies, enteritis, intestinal neoplasia, blunt trauma, and gastric dilatation volvulus (GDV).

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Acute-onset abdominal distension, pain, vomiting, and hematochezia

PHYSICAL EXAM FINDINGS

- Physical findings consistent with hypovolemic shock: tachycardia (or bradycardia in cats), weak pulses, pale mucous membranes, prolonged capillary refill time, weakness or collapse
- Abdominal distension, palpably gas-filled intestinal loops

ETIOLOGY AND PATHOPHYSIOLOGY

- Twisting of intestine occurs around mesenteric axis or root, causing vascular occlusion to the intestines.
- Thin-walled veins and lymphatics become obstructed, causing edema in the intestinal wall.
- Blood flow through cranial mesenteric artery and its branches is partially or completely occluded due to twisting.
- Ischemic necrosis of intestine occurs, and blood is lost into the intestinal lumen.
- Endotoxins and bacteria translocate into the abdomen through the damaged intestinal mucosa.
- Patients eventually die from circulatory shock and endotoxemia/sepsis.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on physical exam and appearance of abdominal radiographs. Differential diagnoses must be ruled out to the extent possible (e.g., ileus due to parvoviral enteritis: testing as appropriate). Confirmation of the diagnosis is made at the time of surgery.

DIFFERENTIAL DIAGNOSIS

Any condition associated with acute abdominal pain or hematochezia and vomiting:

- Gastric dilatation/volvulus (GDV)
- Cecocolic volvulus
- Intussusception
- Splenic torsion

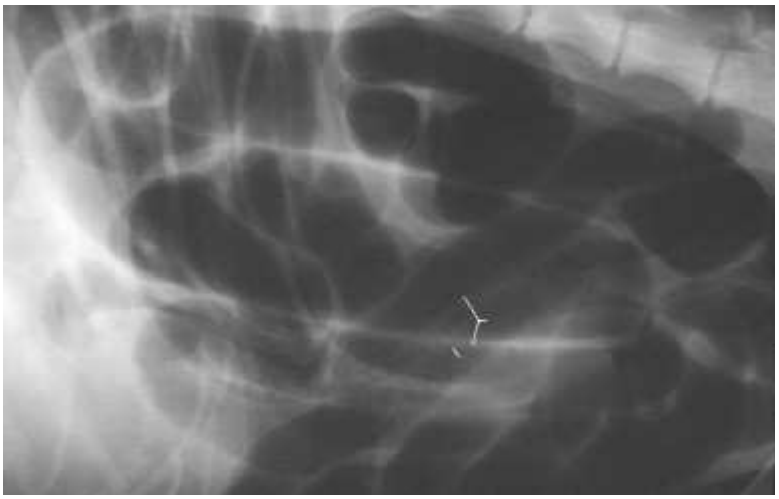
- Gastrointestinal obstruction or rupture
- Peritonitis
- Pancreatitis
- Hemorrhagic gastroenteritis
- Parvoviral enteritis

INITIAL DATABASE

- Abdominal radiography: multiple severely distended gas-filled intestinal loops; poor abdominal detail associated with peritoneal fluid; concurrent GDV
- CBC:
  - Packed cell volume usually normal
- Serum biochemistry profile:
  - Hypoproteinemia, hypokalemia
- Preoperative laboratory evaluation is often limited to on-site tests because of the potentially rapid deterioration of the patient's condition with mesenteric volvulus.
- Abdominocentesis (see p. 1193) with fluid evaluation: modified transudate (early) or septic exudate (eventually, with bacterial translocation or peritonitis). With bowel necrosis, the fluid may be dark and fetid.

ADVANCED OR CONFIRMATORY TESTING

Surgical confirmation of diagnosis



MESENTERIC VOLVULUS Lateral abdominal radiograph of dog with mesenteric volvulus; cranial is to the left. Marked gas distension of bowel present; a differential diagnosis would be severe enteritis.

(Courtesy Dr. Richard Walshaw.)

MESENTERIC VOLVULUS Same dog, gross appearance of bowel during exploratory laparotomy. Severe discoloration of much of small intestine and volvulus of mesenteric root are diagnostic.

(Courtesy Dr. Richard Walshaw.)

TREATMENT

TREATMENT OVERVIEW

Patients with mesenteric volvulus should be treated for circulatory shock as appropriate and have immediate surgical intervention to correct the volvulus and resect diseased bowel.

ACUTE GENERAL TREATMENT

- Crystalloids should be administered at shock doses (90 ml/kg/hr). Colloid boluses of 5 ml/kg can be administered simultaneously.
- Treat endotoxemia/sepsis with antibiotics:
  - Third-generation cephalosporin. 22 mg/kg IV q 2 h during perioperative period, then q 6 h postoperatively; *or*
  - Ampicillin, 22 mg/kg IV q 6 h combined with enrofloxacin, 5-10 mg/kg IV q 24 h (5 mg/kg maximum in cats)
- Correct hypokalemia and acid-base abnormalities with fluid therapy.
- If only parts of the intestine are devitalized, resect affected segment(s) before derotation, to reduce reperfusion effects.
- Perform derotation of intestines and monitor for perfusion.
- Perform thorough exploratory for associated conditions.
- Lavage abdomen, and consider postoperative drainage if peritonitis is present.

POSSIBLE COMPLICATIONS

- Septic peritonitis if diseased bowel not removed, contamination of abdomen not cleared, or resection and anastomosis site dehiscence
- Reperfusion injury
- Short bowel syndrome if >70% of small intestine resected

RECOMMENDED MONITORING

- Postoperative monitoring of hydration and electrolyte concentrations
- Blood pressure monitoring for hypotension
- Body temperature and blood glucose monitoring for sepsis

PROGNOSIS AND OUTCOME

- Grave prognosis unless volvulus recognized and treated immediately
- Most reports of mesenteric volvulus cite a 100% mortality rate unless the volvulus is found incidentally during exploratory celiotomy.
- One study reported a 58% mortality rate in patients with mesenteric volvulus presenting in shock and attributed increased survival to rapid initiation of treatment.

PEARLS & CONSIDERATIONS

COMMENTS

- Surgery should not be delayed if an animal presents in shock with multiple gas-filled intestinal loops on radiographs, but parvoviral enteritis should be ruled out.
- Consideration should be given to the use of drugs that block the formation of, or scavenge, oxygen free radicals (i.e., corticosteroids).

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Meningioma

BASIC INFORMATION

DEFINITION

A neoplasm of the meninges surrounding the brain or spinal cord

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Meningiomas occur in both dogs and cats and usually affect older patients.
- Dogs are usually older than 8 years, and females are affected slightly more than males.
- Cats are usually older than 10 years, and males are affected slightly more often than females.

GENETICS & BREED PREDISPOSITION

- **In** dogs, dolichocephalic breeds are more likely to develop meningiomas than other breeds.
- There is no breed predisposition in cats.

GEOGRAPHY AND SEASONALITY: Reported worldwide

ASSOCIATED CONDITIONS & DISORDERS: Meningiomas have been reported to occur in young cats with mucopolysaccharidosis type I.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Historic findings in general reflect neurologic compromise, but specific signs depend on lesion location.
- Clinical signs are often insidious and progressive; less commonly, acute onset of clinical signs is possible.
- The most common chief complaints for intracranial meningiomas include seizures, circling, behavior change (aggression), altered consciousness, and nonspecific signs such as inappetence and lethargy.
- The most common chief complaints for spinal meningiomas include acute to chronic onset of paresis, ataxia, and neck or back pain.

PHYSICAL EXAM FINDINGS

- Neurologic exam findings (see p. 1311) vary depending on lesion location.
- Cerebral meningioma: seizures, contralateral menace and postural reaction deficits, behavior change, contralateral hemiparesis
- Brainstem meningioma: ipsilateral cranial nerve deficits, hemiparesis or tetraparesis or hemiplegia or tetraplegia, or signs of central vestibular dysfunction
- Cerebellar meningioma: hypermetria, intention tremors, truncal sway, broad-based stance
- Spinal meningioma: paresis, ataxia, spinal pain

ETIOLOGY AND PATHOPHYSIOLOGY

- Etiology is unknown.
- Meningiomas usually occur as solitary masses, but multiple meningiomas are relatively common in cats.
- By definition, they originate on the periphery (neoplastic outgrowths of the meninges), adjacent to cranial or vertebral bone.
- Biological behavior and histopathologic characteristics are benign; clinical effects are due to space-occupying nature within confines of skull or vertebral canal.
- Most commonly reported in the supratentorial compartment (rostral to the tentorium cerebelli, including the cerebrum and diencephalon) in the brain
- Tumor tends to invade into the brain parenchyma in dogs but not in cats.
- Cervical portion of spinal cord is the most commonly affected segment in cases of spinal meningioma, but any location is possible.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected in a middle-aged to older dog or cat with neurologic deficits suggesting a slowly growing intracranial or spinal lesion. Advanced imaging (preferably MRI) is the clinical confirmatory test of choice; the final diagnosis is obtained histologically.

DIFFERENTIAL DIAGNOSIS

- Other brain tumors (e.g., glioma, lymphoma, metastatic tumors)
- Infectious diseases (bacterial, viral, fungal, protozoal)
- Inflammatory diseases (e.g., granulomatous meningoencephalomyelitis)
- Intervertebral disk disease
- Diskospondylitis

INITIAL DATABASE

- CBC/serum biochemical profile/urinalysis: usually normal
- Survey thoracic and abdominal radiographs should be performed in older patients to rule out extracranial and/or concurrent diseases.

ADVANCED OR CONFIRMATORY TESTING

- CT (see p. 1233) or MRI (see p. 1302): intracranial mass located outside the brain or spinal cord parenchyma, with marked, often homogeneous, contrast enhancement. Compression of underlying brain or spinal cord is common.
- Cerebrospinal fluid analysis: used as an adjunct to advanced imaging, primarily to rule out encephalitis or myelitis. Results are generally nonspecific with meningioma and reveal normal to mildly elevated protein. Sterile neutrophilic pleocytosis is relatively common with meningioma but is not pathognomonic.
- Histopathologic evaluation is required for definitive diagnosis. Tissue samples can be obtained via surgical excision or stereotactic brain biopsy (see p. 1214).

TREATMENT

TREATMENT OVERVIEW

Definitive treatment involving surgical excision and/or radiation therapy

ACUTE GENERAL TREATMENT

- Cluster seizures or status epilepticus: see p. 1425
- Cerebral edema/brain herniation: mannitol, 0.5 g/kg IV slowly over 15 to 20 minutes; furosemide (2 mg/kg IV) has synergistic effects with mannitol and can be given if needed.

CHRONIC TREATMENT

- Surgical excision for histologic diagnosis and definitive treatment if tumor is accessible
  - In general, tumors located in superficial (dorsal or lateral) regions of the skull/vertebrae overlying cerebrum, cerebellum, and spinal cord are the best candidates for surgical excision.
- Radiation therapy: used as an adjunctive treatment to surgery or as a primary treatment
- Chemotherapy: generally less effective because the blood-brain barrier (BBB) prevents most chemotherapeutic agents from entering the brain and spinal cord.
  - There are special handling requirements and potentially life-threatening adverse patient effects associated with these drugs; consultation with an oncologist for appropriate usage and the most current treatment recommendations is indicated.
  - Hydroxyurea (20 mg/kg PO q 24 h) crosses the BBB and appears to be effective in dogs as it is in humans with intracranial meningioma. Possible adverse effects include bone marrow suppression (anemia, thrombocytopenia, leukopenia), pulmonary fibrosis, gastrointestinal upset, stomatitis, sloughing of nails, alopecia, and dysuria. Methemoglobinemia has been reported in cats at high dosages (>500 mg).
  - Anecdotally, nitrosourea agents such as lomustine (CCNU; 60-90 mg/m^2 PO q 6 weeks) or carmustine (BCNU 50

mg/m^2 IV q 6 weeks), which can cross the BBB, appear to have some effect; these agents are more specifically used for treating patients with gliomas. The most serious potential adverse effects are bone marrow suppression (anemia, thrombocytopenia, leukopenia) and hepatotoxicosis.

- Seizures: anticonvulsants should be used if more than one seizure occurs every 6 to 8 weeks (see p. 1009).
- Cerebral edema: prednisone, 0.5 mg/kg PO q 12 h initially, then taper to lowest dose that will control clinical signs.

DRUG INTERACTIONS

- Drug interactions or altered metabolism of medications have been reported between corticosteroids and amphotericin B, furosemide, thiazide diuretics, digitalis glycosides, cyclosporine, phenytoin, phenobarbital, and mitotane.
- Corticosteroids should not be given concurrently with nonsteroidal antiinflammatory drugs or other potentially gastrointestinally ulcerogenic medications.
- Phenobarbital: may cause excessive sedation in patients with intracranial tumors, even at low doses

POSSIBLE COMPLICATIONS

Progression of clinical signs, including status epilepticus, brain herniation, and sudden death

RECOMMENDED MONITORING

Serial neurologic exam every 4-6 weeks. Therapeutic drug monitoring of serum levels of anticonvulsants if relevant.

PROGNOSIS AND OUTCOME

- Dogs: prognosis is fair. Median survival time for cerebral meningioma is 5-9 months with surgery alone and 16-30 months with surgery and radiation therapy. Radiation therapy alone yields a survival time of approximately 6-12 months.
- Cats: prognosis is good after surgical excision, with a median survival time of approximately 2 years with surgical excision alone. Surgical excision can be curative in cats.
- Prognosis for meningiomas in other anatomic locations is fair to guarded.
- Many patients treated with supportive nonspecific treatments (e.g., anticonvulsants, corticosteroids) are euthanized within 3 months because of progression of clinical signs.
- Dogs with intracranial meningiomas treated with oral hydroxyurea have a mean survival time of approximately 7 months.

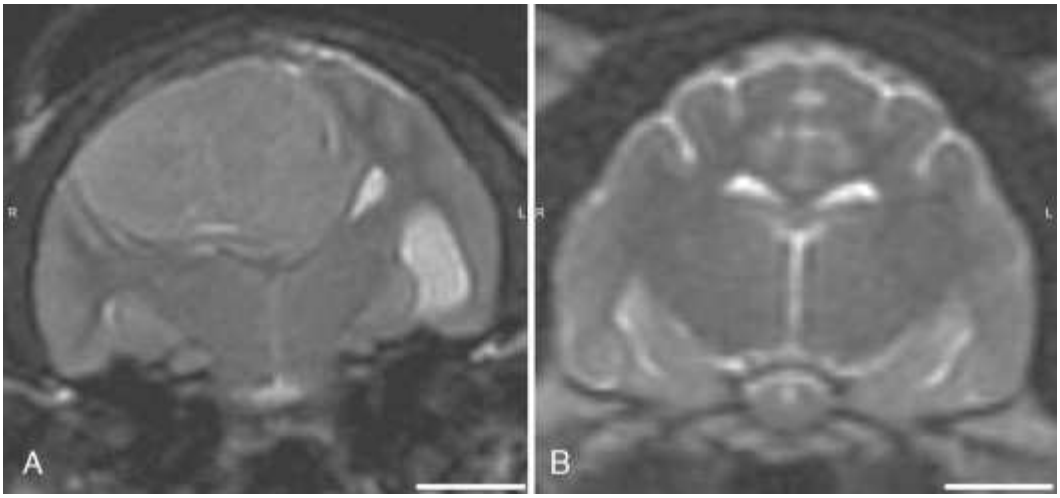
PEARLS & CONSIDERATIONS

COMMENTS

- Meningiomas are the most common primary brain tumor in dogs and cats.
- Surgical excision followed by radiation therapy provides the longest survival times for dogs.
- Surgical excision alone provides prolonged survival times for cats and may be curative in some cases.
- In canine intracranial meningioma cases with seizure activity, relatively nonsedative anticonvulsant drugs (e.g., felbamate, zonisamide, levetiracetam) should be considered, especially if surgical removal of the tumor is planned (see p. 1009and p. 353).

CLIENT EDUCATION

- With patients receiving corticosteroids, warn owner of expected side effects (e.g., polyuria, polydipsia, polyphagia, weight gain) and of effects warranting notification (obesity, signs of gastrointestinal ulceration, signs of iatrogenic hyperadrenocorticism).
- Phenobarbital (see p. 871): short-term side effects include sedation/lethargy and pelvic limb weakness and ataxia. Long-term side effects include polyuria, polydipsia, polyphagia, weight gain. Less common adverse effects warranting intervention include hepatotoxicity, blood dyscrasias.



MENINGIOMA A, Brain MRI of a patient with meningioma *(left panel).***B**, Normal patient for comparison *(right panel),* T2-weighted image. Patient's right is on the left of each image. Patient with meningioma has a large, sessile mass originating from the right dorsal calvarium; severe compression and displacement of right cerebral hemisphere and midline shift are seen. Bar = 1 cm.

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Melena

BASIC INFORMATION

DEFINITION

Dark, tarlike, often foul-smelling stools, as a result of digested blood (specifically oxidized hemoglobin)

EPIDEMIOLOGY

SPECIES, AGE, SEX: Any age, breed, sex
RISK FACTORS: Anything that will cause hemorrhage into the proximal or mid-gastrointestinal (GI) tract (esophagus, stomach, small intestine) or the mouth, pharynx, nose, or lungs

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- The patient will normally present for signs associated with blood loss (i.e., weakness, pale mucous membranes, bleeding from other sites or due to the melena [foul-smelling flatulence or black tarry feces]).
- Medication history includes those known to have gastrointestinal ulcerogenic potential (e.g., glucocorticoids, nonsteroidal antiinflammatory drugs [NSAIDs]).
- Intoxication history: known exposure or accessibility of vitamin K antagonists (rodenticides, pharmaceutical) in the environment
- Specific questions related to potential specific sources of bleeding: coughing, sneezing, vomiting, diarrhea
- Some patients have a history of recent surgical skin lump removal (possibility of mast cell tumor).
- Overdiagnosis due to leading questions (e.g., “Are the stools dark and tarry?”) should be avoided; open-ended questions are preferred (e.g., “Have the color and consistency of the stools changed? How so?”) to avoid this error.
- Rule out false-positive results:
    - Animals eating meat-based diets
    - Diets high in iron
    - Drugs such as charcoal and bismuth
    - Normal variation

PHYSICAL EXAM FINDINGS

- Rectal exam to confirm the diagnosis
- Evaluation for petechial hemorrhages on the mucous membranes and for signs of bleeding on the skin
- Auscultation of the chest for signs of lung hemorrhage (bronchovesicular sounds that are either louder [interstitial or airway hemorrhage] or softer [pleural effusion])
- Thorough abdominal palpation: abnormal GI loops or masses
- Careful examination of the skin for suspect mast cell tumors
- Additionally, specific aspects of the physical exam will vary depending on the source of bleeding. The blood can originate from the mouth, nose, lungs, pharynx, esophagus, stomach, or small intestine.

ETIOLOGY AND PATHOPHYSIOLOGY

- Blood presented to proximal or mid-GI tract (via any route already mentioned).
- Slow GI transit time of longer than 8 hours (in humans) allows greater degree of oxidation of hemoglobin. Melena occurs based on the duration of the presence of blood in the GI tract, rather than the anatomic site of blood loss.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Gross inspection of feces should allow confirmation of melena. If uncertainty persists, a fecal occult blood test is indicated. Diagnosis of the source of melena begins with history and physical exam in an attempt to differentiate generalized bleeding disorders from primary gastrointestinal bleeding.

DIFFERENTIAL DIAGNOSIS

- GI bleeding (stomach, small intestine; or large intestine in anorexic animals with slow GI transit time). Examples: hemorrhagic gastroenteritis, foreign body, intussusception, volvulus, inflammatory bowel disease, helminthiasis, or neoplasia.
- Liver or renal failure (coagulopathy or gastric ulceration)
- Pulmonary or upper respiratory tract bleed with swallowing of blood
- Shock (shock gut)
- Pancreatitis
- Hypoadrenocorticism
- Mast cell tumor or (rarely) gastrinoma
- High meat-based diet or diet high in iron
- Drugs such as charcoal and bismuth darken the color of feces but do not signify digested blood.

INITIAL DATABASE

- Recheck history and repeat abdominal palpation
- CBC, serum biochemistry profile (including preprandial and postprandial bile acids if liver disease suspected), urinalysis. Thrombocytopenia may explain or be a result of hemorrhage. Microcytosis and hypochromia suggest chronic blood loss.
- Fecal flotation
- Imaging: survey radiographs of chest and abdomen; abdominal ultrasound
- Coagulation profile

ADVANCED OR CONFIRMATORY TESTING

- If still no diagnosis:
  - Repeat abdominal ultrasound exam
  - Thorough nasal and pharyngeal exam [with radiographs]; systemic blood pressure measurement if epistaxis is present
  - Endoscopy (see p. 1284)
  - Exploratory laparotomy:
    - Biopsy, aspiration, and/or resection of any lesions seen
    - Biopsies of liver, stomach, duodenum, ileum, and jejunum if no macroscopic lesion seen
- If still no diagnosis:
  - Scintigraphy (radiolabeled albumin)
  - Arteriography
  - Small-bowel radiographic contrast study

TREATMENT 

TREATMENT OVERVIEW

- Control hemorrhage and any secondary complications of hemorrhage
- Cure the trigger

ACUTE GENERAL TREATMENT

- Largely depends on underlying cause
- Identify shock early, and treat aggressively with IV fluids.
- Blood transfusion: if anemia with resultant clinical signs or for coagulopathy
- Plasma transfusion: for coagulopathy
- Antiemetics and antiulcer therapy as needed
- Stop the inciting medications

DRUG INTERACTIONS

Sucralfate inhibits the absorption of fluoroquinolone antibiotics for up to 8 hours, so patients receiving sucralfate and requiring quinolone antibiotics should receive the quinolones parenterally if feasible.

PROGNOSIS AND OUTCOME 

Dependent on the trigger

PEARLS & CONSIDERATIONS

COMMENTS

These cases generally are far more difficult to diagnose than hematochezia cases. A thorough and methodical approach is essential.

CLIENT EDUCATION

Advise all owners on the potential dangers of NSAIDs.

SUGGESTED READING

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Melanoma

BASIC INFORMATION

DEFINITION

- Melanoma is a common neoplasm in the dog and is rare in the cat.
- Classification of melanomas by location generally has more clinical utility than by histologic subtype.
- Oral melanomas are uniformly malignant, locally invasive, and highly metastatic (>60%) tumors (see p. 708)
- Subungual (nail bed) melanomas are locally invasive tumors with a lower rate of metastasis (30%-60%)
- Cutaneous melanomas are generally (but not always) benign.
- Ocular melanomas are discussed elsewhere in this text (see p. 620).

SYNONYMS

Malignant melanoma, melanocytic tumor, melanocytoma

EPIDEMIOLOGY

SPECIES, AGE, SEX: Melanoma generally occurs in older patients (9-12 years).

GENETICS & BREED PREDISPOSITION

- Predisposed dog breeds include chow chow, Doberman pinscher, golden retriever, Gordon setter, Irish setter, giant schnauzer, miniature schnauzer, Scottish terrier.
- Breed predisposition suggests an underlying genetic mechanism for melanoma in veterinary patients.
- Black dogs may be predisposed, but any color dog may be affected.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Oral melanoma:
  - Detection of an oral mass by a veterinarian during routine examination or dental prophylaxis (common)
  - Identification of an oral mass by the owner
  - Recent onset of halitosis and ptyalism
- Cutaneous or subungual (nail bed) melanomas:
  - Identification of a mass by the owner

PHYSICAL EXAM FINDINGS

- Examination typically reveals a mass lesion.
- Oral examination should be thorough; some tumors are located at the base of the tongue or in the tonsils.
- Cutaneous and subungual tumors may become ulcerated.
- Melanomas may be pigmented or amelanotic.
- Thorough examination of draining lymph nodes is always indicated, but cytologic evaluation should be performed regardless of physical exam findings.

ETIOLOGY AND PATHOPHYSIOLOGY

- Underlying genetic mutations and ultraviolet light exposure are known etiologic agents in humans.
- Melanomas do not have to arise from pigmented skin.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Biopsy of an identified mass is the test of choice to establish a diagnosis of melanoma.

DIFFERENTIAL DIAGNOSIS

- Oral: squamous cell carcinoma, soft tissue sarcoma, epulides
- Cutaneous: any mass lesion of skin (neoplastic or non-neoplastic)
- Subungual: squamous cell carcinoma, nail bed infection

INITIAL DATABASE

CBC, serum biochemistry profile, urinalysis, lymph node aspiration, thoracic radiographs, abdominal ultrasound (in patients with hind limb or caudally located masses)

ADVANCED OR CONFIRMATORY TESTING

- Biopsy and histopathologic examination of tissue
- Immunohistochemical staining with S-100 or Melan-A may confirm the diagnosis of melanoma in undifferentiated and amelanotic tumors.
- Determination of mitotic index may be used for distinguishing benign and malignant canine cutaneous melanomas.
    - Determination of mitotic index requires histopathologic evaluation of tissue and cannot be reliably assessed on fine-needle aspiration/cytology.
    - Tumors with a mitotic index of <3 are typically benign; those ≥3 are generally malignant.

TREATMENT

TREATMENT OVERVIEW

Determination of an appropriate treatment plan for a patient with melanoma requires a thorough understanding of the patient's underlying prognosis. Evaluation of the patient to establish both local and metastatic disease status is essential. Goals of treatment are long-term disease control in patients amenable to definitive therapy and palliation of clinical signs in patients not treated definitively or those with metastatic disease. A general treatment overview is available on .

ACUTE GENERAL TREATMENT

- Oral melanoma:
    - Radical excision of mass indicated if:
        - Wide surgical margins (>2 cm, including underlying bone) can be obtained, and
        - Patient has no regional lymph node or distant metastasis
    - Removal of macroscopic (measurable) tumor followed by definitive course of radiation therapy to primary tumor site and regional lymph nodes indicated if:
        - Radical excision is not possible or regional lymph node metastasis is identified; and
        - Patient has no distant metastatic disease
        - Radiotherapy dosing; see Pearls & Considerations below.
    - Definitive course of radiation therapy alone to primary tumor and regional lymph nodes is indicated if:
        - Removal of macroscopic tumor burden is not possible; and
        - Patient has no distant metastatic disease
    - Palliative course of radiation therapy to tumor could be considered if:
        - The patient has distant metastatic disease; and/or
        - Financial or other restrictions preclude definitive therapy with surgery, radiotherapy, or both.
    - Chemotherapy indicated for all patients treated definitively with surgery and/or radiotherapy, owing to high rate of metastatic disease
        - Systemic therapy with platinum (carboplatin or cisplatin) chemotherapeutic agents, given reported activity of carboplatin in dogs with melanoma
        - Chemotherapy may benefit patients treated with palliative radiotherapy and those with evidence of distant metastasis.
    - DNA-based melanoma vaccine indicated for all patients where local/regional control has been attained.
- Subungual (nail bed) melanoma:
    - Radical excision of mass indicated if:
        - Wide surgical margins (>2 cm, to include underlying bone) are possible; and
        - Patient has no distant metastatic disease.
    - Limb amputation should be performed if wide surgical margins cannot be obtained with local resection (i.e., digital amputation)

- Limb amputation including removal of lymph nodes should be performed in patients with regional lymph node metastasis.
- Removal of macroscopic (measurable) tumor followed by definitive course of radiotherapy to primary tumor site and regional lymph nodes is indicated if:
  - Digital amputation not possible or clients decline amputation
  - Regional lymph node metastasis is identified
  - Patient has no distant metastatic disease
- Palliative course of radiotherapy could be considered if:
  - Patient has distant metastatic disease and clinical signs associated with local disease result in decreased quality of life for patient
- DNA-based vaccine and chemotherapy are indicated for all patients treated definitively with surgery and/or radiotherapy, owing to the high rate of metastatic disease in patients with subungual melanoma.

- Cutaneous melanoma
  - Surgical resection is the treatment of choice for benign melanomas (<3 mitoses/10 hpf)
  - Radical excision of malignant cutaneous melanoma (≥3 mitoses/10 hpf) is indicated if:
    - Wide surgical margins (<2 cm) can be obtained; and
    - Patient has no regional lymph node or distant metastatic disease
  - Removal of macroscopic (measurable) tumor followed by definitive course of radiation therapy to primary tumor site and regional lymph nodes are indicated if:
    - Radical excision is not possible or if regional lymph node metastasis is identified
    - Patient has no distant metastatic disease
  - Palliative course of radiation therapy could be considered if:
    - Patient has distant metastatic disease and clinical signs associated with local disease result in decreased quality of life for the patient
  - DNA-based vaccine and chemotherapy indicated for all patients with malignant cutaneous melanomas treated definitively with surgery and/or radiation therapy
    - Refer to oral melanoma section for comments regarding chemotherapy.

POSSIBLE COMPLICATIONS

Potential complications or therapy for patients with melanoma are those typically encountered after treatment with surgery, radiation, and chemotherapy.

RECOMMENDED MONITORING

After treatment, patients should be monitored with routine examination (determination of local disease status) and thoracic radiographs (identify metastatic disease).

PROGNOSIS AND OUTCOME

- Oral melanoma:
  - Prognosis:
    - Conservative surgery alone: median survival 3-4 months; local recurrence rate >70%
    - Radical surgery alone: median survival 9 to 10 months; local recurrence rate 20%-50%
    - Radiation therapy for microscopic tumors: median survival 15 months; local recurrence rate 26%
    - Radiation therapy for macroscopic tumors: response rate 82%; median survival 5 months; local progression/recurrence 45%
    - Chemotherapy for macroscopic tumors: response rate 28%; efficacy in adjuvant setting unknown
    - Prognosis for definitively treated feline oral melanoma is not known.
  - Prognostic factors:
    - Most apply to patients treated with radiotherapy.
    - Reported negative prognostic factors include macroscopic tumor burden, caudal tumor location, bone lysis; all oral melanomas should be considered malignant regardless of mitotic index.
    - In one study, median survival correlated with the number of negative prognostic factors present: 0 = 21 months, 1 = 11 months; 2 = 5 months; 3 = 3 months.
- Subungual melanoma:
  - Prognosis:
    - Surgical excision (local or limb amputation): median survival 12 months; local recurrence rate 30% (local resection only)
    - Role of radiotherapy and chemotherapy undetermined for this location
    - Prognostic factors: none identified
    - Prognosis is unknown for feline subungual melanoma.
- Cutaneous melanoma:

- Prognosis:
  - Surgical excision: median survival 24 months (benign); 7-11 months (malignant)
  - Efficacy of radiotherapy and chemotherapy is undetermined for this location.
  - Median survival for feline cutaneous melanoma treated with surgery alone is 12 months.
  - Mitotic index is not uniformly predictive of biological behavior.
- Prognostic factors:
  - Mitotic index is the most important prognostic factor: ≥3 indicates malignant tumor.
  - Breed: Doberman pinschers and miniature schnauzers more likely have benign melanoma (75%); miniature poodles more likely have malignant melanomas (85%).

PEARLS & CONSIDERATIONS

COMMENTS

- Radiotherapy treatment:
  - Melanoma has a greater capacity for sublethal damage repair and therefore is best treated with a hypofractionated (larger doses per fraction) treatment protocol instead of a conventional protocol such as 3-Gy doses given in 16 to 19 fractions.
  - Four reported veterinary protocols for melanoma are: 10 Gy × 3; 9 Gy × 4; 8 Gy × 3; 4 Gy × 12. The optimal protocol remains to be determined.
  - Because late-responding normal tissues (bone, muscle, central nervous system) are more susceptible to toxicosis with larger doses of radiation, large doses (8-10 Gy) should be avoided in patients in which long-term survival (<12 months) is expected.
    - In patients with probable long-term survival (e.g., dog with no negative prognostic factors), a protocol utilizing smaller doses per fraction (4-6 Gy) may be advisable.
    - In patients treated definitively but in which long-term survival is unlikely (e.g., with caudally located, macroscopic tumor) or in patients treated palliatively, a protocol utilizing larger doses per fraction is reasonable, since long-term survival and therefore late-responding tissue toxicity are unlikely.
- Chemotherapy:
  - In patients failing platinum chemotherapy, there is little information regarding rescue chemotherapy agents for melanoma.
  - Information from the veterinary and human literature may support the use of dacarbazine, melphalan, CCNU, piroxicam, and interferon.
- DNA-based vaccine:
  - Early studies indicate that patients with locally/regionally controlled disease experience a longer survival when the tyrosinase DNA vaccine is administered.
  - The utility of tyrosinase DNA vaccination in patients with advanced disease is unclear.

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Megaesophagus

BASIC INFORMATION

DEFINITION

Dilatation of the esophagus due to weakness of the esophageal musculature from any cause. This is to be distinguished from dilatation of the esophagus orad to an obstruction.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs and cats of any age or sex. Acquired megaesophagus usually occurs after 2-3 years of age. Cats are less commonly affected.

GENETICS & BREED PREDISPOSITION

- For congenital megaesophagus:
  - Cats: Siamese
  - Dogs: German shepherds, Great Danes, Labrador retrievers, miniature schnauzers, Irish setters, sharpeis, fox terriers, Newfoundlands (but any dog can be affected).
- For acquired megaesophagus in dogs: black standard poodles (secondary to hypoadrenocorticism), but any dog can be affected.

RISK FACTORS: Any neuromuscular disease can cause acquired megaesophagus; localized myasthenia gravis is the most commonly identified cause.

ASSOCIATED CONDITIONS & DISORDERS

- Coughing due to tracheobronchitis or pneumonia secondary to aspiration
- Aspiration pneumonia is the most common cause of death.
- Weakness due to myopathy, neuropathy, or junctionopathy in the case of acquired megaesophagus

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Congenital megaesophagus
- Acquired megaesophagus

HISTORY, CHIEF COMPLAINT

- Regurgitation (must distinguish from vomiting) is the most common complaint.
- Cough (due to aspiration): this is sometimes seen before regurgitation is reported.
- Drooling (due to difficulty swallowing)

PHYSICAL EXAM FINDINGS

- Weight loss or failure to gain weight (if patient is losing excessive calories or has chronic pulmonary infection)
- Pulmonary crackles/easily elicited cough (due to aspiration pneumonia)
- Fever and signs of systemic illness (e.g., anorexia, lethargy) when sepsis from aspiration is present
- Bellows-like action at thoracic inlet, associated with breathing (due to filling and emptying of distended esophagus with air, associated with respirations)
- Nasal discharge (if pneumonia or rhinitis secondary to regurgitation is present)

ETIOLOGY AND PATHOPHYSIOLOGY

- Congenital or idiopathic megaesophagus:
  - Considered to involve the loss of peristaltic function
  - This defect can occur in any part of the neural reflex that controls the pharyngeal and esophageal phases of

swallowing, including the sensory receptors, the afferent nerves (glossopharyngeal and vagus), the tractus solitarius (leading to the nucleus solitarius), the swallowing center (near the lateral reticular formation), the lower motor neurons of the nucleus ambiguus, the efferent somatic and parasympathetic nerve fibers in the vagus, the myoneural junction in the esophagus itself, the esophageal striated muscle, and potentially the esophageal smooth muscle in the cat.
    - Most evidence suggests that the problem resides in the afferent limb of the reflex arc. This is supported by the fact that dogs with megaesophagus are prone to aspiration pneumonia, which is increased in dogs with loss of the afferent arc (abnormal respiratory reflexes also occur).
- Secondary megaesophagus; etiopathogenesis relates to primary cause:
    - Neurologic (polyradiculoneuritis, dysautonomia, demyelinating neuropathies, lead, etc.)
    - Neuromuscular (botulism, tetanus, myasthenia gravis)
    - Muscular (e.g., toxoplasmosis, polymyositis, systemic lupus erythematosus)
- Other causes of megaesophagus include certain metabolic conditions (hypoadrenocorticism).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected immediately in any patient that regurgitates. An essential diagnostic point is determining through simple questioning whether “vomiting” observed by the owner is in fact regurgitation. Thoracic radiographs confirm the diagnosis in most cases. Additional diagnostic tests are generally appropriate for evaluating possible underlying causes which present therapeutic opportunities.

DIFFERENTIAL DIAGNOSIS

Acquired megaesophagus in the dog:

- Myasthenia gravis (either generalized or localized)
- Hypoadrenocorticism
- Dysautonomia
- Polymyopathies/polyneuropathies of various causes
- Lead intoxication
- Organophosphate intoxication
- Botulism or tetanus
- Esophagitis
- Systemic lupus erythematosus
- Dermatomyositis
- Idiopathic

Acquired megaesophagus in the cat:

- Dysautonomia
- Myasthenia gravis
- Idiopathic (43% of feline cases)

INITIAL DATABASE

- CBC: look for evidence of inflammation consistent with aspiration pneumonia.
- Plain thoracic radiographs: look for megaesophagus (usually seen but is not always obvious) and for pneumonia (especially in right middle lung lobe; need ventrodorsal or dorsoventral projection to reliably see this lesion).
- Contrast esophagram using radiographs: if needed
    - Not always needed, as plain films can be confirmatory in many cases
    - Indicated if clinical signs suggest esophageal disease, but plain films are equivocal or interpreted as normal.
    - Can reveal unsuspected esophageal obstruction or segmental weakness
- Contrast esophagram using fluoroscopy (if needed): will detect megaesophagus missed by radiography, especially if only a segment of the esophagus is affected (especially cervical esophagus) or if there is only partial loss of muscular tone (see p. 1205).

ADVANCED OR CONFIRMATORY TESTING

- Antibodies against acetylcholine receptors (in dogs): when looking for cause of acquired megaesophagus (see p. 736)
- Resting serum cortisol concentration ± ACTH stimulation test (in dogs): when looking for cause of acquired megaesophagus (see p. 573)

- Serum creatine kinase determination: various myopathies
- Electromyography/motor nerve conduction velocity (see online chapter: Electromyography and Nerve Conduction Velocity): polymyopathy/polyneuropathy

TREATMENT

TREATMENT OVERVIEW

Treat acquired megaesophagus by finding and resolving the underlying cause (accomplished in approximately 15%-20% of dogs); treat aspiration pneumonia if present. If an underlying cause cannot be found, then treat as idiopathic megaesophagus. For idiopathic megaesophagus, try to minimize regurgitation by modifying feeding practices, and treat aspiration pneumonia when present.

ACUTE GENERAL TREATMENT

- Treat pneumonia if present (see p. 1583).
- Treat underling cause if found (see pp. 736 and p. 573).
- Feeding modification:
  - Feed from an elevated platform such that the patient's esophagus is as close to being perpendicular to the floor as possible so gravity aids in food/water emptying from the esophagus into the stomach. Probably beneficial to maintain this position for several minutes after eating to enhance food emptying into the stomach.
  - Feed different consistencies of food to find which is best tolerated: feeding a gruel is usually the best choice, but some animals fare better if fed canned or solid food or meatballs.
  - Feed several small meals per day (or free choice in the case of dry kibble) to minimize retention of large amounts in esophagus.
- Prokinetic drugs may be tried.
  - Only indicated when gastroesophageal reflux is suspected or confirmed, to increase normograde gastric emptying and reduce the volume of acid reflux. Prokinetic drugs are often useful for treating gastric motility disorders, but they do not increase esophageal motility to any clinically appreciable degree. Options include:
    - Cisapride (0.1-0.5 mg/kg PO q 8-12 h). Cisapride increases lower-esophageal tone (most effective prokinetic).
    - Metoclopramide (0.2-0.4 mg/kg PO, IM, or SQ q 8-12 h). The increase in lower-esophageal sphincter tone described for metoclopramide is not thought to be clinically significant and does not contraindicate usage in megaesophagus.
    - Erythromycin (2 mg/kg PO q 12-24 h). This drug stimulates motilin receptors, thereby enhancing gastric peristalsis.
    - Ranitidine (2.2 mg/kg PO, q 8-12 h). This H2 receptor antagonist has prokinetic activity.
- Gastric acid-reducing therapy: recommended if gastroesophageal reflux is documented or likely.
  - Omeprazole (1 mg/kg PO q 24 h); most effective drug

CHRONIC TREATMENT

- Ongoing implementation of measures described in acute treatment
- Treat specific conditions identified as indicated (e.g., hypoadrenocorticism, myasthenia gravis).
- Can place gastrostomy tube (see p. 1270) to minimize regurgitation of food (especially if waiting for treatment of underlying cause to succeed)
  - Dog can still swallow, regurgitate, and aspirate saliva, despite gastrostomy tube.

POSSIBLE COMPLICATIONS

- Aspiration pneumonia
- Infected stoma (gastrostomy tube)

PROGNOSIS AND OUTCOME

- If the underlying cause can be found and cured, the outlook is usually good, assuming that the patient does not die first from aspiration pneumonia.
- If the underlying cause cannot be found and treated, the outlook is guarded to poor. Many such patients die of aspiration pneumonia.
- The esophageal function of some dogs with congenital megaesophagus will spontaneously improve over time; however, one cannot predict which patients will improve.

PEARLS & CONSIDERATIONS

COMMENTS

- Certain drugs used for restraint (e.g., ketamine, xylazine) cause temporary megaesophagus.
- Some dogs with apparent megaesophagus on plain radiographs have normal function during barium-contrast esophagram, and the radiographic megaesophagus will spontaneously resolve.
- Radiography is the preferred way to diagnose megaesophagus; endoscopy is often the preferred way to diagnose esophagitis or the cause of esophageal obstruction, as well as other morphologic changes (e.g., hiatal hernia).
- The severity of radiographic dilation of esophagus is not always proportional to the severity of regurgitation or aspiration.
- Mild aspiration pneumonia is often missed on lateral radiographs; dorsoventral radiographs are more sensitive for finding this lesion.
- Any unexplained bacterial pneumonia in a dog could be caused by occult esophageal dysfunction; it is often reasonable to perform contrast radiographs looking for esophageal weakness in dogs with pneumonia that do not have esophageal dilation on plain radiographs.
- If a dog with megaesophagus vomits, esophagitis typically occurs due to gastric acid entering and not exiting the esophageal lumen.
- Surgery (cardiomyotomy) is not helpful or indicated in dogs with megaesophagus; true achalasia (which is helped by such surgery) is exceptionally rare in dogs.

PREVENTION

Do not breed animals with known history of producing litters with megaesophagus.

CLIENT EDUCATION

Aspiration pneumonia can occur at any time, even in dogs with mild radiographic signs of megaesophagus.

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Mediastinal Disease

BASIC INFORMATION

DEFINITION

Disorders of the mediastinum, the potential space between the right and left lungs

EPIDEMIOLOGY

SPECIES, AGE, SEX: Mediastinal lymphosarcoma: young cats overrepresented. Other mediastinal masses more commonly affect middle-aged or older animals.

GENETICS & BREED PREDISPOSITION: Mediastinal lymphoma: Oriental-breed cats

RISK FACTORS

- Mediastinal lymphoma: feline leukemia virus infection (FeLV; see p. 385)
- Pneumomediastinum: tracheal laceration/avulsion; traumatic or iatrogenic
- Mediastinitis: esophageal foreign body or rupture

CONTAGION & ZOONOSIS: FeLV infection

ASSOCIATED CONDITIONS & DISORDERS: Mediastinal masses:

- Acquired myasthenia gravis (thymoma)
- Polyuria and polydipsia (lymphoma)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Pneumomediastinum
- Mediastinitis
- Mediastinal masses
- Mediastinal hemorrhage

HISTORY, CHIEF COMPLAINT

- Pneumomediastinum:
  - History of trauma
  - Recent anesthesia: overinflated endotracheal tube cuff, with tracheal necrosis; turning patient without disconnection of endotracheal tube
  - Recent transtracheal wash
  - Recent jugular venipuncture
  - Subcutaneous emphysema
- Mediastinitis (acute):
  - Obtundation
  - Inappetence
  - Dysphagia
  - Regurgitation
- Mediastinal masses:
  - Inappetence
  - Lethargy
  - Polyuria/polydipsia
  - Dysphagia or regurgitation
  - Cough
  - Dyspnea
  - Facial, neck, and/or forelimb swelling
- Mediastinal hemorrhage:

- Lethargy
- Weakness
- Tachypnea

PHYSICAL EXAM FINDINGS

- Pneumomediastinum:
  - Can be an incidental finding
  - Subcutaneous emphysema (see online chapter: Subcutaneous Emphysema)
  - Respiratory signs if severe:
    - Dyspnea
    - Muffled breath sounds
    - Hyperresonant thoracic percussion from pneumothorax
  - Jugular venous distention
  - Shock
- Mediastinitis:
  - Fever
  - Dyspnea, tachypnea, cough
  - Edema of head, neck, forelimbs secondary to cranial vena cava syndrome (see p. 263)
  - Dysphagia
  - Regurgitation
  - Thoracic pain
  - Reduced thoracic compressibility
- Mediastinal masses:
  - Poor compressibility of cranial thorax (especially cats)
  - Cranial vena cava syndrome (see p. 263)
  - Respiratory or gastrointestinal signs as mentioned previously
  - Occasionally paraneoplastic signs:
    - Weakness
    - Stridor if secondary laryngeal paralysis
  - Horner's syndrome possible
- Mediastinal hemorrhage:
  - Pale mucous membranes
  - Tachycardia
  - Weakness

ETIOLOGY AND PATHOPHYSIOLOGY

- Pneumomediastinum:
  - Air enters from:
    - Penetrating neck wounds
    - Tracheal laceration
    - Occasionally from esophageal air leakage
    - Positive-pressure ventilation
- Mediastinitis:
  -
    - Hematogenous infection
    - Penetrating wounds and migrating foreign bodies
    - Extension from surrounding tissues (especially esophagus)
    - Acute mediastinitis *(Staphylococcus* spp., *Streptococcus* spp., *Escherichia coli, Corynebacterium* spp.)
    - Chronic bacterial *(Nocardia, Actinomyces, Staphylococcus* spp.) or fungal (histoplasmosis, blastomycosis, cryptococcosis) infection also possible
    - Clinical signs due to sepsis, pleural effusion, and compression of vascular or respiratory structures
- Mediastinal masses:
  - Lymphoma, thymoma, thyroid neoplasia, chemodectoma, thymic cysts, granulomas
  - Clinical signs reflect compression of respiratory, cardiovascular, gastrointestinal structures, possibly pleural effusion, or sometimes neurologic abnormalities (Horner's syndrome, laryngeal paralysis).
  - Occasionally, paraneoplastic syndromes:
    - Hypercalcemia
    - Myasthenia gravis
- Mediastinal hemorrhage:
  - Trauma
  - Coagulopathy
  - Spontaneous thymic hemorrhage possibly associated with thymic involution

- Neoplastic disease
- Thyroid carcinoma
- Clinical signs are often related to acute blood loss.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Thoracic radiographs are typically the initial step in a diagnostic evaluation. If there is a mass lesion, advanced imaging such as CT scanning is often indicated, but fine-needle aspiration and cytologic analysis, or needle or surgical biopsy and histopathology, are typically required to define the nature of the disease process.

DIFFERENTIAL DIAGNOSIS

- Pneumomediastinum:
  - Tracheal trauma
  - Pneumothorax
- Mediastinitis:
  - Other causes of sepsis
  - Mediastinal masses/fat/fluid
  - Pleural effusions
- Mediastinal masses:
  - Mediastinitis
  - Pleural space disease
  - Pulmonary masses
  - Thoracic wall masses
  - Mediastinal fat or fluid
  - Normal thymic enlargement (young animals)
- Mediastinal hemorrhage:
  - Mediastinitis
  - Mediastinal fat or fluid
  - Mediastinal mass
  - Normal thymic enlargement (young animals)
  - Thymic hemorrhage (rare)

INITIAL DATABASE

- Thoracic radiographs:
  - Pneumomediastinum:
    - Visualization of mediastinal vascular structures not normally seen (e.g., branches of aorta) is pathognomonic.
    - Subcutaneous emphysema
  - Mediastinitis and mediastinal masses:
    - Mediastinal widening on dorsoventral or ventrodorsal views
    - Dorsal displacement of trachea on lateral view possible
    - Acute mediastinitis may cause no changes.
    - Pleural fluid possible
    - Gas in fascial planes of neck
- Abdominal radiographs: pneumoretroperitoneum possible
- CBC:
  - Leukocytosis if inflammation
  - Rarely cytopenias or leukemia
  - Anemia if mediastinal hemorrhage
- Serum biochemistry panel: hypercalcemia possible
- FeLV test
- Thoracic ultrasonography may identify:
  - Presence/structure of masses
  - Pleural effusion
  - Lymphadenomegaly
  - Vascularity/vascular invasiveness of mass (impacts biopsy/excision possibilities)
  - Mediastinal fluid if hemorrhage
- Fine-needle aspiration cytologic analysis:
  - Risks include hemothorax, pneumothorax, or nondiagnostic sample
  - If inflammatory: culture (aerobic, anaerobic, *Nocardia, Actinomyces,* ± fungal) indicated

- Thoracocentesis for cytology and culture if fluid present

ADVANCED OR CONFIRMATORY TESTING

- Tracheoscopy/bronchoscopy if pneumomediastinum (and patient stable)
- Contrast (water-soluble) esophagram if suspect rupture. See p. 1205.
- Esophagoscopy if suspect esophageal disease
- Cytologic evaluation of respiratory wash samples if underlying pulmonary disease
- Echocardiography if heart base mass
- Arterial blood gas to assess respiratory function
- Coagulation testing (prothrombin time, partial thromboplastin time [PT, PTT]) if hemorrhage
- CT or MRI will better delineate nature and extent of space-occupying disease and address possible metastatic disease (CT).
- Fungal serologic evaluation if possible fungal mediastinitis
- Biopsy for histopathologic evaluation can be obtained transthoracically (Trucut) or via thoracoscopy or thoracotomy.
- Flow cytometry can be helpful in distinguishing thymoma from thymic lymphoma.

TREATMENT

TREATMENT OVERVIEW

Many cases of pneumomediastinum will resolve over time with conservative management. Nonlymphoid cranial mediastinal masses typically require surgical intervention, whereas lymphoid neoplasia is treated nonsurgically.

ACUTE GENERAL TREATMENT

- Pneumomediastinum:
  - If mild signs, cage rest is sufficient; subcutaneous emphysema typically resolves in approximately 2 weeks.
  - If signs more marked, provide supplemental oxygen.
  - Drain subcutaneous emphysema only if causing discomfort (see p. 1060).
  - If tracheal tear/laceration, consider surgical repair (see p. 1108).
  - Thoracocentesis if pneumothorax
- Mediastinitis:
  - Broad-spectrum empirical antimicrobial therapy while culture/sensitivity results are pending
  - Severe systemic signs may require intravenous fluids and/or additional supportive therapy.
  - Esophageal laceration/rupture may require surgery.
- Mediastinal masses:
  - Surgery, chemotherapy, radiation therapy, or a combination based on type of mass
  - Mediastinal cysts are either drained transthoracically or excised.
- Mediastinal hemorrhage:
  - Volume support: crystalloid or colloids
  - Blood transfusion if severe o If coagulopathy, treat with vitamin K, 2.5 mg/kg SQ in multiple sites initially, and possibly a fresh frozen plasma transfusion.

CHRONIC TREATMENT

- Pneumomediastinum: cage rest as above
- Mediastinitis: long-term (minimum 4-6 weeks) antimicrobial therapy based on culture and sensitivity results
  - Fungal mediastinitis may require months of therapy.
  - Large granulomas causing cranial vena cava syndrome may require surgical excision/debulking.
- Mediastinal masses:
  - Chemotherapy or radiation therapy for lymphoma
  - Radiation therapy for incompletely resected thymoma

POSSIBLE COMPLICATIONS

- Pneumothorax, pleural effusion, pyothorax from thoracostomy tubes
- Gastrointestinal and/or myelotoxicity for many chemotherapeutics
- Individual toxicities for particular drugs:
  - Renal: aminoglycosides, amphotericin B
  - Hepatic: azole antifungals
- Surgery entails risks of anesthesia, hemorrhage, infection.

RECOMMENDED MONITORING

- Clinical signs
- Pulse oximetry, arterial blood gases
- Thoracic radiographs
- Pleural fluid volume if thoracostomy tube
- CBC (chemotherapy)
- Serum chemistries for renal and hepatic function, depending on antimicrobials or other drugs administered

PROGNOSIS AND OUTCOME

- Pneumomediastinum: good if underlying disease resolves or can be corrected
- Mediastinitis: variable depending on severity; chronic cases may be hard to resolve.
- Mediastinal masses:
  - Lymphoma: chemotherapy usually palliative
  - Others: surgery for cure or palliation. The prognosis for dogs and cats with surgical excision of thymoma is generally good.
- Mediastinal hemorrhage: prognosis variable, depending on cause and severity

PEARLS & CONSIDERATIONS

COMMENTS

- Advanced imaging helps define internal structure and extent of mediastinal masses and detect pulmonary metastases.
- In patients at risk of foreign body inhalation (hunting or field trial dogs), consider *Nocardia, Actinomyces* as causes of mediastinitis.

PREVENTION

Avoid iatrogenic tracheal injury associated with:

- Intubating with a stylet
- Overinflation of endotracheal tube cuffs
- Rotating a patient while attached to anesthetic circuit
- Traumatic jugular venipuncture

TECHNICIAN TIPS

- The complications of a fine-needle aspirate of a mediastinal mass include pneumothorax and hemothorax. If your patient suddenly develops a high respiratory rate or effort after the procedure, alert the attending clinician as soon as possible.
- Dogs that present with swollen front legs, neck, and face often have disease in the mediastinum.
- Cats with mediastinal masses can be very fragile (unstable respiratory/cardiovascular status). Minimize handling and avoid ventrodorsal projection for thoracic radiographs.

SUGGESTED READING

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MDR1 Mutation

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

The MDR (multidrug resistance) 1 mutation causes enhanced sensitivity to a number of drugs such that affected dogs are extremely susceptible to adverse drug reactions at doses of drugs otherwise well tolerated by normal dogs.

SYNONYMS

Ivermectin or avermectin sensitivity; ABCB1, ABCB1-1 delta, or MDR1-1Δ gene mutation

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs **GENETICS** & **BREED PREDISPOSITION:** Herding breeds (collie, Australian shepherd, Shetland sheepdog, Old English sheepdog, English shepherd, border collie, German shepherd, McNab), sight hound breeds (long-haired whippet, silken windhound)

RISK FACTORS: Breed is a risk factor, based on the percentage of animals known to harbor the MDR1 mutation:

- Australian shepherd: 50%
- Border collie: 5%
- Collie: 75%
- English shepherd: 15%
- German shepherd: 5%
- Longhaired whippet: 65%
- McNab: 30%
- Old English sheepdog: 35%
- Shetland sheepdog: 15%
- Silken windhound: 35%
- Mixed breed dogs (presumed to be herding breed crosses): 10%

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Depends on the particular drug to which the animal is exposed:
  - Exposure to macrocyclic lactones (i.e., ivermectin, milbemycin, selamectin, moxidectin, etc.) may result in neurologic toxicosis. Note: Use of these drugs as labeled for heart-worm prevention is safe even for dogs with the MDR1 mutation. Neurologic toxicosis occurs only with higher doses (e.g., for treatment of mange, or accidental overdose).
  - Exposure to loperamide may result in neurologic toxicosis.
  - Exposure to some chemotherapeutic drugs (vinca alkaloids, anthracyclines such as doxorubicin) can result in severe gastrointestinal signs and/or severe myelosuppression.
  - Exposure to some antiemetics (ondansetron, possibly maropitant) may result in neurologic toxicosis.
  - Exposure to some preanesthetic agents (acepromazine, butorphanol) may result in more profound and prolonged sedation than expected for the dose administered.
- Onset of signs occurs within hours to days after drug exposure.
- Of note, exposure to macrocyclic lactones can occur through ingestion of feces of animals, particularly livestock, recently treated with these agents. Additionally, several pesticides contain avermectins and have caused neurologic toxicosis in dogs that were inadvertently exposed.

PHYSICAL EXAM FINDINGS: Determined by drug to which the dog has been exposed (see above):

- Macrocyclic lactones: mydriasis, hyper-salivation, ataxia, blindness, paresis, stupor, muscle tremors; may progress to coma
- Loperamide: paresis, ataxia, stupor
- Chemotherapeutic agents: anorexia; vomiting, diarrhea; signs of opportunistic infections or hemorrhage possible if neutropenia orthrombocytopenia, respectively
- Antiemetics: signs of mild to moderate central nervous system (CNS) dysfunction (usually depression)
- Preanesthetic agents: prolonged and more profound CNS depression

ETIOLOGY AND PATHOPHYSIOLOGY

- The MDR1 mutation is inherited in a simple Mendelian fashion.
- The MDR1 mutation itself is a 4-base-pair deletion mutation that results in dysfunction of P-glycoprotein, the product of the MDR1 gene.
- P-glycoprotein protects individuals from a number of drugs by restricting their access to the brain and enhancing their export from the body.

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

Screening for the MDR1 mutation can be performed preemptively in a dog of a high-prevalence breed. Otherwise, the mutation is suspected when signs of drug toxicosis have occurred despite the use of normal drug dosages. In either situation, confirmation is via genotyping.

DIFFERENTIAL DIAGNOSIS

- Idiopathic drug sensitivity
- Overdose

INITIAL DATABASE

Initial diagnostic tests are those that would be performed in any suspected case of toxicosis for the particular agent (e.g., CBC for chemotherapeutic drugs with myelosuppressive potential).

ADVANCED OR CONFIRMATORY TESTING

Definitive diagnosis consists of genotyping the dog. A DNA sample (cheek swab, using purpose-made kit) can be submitted to the Veterinary Clinical Pharmacology Laboratory at Washington State University. A DNA swab kit can be obtained at: www.vetmed.wsu.edu/vcpl.

TREATMENT 

TREATMENT OVERVIEW

- While there is no treatment that can alter the dog's MDR1 genotype, treatment of clinical signs resulting from drug exposure should be aimed at the particular drug involved.

ACUTE AND CHRONIC TREATMENT

- For macrocyclic lactones, supportive care is indicated (see p. 625). Administration of CNS depressants such as diazepam should be avoided. Recently the use of intravenous lipid emulsion for reversal of macrocyclic lactone toxicity has been discussed, but there are no clinical studies in dogs at this time.
- For loperamide, an opioid antagonist such as naloxone can reverse CNS depression.
- Chemotherapeutic agents, antiemetic agents, preanesthetic agents: supportive care (see p. 188)

PROGNOSIS AND OUTCOME 

- Clinical signs tend to be milder, and clinical outcome better, in dogs heterozygous for the MDR1 mutation (MDR1 mutant/normal).
- For dogs homozygous for the MDR1 mutation (MDR1 mutant/mutant), the prognosis is guarded for dogs exposed to doses of ivermectin used for treating mange (300-600 mcg/kg or higher) and customary doses of vincristine (0.5-0.7 mg/m^2) and doxorubicin (30 mg/m^2)

PEARLS & CONSIDERATIONS 

COMMENTS

- The MDR1 mutation (and exposure to a macrocyclic lactone or loperamide) should be considered in any herding-breed dog that develops unexplained signs of neurologic toxicosis.
- Prior to treatment with chemotherapeutic agents and/or off-label (i.e., anti-mange) doses of macrocyclic lactones, mixed-breed dogs or breeds listed above should be tested for the MDR1 mutation.
- The MDR1 mutation may explain the intolerance to stress and illness anecdotally observed in some breeds. In collies, the MDR1 mutation is associated with lower plasma cortisol concentrations at baseline and after ACTH stimulation. Since P-glycoprotein limits glucocorticoid passage into the brain, MDR1 mutation could favor such passage, increasing feedback inhibition and creating a state of relative adrenal insufficiency.

PREVENTION

- Treatment planning in dogs identified as having the MDR1 mutation (hetero-or homozygous): depending on the drug involved, patients requiring treatment with such drugs as those listed above may need to receive either a decreased drug dosage or an alternative drug. Studies to determine appropriate dosage adjustments have not yet been conducted.

CLIENT EDUCATION

Owners should be aware of drug sensitivities if their dog has the MDR1 mutation. Breeders should consider the MDR1 mutation as part of a comprehensive genetic assessment of their breeding program.

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Masticatory Myositis

BASIC INFORMATION

DEFINITION

Masticatory myositis (MM) is an autoimmune disease affecting the muscles of mastication in dogs.

SYNONYMS

Masticatory muscle myositis (redundant because myositis by definition is muscle inflammation); eosinophilic myositis, atrophic myositis: incomplete (likely represent acute and chronic stages of a single disease)

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs of any age or breed, either sex.

GENETICS & BREED PREDISPOSITION

- Large-breed, young-adult to middle-aged dogs most commonly affected
- Overrepresentation in German shepherds
- Especially severe inflammation and myofiber destruction in rottweiler, Samoyed, and Doberman
- Reported in Cavalier King Charles spaniel littermates, with clinical signs beginning before 12 weeks of age

GEOGRAPHY AND SEASONALITY: Higher incidence reported to occur in the summer and fall

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Acute versus chronic

- An acute stage (painful muscle swelling/inflammation) may be followed by a latent stage (apparently healthy animal) which is then either followed by a chronic stage (muscle atrophy) or a recurrent acute stage.
- Untreated acute episodes last 2-3 weeks, and relapses in weeks or months frequently occur.
- The chronic form may develop without the client having observed acute signs.

HISTORY, CHIEF COMPLAINT:

Acute:

- Decreased activity, lethargy
- Fever, regional lymphadenopathy
- Dysphagia, reluctance to eat, weight loss
- Drooling of saliva, change in bark (more high-pitched)
- Pain on yawning or when grabbing toys

Chronic:

- Dogs usually bright, alert, and otherwise normal, but progressive atrophy of masticatory muscles

PHYSICAL EXAM FINDINGS: Acute:

- Visible or palpable swelling of the masticatory muscles
- Exophthalmos due to swelling of temporal and pterygoid muscles; inability to blink properly, ocular discharge, conjunctivitis, and keratitis; occasionally blindness due to optic nerve compression
- Pain on palpation of masticatory muscles and regional lymph nodes
- Resistance or inability to open the mouth (trismus)

Chronic:

- Moderate to severe atrophy of masticatory muscles
- Enophthalmos due to atrophy of temporal and pterygoid muscles (globes sinking into their orbits)
- Inability to fully open the mouth (trismus)
- In rare cases, open bite presentation due to inability to completely close the mouth

ETIOLOGY AND PATHOPHYSIOLOGY

- Masticatory myositis (MM) is an autoimmune disease affecting the muscles of mastication in dogs.
- Temporal, masseter, and (medial and lateral) pterygoid muscles (but not digastricus muscles) possess 2M fibers that differ from the common type 2C fibers of limb muscles.
- In dogs with MM, autoantibodies target the unique myosin component of type 2M fibers, resulting in inflammation, necrosis, and phagocytosis of muscle tissue.
- It has been speculated that autoantibodies are generated in response to an infectious agent cross-reacting with endogenous antigens.

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

A diagnosis of MM can be made if clinical and histopathologic signs of myositis are limited to masticatory muscles, and antibodies against type 2M fibers are identified in serum or immune complexes found in biopsied muscle samples.

DIFFERENTIAL DIAGNOSIS

Masticatory myositis must be differentiated from a variety of disorders of the head and neck that can make a dog unwilling or unable to open its mouth.

- Maxillofacial trauma
- Temporomandibular joint disease
- Bone and soft-tissue neoplasia
- Foreign-body penetration (caudal to last maxillary molar, tonsillar region, pharyngeal wall, sublingual tissues)
- Ocular disease and space-occupying orbital/retrobulbar lesions
- Ear disease (e.g., otitis externa, neoplasia in ear canal)
- Other inflammatory muscle disorders (polymyositis, extraocular myositis, dermatomyositis, laryngeal myositis)
- Tetanus
- Chronic exposure to glucocorticosteroids (catabolic to muscle)
- Craniomandibular osteopathy (excessive bone deposition along caudal mandible and temporal bone region).

INITIAL DATABASE

- CBC (occasionally leukocytosis with eosinophilia)
- Serum biochemistry profile (occasionally increased serum globulin, total protein, and hepatic enzyme activities)
- Serum creatine kinase (normal or slightly elevated)
- Urinalysis (generally unremarkable; proteinuria uncommon)
- Orofacial examination: check for facial asymmetry, look for masticatory muscle swelling or atrophy, evaluate presence of pain on palpation or jaw manipulation, measure range of mandibular motion with a ruler as the distance between the incisal edges of the maxillary and mandibular first incisors.

ADVANCED OR CONFIRMATORY TESTING

- Serum type 2M fiber antibody titer (<1:100 = negative; 1:100 = borderline; >1:100 = positive; circulating antibodies against type 2M fibers detected in serum from 81% of dogs with MM)
- General anesthesia allows assessment of jaw tone without conscious resistance from the patient (occasionally requiring temporary tracheostomy for intubation).
- Skull radiographs: to rule out skeletal abnormalities in dogs that cannot open their mouths
- CT: for ruling out most differentials of MM, allowing CT-guided fine-needle aspiration, showing changes in size (larger due to edema or inflammation; smaller due to atrophy, necrosis or fibrosis), pre-contrast tissue attenuation (hypoattenuated due to edema) and contrast enhancement (heterogeneously enhanced due to inflammation) of affected masticatory muscles and lymphadenopathy
- MRI:

    - Advantages compared with CT: superb characterization of soft tissues and very sensitive in detecting early signs of muscle edema
    - Disadvantages compared with CT: more time-consuming and costly; less readily available; does not record signals from cortical or lamellar bone; not useable for fine-needle aspiration
- Electromyography (less useful in dogs with chronic MM): to demonstrate spontaneous electrical activity (i.e., increased insertional activity, fibrillation potentials, positive sharp waves, and bizarre high-frequency discharges), differentiate MM from neuropathy (denervation atrophy) or polymyositis, and facilitate selection of sites for muscle biopsy (though less helpful than CT)
- Muscle biopsy: (see p. 1305)

TREATMENT

TREATMENT OVERVIEW

The goal of therapy is to alleviate pain, blunt the inflammatory response, prevent muscle fibrosis, and restore normal opening and closing of the mouth.

ACUTE GENERAL TREATMENT

Glucocorticosteroid therapy should not be started prior to blood collection and muscle sampling:

- Dexamethasone, 0.4 mg/kg IV (once after blood collection and muscle biopsy): initially helpful in reducing the degree of inflammation in dogs with acute MM that can barely open the mouth.
- Prednisone, 1-2 mg/kg PO q 12 h (upon patient discharge): usually results in rapid (within days) improvement of clinical signs; after approximately 2-3 weeks, dosage can be decreased to 1 mg/kg q 24 h, and then slowly tapered to the lowest possible alternate-day effective dosage over a period of 8-12 months.

CHRONIC TREATMENT

- It is usually necessary to maintain dogs on a low-dose, alternate-day oral prednisone therapy to prevent relapses.
- Dogs unable to receive corticosteroids, unresponsive to corticosteroids alone, or showing unacceptable side effects in response to corticosteroids may instead benefit from administration of azathioprine (1-2 mg/kg PO q 24 h).

NUTRITION/DIET

Feeding tube placement (see p. 1270 and p. 1267), temporarily (treatment response) or permanent (lifelong)

POSSIBLE COMPLICATIONS

- Corticosteroids: typical effects
- Azathioprine: myelotoxicity (leukopenia, anemia, thrombocytopenia), acute pancreatitis, and hepatotoxicity
- Progressive inability to open the mouth (leading to starvation from inability to prehend)

RECOMMENDED MONITORING

- Physical examination (focus on body weight, muscle atrophy, pain on head palpation/jaw manipulation, and range of mandibular motion measured with a ruler) at 2 weeks, 1, 2, 6, 9, and 12 months after initiation of prednisone therapy and once every 6-12 months thereafter
- Serum type 2M fiber antibody titer at 2, 6, 9, and 12 months after initiation of prednisone therapy and once every 6-12 months thereafter (determining antibody titer is particularly important prior to decreasing prednisone doses when they are already very low [i.e., below 0.1-0.2 mg/kg q 24-48 h])
- CBC and serum biochemistry profile at 6 and 12 months after initiation of prednisone therapy (sooner and shorter interval if receiving azathioprine) and once every 12 months thereafter

PROGNOSIS AND OUTCOME

- Good prognosis for acute MM when initiation of treatment is prompt and therapy is long term. Inadequate dosing or treatment for an insufficient period of time is associated with a high rate of relapse. Dogs with relapses when the dose is lowered should be reinstituted at the maximum prednisone dose.
- Fair to guarded prognosis for chronic MM when extensive atrophy and fibrosis of masticatory muscles led to progressive

inability to open the mouth.

PEARLS & CONSIDERATIONS

COMMENTS

- MM is a leading differential diagnosis in a dog with difficulty, unwillingness, or inability to fully open the mouth; masticatory muscle swelling or atrophy; and pain upon palpation of the head (muscles, jaws, etc.).
- Clinical signs of MM are usually bilateral, but because they are not always equal in severity or time of onset, muscle swelling and atrophy may sometimes appear unilaterally.
- Treatment with corticosteroids prior to blood collection can result in false-negative serum type 2M fiber antibody titer results. Destruction of type 2M fibers and replacement with scar tissue may also lead to a decreased antigenic stimulus for autoantibody production in dogs with chronic MM.
- Serum creatine kinase is more likely to be high in dogs with acute than chronic MM but is generally lower than in dogs with polymyositis, owing to less muscle mass affected.
- Myotomy of affected muscles and slow traction to force open the mouth are considered to be experimental procedures that have not been evaluated in controlled studies and may be associated with increased morbidity and high rate of complications (iatrogenic jaw fracture).

TECHNICIAN TIPS

Technicians caring for these patients should be familiar with assisted feeding techniques, including the use and care of feeding tubes.

SUGGESTED READING

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Mast Cell Tumors, Dog

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Canine mast cell tumors (MCTs) are neoplastic accumulations of cells that can degranulate, a process resulting in the release of bioactive substances that can produce cutaneous or systemic clinical signs.

SYNONYMS

Mastocytoma, systemic mastocytosis (metastatic MCT)

EPIDEMIOLOGY

SPECIES, AGE, SEX: Can occur in any age dog; the median age in dogs is 8 years.

GENETICS & BREED PREDISPOSITION: Breeds predisposed to MCT include boxer, Boston terrier, golden retriever, Labrador retriever, Pug, sharpei, Staffordshire bull terrier, Jack Russell terrier

ASSOCIATED CONDITIONS & DISORDERS: Caused by mast cell degranulation: gastrointestinal ulceration, pruritus, hypotension, delayed wound healing

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Most dogs show no clinical signs and are evaluated for an incidentally discovered cutaneous or subcutaneous mass. Some lesions are pruritic. MCTs often remain unchanged in size for months to years before presentation.
- Occasionally, dogs are evaluated because of signs related to gastric ulceration (vomiting, diarrhea, weight loss, melena) secondary to histamine-induced gastric acid secretion.

PHYSICAL EXAM FINDINGS

- Mast cell tumors have a highly variable appearance and may be mistaken for lipomas, skin tags, or insect bites. For this reason, skin and subcutaneous masses should always be aspirated and examined cytologically to obtain a diagnosis.
- Some dogs have multiple cutaneous MCTs, so a thorough examination of the entire skin surface is indicated.
- Because of the presence of histamine in mast cell granules, MCTs sometimes shrink and swell intermittently as degranulation (release of granules from the mast cell cytoplasm) occurs. Degranulation can result from manipulation of the tumor or can be spontaneous.
- Because of the presence of heparin in mast cell granules, MCT may bleed excessively when aspirated, but this is rarely clinically significant.
- Peritumoral bruising and edema (termed *Darier's sign)* and hyperemia (see p. 555) are uncommon but are associated with aggressive-behaving MCTs.

ETIOLOGY AND PATHOPHYSIOLOGY

- Mast cells participate in allergic and inflammatory responses. They contain preformed granules consisting of histamine, heparin, and other cytokines that are released on activation of the cells (degranulation). Cytokine release causes clinical signs.
- Mast cell tumors are accumulations of mast cells with malignant potential.
- Mast cell tumors occur primarily in the skin and subcutaneous tissues, and rarely in extracutaneous sites (GI tract, spinal cord, lung, nasal cavity) in dogs.
- MCTs most commonly metastasize to regional lymph nodes followed by spleen, liver, mesenteric lymph nodes, other cutaneous sites, and bone marrow.
- Chronic inflammatory skin diseases or mutations in a protooncogene, c-KIT, may predispose dogs to mast cell neoplasia; c-KIT encodes the receptor tyrosine kinase KIT, which promotes mast cell growth and differentiation. Mutations in c-KIT (present in about 20%-30% of canine MCT) allow abnormal continuous activation of the receptor and predispose dogs to aggressive MCT that are more likely to recur and metastasize. Inhibition of receptor tyrosine kinases through targeted therapies (see treatment below) holds promise in the treatment of advanced local or metastatic MCT.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis of MCT is generally straightforward: microscopic examination of cytologic preparations or tissue samples reveals characteristic intracytoplasmic granules. Regional lymph nodes should be aspirated whenever possible, and additional staging tests should be considered if signs of aggressive tumoral behavior are present, including peritumoral edema, swelling, or bruising, or if tumors are recurrent.

DIFFERENTIAL DIAGNOSIS

- Gross appearance and palpation:
  - Hemangiosarcoma or hemangioma, cutaneous
  - Plasma cell tumor, histiocytoma, transmissible venereal tumor, lymphoma, amelanotic melanoma, squamous cell carcinoma
  - Lipoma
  - Phlebectasia
  - Granuloma
  - Abscess
- Cytologically, other round cell tumors (histiocytoma, lymphoma) may have a similar appearance.

INITIAL DATABASE

- MCTs are readily diagnosed cytologically by their characteristic blue-or-purple-staining intracytoplasmic granules. In poorly differentiated MCTs, these granules may not be visible, especially with Diff-Quik stain (in-clinic stain). Wright's stain (used in most university and commercial clinical pathology laboratories) is more sensitive to detect granules.
- Before surgical excision, a CBC, serum chemistry panel, urinalysis, and regional lymph node aspirate (regardless of size of the lymph node) should be obtained.
  - CBC abnormalities associated with MCT can include eosinophilia, basophilia, and regenerative or nonregenerative anemia.
- Complete staging for systemic mast cell disease is indicated before surgery in the following patients:
  - Lymph node metastasis is present.
  - Peritumoral edema or bruising is present.
  - Tumors are recurrent.
  - Tumors are located on the prepuce, scrotum, muzzle, digit, pinna or ear canal, or oral mucosa (locations associated with a high rate of metastasis). Tumors located on mucous membranes have a worse prognosis when compared to MCT of haired skin.
- Complete systemic staging to examine for evidence of MCT metastasis includes a CBC, serum chemistry panel, urinalysis, abdominal ultrasound, bone marrow aspiration cytologic study, regional lymph node aspirate or biopsy, and biopsy of the primary tumor.
- Splenic/liver aspirates are indicated if these organs are enlarged or have an abnormal echotexture ultrasonographically.
- The buffy coat smear can be part of complete staging for dogs with MCT, but it has a high rate of false-positive results and must be interpreted along with other staging tests to confirm metastasis.

ADVANCED OR CONFIRMATORY TESTING

- MCTs are categorized into grades based on their histologic appearance (Patnaik grading system):
  - Grade I = well-differentiated tumors
  - Grade II = intermediately differentiated tumors
  - Grade III = poorly differentiated tumors
- This grading system is the most consistent prognostic indicator for metastasis, disease-free interval, and survival for dogs with MCT. The metastatic rate for grade I and II tumors is <10%, and for grade III tumors it is >50%.
- The mitotic index ([MI]; # mitotic figures/high-power field) correlates with grade and prognosis. Dogs having cutaneous MCT with a MI < 5 had a median survival time (MST) of 70 months, compared to 5 months if the MI > 5.
- Mast cell granules may not be present or visible in highly anaplastic MCT; CD-117 (c-KIT) immunohistochemistry can be used to confirm a diagnosis of MCT.
- Normal lymph nodes may contain scattered mast cells; increased numbers or clusters of mast cells in a lymph node draining a MCT suggest metastasis.
- The liver, spleen, and bone marrow normally contain a few mast cells, but increased numbers or clusters of mast cells suggest MCT metastasis.
- Thoracic radiographs are of limited usefulness in dogs with MCT. Uncommonly, malignant pleural effusion containing mast cells occurs.

- Abdominal ultrasound:
  - Affected lymph nodes may be enlarged, hypo- or hyperechoic, or irregular.
  - Splenic/hepatic infiltration: hypoechoic lesions throughout the parenchyma, rarely a solitary mass

TREATMENT

TREATMENT OVERVIEW

Mast cell tumors have a wide variety of biological behaviors and outcomes, and treatment may include surgery, radiation therapy, chemotherapy, or a combination of these modalities. Newer targeted therapies are now available and may be indicated in patients with nonresectable or recurrent tumors. Consultation with an oncologist for current treatment options is warranted in these cases.

ACUTE GENERAL TREATMENT

- Surgery is the primary treatment modality for MCT.
  - For most MCT, tumors should be surgically excised with 2 cm or greater lateral margins and 1 fascial plane deep to the tumor.
  - All tissue should be submitted for histologic evaluation of grade and margins. Margins should be inked with a marking system before placement in formalin.
  - Histamine blockers are indicated in dogs with MCT before surgical excision (begin therapy a few days before and premedicate patient immediately prior to surgery) or in cases of nonresectable or metastatic disease:
    - H2 blocker: diphenhydramine (1-2 mg/kg PO or SQ q 12 h)
    - H2 blockers: ranitidine (1-2 mg/ kg PO or SQ q 12 h); or famotidine (0.5-1 mg/kg PO or SQ q 12 h).
  - Proton pump inhibitors (omeprazole, 0.5-1 mg/kg PO once daily) are indicated in dogs with MCT and suspected or confirmed gastric ulceration.
  - Perioperative complications may include hypotension and hemorrhage. Postoperative complications can include poor wound healing after resection of large or infiltrative MCT.
- For tumors that are not surgically resectable, owing to size, invasiveness, or metastasis, chemotherapy or radiation therapy (RT) before or instead of surgery may be indicated.
- Mast cell tumors are responsive to RT:
  - Treating MCT in a microscopic disease setting (i.e., postsurgical resection) yields better results than if treatment is performed in a setting of macroscopic (measurable) disease.
  - Potential indications for RT for mast cell tumors include incompletely excised grade I and II MCT where wider surgical excision is not possible; as an adjunct to surgery and chemotherapy in dogs with grade III MCT; and to attempt cytoreduction of nonresectable MCT.
  - Regional (draining) lymph nodes should be irradiated prophylactically, since one study demonstrated improved survival times versus patients whose nodes were not irradiated.
- The goal of chemotherapy is to delay or prevent metastasis and possibly local recurrence or to attempt to cytoreduce or slow progression of nonresectable tumors or metastatic lesions. Potential indications for chemotherapy in dogs with MCT include:
  - Dogs with grade III MCT (because at least 50% will develop metastasis) or tumors with MI > 5
  - Dogs with metastasis at diagnosis or with recurrent tumors
  - Dogs with tumors in locations associated with aggressive behavior (see above)
  - Before attempting surgical excision in large, fixed tumors or tumors with peritumoral edema or bruising
- Chemotherapy drugs considered to be effective in the treatment of MCT include CCNU (lomustine), prednisone, vinblastine, vinorelbine, chlorambucil, cyclophosphamide, and others. Special handling requirements and potentially severe or life-threatening adverse patient effects exist with these chemotherapeutic drugs; these concerns and rapid evolution of protocols warrant consultation with/referral to an oncologist.
- Targeted therapy: receptor tyrosine kinase inhibitors such as toceranib (Palladia; 2.2-3.25 mg/kg PO q 48 h; intolerance may warrant decrease to Mon-Wed-Fri dosage schedule) and mastinib inhibit normal and mutated KIT (see pathogenesis). They are indicated for use in dogs with metastatic, recurrent, or nonresectable grade II and III MCT. Consultation with an oncologist is recommended.

PROGNOSIS AND OUTCOME

- The most significant prognostic indicator for MCT is tumor grade. For dogs with completely excised grade I and II MCT, the prognosis is excellent; approximately 5% of these tumors will recur locally or metastasize.
- For dogs with incompletely excised grade I and II tumors, RT provides excellent long-term tumor control, with 80%-90% of dogs free of tumor 2-5 years after treatment. In one study, <25% of incompletely excised grade II MCT recurred following incomplete excision.
- For dogs with grade III MCT, survival times are unpredictable because of the possibility of metastasis and tumor recurrence. A recent study suggests that with effective local control, 70% of dogs with grade III MCT were alive 1 year after treatment. In

another study, dogs with grade III MCT treated with prednisone and vinblastine had a median survival time > 1300 days.
- Mitotic index correlates with grade, and MI > 5 (see above) warrants a guarded prognosis.
- Approximately 10%-40% of dogs develop additional cutaneous MCT in their lifetime.

PEARLS & CONSIDERATIONS

COMMENTS

- It is recommended to schedule patients for rechecks including thorough physical examinations every 4-6 months (or more often if indicated) to try to detect new MCT as soon as possible.
- Grossly, fine-needle aspirates of mast cell tumors can look transparent and watery and are indistinguishable from fat. All fine-needle aspirations must be examined cytologically to differentiate fat from MCT.
- Buffy coat exams frequently are falsely positive and are inferior to bone marrow aspiration and cytologic evaluation for assessing hematologic involvement.
- Because of interpathologist variation when assigning histologic grades to MCT in dogs, the clinician must consider factors including tumor grade, MI, location and size of the tumor, presence of regional and systemic metastasis, and completeness of surgical excision to determine an appropriate treatment plan and prognosis.
- Intralesional therapies such as deionized water or corticosteroids may provide temporary shrinkage of MCT but are rarely effective for long-term tumor control and are not recommended.

CLIENT EDUCATION

Any new masses on the skin should be evaluated as soon as possible.

SUGGESTED READING

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Mast Cell Tumors, Cat

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Feline mast cell tumors are neoplastic accumulations of mast cells in cats. Mast cell tumors (MCTs) produce deleterious effects when the mast cells degranulate, a process resulting in the release of bioactive substances that can produce cutaneous or systemic clinical signs depending on tumor location. Cutaneous MCTs are common, splenic MCT is uncommon, and visceral MCTs are rare.

SYNONYMS

Mastocytoma, splenic or visceral mastocytosis

EPIDEMIOLOGY

SPECIES, AGE, SEX: MCT is primarily a disease of older cats, although all ages can be affected. Males may be predisposed.

GENETICS & BREED PREDISPOSITION: Siamese (possibly)

ASSOCIATED CONDITIONS & DISORDERS: Related to mast cell degranulation:

- Gastrointestinal ulceration
- Pruritus
- Hypotension
- Delayed wound healing

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: In cats, there are two distinct presentations:

- Cutaneous MCTs
- Splenic or visceral MCTs

HISTORY, CHIEF COMPLAINT

- Most cats with cutaneous MCT show no clinical signs, although some lesions are pruritic. MCTs often remain unchanged in size for months or years prior to presentation.
- Cats with splenic or visceral MCTs display nonspecific signs of illness (weakness, lethargy, anorexia) or gastric ulceration-associated bruxism, vomiting, diarrhea, weight loss, and melena. Abdominal distension secondary to ascites and splenomegaly may also occur.

PHYSICAL EXAM FINDINGS

- Although most cutaneous MCTs are found on the head, a thorough examination of the skin is indicated. Tumors are usually alopecic, small (<5 mm), round, and pink or white. Some MCTs are plaquelike. Regional lymph nodes may be normal in size even if metastasis is present.
- Approximately 15% of cats with cutaneous MCTs have concurrent splenic or visceral MCTs.
- Physical exam findings in cats with splenic or visceral MCTs include splenomegaly, ascites, abdominal mass, bowel wall thickening, abdominal pain, and mucous membrane pallor secondary to anemia (induced by gastrointestinal ulceration and bleeding, or rarely myelophthisis).

ETIOLOGY AND PATHOPHYSIOLOGY

- Mast cells participate in allergic and inflammatory responses.
- Mast cells contain preformed granules consisting of histamine, heparin, and other cytokines that are released upon activation of the cells (degranulation). Cytokine release causes clinical signs.
- Mast cell tumors are accumulations of mast cells with malignant potential.
- Mast cell tumors have a variable potential for metastasis (visceral MCT > cutaneous MCT); when it occurs, regional lymph nodes, spleen, liver, bone marrow, mesenteric lymph nodes, and other cutaneous sites can be affected.

- The etiology of feline MCTs is unknown.
- Feline leukemia virus (FeLV), feline immunodeficiency virus (FIV) infection: not associated with the development of feline MCT.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Cutaneous MCT should be suspected in cats with small pimple-like lesions of the head and neck; fine-needle aspirate is usually diagnostic. Any cat with splenomegaly or ascites should be suspected to have splenic MCT, and fine-needle aspiration of the spleen should be performed.

DIFFERENTIAL DIAGNOSIS

- Cutaneous form: histiocytoma, lymphoma, eosinophilic granuloma complex, and lipoma
- Splenic and visceral forms: splenomegaly: infectious splenitis, lymphoma, myeloproliferative disease, and hemangiosarcoma
- Visceral lesions: inflammatory bowel disease, lymphoma, intestinal adenocarcinoma or sarcoma, and granulomas

INITIAL DATABASE

Cutaneous form:

- The diagnosis of MCTs is frequently obtained by fine-needle aspiration of the lesion for cytologic examination.
- Prior to treatment, CBC, serum biochemistry panel, serum thyroxine (T4), urinalysis, FeLV/FIV test, and a regional lymph node aspirate should be obtained.
- Staging for systemic mast cell disease is indicated prior to surgery in patients with the following:
    - Lymph node metastasis is present.
    - Peritumoral edema or bruising is present.
    - Tumors are recurrent or multiple.
    - There is any suspicion of splenic or visceral MCTs (e.g., splenomegaly).
- Complete staging for metastasis includes CBC, serum biochemistry panel, urinalysis, serum T4 level, FeLV/ FIV tests, buffy coat smear, thoracic and abdominal radiographs, abdominal ultrasound, bone marrow aspirate, regional lymph node aspirate or biopsy, and aspirate or biopsy of the primary tumor. Splenic/liver aspirates are indicated if these organs are enlarged or have an abnormal echotexture.

Visceral and splenic forms:

- All cats with the splenic or visceral form of MCTs should have complete staging prior to definitive therapy.

ADVANCED OR CONFIRMATORY TESTING

- Cytologically, mast cells have a round nucleus and intracytoplasmic granules are almost always present.
- The histologic grading system used for canine cutaneous MCTs is not clinically significant in cats. Some feline dermal MCT have histologic characteristics that would suggest aggressive behavior (anisokaryosis/ -cytosis, nuclear atypia, multiple nucleoli), but in one study 14/15 cats whose tumors fit this description did not develop tumor recurrence or metastasis. A high mitotic index (≥1-2 mitoses/high power field) is likely related to a malignant phenotype.
- CBC abnormalities associated with MCTs can include eosinophilia, basophilia, and regenerative or nonregenerative anemia.
- Normal lymph nodes may contain scattered mast cells; metastasis to regional lymph nodes is documented by the presence of increased numbers or clusters of mast cells in a lymph node draining an MCT.
- The buffy coat smear is more specific in cats than dogs. A positive test supports a diagnosis of mast cell metastasis in cats with MCT.
- The liver, spleen, and bone marrow normally contain a few mast cells; increased numbers or clusters of mast cells are supportive of MCT metastasis.
- Thoracic radiographs: limited usefulness. Uncommonly, pleural effusion containing mast cells occurs with MCTs, and mediastinal MCTs have been reported.
- Abdominal ultrasound:
    - Affected lymph nodes may be enlarged or irregular.
    - Splenic/hepatic infiltration: hypoechoic lesions throughout the parenchyma, rarely a solitary mass
    - Gastrointestinal tract lesions may be solitary or diffuse throughout the bowel.

TREATMENT

TREATMENT OVERVIEW

In most cases, the goal of therapy is to control the local disease to prevent recurrence and metastasis. In cases presenting with metastasis or nonresectable local disease, the goals are to minimize tumor volume and secondary GI signs and to maintain quality of life.

ACUTE AND CHRONIC TREATMENT

Cutaneous form:

- Treatment options include surgery and radiation therapy.
- Spontaneous resolution is rare.
- Chemotherapy may play a role in some cats with cutaneous MCTs.
- Surgery is the primary treatment for cutaneous MCTs.
    - Wide surgical margins are not as important in cats as in dogs, since recurrence following incomplete excision is uncommon in the cat.
    - All tissue should be submitted for histologic evaluation; margins should be inked prior to placement in formalin.
    - Treatment with antihistamines for at least 48 hours prior to surgery is recommended (to reduce effects of mast cell degranulation induced by surgical manipulation of the tumor).
    - Postoperative complications are uncommon; wound healing should be monitored following resection of large, infiltrative MCTs.
- Mast cell tumors in locations that preclude complete excision (i.e., periocular, pinna) are common; radiation therapy may be effective as a primary or adjunct (postoperative) treatment. External beam radiation therapy (via linear accelerator) is uncommonly used to treat cats with MCT, but strontium-90 plesiotherapy (radiation source applied directly to the tumor) is a very useful treatment to prevent recurrence of superficial (<4 mm deep) feline cutaneous MCT.
- Nonresectable (large/highly invasive/ metastatic) tumors may require chemotherapy or radiation therapy prior to or instead of surgery.

Visceral form:

- Surgery is the primary treatment modality for visceral MCTs.
- Exploratory laparotomy is indicated, with incisional liver and mesenteric lymph node biopsies even if the tissue appears normal. Bowel-wall masses should be resected if possible.
- Splenectomy is the treatment of choice in cats with splenic MCTs, even if metastasis or cutaneous MCT is present. Following splenectomy, disseminated disease often resolves or improves significantly.
- Take care not to excessively manipulate known tumor tissue, since degranulation can result in anaphylaxis and hypotension during surgery.

Chemotherapy for feline MCT:

- The goal of chemotherapy is to delay or prevent metastasis or to attempt cytoreduction for nonresectable tumors or metastases. A single study evaluating the use of lomustine (50-60 mg/m^2 PO q 3-6 wk, based on neutrophil count) in cats with measurable MCT revealed a response rate of 50% with a median duration of response of 168 days. Other drugs that may be effective in the treatment of MCTs include prednisone and vinblastine. Special handling requirements and potentially severe or life-threatening adverse patient effects exist with these chemotherapeutic drugs; these concerns and rapid evolution of protocols warrant consultation with/referral to an oncologist.
- Potential indications for chemotherapy in cats with MCTs include: multiple or recurrent cutaneous MCTs, presence of metastasis at the time of diagnosis, or prior to attempting surgical excision in large, infiltrative tumors.

Adjunctive therapies:

- Antihistamines are indicated in cats with MCTs prior to surgical excision or in cases of nonresectable or metastatic disease.
- H2 blockers: cyproheptadine (2 mg/ cat PO q 12-24 h) or diphenhydramine (1-2 mg/kg PO or SQ q 12 h); cyproheptadine is recommended for feline MCT due to its antiserotonin properties and ease of administration as compared to diphenhydramine.
- H2 blockers: ranitidine (1-2 mg/kg PO or SQ q 12 h) or famotidine (0.5 mg/ kg PO or SQ q 12-24 h)
- Proton pump inhibitors (omeprazole, 0.7 mg/kg PO q 24 h) are indicated in cats at risk for or that have developed gastric ulceration.
- Supportive care including nutritional and blood-product support and analgesia are indicated perioperatively as needed.

PROGNOSIS AND OUTCOME

- The prognosis for cats with cutaneous MCTs is good, and recurrence after excision or strontium irradiation is uncommon.

Some cats will develop multiple cutaneous MCTs, regional lymph node metastasis, or splenic or visceral MCTs, and currently there is no reliable way to predict in which cases this type of progression will occur; client education and frequent rechecks are recommended.

- In one study, cats with solitary dermal MCT with or without regional lymph node involvement had longer median survival times (MST) (MST was not reached in cats with solitary tumors +/− lymph node involvement) as compared to cats with multiple cutaneous MCT or cats with cutaneous tumors + distant metastasis (MST 582 days in this group of cats). Survival times were longer in cats with cutaneous tumors as compared to those with splenic or visceral tumors.
- The prognosis for cats with solitary splenic MCT is good (MST following splenectomy: 19 months).
- For cats with splenic MCT with other sites involved, the prognosis can be good, and the remaining mast cell disease may resolve following splenectomy. There is no reliable way to predict tumor behavior, so chemotherapy can be considered if metastatic sites do not resolve within 2 months of splenectomy or if clinical signs persist despite splenectomy.
- Primary gastrointestinal MCTs have the poorest prognosis, which may improve if the lesions are surgically resectable. The role of adjuvant chemotherapy is unclear but should be considered.

PEARLS & CONSIDERATIONS

COMMENTS

Many cats with mast cell disease will develop additional MCTs during their lifetime, including cutaneous, splenic, or visceral forms. It is wise to schedule patients for rechecks at least every 4-6 months (or more often if indicated) for physical examinations and possibly restaging.

CLIENT EDUCATION

Any new skin masses or signs of illness should be evaluated as soon as possible.

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Mass: Cutaneous, Subcutaneous

BASIC INFORMATION

DEFINITION

A lump made up of cohering cells in the skin (cutaneous) or soft tissue between the skin and underlying fascia, muscle, or bone (subcutaneous). A very common condition in dogs, and common in cats.

SYNONYMS

Bump, growth, lump, nodule, tumor

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Older animals more commonly develop benign and malignant neoplasms.
- Eosinophilic lesions and plasma-cell pododermatitis or stomatitis (cats)
- Canine juvenile cellulitis (puppies)
- Histiocytomas and viral papillomas (young dogs)
- Intact male cats are prone to abscesses because of fighting behavior.
- Mammary tumors (intact female dogs)
- Perianal gland tumors (intact male dogs)

GENETICS & BREED PREDISPOSITION

- Malignant tumors are more common in purebred dogs versus crossbred dogs.
- Boxers are prone to a variety of benign and malignant neoplasms.
- Cutaneous histiocytoma (flat-coated retrievers)
- Keratinous cysts and nodular dermato-fibrosis syndrome (German shepherds)
- Idiopathic focal mucinosis (Doberman pinschers)
- Dermatophyte pseudomycetoma (Persian cats)

RISK FACTORS: Long-term exposure to sunlight increases the risk of cutaneous hemangioma and hemangiosarcoma (dogs) and squamous cell carcinoma (dogs and cats).

CONTAGION & ZOONOSIS: Transmissible venereal tumors and viral papilomas are contagious between dogs.

GEOGRAPHY AND SEASONALITY: Transmissible venereal tumor is more prevalent in temperate climates.

ASSOCIATED CONDITIONS & DISORDERS: Nodular dermatofibrosis syndrome in German shepherds may be associated with renal adenocarcinoma and uterine leiomyoma.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Most commonly, the pet owner visualizes or feels the mass, but it may be found incidentally by the veterinarian on physical examination.
- Historic information obtained should include:
  - Presence of similar lesions
  - Rapidity of onset (malignant tumors tend to grow rapidly)
  - Evidence of pruritus or pain
  - Presence of other animals in the household
  - Possibility of exposure to anticoagulant rodenticides (hematomas)
  - Known trauma
  - In cats, indoor/outdoor status should be known (increased risk of bite or scratch wounds, foreign bodies, other trauma).

PHYSICAL EXAM FINDINGS

- Characterize the mass in terms of size, shape, location, consistency, depth, ulceration, and whether it is freely movable. Malignant tumors are more likely to be ulcerated, fixed to underlying structures, and have poorly defined margins.
- Examine local lymph nodes and possible sites of metastasis (e.g., lungs, abdomen). Local lymph nodes may be enlarged due to inflammation (i.e., reactive lymph node) or metastasis.
- A complete physical exam is essential to identify any associated abnormalities.

ETIOLOGY AND PATHOPHYSIOLOGY

- A neoplasm is caused by progressive, uncontrolled growth of cells. Unlike benign neoplasms, malignant neoplasia shows a greater degree of anaplasia and exhibits invasive and metastatic properties. Most have an unknown cause, but some may be induced by irritation, trauma, viruses, vaccinations, ultraviolet radiation exposure, thermal injury, immunologic or genetic influences, or hormones.
- Cysts are accumulation of material (keratin, serum, glandular product) within a membrane. May arise from idiopathic, traumatic, congenital, follicular, or pilar causes.
- A granuloma is a focal accumulation of mononuclear inflammatory cells due to bacteria, mycoses, mycobacteria, dermatophytes, parasites, endogenous or exogenous foreign objects, allergic, or idiopathic causes. Pyogranulomas also include neutrophilic inflammation.
- Keratoses are solid circumscribed lesions caused by overproduction of keratin.
- A hamartoma is a benign, disorganized overgrowth of normal cells within a tissue, whereas a nevus is a hamartoma arising from any skin component.
- A hematoma is local extravasation of blood due to trauma and/or bleeding disorder.
- Abscesses result from a local accumulation of neutrophils and necrotic tissue cells, usually secondary to a bacterial or fungal infectious agent.
- Urticaria is a group of wheals in the dermis caused by a hypersensitivity reaction to insect bites, food, irritants, drugs, allergens, or physical stimuli. Angioedema is a hypersensitivity reaction that occurs below the dermis.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Cytologic analysis of a fine-needle aspirate, impression smear, scrape, or swab sample from a mass may provide a tentative or sometimes a definitive diagnosis; histopathologic evaluation of an incisional or excisional biopsy may be necessary for final diagnosis.

DIFFERENTIAL DIAGNOSIS

- Neoplasm:
  - Benign
  - Malignant:
    - Epithelial
    - Glandular
    - Mesenchymal
    - Round cell
- Pseudoneoplasm:
  - Cyst
  - (Pyo)granuloma
  - Keratoses
  - Hamartoma/nevus
  - Acral lick dermatitis
  - Feline plasma cell pododermatitis or stomatitis
  - Calcinosis cutis
  - Calcinosis circumscripta
  - Canine juvenile cellulitis
  - Nodular sterile panniculitis
  - Idiopathic lichenoid dermatitis (coalescent plaques)
  - Idiopathic focal mucinosis (Doberman pinschers)
  - Eosinophilic lesions:
    - Eosinophilic plaque
    - Indolent ulcer
    - Collagenolytic granuloma
- Hematoma

- Abscess
- Urticaria
- Angioedema
- Normal structures:
  - Lymph node
  - Salivary gland
  - Bulbus glandis (transient preputial “mass” in male dogs)

INITIAL DATABASE

- Confirm that the mass is not a normal structure (anatomic location).
- Cytologic examination of samples obtained from a mass via fine-needle aspiration, impression smear, scrape, or swab may provide a diagnosis.
- Fine-needle aspiration cytologic evaluation of a local lymph node may help discern an inflammatory reaction from metastasis.
- Examination for evidence of distant metastasis via three-view thoracic radiographs and/or abdominal ultrasound
- Preoperative blood work (e.g., CBC, serum biochemical profile, urinalysis, depending on the age of the patient) if a biopsy is planned

ADVANCED OR CONFIRMATORY TESTING

Histopathologic evaluation +/− bacterial and fungal culture of an incisional or excisional biopsy sample generally is necessary for a definitive diagnosis.

TREATMENT 

TREATMENT OVERVIEW

Eliminating the mass via surgery and/or medical management is ideal if possible; however, known benign neoplasms or pseudoneoplasms may not require treatment if they are not causing harm to the patient.

ACUTE AND CHRONIC TREATMENT

- Many cutaneous or subcutaneous masses can be successfully removed surgically and possibly cured if not malignant.
- Drainage and antibacterial therapy based on culture and sensitivity information is recommended for most abscesses.
- Medical therapy without surgical removal may be appropriate in cases of eosinophilic lesions, urticaria and angioedema, dermatophytic pseudomycetoma, hematomas, and some round cell tumors.

PROGNOSIS AND OUTCOME 

- Depends on the diagnosis
- Many benign growths can be cured with complete surgical removal or appropriate medical therapy.
- Therapy for malignant neoplasms rarely results in a cure, but long remissions can be obtained in many cases.

PEARLS & CONSIDERATIONS 

COMMENTS

- Cytologic examination of a sample obtained by fine-needle aspiration from a cutaneous or subcutaneous mass is a simple and inexpensive diagnostic aid that should be recommended in most cases.
- Establishing a diagnosis via physical examination alone and treating with clinical neglect can lead to inappropriate patient outcomes.

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EDITOR: ETIENNE CÔTÉ

Mass, Splenic

BASIC INFORMATION

DEFINITION

Diffuse nodular or focal enlargement of the spleen

EPIDEMIOLOGY

GENETICS & BREED PREDISPOSITION

- Large- to giant-breed, geriatric dogs: German shepherds, great Danes, retrievers
- Cats: splenic lesions are less common and when present usually consist of diffuse splenomegaly (see p. 1428).

ASSOCIATED CONDITIONS & DISORDERS

- Anemia
- Hemoabdomen
- Disseminated intravascular coagulation (DIC)
- Metastasis

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Diffuse, nodular splenic enlargement (multiple masses)
- Focal splenic enlargement (single mass)

HISTORY, CHIEF COMPLAINT

- Incidental finding (no clinical signs)
- Nonspecific signs: inappetence, lethargy, weight loss, vomiting, diarrhea, discolored urine (hemoglobinuria due to hemolysis)
- Abdominal enlargement
- Weakness, collapse

PHYSICAL EXAM FINDINGS: Variable, depending on etiology of splenic mass:

- Abdominal distension:
  - Fluid (palpable fluid wave possible)
  - Mass
- Pale mucous membranes, poor or nonpalpable pulses, weakness, tachycardia and tachypnea:
  - Acute blood loss despite normal coagulation (e.g., mass rupture)
  - Bleeding/coagulation disorder
- Nonspecific findings:
  - Fever, dehydration
- Associated findings depending on etiology
  - Peripheral lymphadenopathy
  - Neoplasia elsewhere

ETIOLOGY AND PATHOPHYSIOLOGY

- Diffuse, nodular splenic enlargement (multiple masses):
  - Diffuse neoplasia (e.g., lymphoma, mast cell neoplasia)
  - Metastatic neoplasia (hemangiosarcoma, mast cell neoplasia)
- Focal splenic enlargement (single mass): hematoma, neoplasia (benign [e.g., hemangioma] or malignant [e.g., hemangiosarcoma, soft-tissue sarcoma])

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis may be suspected from signalment, history, and physical examination findings alone. Confirmation requires further diagnostic testing, notably diagnostic imaging, to determine that the mass is splenic in origin and define the underlying etiology.

DIFFERENTIAL DIAGNOSIS

Mass arising from/involving another abdominal organ:

- Liver (diffuse hepatomegaly, neoplasia [benign [e.g., hepatocellular adenoma] or malignant [e.g., hepatocellular carcinoma, hemangiosarcoma])
- Kidney
  - Neoplasia (renal adenocarcinoma, lymphoma, hemangiosarcoma)
  - Hydronephrosis
  - Cyst/polycystic renal disease
  - Perirenal pseudocyst
- Stomach: gastric dilatation/volvulus
- Abdominal cavity: omental mass
- Paraprostatic cyst

INITIAL DATABASE

Some, all, or none of these abnormalities may be present, depending on the case:

- CBC, serum biochemistry profile, urinalysis:
  - Hemorrhage (regenerative anemia, mild panhypoproteinemia)
  - Mass-associated hemolysis (schistocytosis)
  - Paraneoplastic immune-mediated hemolytic anemia (anemia, spherocytosis)
  - Involvement of other organ systems
- Survey abdominal radiographs:
  - Determine if mass appears to be arising from spleen
  - Evidence of other intraabdominal disease
  - Lymphadenopathy
- Survey thoracic radiographs:
  - Metastatic disease
  - Lymphadenopathy

ADVANCED OR CONFIRMATORY TESTING

- Ultrasound examination:
  - Confirmation of origin of mass
  - Involvement of other organs
  - Metastatic disease
  - Identification of free abdominal fluid for centesis
- Coagulation profile:
  - Hemangiosarcoma potentially can be associated with coagulation dis-orders
  - Prothrombin time, partial thromboplastin time, platelet count, antithrombin lll, fibrin degradation products, D-dimer
- Electrocardiogram (ECG):
  - Ventricular arrhythmias possible; other arrhythmias occasionally:
    - Common in dogs with splenic hemangiosarcoma
- Fine-needle aspiration cytologic analysis/needle biopsy (ultrasound guided); often contraindicated if splenic mass is highly vascular (poor diagnostic yield, and risk of rupture):
  - Benign versus malignant disease
  - Type of malignancy:
    - Primary versus metastatic
  - May be a low-yield procedure with certain malignancies (hemangiosarcoma):
    - May only obtain blood
    - Miss focus of neoplastic cells
  - Concern about seeding tumor cells throughout abdominal cavity
- Echocardiography:
  - Rule out presence of cardiac hemangiosarcoma

TREATMENT

TREATMENT OVERVIEW

Treatment of a splenic mass depends upon the etiology of the mass (surgical or nonsurgical) and whether the mass has ruptured and is causing potentially fatal intraabdominal hemorrhage (splenic hemangiosarcoma, others), requiring intensive care and immediate intervention.

ACUTE GENERAL TREATMENT

Dependent upon etiology of splenic mass:

- Nonsurgically treated splenic masses:
  - Neoplasia; lymphoma, mast cell neoplasia (dog ± cat): chemotherapy
  - Diffuse metastatic disease; hemangiosarcoma: palliative, nonsurgical treatment
- Surgically treated splenic masses (splenectomy with histopathologic examination of excised spleen):
  - Benign disease (hematoma, hemangioma)
  - Malignant disease without widespread metastasis (hemangioma, soft-tissue sarcoma)
  - Malignant disease with evidence of metastasis, as part of multimodality treatment plan: mast cell neoplasia (cat)
- Prior to splenectomy, if acute intraabdominal hemorrhage has occurred:
  - Support cardiovascular system by replacing intravascular volume and reestablishing peripheral tissue perfusion, replacing blood loss if significant, and maintaining a perfusing cardiac rhythm.
  - Definitive surgical therapy is recommended as soon after stabilization as possible.
  - Abdominal wrap/gentle abdominal pressure bandage to reduce rate of bleeding if surgery is delayed; ensure ventilation is not compromised.
- Treat any coagulation disorder:
  - Fresh frozen plasma
  - Fresh whole blood
- Correct or control cardiac arrhythmias such as premature ventricular complexes and ventricular tachycardia (see p. 1165):
  - In an anemic or hypokalemic patient, correction of these problems often resolves the ventricular arrhythmia without antiarrhythmic drugs.
  - Lidocaine:
    - 2-4 mg/kg, intravenous bolus
    - 50 mcg/kg/min continuous rate IV infusion

CHRONIC TREATMENT

- Continued supportive care in the postoperative period:
  - Intravenous fluid therapy
  - Transfusion therapy (see p. 1347)
  - Treatment of cardiac arrhythmias
- Long-term treatment dependent upon etiology of splenic mass:
  - Chemotherapy for certain types of neoplasia (lymphoma, mast cell neoplasia, hemangiosarcoma without gross metastatic disease)

DRUG INTERACTIONS

- Avoid thiobarbiturates as part of anesthetic protocol:
  - Cause relaxation of smooth muscle of the splenic capsule (red blood cell sequestration causing splenic congestions +/- increasing difficulty of removal of spleen, quantity of blood removed from patient [in spleen])
  - Potentially contraindicated if preexisting ventricular arrhythmias exist. Thiopental causes arrhythmias in approximately 40% of dogs.
- Avoid acepromazine or other phenothiazine tranquilizers as part of anesthetic protocol:
  - Cause hypotension via central mechanisms and through alpha-adrenergic actions
  - May cause cardiovascular collapse secondary to bradycardia and hypotension

POSSIBLE COMPLICATIONS

- Associated with preoperative rupture of the splenic mass:
  - Hypotension
  - Hemorrhagic/hypovolemic shock
  - Cardiovascular collapse and death

- Associated with splenectomy:
  - Hemorrhage
  - Coagulation disorders
  - Sepsis:
    - Loss of white blood cell reservoir
    - Loss of phagocytic function of spleen
- Anemia:
  - Loss of RBC reservoir
  - Decreased hematopoiesis
  - Altered iron metabolism
- Diminished immune function
- Portal vein thrombosis
  - Uncommon
- Acute onset of shock often fatal due to intestinal ischemia
- Pancreatitis:
  - Inadvertent ligation of pancreatic branch of splenic artery and vein
  - Traumatic handling or retraction of pancreas during splenectomy

RECOMMENDED MONITORING

- Postoperative patient monitoring
- Detection of ongoing hemorrhage:
  - Packed cell volume (PCV), CBC
- Maintenance of normovolemia and tissue perfusion:
  - PCV, total solids
  - Urine output
  - Blood pressure
- Continuation/development of cardiac arrhythmias (ventricular premature complexes):
  - ECG monitoring
  - Appropriate treatment, if indicated
  - See Acute General Treatment above.
- Long-term monitoring dependent upon etiology of splenic mass; may include:
  - Repeat radiographs and ultrasound examination to detect recurrence of malignancy/development of metastasis
  - Monitoring associated with adjuvant chemotherapy:
    - Periodic blood tests
    - Echocardiogram

PROGNOSIS AND OUTCOME

Dependent upon etiology of splenic mass:

- Hemangiosarcoma in dogs:
  - Most common malignant splenic neoplasm
  - Median survival time post splenectomy ranges from 10-23 weeks.
- Postsplenectomy survival times:
  - 2-month survival times: 83% if non-neoplastic disease, 31% if hemangiosarcoma
  - 12-month survival times: 64% if non-neoplastic disease, 7% if neoplastic
  - Cats with systemic mastocytosis that undergo splenectomy often have extended survival times and may be cured.
- Preoperatively, dogs with anemia, nucleated RBC, abnormal RBC morphology, or splenic rupture are more likely to have malignant splenic neoplasia. NOTE: These findings should not lead to the definitive conclusion that the splenic mass is due to malignant neoplasia.

PEARLS & CONSIDERATIONS

COMMENTS

- In the dog, a splenic mass may be a non-neoplastic (hematoma) or benign (hemangioma) or malignant (hemangiosarcoma) neoplasm. A single biopsy may result in a false-negative diagnosis. Therefore, the *entire* spleen should always be submitted for histopathologic examination.
- It can be difficult to differentiate splenic masses by their gross appearance. Therefore, a diagnosis is always based on histopathologic examination, not on gross appearance.

    - Over 50% of dogs have malignant disease, and over 40% have benign disease.
- An echocardiogram is recommended prior to splenectomy to rule out presence of primary cardiac hemangiosarcoma. The splenic hemangiosarcoma may represent metastatic disease.

CLIENT EDUCATION

- Splenic masses may rupture and cause lethal intraabdominal hemorrhage.
- Over 50% of splenic masses in the dog are malignant neoplasms.
    - Splenectomy does not extend survival time with regard to the malignancy.
    - Splenectomy prevents exsanguinations.
    - Splenectomy improves the quality of life for the patient.

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Mass, Pancreatic

BASIC INFORMATION

DEFINITION

Mass visualized in the pancreas via ultrasonography or during exploratory celiotomy; very rarely identified as an incidental finding on abdominal palpation

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs:

- Masses associated with pancreatitis: older intact or spayed females are overrepresented.
- Endocrine pancreatic neoplasia: middle-aged to older dogs are overrepresented.

Cats:

- Exocrine pancreatic neoplasia: middle-aged to older cats

RISK FACTORS: Dogs: pancreatitis-associated masses from a high-fat diet

ASSOCIATED CONDITIONS & DISORDERS: Dogs:

- Pancreatitis-associated masses:
  - Hyperadrenocorticism
  - Diabetes mellitus
  - Hyperlipidemia
  - Biliary obstruction secondary to the mass
- Exocrine pancreatic neoplasia:
  - Biliary obstruction
  - Paraneoplastic alopecia or pan-niculitis
- Endocrine pancreatic mass:
  - Insulinoma: hypoglycemia: weakness, collapse, possibly seizures
  - Gastrinoma: gastric ulceration, vomiting, melena, anemia

Cats:

- Exocrine pancreatic neoplasia:
  - Biliary obstruction
  - Paraneoplastic alopecia
- Endocrine pancreatic mass
  - Gastrinoma (rare): gastric ulceration, vomiting, melena, anemia, lethargy

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Dogs:

- Associated with pancreatitis:
  - Inflammatory/necrotic mass
  - Abscess
  - Pseudocyst
- Nodular hyperplasia
- Neoplasia (primary pancreatic): exocrine (adenocarcinoma) or endocrine (e.g., insulinoma, rarely gastrinoma)
- Metastatic or local extension of another primary neoplasm
- Icterus secondary to biliary obstruction

Cats:

- Associated with pancreatitis

- Exocrine neoplasia
- Icterus secondary to biliary obstruction
- Endocrine neoplasia (i.e., insulinoma, gastrinoma): extremely rare

HISTORY, CHIEF COMPLAINT

- Pancreatitis: vomiting, anorexia, lethargy, inappetence, diarrhea
- Exocrine neoplasia: similar but may include weight loss
- Secondary biliary obstruction: similar; some owners may also note icterus
- Endocrine neoplasia:
  - Insulinoma: weakness, lethargy, altered neurologic state
  - Gastrinoma (rare): vomiting, melena, anemia, lethargy

PHYSICAL EXAM FINDINGS

- Mass may be palpable.
- Otherwise, variable depending on etiology of pancreatic mass:
  - Pancreatitis, exocrine pancreatic neoplasia
    - Abdominal pain, dehydration, icterus, palpable abdominal mass, pyrexia
  - Endocrine pancreatic neoplasia
    - Neurologic findings associated with hypoglycemia

ETIOLOGY AND PATHOPHYSIOLOGY

- Pancreatitis (see p. 817 and 820)
- Exocrine pancreatic neoplasia: etiology unknown
- Secondary biliary obstruction: lack of bile secretion into the intestine results in a lack of digestion and absorption of fat and fat-soluble vitamins, most importantly vitamin K; development of significant coagulopathy.
- Endocrine pancreatic neoplasia: inappropriate, excessive insulin secretion leads to persistent, profound hypoglycemia (see p. 613and online chapter: Gastrointestinal Endocrine Disease).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Presenting history and physical examination findings are often nonspecific, so diagnosis is based on results from the initial database and particularly on diagnostic imaging.

DIFFERENTIAL DIAGNOSIS

- Pancreatitis: inflammation, necrosis, abscess, pseudocyst, fibrosis
- Exocrine neoplasm: adenocarcinoma
- Metastasis of another primary neoplasm to the pancreas: gastric or duodenal adenocarcinoma, leiomyosarcoma, lymphoma

INITIAL DATABASE

- CBC: inflammatory leukogram with or without evidence of inflammation (e.g., with pancreatitis): left shift, toxic neutrophil changes
- Serum biochemistry profile, urinalysis: reflect underlying disorder
  - Elevated amylase, lipase, ± bilirubin, ± liver enzyme concentrations: pancreatitis
  - Hypoglycemia: insulinoma
  - Hyperbilirubinemia, bilirubinuria: secondary biliary obstruction
- Survey abdominal radiographs:
  - Mass effect in region of pancreas: may displace duodenum laterally, pylorus cranially
  - Possible increased radiopacity in area of pancreas (pancreatitis)
  - Diffuse granular appearance to abdomen: carcinomatosis
- Survey thoracic radiographs: help rule out metastatic disease if neoplasia suspected

ADVANCED OR CONFIRMATORY TESTING

- Abdominal ultrasound examination:
  - Pancreas, morphology/echogenicity of mass:

        - Generalized inflammation of pancreas and surrounding structures: pancreatitis
        - Fluid-filled mass: pancreatic abscess (mixed echogenicity common), cyst (contents generally anechoic)
        - Solid mass (head of pancreas): exocrine neoplasia
        - Small, isolated, well-defined mass: insulinoma (hepatic metastases commonly present at time of diagnosis)
    - Evaluation of adjacent organs:
        - Extension of pancreatic disease into duodenum:
            - Inflammation
            - Neoplasia
        - Extension of duodenal disease into pancreas:
            - Neoplasia
        - Evidence of metastatic disease:
            - Regional lymph nodes
            - Liver
            - Carcinomatosis (ascites usually is also present)
    - Evidence of secondary biliary obstruction; any mass when sufficiently large:
        - Common bile duct dilation
    - Possible ultrasound-guided fine-needle aspiration (cytologic examination) or needle biopsy of pan-creatic mass:
        - Possible metastatic sites:
            - Regional lymph nodes
            - Liver
    - Suspected insulinoma:
        - Simultaneous measurement of fasting blood glucose and serum insulin concentrations, (see p. 613and p. 444).

TREATMENT

TREATMENT OVERVIEW

Treatment of this problem depends on the etiology of the pancreatic mass and typically includes intensive supportive care, surgical correction and/or nutritional support.

ACUTE GENERAL TREATMENT

Dependent on etiology of pancreatic mass but may include:

- Rehydration by IV administration of balanced electrolyte solution and possibly colloid solutions:
    - Correction of fluid deficits
    - Normalization of serum electrolyte concentrations
- Possible administration of fresh frozen plasma (see p. 1347):
    - Hypoproteinemia
    - Possible coagulopathy
- Treat hypoglycemia if present:
    - Addition of dextrose (5%) to IV fluids
    - Change of diet and feeding schedule
    - Corticosteroids
- Vitamin K administration if biliary obstruction (vitamin K1 2.5-5 mg/kg SQ or IM q 12 h for 3 days, then once weekly until obstruction relieved)
- Exploratory laparotomy:
    - Identifying pancreatic mass and extent of intraabdominal disease
    - Removing mass or performing biopsy
    - Draining and omentalizing pancreatic abscess if present
    - Performing biopsy of possible metastatic lesions
    - Correcting biliary obstruction
    - Placing feeding tube for nutritional support

NUTRITION/DIET

Animal that has pancreatitis: in patients that have undergone extensive pancreatic/duodenal resections, parenteral and enteral nutritional support should be provided postoperatively (see p. 1322and p. 1273).

POSSIBLE COMPLICATIONS

- Ongoing or recurrent pancreatitis

- latrogenically induced pancreatitis
- Persistent hypoglycemia: incomplete removal of primary tumor or functioning metastatic lesions

RECOMMENDED MONITORING

- Dependent on etiology of pancreatic mass but may include:
  - CBC and serum biochemistry profile
  - Blood glucose concentrations
  - Serum amylase and lipase concentrations
- Repeat abdominal ultrasound examination for chronological assessment:
  - Resolution or progression of pancreatic disease
  - Regrowth of pancreatic neoplasm
  - Development of metastatic disease

PROGNOSIS AND OUTCOME 

- Fair to guarded in animals with pancreatitis with or without secondary development of abscesses
- Poor in animals with malignant exocrine pancreatic neoplasia (adenocarcinoma)
- Insulinoma:
  - Persistent hypoglycemia or inability to completely resect all neoplastic disease indicates a poor prognosis.
  - Resolution of hypoglycemia or complete resection of neoplastic disease indicates a good prognosis.

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Mass, Abdominal

BASIC INFORMATION

DEFINITION

An abnormal confluence or collection of inflammatory cells, infectious organisms, or neoplastic cells within the abdominal cavity

EPIDEMIOLOGY

SPECIES, AGE, SEX: Any; based on the origin of the mass

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Variable, from overt illness to incidental discovery on routine exam
- Dependent on organ system affected and systemic involvement

PHYSICAL EXAM FINDINGS

- Specific abdominal findings may include distension, pain, palpable mass, free fluid/ballotable (fluid-wave) ascites.
- All dogs with abdominal masses require a digital rectal examination (see p. 1333).

ETIOLOGY AND PATHOPHYSIOLOGY

Variable, depending on organ system affected and systemic involvement

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on physical examination findings. Due to the extensive list of rule-outs for this problem, confirmation of the underlying etiology of the mass requires diagnostic imaging and diagnostic sampling of specimens in virtually all cases.

DIFFERENTIAL DIAGNOSIS

Common differential diagnoses for abdominal masses include:

- Spleen: malignant neoplasia (hemangiosarcoma, fibrosarcoma, chondrosarcoma, lymphoma, mastocytosis), benign neoplasia (hemangioma, lipoma), splenic abscess, splenic torsion, hematoma, splenic congestion secondary to drug administration or other toxins, mastocytosis, autoimmune disease, systemic infection/ inflammation, normal folded spleen
- Liver: malignant neoplasia (hepatocellular carcinoma, lymphoma, hemangiosarcoma, mastocytosis, etc.), benign neoplasia (biliary [cyst]adenoma, lipoma, etc.), abscess, hematoma (trauma), chronic passive congestion, regenerative nodular hyperplasia
- Lymphadenopathy: reactive versus infiltrated
- Gastrointestinal tract: malignant neoplasia (leiomyosarcoma, adenocarcinoma, etc.), benign neoplasia (adenoma, leiomyoma, etc.), foreign body, intestinal volvulus, trichobezoar, ileus, gastric dilation-volvulus, fecal material
- Granuloma: secondary to foreign body reaction (retained suture material or gauze), infectious organisms such as protozoa or fungi
- Pancreas: abscess, hemorrhagic pancreatitis, phlegmon
- Uterus: uterine torsion, pyometra, mucometra/hydrometra, pregnancy.
- Ovary: cyst, neoplasia (papillary adenoma/adenocarcinoma, granulosa cell tumor, etc.)
- Prostate: benign prostatic hypertrophy, prostatitis, prostatic abscess, prostatic cyst, paraprostatic cyst
- Testicles: neoplasm of cryptorchid testicle, torsion of cryptorchid testicle
- Urinary bladder: malignant neoplasia (transitional cell carcinoma, others), cystitis, urolith
- Kidney: malignant neoplasia (renal cell carcinoma, lymphoma, hemangiosarcoma, etc.), benign neoplasia, polycystic renal

disease, toxin ingestion (ethylene glycol), pyelonephritis, hydronephrosis, perirenal pseudocysts
- Adrenal glands: malignant or benign neoplasia (adenocarcinoma, lymphoma; adenoma)
- Peritoneal cavity and mesentery: cyst, malignant neoplasia (carcinomatosis, mesothelioma), benign neoplasia (lipoma, other)

INITIAL DATABASE

- CBC, serum biochemistry profile, urinalysis: results depend on underlying cause.
  - Avoid cystocentesis if ascites, caudal abdominal mass, or evidence of bleeding disorder.
- Urine culture and sensitivity: if involvement of urinary tract
- Survey abdominal radiographs:
  - Complementary to ultrasound; may be superior if mass is extremely large or if vertebral involvement is possible
- Abdominal ultrasound helps determine:
  - Origin of the mass
  - Texture and vascularity of the mass (fine-needle aspirate/core biopsy possible?)
  - Invasiveness of the mass/amenability to surgical removal
  - Presence of free fluid for aspiration and cytologic analysis
  - Presence of visible lesions consistent with metastasis

ADVANCED OR CONFIRMATORY TESTING

- Contrast radiographic studies of urogenital tract
- Nuclear scintigraphy (liver, renal)
- CT, MRI
- Abdominal exploratory celiotomy and tissue sampling for histopathologic examination

TREATMENT

TREATMENT OVERVIEW

Remove mass if possible.

- Rationale: pathologic discrete abdominal masses often produce one or more of the following sequelae:
  - Localized or systemic infection
  - Signs of pain or organ dysfunction (mechanical compression; see p. 4)
  - Ongoing growth and potential for metastasis or local invasion
  - Death from hemorrhage, metastasis, infection/sepsis, shock, or organ failure

ACUTE GENERAL TREATMENT

- Variable, depending on the origin of the mass
- The usual treatment of choice for pathologic discrete abdominal masses is medical stabilization of the patient (if necessary) followed by surgical removal.

CHRONIC TREATMENT

- Variable, depending on the origin of the mass
- Adjunct therapy including intravenous fluid therapy, blood products (see p. 1347), nutritional supplementation, chemotherapy, or antimicrobial medication administration may be indicated, depending on origin of mass and final histopathologic diagnosis.

POSSIBLE COMPLICATIONS

- Recurrence of infection or neoplasia
- Metastasis
- Hemorrhage
- Shock
- Weight loss, anorexia
- Peritonitis

RECOMMENDED MONITORING

Variable, depending on source of abdominal mass

PROGNOSIS AND OUTCOME

Variable, depending on source of abdominal mass

PEARLS & CONSIDERATIONS

COMMENTS

- Some normal processes (folded spleen, pregnancy) cause an abdominal mass effect and must be ruled out before proceeding to treatment.
- Some masses (including very large ones) are benign (e.g., intraabdominal lipoma), and therefore the presence of a mass does not by itself confer any particular prognosis.
- Abdominal masses may be suspected as being pathologic via careful abdominal palpation and abdominal ultrasound and, if so, are definitively diagnosed by surgical exploration and histopathologic examination.
- Nonresectable discrete masses may be treated with alternative therapies depending on the diagnosis; however, prognosis is generally poorer for a patient with a nonresectable mass.

PREVENTION

Variable, depending on the origin of the mass

CLIENT EDUCATION

- Tests including laboratory evaluation, imaging, and biopsy are necessary in most cases for definitive assessment of an abdominal mass.
- Definitive treatment and outcome for a patient with an abdominal mass are dependent on the origin of the mass, whether the mass is resectable, and if the mass is causing any systemic effects.

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Marijuana Toxicosis

BASIC INFORMATION

DEFINITION

Common toxicosis resulting from ingestion of *Cannabis sativa* and characterized by any of the following signs: central nervous system (CNS) depression, ataxia, vomiting, hypothermia, urinary incontinence, bradycardia, hyperreflexia, possibly coma and seizures.

SYNONYMS

Common street names: *Cannabis sativa,* grass, hashish, hemp (not to be confused with textile hemp, which is THC-deficient), marijuana, Mary Jane, pot, reefer, THC

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Most commonly exposed animals: dogs (96%), cats (3%), other species (1%)
- Dogs exposed are commonly under the age of 5 years.

ASSOCIATED CONDITIONS AND DISORDERS: In humans with a history of seizures, use of marijuana has been associated with lowering the seizure threshold.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- History of exposure to marijuana
- Ataxia, CNS depression, tremors, vomiting within 15 to 30 minutes of ingestion
- Specific history of exposure may be withheld by owner, owing to illicit nature of marijuana.

PHYSICAL EXAM FINDINGS

- Common:
  - Bradycardia
  - Hypothermia (body temperature: 98○F-99○F [36.7○C-37.2○C])
  - Mydriasis
  - Vomiting
  - Urinary incontinence/dribbling
  - Weakness, ataxia
- Possible:
  - Hyperesthesia
  - Hypersalivation
  - Recumbency
  - Tachycardia
  - Tremors
  - Coma

ETIOLOGY AND PATHOPHYSIOLOGY

Source:

- *Marijuana* refers to a mixture of cut and dried flowers, leaves, and stems of the leafy green hemp plant, *Cannabis sativa.* It grows in warm, moist climates or is grown artificially indoors (greenhouses) and can be rolled into cigarettes or in some cases baked into food, especially brownies.
- Exposure to marijuana in pet animals is mostly accidental, but occasionally is intentional or malicious. Sometimes drug-detection dogs ingest large amounts of marijuana accidentally.

- Marijuana is a Schedule I controlled substance commonly used as an illicit recreational drug.
- It is also used for treating nausea for chemotherapy patients and to decrease intraocular pressure in glaucoma patients. A synthetic THC is available under the trade names Marinol and Cesamet for treatment of these conditions.

Mechanism of toxicosis:

- The predominant psychoactive portion of marijuana is Δ-9-tetrahydrocannabinol (THC). THC is believed to act on a unique receptor in the brain that is selective for cannabinoids and is primarily responsible for CNS effects (ataxia and depression).
- Cannabinoids also enhance CNS formation of norepinephrine, dopamine, and serotonin and stimulate release of dopamine and enhance γ-aminobutyric acid (GABA) turnover.
- When taken orally, THC goes through substantial initial hepatic metabolism (first-pass effect). It is highly lipophilic and distributes to brain and other fatty tissues after absorption.
- Clinical signs in dogs may last 24-96 hours.
- Oral LD^{50} of THC in rats = 666 mg/kg, mice = 482 mg/kg. Clinical effects of marijuana are seen at much lower doses than this.
- Concentration of THC in marijuana varies between 1% and 8%.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Intoxication is typically suspected in one of two contexts: history of known or suspected ingestion provided by the owner or presence of typical clinical signs without such a history, as some clients may be reluctant to admit exposure or may not be aware that the agent is in their house. Exposure can be confirmed with a more thorough medical history or via a positive result when the pet's urine is evaluated with an over-the-counter illicit drug test kit. A low rate of life-threatening intoxications means a test kit may be obtained at some point during the first few hours of treatment/observation if definitive confirmation is needed (e.g., uncertain history).

DIFFERENTIAL DIAGNOSIS

Toxicologic:

- Ethylene glycol toxicosis
- Macadamia nut toxicosis
- Ivermectin toxicosis
- Other CNS depressants such as benzodiazepines, barbiturates

Spontaneous, Nontoxicologic:

Overall, the onset of clinical signs can mimic metabolic or toxic CNS disorders, but acute decompensation of primary CNS diseases (e.g., granulomatous meningoencephalitis, neoplasia, others) is possible, especially in an animal that is not closely observed by its owner. A sudden onset of signs, with near-complete resolution and no recurrence all within 24 hours, makes intoxication much more likely than these nontoxicologic diagnoses.

INITIAL DATABASE

- Arterial blood pressure (normal or below normal; normal [systolic] >120 mm Hg in clinical setting)
- CBC, serum biochemistry panel, urinalysis (to assess for preexisting conditions): no significant changes expected

ADVANCED OR CONFIRMATORY TESTING

- Over-the-counter illicit drug test kits (urine) may help confirm exposure during the early course of exposure. Caution: such kits have not been validated in dogs, and some do not appear to be accurate; a negative result does not preclude exposure.
- Rapid analysis at human hospital labs is also an option for confirmation.

TREATMENT

TREATMENT OVERVIEW

Treatment goals are early decontamination (induction of emesis and administration of activated charcoal) of the patient, correcting hypothermia, and providing supportive care. In a patient showing no clinical signs and presenting more than 1 hour after possible

ingestion, treating with activated charcoal only and monitoring for onset of signs, without further treatment if no signs emerge, is acceptable.

ACUTE GENERAL TREATMENT

- Decontamination of the patient:
  - Emesis: can be induced within 15-30 minutes of exposure as long as no overt clinical signs of toxicosis are present. Use hydrogen peroxide at 2.2 mL/kg PO; max 45 mL. Repeat once if emesis does not occur first time.
  - Apomorphine: not likely to work as an emetic because of the strong central antiemetic effect of marijuana
  - Activated charcoal: very beneficial. Indicated when emesis is absent in patients with or without clinical signs. In patients with clinical signs or large ingestions, multiple doses can be used every 8 hours to reduce enterohepatic recirculation; 1-3 g/kg or labeled dosage of commercial products. Caution: risk of hypernatremia when using repeated doses of charcoal products containing a purgative (e.g., Toxiban)
- Supportive care:
  - IV fluids as needed for dehydration, hypovolemia
  - Thermoregulation (heating pads for hypothermia)
  - Monitor cardiovascular function. Atropine, 0.022-0.044 mg/kg IM or SQ can be given for bradycardia in normotensive patients.
  - Control tremors with diazepam at a low dose of 0.25 mg/kg IV.
  - Monitor for signs of aspiration pneumonia in recumbent animals. Pass cuffed endotracheal tube if needed, ensuring a mouth gag/speculum is also used in order to avoid the patient biting and transecting the tube when recovering.
  - Control severe vomiting with metoclopramide, 0.2-0.4 mg/kg q 6 h PO, SQ, or IM; or maropitant, 1 mg/kg SQ or 2 mg/kg PO q 24 h, once ingested material has been expelled.

DRUG INTERACTIONS

Other CNS depressants (barbiturates, benzodiazepines) may exacerbate signs.

RECOMMENDED MONITORING

- Heart rate
- Blood pressure
- Body temperature

PROGNOSIS AND OUTCOME

- Excellent with treatment
- Fatalities are extremely rare.

PEARLS & CONSIDERATIONS

COMMENTS

- Until proven otherwise, a dog presenting with acute-onset ataxia, CNS depression, and urinary incontinence that improves with stimulation and then gets worse again with decreased stimulation should be considered suspect of marijuana ingestion.
- Marijuana may be mixed with other substances for smoking (e.g., phencyclidine [PCP]) which may alter the patient's signs.

TECHNICIAN TIP

Some owners may mention the possibility of this type of drug exposure in the veterinarian's absence (due to embarrassment, oversight, or fear of consequences). If the client raises the possibility with any member of the technical staff, this valuable piece of information could determine the course of treatment and the patient's outcome and therefore should be mentioned to the attending veterinarian.

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Mammary Gland Neoplasia, Dog

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Mammary gland tumors are benign or malignant neoplasms arising from mammary tissue.

SYNONYMS

Mammary cancer, breast cancer Benign mammary tumors:

- Adenoma/cystadenoma (very common)
- Benign mixed mammary tumor (very common)
- Fibroadenoma (uncommon)

Malignant mammary tumors:

- Adenocarcinoma/cystadenocarcinoma (common)
- Carcinoma (common)
- Inflammatory carcinoma (uncommon)
- Malignant mixed mammary tumor (uncommon)
- Carcinosarcoma (rare)
- Sarcoma (uncommon)

Note: Different pathologic classification schemes exist.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Mammary gland tumors are the most common tumor in female dogs, according to some surveys.
  - Incidence ~ 2:1000.
  - Due to the common practice of early-age ovariohysterectomy (OHE), the incidence has decreased in the United States. In European countries, mammary tumors represent 40%-50% of all tumors in female dogs.
- Greater prevalence with older age; median age 10-11 years
- Mammary gland tumors in male dogs are uncommon (approximately 1% of mammary tumors occur in males).

GENETICS & BREED PREDISPOSITION

- Breeds at increased risk include:
  - Spaniel breeds
  - Pointer breeds
  - Poodles
  - Dachshunds
  - German shepherds
  - Yorkshire terriers
- A genetic factor in the development of mammary tumors seems to be present; however, a specific, common mutation has not been identified. The following genes have been found to be mutated in select canine mammary gland tumors:
  - p53
  - c-erb-2 (Her-2/neu)
  - BCRA 1, 2

RISK FACTORS

- Timing of OHE: the relative risk for developing mammary gland tumors:
  - 0.5% if OHE is performed before the first estrus
  - 8% if OHE is performed between the first and second estrus
  - 26% if OHE performed between the second and third estrus

- Intact females and females neutered after 2 years of age have a sevenfold greater risk of mammary neoplasia compared to those neutered before age 6 months.
- Body condition/diet: reduced risk in dogs with lean body condition at age 9-12 months
- Progesterone treatment: increases the risk for the development of benign and malignant mammary tumors.
- Pregnancy, lactation, pseudopregnancy:
  - Unlike people, pregnancy does not afford a protective effect against the development of mammary tumors in dogs.
  - Lactation and pseudopregnancy also do not seem to have an influence.

ASSOCIATED CONDITIONS & DISORDERS: Ovarian cysts, cystic endometrial hyperplasia

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Clinical staging:
  - Tumor: T1, <3 cm; T2, 3-5 cm; T3, >5 cm
  - Regional lymph node: N0, no metastasis; N1, metastasis detected
  - Distant metastasis: M0, no metastasis; M1, metastasis detected
- Histologic staging:
  - 0 Without stromal invasion
  - I With stromal invasion
  - II With neoplastic emboli in vessels

Stage Grouping	T	N	M
I	T1	N0	M0
II	T2	N0	M0
III	T3	N0	M0
IV	T1-3	N1	M0
V	T1-3	N0, N1	M1

HISTORY, CHIEF COMPLAINT

- Owners may note a swelling, “lump,” or ulceration in their dog's mammary chain, or these may be incidental findings on routine physical examination.
- Duration of clinical signs is highly variable, ranging from days to months.
- In cases of metastasis or inflammatory carcinoma, dogs may be presented due to general signs of illness or specific complaints attributable to a certain site of metastasis (e.g., lameness in cases of bone metastasis).

PHYSICAL EXAM FINDINGS

- Variable depending on extent and stage of the disease
- Single or multiple nodules may be present. Multiple tumors are common in dogs, and both mammary chains may be affected. Multiple tumor types are common.
- Signs of malignancy include fixation to skin or underlying structures, rapid increase in size, ill-defined borders, ulceration, pain, inflammation or edema.
  - Absence of these signs does not exclude malignancy.
- Inflammatory carcinomas present with diffuse, firm, and painful swelling of the affected gland or chain. The adjacent extremity may be affected. Cutaneous involvement in form of small beadlike nodules may also be found.
- Regional lymph nodes (inguinal and axillary) may be enlarged (due to metastasis or reactive hyperplasia) or normal on palpation. The internal iliac, popliteal, and prescapular nodes may also be affected.

ETIOLOGY AND PATHOPHYSIOLOGY

- Estimates of malignancy rates range from 30%-50%.
- Metastasis most common to the regional lymph nodes and lungs
- Tumors are classified according to their tissue of origin into epithelial, mesenchymal, and mixed tumors.
  - Inflammatory carcinoma is not a specific histologic subtype but an aggressive high-grade carcinoma with invasion into the dermis and dermal lymphatics. The inflammatory cell infiltrate is moderate in most cases and consists of lymphocytes, plasma cells, and macro-phages.

- Primary mesenchymal mammary tumors (e.g., fibrosarcoma, osteosarcoma) are infrequent. Malignant mesenchymal mammary tumors often behave aggressively, with frequent metastasis and a short survival.
- Mixed mammary tumors consist of epithelial, myoepithelial, and mesenchymal tissue. Most mixed mammary tumors are benign. Malignant mixed mammary tumors and carcinosarcomas are rare exceptions.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on the presence of a mass in the mammary chain. Histologic evaluation is required for definitive diagnosis which is usually obtained from an excisional biopsy.

DIFFERENTIAL DIAGNOSIS

- Mastitis
- Other cutaneous and subcutaneous tumors
- Inguinal/axillary lymphadenopathy (reactive, neoplastic)
- Inguinal hernia

INITIAL DATABASE

- Physical examination:
  - Measure primary tumor (T)
  - Describe possible signs of invasiveness (ulceration, fixation)
  - Evaluation of regional lymph nodes (N): palpation and cytologic study
- Thoracic radiographs (three views)
- Abdominal ultrasound in case of suspected metastasis to abdominal organs or lymph nodes
- CBC, serum biochemistry profile, urinalysis
- Coagulation profile in cases of suspected inflammatory carcinoma (risk of disseminated intravascular coagulation)

ADVANCED OR CONFIRMATORY TESTING

- Excisional biopsy of the tumor and thorough histologic examination are necessary to obtain a definitive diagnosis.
- Fine-needle aspiration cytology is *not* recommended:
  - Poor differentiation between malignant and benign mammary tumors, owing to their heterogeneous composition
- Incisional biopsy also may not represent the whole tumor and is not recommended.
- Lymph node metastasis: fine-needle aspiration and cytologic evaluation of lymph nodes has been shown to increase diagnostic accuracy of mammary tumor metastasis. Metastases may be present in palpably normal nodes.
- Advanced imaging (CT, MRI) may be more sensitive to detect metastatic lesions in the thoracic and abdominal cavities and should be considered in cases in which metastasis is strongly suspected but cannot be detected on radiographs or ultrasound.

TREATMENT

TREATMENT OVERVIEW

Treatment consists of complete surgical removal of the mammary tumor(s). The role of chemotherapeutics to delay the onset of metastatic disease has not been well defined in dogs. For dogs with inoperable tumors or inflammatory carcinomas, palliation with piroxicam or other antiinflarnmatory medications may improve quality of life.

ACUTE GENERAL TREATMENT

- Mainstay of treatment is surgical excision of the mammary tumor(s) with wide margins (at least 2 cm in all planes if possible).
- Type of surgery (nodulectomy, regional or radical mastectomy) depends on the size, location, and number of tumors present.
  - Type of surgery does not influence survival so long as the entire tumor is removed with histologically clean margins.
- Lumpectomy possible for freely move-able tumors <5 mm but increases risk of local recunence of carcinoma.
- Simple or radical (block or unilateral chain resection) mastectomy: both increase disease-free interval.
- Unilateral radical chain mastectomy will decrease the chances of tumor development in the remaining mammary tissue. In one study, 58% of dogs that underwent a regional mastectomy for a solitary mammary tumor developed a new tumor in the ipsilateral mammary chain after the first surgery.

- Removal of inguinal lymph node with caudal gland tumors; excise axillary nodes only if metastasis is suspected.
- Inflammatory carcinoma is nonresectable; palliative surgery may be possible in select cases.

CHRONIC TREATMENT

- Chemotherapy: limited information available
  - Antitumor activity has been demonstrated in vitro, in select patients with gross metastatic disease, and as adjuvant treatment in a small group of dogs with advanced-stage disease. High-risk patients may therefore benefit from adjuvant chemotherapy.
  - Chemotherapeutics studied for monotherapy include doxorubicin (30 mg/m^2 IV), 5-fluorouracil (150 mg/m^2 IV), cyclophosphamide (200 mg/m^2 IV), and platinum compounds (cisplatin, 50-70 mg/m^2 IV plus saline diuresis; carboplatin, 250-350 mg/m^2 IV). Special handling requirements and potentially severe, life-threatening adverse patient effects exist for these drugs.
  - Consultation with an oncologist for the most current treatment recommendations is indicated.
- OHE at time of mammary tumor surgery: benefit is controversial, with some studies reporting increased survival and others showing no difference.
- Radiation therapy: limited information available. May be of use in the palliative setting or to improve local control in inoperable cases.
- Antiestrogen therapy (tamoxifen): not recommended. Most anaplastic mammary tumors lack estrogen receptors, so antiestrogen therapy may not be beneficial for most cases in which systemic therapy is indicated. In addition, estrogen-like side effects including vulvar swelling, vaginal discharge, stump pyometra, signs of estrus, and urinary tract infection may occur in dogs treated with antiestrogen drugs.
- Pain medication: analgesics should be considered in the palliative treatment of advanced stage disease or inflammatory carcinoma. Options include nonsteroidal antiinflammatories (including carprofen, 2 mg/kg PO q 12 h; or etodolac, 10-15 mg/kg PO q 24 h; or deracoxib, 1-2 mg/kg PO q 24 h; or meloxicam, 0.1 mg/kg PO q 24 h; or piroxicam, 0.3 mg/kg q 24 h).

POSSIBLE COMPLICATIONS

See Chemotherapy: Adverse Reactions, p. 188.

RECOMMENDED MONITORING

Regular examination of surgical site and local lymph nodes: radiology or other imaging techniques if indicated (e.g., diagnosis of malignancy, respiratory signs, other signs suggestive of internal metastasis)

PROGNOSIS AND OUTCOME

- Dogs with benign mammary tumors are cured by surgical excision so long as histologically clean margins are achieved.
- Prognosis for dogs with malignant mammary gland tumors is extremely variable and ranges from a cure with surgery (especially low-grade malignancy) to rapid recurrence and metastasis within the first year after surgical excision. Prognostic factors include:
  - Tumor size: tumors <3 cm have a better prognosis than tumors >3 cm.
  - Tumor histologic characteristics
    - Epithelial tumors (adenocarcinomas, cystadenocarcinomas. carcinomas) may have a better prognosis than sarcomas, malignant mixed tumors, and carcinosarcoma. Median survival = 6.5 months (solid carcinoma), 12 months (invasive tumor), 29 months (noninvasive tumor), 10 months (sarcoma), 18 months (carcinosarcoma).
    - Inflammatory carcinomas have a grave prognosis.
    - Anaplastic and high-grade, invasive tumors with stromal or lymphatic or vascular infiltration carry a worse prognosis than well-differentiated low-grade or noninvasive lesions.
  - Clinical stage: a worse prognosis is associated with:
    - Large tumors (stages II-V)
    - Lymph node involvement (stages IV-V)
    - Distant metastasis (stage V)
- Disease-free interval of 24 months for malignant tumors = 27%-55%.

PEARLS & CONSIDERATIONS

COMMENTS

- Canine mammary tumors represent a heterogeneous group of tumors with different prognoses.

- Multicentric mammary tumors occur in >50% of affected dogs; multiple tumor types occurring concunently or sequentially are common.
- Highest-risk patients that will benefit most from postoperative adjuvant chemotherapy still need to be identified. These may include patients with advanced clinical stages (II-V), histologic evidence of vascular/lymphatic invasion, and/or high degree of anaplasia on histopathologic evaluation.
- The benefit of OHE at the time of mammary tumor surgery remains controversial, but a subset of dogs with differentiated estrogen receptor-positive tumors may indeed benefit from concurrent OHE.

PREVENTION

OHE at age <6 months is not preventive but will significantly reduce risk.

CLIENT EDUCATION

- Early age OHE of bitches not intended for breeding
- Regular examination of the mammary chain
- Prompt presentation for veterinary examination if abnormalities are found

SUGGESTED READING

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Mammary Gland Neoplasia, Cat

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Mammary gland tumors are benign or malignant neoplasms arising from mammary tissue.

SYNONYM

Mammary cancer, mammary tumor Specific mammary neoplasms:

- Adenocarcinoma
- Adenoma/cystadenoma
- Carcinoma
- Duct papilloma
- Fibroadenoma
- Inflammatory carcinoma

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Mammary gland tumors represent less than 20% of all tumors in female cats.
- Incidence ≅0.25:1000.
- Mean age is 10-12 years. Males may be slightly older, with a mean age of 12.8 years.
- Most common: malignant epithelial carcinoma/adenocarcinoma (female), mammary carcinoma (male)
- Mixed mammary tumors and sarcomas are extremely rare to nonexistent.
- Siamese cats may develop mammary tumors at an earlier age than other cats.
- Mammary tumors are rare in male cats (1%-2% of feline mammary carcinomas).

GENETICS & BREED PREDISPOSITION

- Siamese cats have a twofold risk of developing mammary gland tumors and have a higher incidence of malignant tumors with lymphatic invasion.
- Persian cats may have a higher incidence of benign mammary tumors.
- A genetic factor in the development of mammary tumors has not been identified. The following oncogenes have shown abnormal expression in select feline mammary gland tumors:
    - p53
    - Her-2 (neu/c-erb-2)

RISK FACTORS: Hormonal factors:

- Ovariohysterectomy (OHE) reduces the risk of developing mammary tumors.
    - OHE < 6 months: 91% risk reduction compared with intact cats
    - OHE 7-12 months: 86% risk reduction compared with intact cats
    - OHE 13-24 months: 11% risk reduction compared with intact cats
    - OHE > 2 years: no benefit
- Treatment with progesterone and estrogen/progesterone combinations is associated with a threefold increased risk of development of benign and malignant mammary tumors in cats (progesterone treatment: 36% of male cats with mammary carcinoma).

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Clinical staging:

- Tumor: T1: <2 cm; T2: 2-3 cm; T3: >3 cm
- Regional lymph node: N0, no metastasis; N1, metastasis detected
- Distant metastasis: M0, no metastasis; M1, metastasis detected

Stage Grouping	T	N	M
I	T1	N0	M0
II	T2	N0	M0
III	T1, T2	N1	M0
	T3	N0, N1	M0
IV	T1-3	N0, N1	M1

HISTORY, CHIEF COMPLAINT

- A swelling, “lump,” or often ulcerated tissue may be noted in a cat's mammary chain.
- In cases of metastasis or inflammatory carcinoma, cats may be presented for general signs of illness or specific complaints attributable to a certain site of metastasis (e.g., dyspnea due to pulmonary metastases or pleural effusion).
- Duration of clinical signs is variable, ranging from a few days to several months.

PHYSICAL EXAM FINDINGS

- Clinical signs vary depending on extent and stage of disease.
- More than 50% of cats will have more than one mammary tumor present, and both mammary chains may be affected simultaneously.
- Tumors may be firm on palpation and occasionally fixed to underlying structures.
- Discrete to infiltrative, soft to firm swelling within mammary gland or overlying skin is most common.
- Ulceration is frequently present.
- Can have associated discharge from nipple.
- Regional lymph nodes (inguinal and axillary) may be enlarged or normal on palpation.
- Lymph node enlargement can indicate metastasis or reactive change secondary to inflammation.
- Inflammatory carcinomas occur rarely in cats after mastectomy for mammary carcinoma. These cats present with local erythema, edema, pain, and involvement of the extremities.

ETIOLOGY AND PATHOPHYSIOLOGY

- The vast majority (85%-93%) of feline mammary tumors are malignant, with more than 80% of feline mammary tumors classified as adenocarcinoma.
    - Metastasis is common (61%). Preferred sites of metastasis include the lungs (76%), pleura (40%), and lymph nodes (27% or more).
- Inflammatory carcinomas occur rarely in cats after mastectomy for mammary carcinoma.
    - These are aggressive anaplastic carcinomas with considerable inflammatory cell infiltrate, intradermal and dermal lymphatic invasion that leads to edema, pain, and rapid metastasis.
- Benign tumors including adenomas, fibroadenomas, and duct papillomas occur uncommonly in cats.

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on the presence of a mass in the mammary chain. Histologic evaluation is required for definitive diagnosis which is usually obtained from an excisional biopsy.

DIFFERENTIAL DIAGNOSIS

- Fibroepithelial hyperplasia: involves multiple glands, most often in young intact females and spayed females given progesterone compounds
- Mastitis
- Other cutaneous and subcutaneous tumors
- Inguinal/axillary lymphadenopathy (reactive, neoplastic)
- Inguinal hernia
- Enlarged inguinal fat pad

INITIAL DATABASE

- Physical examination:
  - Measure primary tumor (T)
  - Describe possible signs of invasiveness (ulceration, fixation)
  - Evaluate regional lymph nodes (N): palpation and cytologic analysis
- Thoracic radiographs (three views) for pulmonary metastasis
- Abdominal ultrasound in case of suspected metastasis to abdominal organs or lymph nodes
- Fine-needle aspiration and cytologic evaluation are of limited utility and generally not recommended. Although seemingly more accurate than in dogs, feline mammary mass aspirates often are not representative of the entire mass, and cytologic criteria of malignancy are not correlated to histologic findings nor clearly defined.
- CBC, serum biochemistry profile, urinalysis, coagulation profile in cases of suspected inflammatory carcinoma

ADVANCED OR CONFIRMATORY TESTING

- Definitive diagnosis is via biopsy and histopathologic evaluation of mammary masses
  - Histologic grading scheme is based primarily on mitotic activity, areas of necrosis, and degree of infiltration into soft tissue and vasculature.
  - Because >85% of feline mammary tumors are malignant, histopathologic examination most often is performed on tumor tissue obtained from a radical mastectomy.
  - When fibroepithelial hyperplasia (see Differential Diagnosis above) or other nonmammary tumors are suspected, incisional (wedge) biopsies may be done.
- Lymph node evaluation:
  - In general, the ipsilateral inguinal lymph node should be removed during radical mastectomy and assessed histopathologically.
  - Axillary lymph nodes may be difficult to isolate, but fine-needle aspiration or biopsies can be done if they are enlarged.
- Distant metastasis:
  - Cytologic evaluation of pleural effusion can aid in the diagnosis of thoracic metastatic disease.
  - Advanced imaging (CT, MRI) may increase diagnostic accuracy of metastatic lesions in the thoracic and abdominal cavities.

TREATMENT

TREATMENT OVERVIEW

Treatment consists of complete surgical removal of the mammary tumor(s). The recommended surgical approach for cats is radical mastectomy. Adjuvant chemotherapy is advised for cats with poor prognostic factors, although the true survival benefit is not known.

ACUTE GENERAL TREATMENT

- Surgery:
  - Radical mastectomy of the affected mammary chain(s) is recommended.
  - In contrast to individual mastectomies or lumpectomies, radical mastectomy significantly reduces the risk for local tumor recurrence.
  - Affected lymph node(s) should be removed along with mammary chain.
  - Fixation of the tumor to underlying muscle or fascia necessitates en bloc removal of these structures.
  - In cats with advanced metastatic disease, local mastectomy to remove ulcerated or infected mammary tumors may be palliative.
  - Inflammatory carcinoma is nonresectable.

CHRONIC TREATMENT

- Chemotherapy:
  - Single-agent doxorubicin, doxorubicin in combination with cyclophosphamide or single-agent carboplatin may lead to complete and partial responses in cats with metastatic disease or nonresectable mammary gland tumors.
  - Adjuvant chemotherapy using the previously mentioned drugs as single agents or in combination is recommended in cats after radical mastectomy. However, a true survival benefit has yet to be proven.
  - Consultation with an oncologist for the most current treatment recommendations is indicated.
- Radiation therapy:
  - Radiation to palliate nonresectable disease may be an option in some cats.
- Immunotherapy:
  - Treatment with levamisole, bacterial vaccines, and other immunomodulators has not led to any improvement in local tumor control or survival.
- Analgesics:

- Analgesics should be used in cats that present with advanced disease.

POSSIBLE COMPLICATIONS

Inflammatory carcinoma after mastectomy for mammary carcinoma: rare

RECOMMENDED MONITORING

Regular examination of surgical site, local lymph nodes, lung fields

PROGNOSIS AND OUTCOME

- Local recurrence rate: 51%-66% (female), 45% (male)
- Prognostic factors for cats with mammary gland carcinomas:
  - Tumor size:
    - >3 cm: median survival of 4-6 months (female), 1.6 months (male)
    - 2-3 cm: median survival of 1-2 years (female), 5.2 months (male)
    - <2 cm: median survival of >3 years after mastectomy (female), 14 months (male)
  - Type of surgery:
    - Radical mastectomy significantly reduces the risk for local tumor recurrence compared with conservative surgery but does not appear to improve survival time. o Degree of histologic differentiation: high grade is associated with a shorter survival time.
  - Other unfavorable prognostic factors include old age of the cat and incomplete surgical excision.
- Benign tumors and low-grade malignant tumors may be cured by wide excision.

PEARLS & CONSIDERATIONS

COMMENTS

- Mammary carcinoma in the cat is a highly malignant neoplastic disease that warrants early diagnosis and an aggressive treatment approach.
- Adjuvant chemotherapy should be considered in cats with resectable mammary carcinoma after radical mastectomy.
- In cats with advanced disease, palliative measures including surgery, chemotherapy, radiation, and analgesics may be considered.

PREVENTION

- Ovariohysterectomy before age 6 months reduces the risk but will not prevent mammary carcinoma in female cats.
- Castration does not prevent mammary carcinoma in male cats.

CLIENT EDUCATION

- Early ovariohysterectomy of queens not intended for breeding
- Regular examination of the mammary chain
- Prompt presentation for veterinary examination when abnormalities are found

SUGGESTED READING

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Mammary Disorders, Non-Neoplastic

BASIC INFORMATION

DEFINITION

- Mastitis: inflammation of the mammary gland, usually septic; blood-milk barrier not intact
- Mammary hyperplasia: aseptic noninflammatory enlargement of mammary glands

SYNONYMS

Mammary hyperplasia, fibroadenomatous mammary hyperplasia, benign feline mammary hyperplasia

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Mastitis: more common in the postpartum bitch than the bitch with overt false pregnancy or the postpartum queen. Occasionally occurs in spayed bitches. Older bitches may be at greater risk (unverified).
- Mammary hyperplasia: usually young intact cats or pregnant queens

GENETICS & BREED PREDISPOSITION: Mastitis: short-legged breeds and dogs with pendulous mammary glands have greater risk of trauma.

RISK FACTORS

- Mastitis: poor hygiene, trauma (environmental or secondarily to puppies nursing), infections from other sites in the body
- Mammary hyperplasia: young intact cats, pregnant queens or cats with false pregnancy. Cats of either sex with recent gonadectomy. Cats of either sex receiving exogenous progestogen treatment.

GEOGRAPHY AND SEASONALITY: Mammary hyperplasia: spring when queens cycle; incidence is 40%-50% post ovulation in cats with false pregnancy.

ASSOCIATED CONDITIONS & DISORDERS

- Mastitis:
  - Bitches and queens with secondary septicemia from other infections may have hematogenous spread to mammary tissue.
  - Galactostasis following weaning or overt pseudopregnancy
  - Benign mammary hyperplasia in queens
  - May be associated with mammary neoplasia
- Mammary hyperplasia:
  - Secondary mastitis and/or necrosis
  - Conditions which may result in treatment with exogenous progestogens

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Mastitis: acute, fulminate or chronic, near subclinical
- Mammary hyperplasia: acute

HISTORY, CHIEF COMPLAINT

- Mastitis:
  - Lactating bitch or queen
    - Uncomfortable dam may or may not want to nurse puppies; neonates do not nurse (crying puppies or kittens)
  - Rarely, pseudopregnant bitch
- Mammary hyperplasia: acute enlargement of mammary glands

PHYSICAL EXAM FINDINGS

- Mastitis:
  - Firm, warm, swollen, often painful mammary gland (one or more)
  - Lethargy
  - Dehydration
  - May be possible to express purulent or discolored milk from gland
  - Gland may abscess, become gangrenous, and rupture.
  - +/− Fever
  - May progress to septic shock
- Mammary hyperplasia
  - Enlarged mammary glands
  - All glands usually involved
  - Can be painful
  - Can develop necrosis

ETIOLOGY AND PATHOPHYSIOLOGY

- Mastitis
  - Possible ascending infection from poor environmental hygiene or traumatic injury from nursing offspring
  - Incidence highest in stimulated mammary glands; may be due to presence of abundant substrate (milk), open ducts, trauma from nursing, and increased trauma because glands are enlarged
- Mammary hyperplasia
  - Hormonally induced condition
    - Hormones include progesterone, growth hormone, and prolactin.
    - Key: high progestogen concentrations, either endogenous or exogenous

DIAGNOSIS

DIAGNOSTIC OVERVIEW

History and physical examination are generally sufficient to formulate a diagnosis: enlarged, painful mammary glands (usually during lactation) in mastitis patients, or rapidly enlarged nonseptic mammary glands in cats with mammary hyperplasia.

DIFFERENTIAL DIAGNOSIS

- Mammary adenocarcinoma (inflamed or septic) usually in older females with no concurrent lactation (see pp. 690 and 692)
- Galactostasis: dam not ill, nonseptic

INITIAL DATABASE

- CBC in mastitis unremarkable or leukocytosis with left shift; if acute sepsis, leukopenia is possible. CBC in mammary hyperplasia normal.
- Cytologic examination of mammary secretions: in mastitis, many toxic neutrophils; in mammary hyperplasia, normal
- Mastitis: pH of mammary secretions will help determine which antibiotic to use.

ADVANCED OR CONFIRMATORY TESTING

- Bacterial culture and sensitivity of mammary secretions
- Biopsy of mammary tissue (to rule out neoplasia and benign mammary hyperplasia)

TREATMENT

TREATMENT OVERVIEW

Goals of treatment are returning the patient to normal mammary function and preventing septicemia. For mammary hyperplasia: prevention of mastitis.

ACUTE GENERAL TREATMENT

- Mastitis:
  - If mammary necrosis is present or milk is too contaminated for puppies and kittens, offspring should be removed and the necrotic tissue surgically drained and débrided.
    - Signs include milk that is grossly purulent, malodorous, or markedly discolored, or hungry neonates that are not nursing on their own or are developing diarrhea, vomiting, or losing weight.
  - Antiprolactin therapy may be administered to stop lactation (cabergoline, 5 mcg/kg PO q 24 h; response usually seen within 3-4 days; over 80% response by day 7).
  - Systemic antibiotic treatment of the dam is required. General guidelines are initially based on Gram stain and on whether neonates are still nursing; subsequently use culture and sensitivity results for definitive treatment. The therapeutic goal is to achieve significant antibiotic concentrations in the milk.
  - While awaiting culture results, the choice of antibiotic for initial empirical treatment is limited (e.g., cefadroxil, 22 mg/kg PO q 8 h or amoxicillin-clavulanic acid 12.75 mg/ kg PO q 12 h) if the dam's offspring continue to nurse.
  - Nursing puppies and kittens can be negatively affected by antibiotic concentrations in the dam's milk.
    - Recommendations for nursing dam:
      - Aerobic bacteria:
        - Gram-negative: cefoxitin, 30 mg/kg IV q 6 h; or chloramphenicol, 40 mg/kg PO q 8h
        - Gram-positive: first-generation cephalosporins (e.g., cefadroxil, 22 mg/kg PO q 8 h; or erythromycin, 10-20 mg/ kg PO q 8 h)
      - Anaerobic bacteria: erythromycin, cefoxitin, chloramphenicol
        - *Mycoplasma:* erythromycin, chloramphenicol
    - Recommendations for dam not nursing neonates:
      - Aerobic bacteria:
        - Gram-negative: quinolones (e.g., enrofloxacin, 5 mg/kg PO q 12 h [5 mg/kg PO q 24 h in cats]), or second- or third-generation cephalosporins (e.g., cefoxitin)
        - Gram-positive: first-generation cephalosporins, amoxicillin/clavulanic acid, or erythromycin
      - Anaerobic bacteria:
        - Penicillin (e.g., procaine penicillin G, 20,000 IU/kg IM or SQ q 12-24 h); metronidazole (15 mg/kg PO q 12 h); clindamycin (5-11 mg/kg PO q 12 h); erythromycin or cefoxitin
        - *Mycoplasma:* tetracyclines (e.g., doxycycline, 5 mg/kg PO q 12 h), erythromycin, or quinolones.
  - Warm packing and ongoing nursing. Unless the gland is necrotic, continued nursing by the offspring and warm packing the affected glands will prevent galactostasis and promote drainage.
- Mammary hyperplasia:
  - Progesterone withdrawal
  - Usually self-limiting in 2-3 weeks
  - If sexually intact, ovariectomy or ovariohysterectomy recommended
  - Pain control
  - Medical therapy
    - Progesterone receptor blocker: aglepristone (15 mg/kg SQ q 24 h × 2 days or 20 mg/kg SQ once). Note: not approved for use in cats in the United States; will abort pregnant cats.
    - Prolactin inhibitor: bromocriptine mesylate (0.25 mg per cat PO q 24 h × 5-7 days. Note: not approved for use in cats in the United States; will abort pregnant cats.
    - Androgens: testosterone enanthate or testosterone cypionate (2 mg/ kg IM once). Note: not approved for use in cats in the United States.

CHRONIC TREATMENT

Mastectomy

BEHAVIOR/EXERCISE

Limit activity which might induce mammary trauma. This may include weaning puppies and kittens.

DRUG INTERACTIONS

Antiprolactinics will stop lactation. Some antibiotics are contraindicated in lactating bitches. Aglepristone is abortifacient in the cat.

POSSIBLE COMPLICATIONS

Systemic antibiotic therapy in lactating dams may interfere with normal bacterial colonization of gastrointestinal flora in nursing neonates, resulting in diarrhea.

RECOMMENDED MONITORING

- Temperature, respiration and heart rate

- Physical signs of septicemia
- Offspring that are nursing: weigh daily to determine adequate milk intake.

PROGNOSIS AND OUTCOME

Prognosis is generally good unless sepsis occurs.

PEARLS & CONSIDERATIONS

COMMENTS

- Neonates 4½ to 5 weeks old should be allowed access to dam's food, and the bitch or queen should have an area where she can remove herself from the neonates (e.g., top of crate, raised platform).
- Neonates will then start eating solid food for a portion of their caloric intake, decreasing the amount of time they are nursing on the mother. Additionally benefits the dam by greatly reducing her metabolic requirements.
- Older neonates with teeth nurse more aggressively and can induce both bite and nail trauma to the mammary gland, greatly increasing the risk of inflammation and infection.
- Frequently, chronic mastitis has been suspected when neonates fail to thrive. However, subclinical mastitis has not been demonstrated in dogs and cats.

PREVENTION

- Adequate husbandry, particularly clean bedding for mother and offspring
- Keep mammary glands clean, monitor glands for trauma from neonate's claws or teeth.
- Clipping neonates' toenails
- Mammary hyperplasia: limit the clinical use of exogenous progestogens.

CLIENT EDUCATION

Primarily husbandry issues of proper hygiene and weaning instructions.

SUGGESTED READING

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Malocclusion

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

An abnormal position of the teeth. In dental malocclusion, one or several teeth is/are in an abnormal position, whereas in skeletal malocclusion there is an upper/lower jaw discrepancy.

SYNONYM

Malalignment of teeth

EPIDEMIOLOGY

SPECIES, AGE, SEX: Malocclusion can be seen in all species, all age groups, and is usually present from the time of eruption of the deciduous or permanent dentition.

GENETICS & BREED PREDISPOSITION: Occlusal development is determined by genetic and environmental factors. Most brachycephalic cats and dogs show malocclusion due to a shortened upper jaw.

RISK FACTORS

- Persistent deciduous teeth
- Facial trauma during tooth and jaw development
- Selective breeding for exaggerated head types

ASSOCIATED CONDITIONS & DISORDERS

- Discomfort and pain can result from maloccluding teeth.
- Linguoverted mandibular canines may lead to oronasal fistula formation.
- Crowded teeth are at risk for early periodontitis from plaque retention.

CLINICAL PRESENTATION

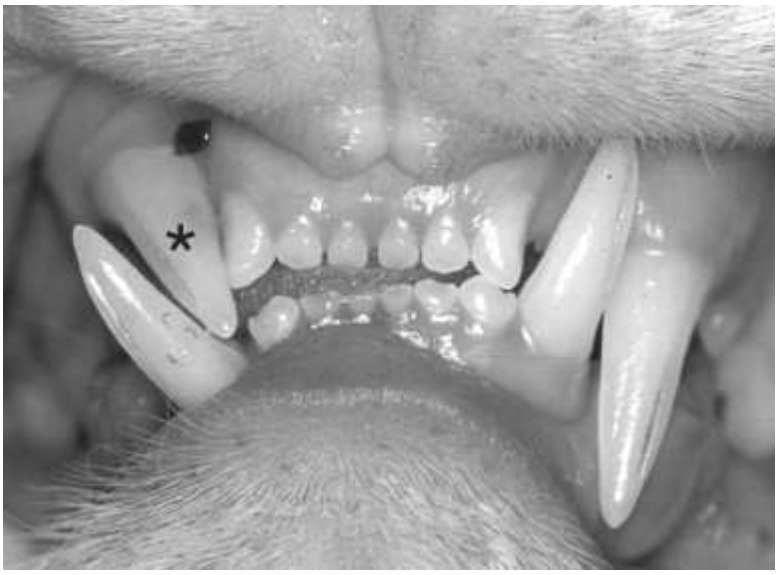
DISEASE FORMS/SUBTYPES

- Dental malocclusion:
  - Neutroclusion (class 1 malocclusion; a normal rostrocaudal relationship of the maxillary and mandibular dental arches, with malposition of one or more individual teeth)
    - Distoversion/mesioversion/lin-guoversion/labioversion/bucco-version: tooth in its anatomically correct position in the dental arch is abnormally angled in a distal/mesial/lingual/labial/buccal direction, respectively.
    - Crossbite: malocclusion in which a mandibular tooth or teeth have a more buccal or labial position than the antagonist maxillary tooth
      - Rostral crossbite: one or more of the mandibular incisor teeth is labial to the opposing maxillary incisor teeth when the mouth is closed
      - Caudal crossbite: one or more of the mandibular cheek teeth is buccal to the opposing maxillary cheek teeth when the mouth is closed
- Symmetric skeletal malocclusion:
  - Mandibular distoclusion (class 2 malocclusion; an abnormal rostrocaudal relationship between the dental arches in which the mandibular arch occludes caudal to its normal position relative to the maxillary arch)
  - Mandibular mesioclusion (class 3 malocclusion; an abnormal rostrocaudal relationship between the dental arches in which the mandibular arch occludes rostral to its normal position relative to the maxillary arch)
- Asymmetric skeletal malocclusion:
  - Maxillary-mandibular asymmetry describes skeletal malocclusions that can occur in a rostrocaudal, side-to-side, or dorsoventral direction.
    - Rostrocaudal: mandibular mesioclusion or distoclusion is present on one side of the face, but the contralateral side retains normal dental alignment.
    - Side-to-side: there is loss of the midline alignment of the maxilla and mandible.
    - Dorsoventral: results in an *open bite,* defined as an abnormal vertical space between opposing dental arches

when the mouth is closed

HISTORY, CHIEF COMPLAINT

- Abnormal incisor occlusion (show and breeding dogs)
- Abnormal tooth position
- Obvious length difference between upper and lower jaws or between left and right



MALOCCLUSION Clinical photograph of a cat with mesioversion of the right maxillary canine tooth *(asterisk).* There is no diastema between the right maxillary canine and third incisor, which the right mandibular canine tooth could occlude into when the mouth is closed (compare with normal left side). Mesioversion of the right maxillary canine tooth resulted in mild labioversion of the right mandibular canine tooth and an open bite (incomplete closure of the mouth).

PHYSICAL EXAM FINDINGS

- Normal occlusion (in the dog):
  - Maxillary incisor teeth are positioned rostral to mandibular incisor teeth. Crown cusps of mandibular incisor teeth contact the cingulum of maxillary incisor teeth.
  - Mandibular canine tooth inclined labially and bisecting the interdental space between the maxillary third incisor tooth and canine tooth
  - Maxillary premolar teeth do not contact mandibular premolar teeth. Crown cusps of mandibular premolar teeth positioned lingual to the arch of maxillary premolar teeth. Crown cusps of mandibular premolar teeth bisect the interdental spaces rostral to corresponding maxillary premolar teeth.
  - Mesial crown cusp of the maxillary fourth premolar tooth positioned lateral to the space between the mandibular fourth premolar and first molar teeth
- Dental malocclusion:
  - Abnormal positioning of one or more teeth
  - No jaw discrepancy
  - Trauma to soft tissue or other teeth
- Skeletal malocclusion:
  - Abnormal maxillary-mandibular incisor relationship
  - Loss of premolar interdigitation
  - Incorrect mandibular canine occlusion
  - Jaw length discrepancy (symmetric or asymmetric)
  - Trauma to soft tissue or other teeth

ETIOLOGY AND PATHOPHYSIOLOGY

- Jaw length, tooth bud position, and tooth size are independently inherited. Unharmonious development of upper and lower jaw and teeth results in malocclusion.
- Persistent deciduous teeth are associated with malpositioned permanent teeth.
- Significant facial trauma at a young age may lead to abnormal development and malocclusion.

- Significant facial trauma at any age may cause changes in jaw relationship.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is based entirely on physical examination to identify malpositioned teeth.

DIFFERENTIAL DIAGNOSIS

- Skeletal malocclusion versus dental malocclusion
- Functional (mal)occlusion versus clinically relevant malocclusion (causing discomfort or pain)

INITIAL DATABASE

Physical examination:

- Look for persistent deciduous teeth.
- Differentiate between dental and skeletal malocclusion.

TREATMENT

TREATMENT OVERVIEW

The goal of treatment is to have a pain-free, comfortable patient with a functional bite. Cosmetic considerations should not play a role.

ACUTE AND CHRONIC TREATMENT

- Extract maloccluding deciduous teeth as early as possible (6-10 weeks of age) if they appear to cause discomfort or interfere with jaw growth.
- Treatment options for maloccluding permanent teeth causing trauma to soft tissue or other teeth:
    - Extraction
    - Surgical crown reduction and vital pulp therapy
    - Orthodontic movement (passive or active)
- Linguoversion of mandibular canines: “Verhaert's rubber ball technique” is useful for young dogs (below 7 months of age) with normal jaw relationships and sufficiently wide diastema between maxillary third incisor and canine teeth. The dog is stimulated to actively play with a smooth-surfaced hard rubber ball for at least 15 minutes 3 times daily.

POSSIBLE COMPLICATIONS

- Inappropriate extraction technique of deciduous teeth may cause trauma to developing permanent teeth.
- Surgical crown reduction may lead to pulpitis and pulp necrosis.
- Orthodontic treatment usually requires several corrective procedures under general anesthesia and may cause soft-tissue trauma from the appliance, tooth ankylosis and root resorption, displacement of anchor tooth, overcorrection of target tooth, avulsion of anchor or target tooth, discomfort, and pain.

RECOMMENDED MONITORING

- Teeth treated by surgical crown reduction should be monitored radiographically after 4-6 months and then on a yearly basis.
- During orthodontic treatment, regular monitoring is necessary to assess tooth movement and to recognize possible complications at an early stage.

PROGNOSIS AND OUTCOME

Prognosis is good once a functional bite has been accomplished.

PEARLS & CONSIDERATIONS

COMMENTS

- Dental malocclusions are not considered inherited unless a familial predisposition exists.
- Skeletal malocclusion is considered inherited unless a developmental cause (e.g., significant facial trauma) can be identified.
- Inherited malocclusion should only be corrected by orthodontic movement if the animal is neutered.

PREVENTION

- Selective breeding
- Remove persistent deciduous teeth

CLIENT EDUCATION

Neuter animals with skeletal malocclusion (if not “normal” for the breed).

SUGGESTED READING

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Malnutrition

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Malnutrition is the inappropriate intake of nutrients, resulting in nutritional deficiencies or excesses.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Malnutrition can affect animals of any species, age, life stage, or lifestyle.

GENETICS & BREED PREDISPOSITION: No specific genetic link or breed disposition is known for malnutrition associated with nutritional deficiencies. An increased prevalence of obesity resulting from excessive caloric intake has been associated with basset hounds, beagles, Cairn terriers, Cavalier King Charles spaniels, cocker spaniels, long-haired dachshunds, Labrador retrievers, and Shetland sheepdogs.

RISK FACTORS

- Animals fed vegetarian, homemade, or single-food diets may be at risk for nutrient deficiencies (see p. 686).
- Animals with a history of chronic vomiting or diarrhea could have altered digestion or absorption, resulting in decreased nutrient assimilation.
- Drugs such as corticosteroids, cancer chemotherapeutic agents, antibiotics, or diuretics may adversely affect nutritional homeostasis.
- Neutering, decreased physical activity, age or calorie-dense foods may predispose dogs or cats to obesity.

GEOGRAPHY AND SEASONALITY: Inadequate food or water intake during severe weather conditions may result in nutrient deprivation.

ASSOCIATED CONDITIONS & DISORDERS

- Decreased protein/calorie intake negatively effects immune function.
- Increased risk of orthopedic problems or diabetes mellitus (cats) with prolonged excessive food intake

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Weight loss, emaciation, low body condition score (1 or 2 on a scale of 1-5 or 1-9). Weight gain, obesity, high body condition score (4 or 5 on a scale of 1-5 or 8 or 9 on a 1-9 scale)

HISTORY, CHIEF COMPLAINT

- Nutrient-deprived animals present with a history of failure to thrive and inappetence or anorexia.
- Overnourished or obese animals often present with clinical signs associated with lameness or endocrinopathy.

PHYSICAL EXAM FINDINGS: Nutrient-deprived animals are often in poor physical appearance: thin body condition; dry, coarse haircoat; flaky skin; hyperkeratosis; muscle wasting; broken or missing teeth; skeletal abnormalities; pressure sores; poor wound healing. Obese animals are also in poor physical condition with fat deposition over the ribs, hips, tail head, and throughout the abdomen. Some are unable to adequately groom themselves, which can result in an unkempt hair coat, dry skin, skinfold dermatitis, and the inability to walk, run, or jump.

ETIOLOGY AND PATHOPHYSIOLOGY

- Inadequate or excessive nutrient intake results in malnutrition.
- Decreased nutrient intake diminishes immune cell response and production, as well as protein turnover, tissue synthesis, and wound healing.
- Altered drug metabolism results from protein/calorie malnutrition and may increase or decrease both drug efficacy and drug toxicity.

- Although not well documented in hospitalized veterinary patients, malnutrition is thought to increase morbidity and mortality.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis of malnutrition is made on the basis of a thorough diet history and the physical examination findings.

DIFFERENTIAL DIAGNOSIS

Gastrointestinal disease: protein-losing enteropathy, lymphocytic-plasmacytic enteritis, inflammatory bowel disease

INITIAL DATABASE

- A thorough diet history should include sufficient information to purchase all food items necessary to feed the patient exactly as the owner does at home.
- The physical examination should include a body weight, body condition score (1-5 or 1-9 scale), and muscle mass score (1-3 scale).
- Laboratory evaluation plays a limited role in diagnosing nutrition-related problems.

TREATMENT

TREATMENT OVERVIEW

The goals of treatment are to correct nutrient deficiencies or excesses and return patient to a normal plane of nutrition and a more appropriate body weight and body condition.

ACUTE GENERAL TREATMENT

- Stabilize patient: rehydrate, correct electrolyte imbalances, hemodynamic abnormalities, and hypothermia before initiating nutritional support.
- Determine whether the gastrointestinal tract is functional and how nutrition support is to be delivered (enteral or parenteral).
- For patients unable or unwilling to prehend, choose the type of feeding tube for enteral delivery that fits your patient (e.g., gastrotomy tube for patients with persistent regurgitation or vomiting, esophagostomy tube for facial trauma). See p. 1267 and p. 1273 .
- Estimate an initial daily caloric goal for resting energy needs based upon animal's current weight (rather than an ideal weight), using the equation: $70 \times BWkg^{0.75}$
- For patients weighing between 15 and 30 kilograms, use the equation: 30 × BWkg + 70. This provides a reasonably accurate assessment of resting energy needs.
- Select a diet or food type that meets the nutritional needs of the patient.
- Determine a feeding regimen (continuous or intermittent feedings) that will deliver the estimated caloric goals over a 24-hour period.
- Administer nutrition to patients by assisted feeding until patient is eating at least 50% resting energy needs.
- Plan to get the animal eating its own food in its own environment as soon as possible.

CHRONIC TREATMENT

- Identify dietary, animal-related, owner-related or environmental issue(s) that caused or contributed to the nutritional deficiency or excess.
- Educate owner(s) about nutritional needs of their animal, given the species, age, life stage, and lifestyle.
- Provide information about, or resources for, complete and balanced homemade diets (website formulation services, laboratory analyses, and continuous monitoring).
- Provide information and support for owners considering a weight management program for their animal.

DRUG INTERACTIONS

Medical therapies instituted for primary conditions will be altered without adequate nutrition support.

RECOMMENDED MONITORING

Client education and repeated follow-up is critical for animals enrolled in weight management programs, or those who are fed homemade or raw meat diets.

PROGNOSIS AND OUTCOME

- Prognosis is good to excellent with immediate identification and correction of nutrient deficiencies or excesses.
- Prognosis is poor to good with prolonged identification and correction of nutrient deficiencies or excesses.

PEARLS & CONSIDERATIONS

COMMENTS

- Obesity prevention is much easier than obesity management. Client education campaigns should focus on prevention at every well-pet visit.
- Obesity management programs should be directed by veterinarians and delivered by trained, licensed veterinary technicians who are excellent communicators.
- Pet owners interested in feeding homemade or raw meat diets should consult with a veterinarian, identify a balanced recipe to use, and plan on regular monitoring of both their pet and the diet (see online chapter: Malnutrition: Home-Prepared Diets).

PREVENTION

- Complete nutritional assessments should be performed daily on hospitalized patients to identify patients at risk of malnutrition before it occurs.
- Clients should be educated on the basic nutrient needs of animals, considering species, age, life stage, and environmental conditions.

TECHNICIAN TIPS

- Technicians can be instrumental in providing client education about the proper diet and feeding management of dogs and cats and in overseeing patients enrolled in weight management programs.
- In the outpatient setting, technicians should ensure that every patient is weighed, body condition scored, and has a diet history taken.
- In the inpatient setting, technicians can aid in identifying patients at risk of malnutrition.

CLIENT EDUCATION

- Consultation for customized homemade diet formulations is available through the American College of Veterinary Nutrition (ACVN.org), or diets can be purchased at www.balanceit.com or www.petdiets.com.
- Homemade diet recipes can be analyzed through the Nutrition Laboratory in the Diagnostic Center for Population and Animal Health at Michigan State University: 517-353-9312.

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Malnutrition, Home-Prepared Diets

DEFINITION

Feeding of an unbalanced diet of uncooked and cooked foods as a sole source of nutrition; this practice is becoming more common among pet owners.

SYNONYMS

Home-cooked diet, homemade diet

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs more likely to be fed home-prepared diets than cats. Young and reproductive animals at increased risk for deficiencies and excess. All animals at risk of illness from foodborne pathogens.

GENETICS & BREED PREDISPOSITION: Dogs and cats: all breeds affected. Dogs: large and giant breeds at increased risk of developmental orthopedic disease. Cats: taurine-deficient cardiomyopathy and/or central retinal degeneration.
CONTAGION & ZOONOSIS: Dogs and cats: *Salmonella, Escherichia coli, Campylobacter, Toxoplasma, Cryptosporidium*

ASSOCIATED CONDITIONS & DISORDERS: Poor skin and coat, obesity, vomiting, diarrhea, pathologic fractures, seizures, pancreatitis (high-fat diet), oral trauma, intestinal obstruction/perforation

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Incidental: no clinical signs
- Overt illness: varies with dietary imbalance/excess or ingredients

HISTORY, CHIEF COMPLAINT: Vomiting, diarrhea, lethargy, decreased activity, poor skin and coat, reproductive failure, fetal resorption, dystocia, failure to gain weight (young), weight loss (adult). May be an incidental finding during routine history-taking.

PHYSICAL EXAMINATION: Varied: dull coarse coat, coat color change, dental fractures, skeletal abnormalities, fractures, heart murmur, loss of vision (cats), abdominal pain, dehydration, poor body condition (obese or cachectic)

ETIOLOGY AND PATHOPHYSIOLOGY

- Essential nutrient deficiency
  - Lethargy, anorexia, reproductive failure: any
  - Poor skin and coat: zinc, iron, iodine, phenylalanine-tyrosine, niacin, biotin, linoleic acid, linolenic acid and/or total protein
  - Osteopenia/osteomalacia: calcium and/or vitamin D
  - Anemia: iron, copper, folate and/or total protein
  - Hypoalbuminemia: individual amino acids, total protein and/or total calories
  - Heart murmur (cats, large-breed dogs, cocker spaniels): taurine
  - Central retinal degeneration (cats): taurine
- Essential nutrient excess
  - Anorexia: vitamin A, vitamin D, iron, calcium, iodine
  - Hypercalcemia: vitamin D
  - Vomiting and/or diarrhea: sodium and/or selenium; total fat (pancreatitis or fat malabsorption)
- Dietary contamination
  - Vomiting and/or diarrhea: foodborne pathogen, bone ingestion
  - Seizures: *Neospora, Toxoplasma*

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

The diagnosis is suspected when an unusual dietary history is revealed, suggestive physical abnormalities are noted, or both.

DIFFERENTIAL DIAGNOSIS

Allergic dermatitis, underlying end-organ disease (hepatic, renal, intestinal, central nervous system)

INITIAL DATABASE

- Diet history: consider adequate energy content, type and amount of protein, source of essential fatty acids, source of calcium, and source of trace minerals and vitamins.
- Serum biochemistry, CBC, urinalysis, may be unremarkable or show nonspecific changes (e.g., hypoalbuminemia, hypocalcemia, hypokalemia, hypomagnesemia, increased alkaline phosphatase, and anemia).

TREATMENT 

TREATMENT OVERVIEW

Manage sequelae of imbalance and correct underlying deficiency.

ACUTE GENERAL TREATMENT

- Varies with imbalance
- Vomiting and/or diarrhea: correct dehydration with intravenous (IV) fluids
- Supplemental calcium gluconate, magnesium sulfate, or balanced B-vitamin solution (IV if needed)
- Foodborne pathogens respond to supportive and antimicrobial therapy unless sustained end-organ damage
- If no clinical signs of disease: dietary deficiencies and/or excesses are corrected with feeding a complete and balanced diet.

POSSIBLE COMPLICATIONS

None known if home-prepared diet complete and balanced

RECOMMENDED MONITORING

- Diet recipes evaluated and balanced by trained veterinary nutritionist
- Physical examination, biochemistry, CBC and urinalysis every 6-12 months
- Diet and supplement review at each visit
- Diet reformulation may be necessary if health status changes.

PROGNOSIS AND OUTCOME 

Good if dietary imbalance corrected

PEARLS & CONSIDERATIONS 

COMMENTS

- Home-prepared diets are becoming more common among dog and cat owners as all or part of the daily diet.
- Normal test results do not rule out deficiency or suboptimal nutrient intake.

PREVENTION

- Client education important to help prevent foodborne illness and dietary imbalances
- Review diet history at each visit; owner substitution of ingredients and omissions of essential nutrients is common.

CLIENT EDUCATION

- Important to understand motivations for feeding home-prepared diets to help direct client education and prevent diet-induced disease.
- Feeding raw meat increases risk of pathogenic bacteria exposure for people and other animals in household; especially at risk are young, old, and immune-compromised adults. Proper food sanitation and hygiene are essential if home-prepared diet

is fed.

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Malignant Fibrous Histiocytoma

BASIC INFORMATION

DEFINITION

An uncommon primary tumor made up of fibrous and inflammatory cells thought to arise from a primitive mesenchymal cell. It is not to be confused with malignant histiocytosis (histiocytic sarcoma), a disease of localized or multisystemic histiocytic infiltration (see p. 535).

SYNONYMS

Epithelioid sarcoma, giant cell fascial sarcoma, giant cell tumor, reticulum cell sarcoma

EPIDEMIOLOGY

SPECIES, AGE, SEX: Malignant fibrous histiocytoma is an uncommon tumor of the skin and subcutaneous tissue of dogs and cats, and can also occur in the spleen in dogs. This tumor type has been reported at injection sites in cats (see p. 610).

GENETICS & BREED PREDISPOSITION: Golden retrievers and rottweilers may be overrepresented.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Different pathologic types include storiform-pleomorphic, inflammatory, and a giant cell variant. The giant cell variant, which occurs in dogs but is very rare in cats, is associated with metastasis and a poor prognosis.
- Malignant fibrous histiocytoma has been reported at injection sites in cats (see p. 610).

HISTORY, CHIEF COMPLAINT

- Pets with malignant fibrous histiocytomas in the skin and subcutaneous tissue usually present for a progressively enlarging mass noticed by the owner.
- Dogs with malignant fibrous histiocytomas of the spleen usually present for signs related to an abdominal mass or abdominal hemorrhage.

PHYSICAL EXAM FINDINGS

- Malignant fibrous histiocytomas in the skin and subcutaneous tissue often present as firm, palpable masses. Occasionally they are hairless or ulcerated.
- Regional lymphadenomegaly may be present secondary to inflammation or (rarely) lymph node metastasis.
- Dogs with splenic tumors may present with abdominal mass, pain, or abdominal enlargement.

ETIOLOGY AND PATHOPHYSIOLOGY

- Malignant fibrous histiocytomas are typically firm, slow-growing tumors that commonly infiltrate into surrounding soft tissues and along fascial planes. Overall they have a moderate metastatic potential, but some variants or grades may be more likely to metastasize (see prognosis).
- Lesions caused by malignant fibrous histiocytoma depend on the location of the primary tumor.
- These tumors are considered a separate entity from the other histiocytic diseases. Peripheral tumors can metastasize, but usually to the lungs.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Definitive diagnosis can only be confirmed via histopathologic analysis, although additional testing such as diagnostic imaging is often helpful in defining the extent of the tumor.

DIFFERENTIAL DIAGNOSIS

- Other skin and subcutaneous tumors:
  - Soft-tissue sarcoma
  - Mast cell tumor
  - Others
- Other splenic tumors:
  - Hemangiosarcoma
  - Lymphoma
  - Others

INITIAL DATABASE

- Fine-needle aspirate cytologic analysis may help identify the tumor type before other diagnostics.
- Three-view thoracic radiographs to rule out pulmonary metastases
- Radiographs of the affected area may reveal involvement of underlying bone.
- Abdominal ultrasound to identify splenic tumors and rule out metastasis. However, abdominal ultrasound cannot be relied on to differentiate malignant fibrous histiocytoma from other splenic tumors.
- Fine needle aspirate of draining lymph nodes to help rule out metastasis

ADVANCED OR CONFIRMATORY TESTING

- CT or MRI may be necessary to delineate the local extent of the tumor and plan for surgery or radiation therapy.
- Biopsy: diagnosis of malignant fibrous histiocytoma is based on histopathologic evaluation of tissue.
  - Special stains may be necessary to differentiate malignant fibrous histiocytoma from other soft-tissue sarcomas, especially poorly differentiated tumors.
  - Care should be taken to differentiate these tumors from other histiocytic tumors, including histiocytic sarcoma and malignant histiocytosis (see p. 535). These other tumors usually have a different prognosis and recommended course of treatment.
  - Histopathologic grade of the tumor is necessary for determining the prognosis and treatment of most soft tissue sarcomas (see p. 610).
    - Histopathologic grading typically involves using the general grading system for soft-tissue sarcomas based on mitotic rate, percent necrosis, and degree of differentiation.
    - Tumors are graded as low, intermediate, or high grade.
    - In most cases, high-grade tumors are larger and more invasive, but gross size and invasiveness cannot be used as a substitute for histopathologic grading.

TREATMENT

TREATMENT OVERVIEW

Definitive treatment is based on complete eradication of the primary tumor whenever possible. However, additional treatment such as chemotherapy may be indicated to prevent or delay metastases or in dogs with high-grade tumors, the giant-cell variant of this tumor or tumors that have already metastasized. Palliative treatment options, such as palliative radiation, may help control pain or discomfort in patients with advanced tumors or in patients where definitive treatment cannot be tolerated.

ACUTE AND CHRONIC TREATMENT

- Aggressive surgical resection, radiation therapy, and/or chemotherapy may be used for treatment (see p. 610).
- Chemotherapy may be indicated to delay or prevent metastasis for malignant fibrous histiocytoma affecting the spleen, high-grade tumors, or giant-cell variants of malignant fibrous histiocytoma.

POSSIBLE COMPLICATIONS

Complications of treatment depend on types of treatments and location of the primary tumor.

RECOMMENDED MONITORING

After appropriate local treatment, follow-up examination should be done routinely to monitor for recurrence (every 2-3 months) and metastasis (thoracic radiographs at 6 months and 1 year). High-grade tumors may require more frequent monitoring (at least every 2-3 months) for metastases during and after chemotherapy administration.

PROGNOSIS AND OUTCOME

- Prognosis is excellent for histologically low- to intermediate-grade tumors with appropriate treatment. This includes either surgical resection with clean histopathologic margins or incomplete resection combined with radiation therapy.
- Dogs with the giant-cell variant of this tumor often have metastases at the time of diagnosis or soon afterward, and prognosis is usually poor despite treatment. Few cats with this variant develop metastases.
- Dogs with splenic tumors are more likely to develop metastases and therefore have a poor prognosis.
- High-grade malignant fibrous histiocytoma: like other soft-tissue sarcomas, prognosis is considered guarded based on the increased likelihood for metastases.

PEARLS & CONSIDERATIONS

COMMENTS

Aside from the giant-cell variant, malignant fibrous histiocytoma should be considered like other soft tissue sarcomas (see p. 1034) in treatment and prognosis. Tumors at injection sites in cats should be treated like injection-site sarcomas (see p. 610).

CLIENT EDUCATION

Pet owners can be educated to monitor their pets for palpable or visible masses and have them evaluated in a timely fashion. Early detection may allow for easier treatment via surgery and may help avoid the need for radiation therapy.

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Malassezia Dermatitis

Additional Images Available on Website

BASIC INFORMATION

DEFINITION

An extremely common pruritic dermatosis caused by the overgrowth of *Malassezia* spp. yeast. Most infections are caused by the lipophilic unicellular organism *Malassezia pachydermatis.*

SYNONYMS

Malasseziasis, yeast dermatitis

EPIDEMIOLOGY

SPECIES, AGE, SEX: Very common in dogs of all ages; uncommon in cats of any age; either sex

GENETICS & BREED PREDISPOSITION: May occur in any breed of dog or cat. Terriers, shih tzus, dachshunds, shar-peis, spaniels, hounds, and German shepherd dogs seem predisposed, likely to underlying conditions favorable to yeast overgrowth. Devon Rex cats are more susceptible.

RISK FACTORS

- Excessive sebum production, poor sebum quality, cutaneous moisture accumulation (particularly in skin folds), a disrupted epidermal surface, and altered host immune defenses. These alterations are often the result of primary underlying diseases (e.g., allergy, endocrinopathy).
- Specific disorders that predispose to cutaneous yeast overgrowth include allergic skin disease (e.g., atopic dermatitis, food allergy, flea allergy, contact allergy), endocrinopathies (e.g., iatrogenic or spontaneous hyper-adrenocorticism, hypothyroidism, hyperthyroidism, diabetes mellitus), primary or secondary cornification disorders, folliculitis (e.g., pyoderma, demodicosis, dermatophytosis), ectoparasitism (e.g., demodicosis, sarcoptic mange, notoedric mange), metabolic diseases (e.g., superficial necrolytic dermatitis, zinc-responsive dermatosis), nutritional deficiencies, cutaneous or internal neoplasia, and in cats, retroviral infections.

CONTAGION & ZOONOSIS: *Malassezia* yeasts have been transmitted from the contaminated hands of dog-owning health care workers to infants in an intensive care nursery, causing mycotic sepsis. Therefore *Malassezia* yeast should be considered a potential zoonotic agent, especially in immunoincompetent individuals.

GEOGRAPHY AND SEASONALITY: *Malassezia* dermatitis may occur more frequently in humid geographic regions, and/or with underlying causes that worsen seasonally (e.g., atopic dermatitis).

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Localized dermatitis: involving the face (perioral, muzzle, ears), ventral aspect of the trunk (neck, axillae, inguinal area), perineal region (ventral tail, perianal area), and paw (interdigital web and nail fold)
- Generalized dermatitis: involving several regions as noted above

HISTORY, CHIEF COMPLAINT: Intense pruritus: most common chief complaint. Rancid offensive odor; an oily coat; hair loss (alopecia); redness (erythroderma); thickened, elephant-like skin (lichenification); scaling (dander); and/or relapsing and remitting dermatitis unresponsive to antibiotics or glucocorticoids are also frequently noted.

PHYSICAL EXAM FINDINGS

- Skin lesions reflect existing pruritus and seborrhea and are not specific to *Malassezia* dermatitis.
- Lesional skin may be erythematous, hyperpigmented, hyperkeratotic, lichenified, scaly, greasy or dry, alopecic, saliva-stained, and excoriated. Hyperpigmented lichenification implies chronicity.
- Intertriginous areas (skin folds) are typically affected. Occasionally, yellow/orange to slate gray seborrheic plaques are present in body folds.
- A brown waxy discharge may be evident in the nail folds, signifying paronychia.

- A brown discoloration around the base of white nails may be seen in dogs with *Malassezia* pododermatitis.
- Follicular casts (keratosebaceous material adhered to the proximal hair shaft) might be suggestive of an underlying keratinization disorder.
- Cats, particularly Devon Rex, may present with alopecia, erythema, and greasy exudation of the axillae, groin, and paws.

MALASSEZIA* DERMATITISMalassezia* dermatitis in a miniature poodle. Alopecia, erythema, and lichenification on the ventral neck.

ETIOLOGY AND PATHOPHYSIOLOGY

Malassezia spp. yeasts are part of the normal skin microflora. They become opportunistic invaders when changes occur in the cutaneous microclimate (e.g., lipid composition, relative humidity) or defense mechanisms (e.g., epidermal barrier dysfunction, immunosuppression). Once colonization takes place, yeasts may release proteases and lipases that alter cutaneous homeostasis, allowing for continued yeast overgrowth. In some atopic dogs with cytologic demonstration of yeasts, *Malassezia* may elicit a type-1 cutaneous hypersensitivity reaction.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Malassezia dermatitis should be considered in any pruritic dog or cat. Confirmation requires typical clinical signs, cytological demonstration of yeast, and most importantly, response to antifungal therapy. Underlying primary conditions must be identified and corrected. Importantly, Devon Rex cats may not have an identifiable predisposing disease.

DIFFERENTIAL DIAGNOSIS

Since *Malassezia* dermatitis is a secondary complication of underlying disorders in most cases, the chief differential diagnosis consists of identifying whether the underlying disorder (see Risk Factors, above) exists in an uncomplicated state or if secondary *Malassezia* dermatitis is present.

INITIAL DATABASE

- Skin cytologic analysis is performed on every case with compatible historical/physical findings.
    - Cytologic examination specimens can be obtained by direct impressions, acetate tape preparations, or dry or wet swabs.

- *Malassezia* are ovoid, monopolar budding yeasts that resemble the shape of footprints or peanuts. They are 3-8 mcm in diameter (the same size as, or slightly smaller than, a red blood cell).
- Yeasts are best visualized using high power (40x) or oil immersion (100x).

- Multiple skin scrapings to exclude superficial and deep ectoparasites
- Especially with cats: dermatophyte culture to exclude ringworm

ADVANCED OR CONFIRMATORY TESTING

- Biopsy and histopathologic analysis: rarely necessary
  - Suggestive but nonspecific findings include parakeratotic hyperkeratosis, epidermal hyperplasia, superficial perivascular dermatitis, and possibly eosinophilic microabscesses.
  - Occasionally, yeast may be found in the superficial keratin layer and/or in hair follicles.
  - Other histopathologic findings may represent changes associated with the underlying dermatosis.
  - Loss of surface scale during processing may decrease the chance of finding yeast organisms.
- Elimination diet trial to exclude food allergy
- Intradermal and/or immunoglobulin (Ig)E serologic testing if history and clinical findings are supportive of atopic dermatitis
- CBC, serum chemistry panel, and urinalysis to screen for internal diseases
- Hormonal testing (e.g., screening tests for hyperadrenocorticism, hypothyroidism, and diabetes mellitus)
- Feline retroviral testing

TREATMENT

TREATMENT OVERVIEW

The main goal your job is to reduce pruritus and remove seborrhea. This is accomplished by killing yeast and controlling for underlying primary diseases and risk factors.

ACUTE GENERAL TREATMENT

- Keratomodulating (antiseborrheic) and antiyeast topical therapies (e.g., sulfur/salicylic acid, phytosphingosine, benzoyl peroxide, selenium sulfide, boric/acetic acid, miconazole, clotrimazole, ketoconazole, terbinafine, enilconazole, lime sulfur, or chlorhexidine) can be applied daily to weekly depending on the formulation used (e.g., shampoo, solution, lotion, spray, wipe, powder).
- Systemic antifungal therapy may be warranted for severe infections or those not responding to sole topical therapy. Duration of systemic therapy should persist beyond (e.g., 1-2 weeks) clinical and cytologic improvement (usually a minimum of 3-4 weeks). Griseofulvin has no effect against *Malassezia* species.
  - Ketoconazole, 5-10 mg/kg PO q 24 h with food; other azoles better suited for cats, *or*
  - Itraconazole, 5-10 mg/kg PO q 24 h with (capsules) or without (suspension) food, *or*
  - Fluconazole, 2.5-5 mg/kg PO q 24 h (generic available in some countries), *or*
  - Terbinafine, 30 mg/kg PO q 24 h with food
- Because dogs with *Malassezia* dermatitis frequently have concurrent staphylococcal pyoderma, treating any secondary bacterial infection with oral antibiotics at an appropriate dose and duration (minimum 21 days) will help improve cutaneous signs.

CHRONIC TREATMENT

- Therapy for underlying predisposing diseases
- Topical keratomodulating and/or antiyeast therapy at reduced frequencies of application if possible
- Azole pulse therapy can be used for remitting and relapsing episodes of *Malassezia* dermatitis, as these drugs concentrate in the skin. Typically, the same initial dose is prescribed for 2 consecutive days per week or given daily for 1-week-on/1-to-4-weeks-off cycles after the initial induction dose described in Acute Treatment above.

DRUG INTERACTIONS

Azole therapy may alter the metabolism or distribution of other prescribed medication by inhibiting cytochrome P450 metabolizing enzymes and P-glycoprotein transporting pumps. Terbinafine does not inhibit these enzymes. Specifically, azoles cannot be given with macrocyclic lactones (e.g., avermectins); if so, dosage reduction and close monitoring is required (see p. 706).

POSSIBLE COMPLICATIONS

- Idiosyncratic cutaneous adverse reactions to topical therapies (e.g., pruritus, erythroderma, papular rash, pustulation, vesiculation, necrosis, ulceration) may occur on the patient or person applying therapy and must be considered along with

reassessment of possible underlying causes in “refractory” cases of *Malassezia* dermatitis.
- The patient may have adverse reactions to systemic azoles (e.g., vomiting, diarrhea, hepatotoxicity, vasculitis, lightening of haircoat, pruritus). Ketoconazole may inhibit cortisol synthesis at doses greater than 10 mg/kg/d.

RECOMMENDED MONITORING

- Clinical signs and skin cytology every 2-4 weeks during therapy
- Other monitoring recommendations are at the discretion of the clinician, based on underlying predisposing diseases.

PROGNOSIS AND OUTCOME

- Failure to detect and treat underlying problems will result in partial treatment success, treatment failure, or relapse.
- For incurable diseases (e.g., primary cornification disorders), therapy for *Malassezia* dermatitis may need to be lifelong.

PEARLS & CONSIDERATIONS

COMMENTS

- *Malassezia* dermatitis is one of the most overlooked causes of pruritus in the dog.
- *Malassezia* dermatitis tends to occur in body areas rich in sebaceous glands and high in relative humidity, and is commonly associated with allergic dermatitis.
- How many yeast are cytologically significant? Finding any yeast from typical clinical lesions is significant.
- Dogs with atopic dermatitis may be hypersensitive to *Malassezia,* resulting in yeast numbers disproportionate to the level of pruritus experienced by the animal.
- Skin culture for *Malassezia* yeast is not recommended in clinical practice, as these organisms are residents on the skin.
- Biopsy with histopathologic evaluation is not considered superior to cytologic evaluation for the diagnosis of *Malassezia* dermatitis (most of the surface scale is lost during biopsy processing) but may be useful in the diagnosis of primary skin disorders in addition to which *Malassezia* dermatitis is a secondary phenomenon.
- Do not use selenium sulfide on cats; it is too irritating to their skin.
- Enilconazole is not approved for small-animal use in some countries.
- Griseofulvin has no effect against *Malassezia* species.
- Cats tend to have gastrointestinal upset with oral ketoconazole, so other systemic antifungals are preferred.
- When given in tablet or capsule form, the azole drugs, ketoconazole and itraconazole, are best absorbed systemically if administered with food; failure to do so may reduce bioavailability of these drugs by up to 40%.

PREVENTION

Correctly identifying and treating for all underlying predisposing factors favorable to yeast overgrowth

TECHNICIAN TIPS

Technicians managing patients with *Malassezia* dermatitis should be proficient in collection and examination of cytologic skin samples, and capable of instructing owners on appropriate use of topical therapy.

SUGGESTED READING

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Negre A, Bensignor E, Guillot J: Evidencebased veterinary dermatology: a systematic review of interventions for *Malassezia* dermatitis in dogs. Vet Dermatol 20:1–12, 2008.

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Macadamia Nut Toxicosis

BASIC INFORMATION

DEFINITION

Acute and often self-limiting toxicosis of dogs resulting from ingestion of macadamia nuts. It is characterized by paresis, depression, vomiting, ataxia, tremors, hyperthermia, abdominal pain, lameness, and/or stiffness. Toxicosis can occur after ingestion of commercially available macadamia nuts or macadamia nut-containing cookies or candies.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Currently, the syndrome has been described in dogs only.
- All breeds, ages, and both sexes are susceptible.

RISK FACTORS

- Dogs develop signs of toxicity after ingesting 2.2-62.4 g/kg macadamia nuts.
- Dogs will readily eat large amounts of chocolate-coated macadamia nuts.

GEOGRAPHY AND SEASONALITY

- Macadamia nuts are obtained from *Macadamia integrifolia* and *Macadamia tetraphylla* trees, mostly cultivated in Hawaii in the United States.
- Toxicosis can occur year round, although it is more likely to occur during holiday seasons.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Severity and onset of signs will depend on amount of macadamia nuts ingested.
- Majority of dogs show clinical signs within 12 hours after ingestion.
- Clinical signs usually resolve within 24-48 hours.

HISTORY, CHIEF COMPLAINT

- History of exposure to macadamia nuts
- Evidence of macadamia nuts in the vomitus or in the stool
- Hind limb weakness, depression, vomiting

PHYSICAL EXAM FINDINGS

- Hind limb weakness with no evidence of central nervous system involvement, musculoskeletal pain, or trauma
  - Rarely, generalized weakness is possible.
  - Forelimb weakness without hind limb weakness is inconsistent with macadamia nut toxicosis.
  - Respiratory muscle paralysis likewise has not been a feature of macadamia nut toxicosis in dogs.
- Mild tremor of hind limbs
- Depression
- Vomiting
- Ataxia
- Hyperthermia (due to tremor; not true fever)

ETIOLOGY AND PATHOPHYSIOLOGY

- Exact cause and mechanism of macadamia nut toxicosis are not clear.
- Evidence suggests that the syndrome is dog specific.
- Toxic principle in macadamia nuts is not known at this time.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is based entirely on history and physical signs: observed or suspected ingestion of macadamia nuts, especially if concurrent signs (paresis, ataxia, stiffness, hyperthermia, and/or vomiting within 12 hours of exposure) are present, is sufficient to warrant treatment.

DIFFERENTIAL DIAGNOSIS

- Rule out other toxicoses that can cause hind limb weakness, ataxia, and vomiting:
  - Ethylene glycol
  - Cholinesterase inhibitor pesticides: organophosphates and carbamates
  - Marijuana (dogs)
  - Phenoxy herbicide (2,4 D)
  - Coral snake bite
  - Bromethalin (dogs)
- Rule out nontoxic causes for hindlimb weakness and ataxia (see p. 837):
  - Systemic disturbances (e.g., anemia, acid-base or electrolyte abnormalities, cardiac arrhythmias)
  - Neuromuscular disorders (polyradiculoneuritis, myasthenia gravis, tick paralysis, botulism)
  - Orthopedic disorders
  - Trauma
  - Right-to-left shunting patent ductus arteriosus (weakness confined to hind limbs)

INITIAL DATABASE

- Abdominal radiographs (may show a large amount of ingesta in the gastrointestinal tract)
- Examination of stomach contents for presence of macadamia nuts (if vomiting occurs)
- Rectal palpation may show presence of macadamia nuts in feces.
- Body temperature
- A complete medical examination is needed if concurrent ingestion of other harmful compound is suspected and to rule out any preexisting condition.

ADVANCED OR CONFIRMATORY TESTING

Serum biochemistry profile: mild elevation in serum triglycerides and serum alkaline phosphatase may be noted but is nonspecific.

TREATMENT

TREATMENT OVERVIEW

Treatment is general and supportive: induction of emesis and administration of activated charcoal if ingestion is suspected or confirmed and patient is stable. Management of complications of severe intoxications (e.g., nursing care if recumbent; treatment of hyperthermia) is applied as needed. Most clinical signs resolve within 24-48 hours with or without treatment.

ACUTE GENERAL TREATMENT

- Decontamination of patient:
  - Emesis (within 2-4 hours after ingestion in dogs not showing overt clinical signs; see p. 1364); *or*
    - Apomorphine (0.03-0.04 mg/kg IV or IM, or crush tablet portion with water and instill into conjunctival sac, rinse after emesis); *or*
    - Hydrogen peroxide 3% (2 mL/kg, max 45 mL PO, repeat in 10-15 minutes if no vomiting)
  - Activated charcoal:
    - Give after inducing emesis or if a few hours have elapsed after exposure; administer activated charcoal (1-4 g/kg) with a cathartic such as 70% sorbitol (3 mL/kg) orally.
  - Warm tap water enema (5-10 mL/ kg) with large ingestion may help move the macadamia nuts more quickly through the gastrointestinal tract.
  - Supportive care:
    - Administer IV fluids as needed.
    - Thermoregulation (cold bath, cooling fans if needed)

RECOMMENDED MONITORING

Serum electrolytes, biochemistry profile, and triglycerides in severely affected dogs

PROGNOSIS AND OUTCOME

- Generally, excellent prognosis
- Dogs recover with or without treatment within 24-48 hours

PEARLS & CONSIDERATIONS

COMMENTS

- Consider concurrent methylxanthine (chocolate) toxicosis if macadamia nuts were covered with chocolate and large amounts of macadamia have been ingested.
- Mild uncomplicated cases may resolve with home observation for 12 hours.

PREVENTION

Keep macadamia nuts out of reach of dogs

SUGGESTED READING

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Nystagmus

BASIC INFORMATION

DEFINITION

Repetitive, rapid, and involuntary movement of the globe of the eye in a horizontal, rotary, or vertical manner

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Any age or breed, either sex
- Idiopathic vestibular disease is more common in older dogs (>8 years) but affects cats of all ages.

GENETICS & BREED PREDISPOSITION

- Cats: pendular nystagmus occurs in otherwise normal Siamese cats. Vestibular nystagmus is a congenital abnormality in Siamese, Tonkinese, and Burmese breeds.
- Dogs: vestibular nystagmus is a congenital abnormality in the Doberman pinscher, cocker spaniel, German shepherd, and other breeds.

GEOGRAPHY AND SEASONALITY: Idiopathic vestibular disease in cats may predominate in late summer/early fall.

ASSOCIATED CONDITIONS & DISORDERS: Frequently associated with head tilt, ataxia, circling, vomiting, and anorexia

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Types of nystagmus:

- Vestibular nystagmus: eye movements are faster in one direction than in the other (fast phase and slow phase for each cycle of the nystagmus); also called *jerk nystagmus*.
- Pendular nystagmus: no fast or slow phase. Pendular nystagmus is uncommon, is a congenital anomaly, and is not associated with vestibular disease or progression of signs.

HISTORY, CHIEF COMPLAINT

- Vestibular nystagmus usually is acute in onset (e.g., idiopathic vestibular disease):
  - The animal may initially exhibit vomiting, followed by vestibular ataxia, circling, or even whole-body rolling.
  - The owners may not notice the nystagmus.
- Much less common are pendular nystagmus or congenital vestibular nystagmus that are present from birth and not associated with deteriorating vestibular function; chief complaint is limited to eye movements.

PHYSICAL EXAM FINDINGS

- Nystagmus due to peripheral vestibular disease (not all signs may be present):
  - Jerk nystagmus (horizontal or rotary) with fast phase away from the side of the vestibular lesion and away from the side of the head tilt
  - The nystagmus may be difficult to observe, especially in the cat, and may be observed only when the animal's head is changed in position (especially dorsal extension of the neck) or when the animal is placed on its back.
  - Head tilt
  - Circling
  - Ataxia with falling to the side of the lesion and to the side of the head tilt
- Nystagmus due to central vestibular disease (not all signs may be present):
  - Jerk nystagmus (horizontal, rotary, or vertical) with fast phase away from the side of the vestibular lesion and away from the side of the head tilt
  - Head tilt toward the side of the lesion
  - Circling
  - Ataxia

- Proprioceptive deficits, motor weakness on the side of the lesion
- Central vestibular disease may (rarely) cause paradoxical signs (the nystagmus fast phase is away from the side of the lesion). Proprioceptive deficits indicate the true side of the lesion (ipsilateral).
- Other cranial nerve deficits (V, VI, VII)

ETIOLOGY AND PATHOPHYSIOLOGY

- The vestibular system allows the body to know its position in space (proprioception) relative to head position, gravity, and linear or rotary acceleration.
- Sensory fibers in the peripheral vestibular system send impulses to the nuclei of cranial nerves III, IV, and VI, coordinating eye movements and allowing the eyes to remain centered on an object until it is beyond the visual field; then, the eyes are able to jerk back to again center on an object ("watching railroad cars go by").
- Damage to the vestibular system can stimulate these eye movements inappropriately, producing nystagmus.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Nystagmus is specific to vestibular dysfunction. Therefore, the diagnostic process identifies whether the brain (central) or inner/middle ear (peripheral) is the site of the lesion, which can usually be determined with a clinical neurologic exam. Further testing is selected based on a differential diagnosis list elaborated from history, physical exam, and neurologic exam findings.

DIFFERENTIAL DIAGNOSIS

- Nystagmus from peripheral vestibular disease:
  - Idiopathic
  - Bacterial infection (otitis media/interna)
  - Neoplasia
  - Hypothyroidism (rare)
  - Post surgery on the middle ear (ear ablation in the dog, removal of polyps in the cat)
  - Congenital or hereditary
- Central vestibular nystagmus:
  - Infection
  - Neoplasia
  - Trauma
- Pendular nystagmus: congenital disease affecting the visual pathway

INITIAL DATABASE

- Neurologic examination (see p. 1311)
- CBC, serum biochemistry profile, urinalysis: usually unremarkable
- Otoscopic exam
  - Otitis externa, polyp, blood (head trauma) possible
  - Careful examination may reveal fluid in the middle ear for cases with infectious causes
- Radiographs of the tympanic bullae

ADVANCED OR CONFIRMATORY TESTING

- MRI or CT of the middle ear and posterior fossa of the brain (see p. 1302 and p. 1233)
- Cerebrospinal fluid (CSF) analysis if signs of central vestibular disease are present (see p. 1228)
- For cases in which there is no nystagmus but other clinical signs suggest vestibular disease, a postrotary nystagmus evaluation may be performed:
  - The animal is rotated in a circle first in one direction for 10 rotations, and the duration of nystagmus is noted.
  - The animal is then rotated in the opposite direction, and the duration of the postrotary nystagmus is again noted.
  - Postrotary nystagmus is usually less or absent when the animal is spun away from the side of the lesion.

TREATMENT

TREATMENT OVERVIEW

Treatment goals are improvement in the clinical condition by decreasing nausea and anorexia, and treatment of the primary cause when possible.

ACUTE GENERAL TREATMENT

- Nystagmus is a clinical sign associated with various underlying causes. Therefore, treatment is aimed at the primary disorder.
- Since it may be difficult for the animal to walk or stand, good nursing care is very important: The animal should be able to get to food and water and should be cleaned after urinating or defecating so urine or fecal scalding is avoided.

POSSIBLE COMPLICATIONS

Treatment of otitis with products that contain aminoglycoside antibiotics may be detrimental (ototoxic), particularly if the tympanum is not intact.

PROGNOSIS AND OUTCOME 

- The prognosis for idiopathic vestibular disease and nystagmus caused by otitis media/interna are good to excellent for both dogs and cats, but recurrence is possible.
- A head tilt may remain after resolution of all other signs.
- The prognosis for neoplasia and virtually all causes of central vestibular nystagmus is guarded to poor.

PEARLS & CONSIDERATIONS 

COMMENTS

- Idiopathic peripheral vestibular disease causes nystagmus in the majority of cases (for cats and dogs); the condition should resolve spontaneously in 1-2 weeks.
- Idiopathic vestibular disease is a diagnosis of exclusion.
- Nearly all patients with nystagmus caused by central vestibular disease will have other central nervous system (CNS) signs (proprioceptive defects, weakness, other cranial nerve involvement).

CLIENT EDUCATION

When idiopathic vestibular disease is the primary consideration, the owners need to know that the problem will usually resolve with time.

SUGGESTED READING

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Nutritional Secondary Hyperparathyroidism

BASIC INFORMATION

DEFINITION

Chronic elevation of circulating parathyroid hormone (PTH) resulting from low serum ionized calcium concentrations (iCa) due to deficiency of absorbed calcium or vitamin D or due to a calcium/phosphorus (Ca:P) imbalance

SYNONYMS

NSHP, nutritional osteodystrophy. The term *rickets* describes bony changes consistent with a vitamin D deficiency.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Nutritional secondary hyperparathyroidism (NSHP) is seen in young, growing animals of any sex or species that have been fed an improperly formulated diet. The condition is occasionally seen in older animals, especially those with malabsorptive disorders.

GENETICS & BREED PREDISPOSITION: Young, large-breed dogs may be at increased risk because of rapid growth rate.

RISK FACTORS

- Animals fed improperly formulated homemade (especially all-meat) diets, particularly during growth. Such diets typically contain decreased calcium and/or increased phosphorus, with a Ca:P ratio of =1:16 (1:1-2:1 for dogs and 1:1-1.5:1 for cats is recommended) and inadequate vitamin D.
- Exotic pets, since dietary requirements for calcium, phosphorus, and vitamin D are not always known
- Animals with severe gastrointestinal disease that limits calcium or vitamin D absorption

GEOGRAPHY AND SEASONALITY: Condition may be more common in winter months in some indoor-housed exotic pets, owing to decreased exposure to sunlight.

ASSOCIATED CONDITIONS & DISORDERS: Animals may have decreased bone density or fractures related to increased circulating PTH.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Inadequate dietary calcium or vitamin D concentration or altered dietary Ca:P ratio
- Inadequate absorption of dietary calcium and vitamin D due to intestinal disease

HISTORY, CHIEF COMPLAINT

- History of a poorly formulated homemade diet
- Excessive use of supplements such as meats, vitamins, and minerals
- History of malabsorption due to intestinal disease
- Reluctance to walk, stiff gait, bone pain, lameness, or limb deformities (pathologic bone fractures); tooth loss; ± neurologic signs if the axial skeleton is involved
- Signs of hypocalcemia: twitching, tremors, stiffness, or seizures (rare)

PHYSICAL EXAM FINDINGS

- Bone palpation may elicit pain; fractures may be noted.
- Swelling of costochondral junctions or metaphyses may be evident.

ETIOLOGY AND PATHOPHYSIOLOGY

- Inadequate calcium absorption decreases iCa, increasing PTH production.

- Inadequate absorbed vitamin D decreases calcitriol production, decreasing iCa and increasing PTH production.
- PTH stimulates renal 1,25-dihydroxyvitamin D (calcitriol, the active metabolite of vitamin D) synthesis and bone resorption and increases renal calcium resorption and phosphorus excretion.
- Calcitriol also stimulates bone resorption to raise iCa into the normal range and decreases PTH production.
- Excessive PTH production reduces bone density, and pathologic fractures may occur.
- Excess circulating phosphorus also inhibits calcitriol synthesis and can lower iCa by the mass law effect.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is strongly suspected in young animals with a history of an inadequate diet, radiographic evidence of diffuse bone loss, and pathologic fractures.

DIFFERENTIAL DIAGNOSIS

- Other causes of lameness, bone pain, loss of bone density, or fractures, including congenital problems in young animals
- Renal secondary hyperparathyroidism (ruled out based on serum biochemistry profile and urinalysis)
- Hyperadrenocorticism associated secondary hyperparathyroidism in older dogs (ruled out based on adrenal function testing and clinical signs)
- Genetic defects in calcitriol production or utilization (rare). Clinical signs are the same in the absence of compatible diet history or malabsorptive disorder.

INITIAL DATABASE

- CBC and serum biochemical profile: serum total calcium concentration normal to low. NOTE: Serum phosphorus and alkaline phosphatase may be elevated in normal animals, especially in those who are young and growing.
- Radiography of the skull, axial skeleton, and limbs: diffusely decreased cortical bone density; fractures possible.
- Dietary history

ADVANCED OR CONFIRMATORY TESTING

- Measure PTH (increased), iCa (low to normal), and 25-hydroxyvitamin D (25-OH-D; typically low) concentrations to confirm the diagnosis.
- Serum calcitriol determination, although helpful, currently is not readily available.
- Vitamin/mineral analysis of homemade diets may be useful.

TREATMENT

TREATMENT OVERVIEW

Goals of treatment are to increase intestinal absorption of calcium and vitamin D and decrease PTH production.

ACUTE GENERAL TREATMENT

- Feed a properly formulated diet.
- Stop the feeding of all supplements.
- Supportive therapy for pain or fractures (cage rest or limited activity as indicated)
- Treatment of malabsorption when present
- Dietary supplementation with oral calcium (25-50 mg/kg elemental Ca [e.g., 62.5-125 mg/kg calcium carbonate] daily) if clinical signs of hypocalcemia are present, discontinuing when signs resolve (see p. 576)

CHRONIC TREATMENT

- Ensure that a properly formulated diet is fed.
- If a homemade diet is fed, a sample of the diet may be sent for vitamin D and mineral analysis.
- Supplemental oral calcium may be indicated in cases of chronic malabsorption.

RECOMMENDED MONITORING

- Clinicians should repeat tests of PTH, iCa, and 25-OH-D concentrations 3-4 weeks after initiating treatment. PTH should be decreased and 25-OH-D increased compared to pretreatment values. Clinicians should monitor the animals monthly until levels are normal.
- Clinicians can measure PTH, iCa, and 25-OH-D concentrations every 3-4 months, even if secondary hyperparathyroidism has resolved and if intestinal malabsorption is present.
- Clinicians should order repeat radiography tests to assess bone density and fracture healing.

PROGNOSIS AND OUTCOME

- Depends on presence of pathologic fractures, which worsen the prognosis because of pain and a potentially long convalescent period.
- Incidentally discovered NSHP that is due to inappropriate diet typically carries a good prognosis.
- For animals with malabsorption, the prognosis depends on the underlying cause and effectiveness of therapy.

PEARLS & CONSIDERATIONS

PREVENTION

Clinicians should inform owners to:

- Feed their pets nutritionally complete and balanced pet foods rather than improperly formulated homemade diets.
- Avoid supplementing balanced diets with meats, vitamins, or minerals.

CLIENT EDUCATION

- Clinicians should explain skeletal problems associated with deficiencies of calcium or vitamin D or with the excess of phosphorus to clients feeding homemade diets to their pets, especially to young, growing animals.
- Clinicians should have the adequacy of homemade diets verified by a veterinary nutritionist.
- Clinicians should suggest periodic nutrient analysis of homemade diets, especially for vitamin D and mineral content.

SUGGESTED READING

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Nonsteroidal Antiinflammatory Drug Toxicosis

BASIC INFORMATION

DEFINITION

A common toxicosis secondary to acute overdose or chronic administration of a nonsteroidal antiinflammatory drug (NSAID), most commonly affecting the gastrointestinal (GI) tract or kidneys. Hepatopathy is also possible.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Cats generally more sensitive than dogs because of deficiency in enzymes which metabolize these drugs.
- Most cases are reported in dogs. All breeds and both sexes are susceptible.
- Elderly and very young animals are at higher risk.

GENETICS & BREED PREDISPOSITION: Labrador retrievers are not considered at greater risk for developing hepatic adverse effects from carprofen administration, despite the fact that one third of the initially reported cases of hepatic syndrome were in Labradors.

RISK FACTORS

- Preexisting renal, cardiovascular, or hepatic disease may increase severity of signs.
- Dehydration, hypotension, and concurrent use of other potentially nephrotoxic drugs can potentiate signs.
- Concurrent use of other NSAIDs or corticosteroids may lead to severe complications.
- Hypoproteinemia or concurrent use of other highly protein-bound drugs can result in higher active drug levels.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Acute toxicosis: after a single large ingestion (usually 5-10 times the recommended dose)
- Chronic toxicosis: in sensitive animals after NSAID use for days, weeks, or months at recommended doses

HISTORY, CHIEF COMPLAINT

- History of exposure (acute or chronic) to an NSAID
- Clinical signs typically begin within hours after acute exposure (exception: days or weeks with chronic therapeutic use or when hepatopathy develops).
- Vomiting (±hematemesis), anorexia, lethargy, diarrhea (melena)
- Polyuria and polydipsia (PU/PD; due to kidney disease/renal failure)

PHYSICAL EXAM FINDINGS

- Variable, from minor GI upset to life-threatening effects of GI perforation
- Minor to moderate toxicosis: signs of abdominal pain, vomiting, diarrhea, lethargy, anorexia
- Severe toxicosis: dehydration, pallor, tachycardia, icterus, bruising (aspirin), hyperthermia (aspirin), ataxia, seizures, sudden death
- Hematemesis or melena is not reliably linked to GI perforation, and absence of hematemesis is not an indicator of absence of perforation.

ETIOLOGY AND PATHOPHYSIOLOGY

- Examples of commonly-implicated NSAIDs:
  - Acetic acid derivatives: diclofenac, etodolac (EtoGesic)*, indomethacin, nabumetone
  - Cyclooxygenase (COX)-2 inhibitors: celecoxib, deracoxib (Deramaxx)*
  - Fenamic acids: meclofenamic acid

- Oxicams: meloxicam (Metacam)*, piroxicam
- Propionic acids: carprofen (Rimadyl)*, flurbiprofen, ibuprofen, ketoprofen, naproxen
- Pyrazolones: phenylbutazone
- Salicylic acid derivatives: aspirin, flunixin meglumine

- NSAIDs inhibit COX enzymes, blocking prostaglandin (PG) production. PGs formed by COX-1 are important for normal physiologic function (GI protection, renal medullary blood flow). PGs formed by COX-2 mediate inflammation. Therefore adverse effects are generally fewer when COX-2 is selectively inhibited.
- NSAID hepatopathy is due to the formation of antigenic proteins that trigger an immune-mediated attack against the liver.

*Approved for use in dogs in the United States

DIAGNOSIS

DIAGNOSTIC OVERVIEW

In most cases, exposure is known (whether acute overdose or ongoing therapeutic administration). In acute overdoses, history and clinical signs may be sufficient to make the diagnosis. In chronic treatment-associated toxicosis, detailed diagnostic testing and/or drug discontinuation to monitor for regression of signs (if mild toxicosis) is often required to distinguish between NSAID toxicosis and naturally occurring disorders mimicking NSAID toxicosis.

DIFFERENTIAL DIAGNOSIS

Any disease process that can cause GI, renal, or hepatic adverse effects.

INITIAL DATABASE

- CBC: anemia from GI hemorrhage (regenerative), leukocytosis (stress or peritonitis) possible
- Serum chemistry profile: azotemia (prerenal or primary renal insult [usually within 24-48 hours after exposure in acute toxicosis]) or elevated liver enzymes and bilirubin (hepatopathy)
- Urinalysis: hematuria, glycosuria, pyuria, proteinuria, casts, and isosthenuria possible with renal injury
- Abdominal radiographs: free air in peritoneal cavity strongly suggests GI tract perforation.

ADVANCED OR CONFIRMATORY TESTING

- Usually, serum/plasma drug levels are not useful clinically.
- Endoscopy (with persistent nonspecific GI signs, especially when NSAID therapy is not discontinued): GI ulceration/irritation /perforation
- Histopathologic evaluation:
  - Stomach (endoscopic or surgical): irritation/duodenal ulceration/hemorrhage; peritonitis if gastric perforation
  - Kidneys (postmortem): renal tubular or papillary necrosis or interstitial nephritis
  - Liver (if persistent enzyme elevation; rarely performed): multifocal to bridging hepatocellular degeneration and necrosis (apoptosis), with mild to moderate periportal inflammation (neutrophils and lymphocytes)

TREATMENT

TREATMENT OVERVIEW

Goals of treatment are decontamination of the patient (induce vomiting and give repeated doses of activated charcoal), preventing/managing/monitoring GI, renal, and hepatic effects, and providing supportive care.

ACUTE GENERAL TREATMENT

- Decontamination of patient:
  - Induction of vomiting (see p. 1364): indicated in any acute overdose patient not showing clinical signs
  - Activated charcoal: 1-3 g/kg PO (or as labeled) with a cathartic, repeated (half dose) q 6-8 h to reduce enterohepatic recirculation of NSAID
- Prevent and/or manage GI effects with combination therapy (sucralfate + H^2 receptor antagonist or proton pump inhibitor + misoprostol):
  - Misoprostol for dogs: 1-3 mcg/kg PO q 8 h. Prostaglandin analog, helps replace NSAID-induced PG depletion.
  - H^2 receptor antagonist: famotidine: 0.5 mg/kg PO, SQ, IM, IV q 12-24 h (dogs, cats)

- Proton pump inhibitor: omeprazole 0.5-1 mg/kg PO q 24 h (dogs, cats)
- Sucralfate: 0.25-1 g PO q 8-12 h (dogs, cats)

- Prevent and/or manage renal effects:
  - Fluid diuresis (2-3 times maintenance rate, barring cardiovascular disease) to enhance NSAID excretion and maintain renal perfusion. For at least 48 h if potential renal toxicity dose has been ingested.
- Prevent and/or manage hepatic effects:
  - Discontinue use of NSAID.
  - Begin IV fluids.
  - Administer vitamin K^1 (1-2 mg/kg PO) if evidence of coagulation disruption.
  - *S*-adenosyl-L-methionine (SAMe), 18 mg/kg PO q 24 h for 1-3 months
- Supportive care:
  - Control vomiting with metoclopramide (0.2-0.4 mg/kg q 6 h PO, SQ, or IM or 1-2 mg/kg/d IV as constant rate infusion) or maropitant, 1 mg/kg SQ q 24 h for up to 5 consecutive days.
  - Correct fluid losses and electrolyte changes.
  - Control seizures with diazepam 1-2 mg/kg IV.
  - Administer a blood transfusion if needed.
  - Treat GI tract perforation (laparotomy, antibiotics) if suspected.

CHRONIC TREATMENT

Some animals may need long-term therapy for renal or hepatic insufficiency.

NUTRITION/DIET

Use appropriate prescription diets in patients with kidney or liver dysfunction.

DRUG INTERACTIONS

- Concurrent use of corticosteroids or other NSAIDs may dramatically increase the risk for adverse effects.
- Increased serum drug levels: phenytoin, valproic acid, oral anticoagulants, sulfonamides, sulfonylurea hypoglycemic agents, ketoconazole, methotrexate, and fluconazole
- Increased risk of nephrotoxicity: aminoglycosides, angiotensin-converting enzyme (ACE) inhibitors, and diuretics

POSSIBLE COMPLICATIONS

- Chronic kidney disease
- Hepatopathy
- GI perforation and peritonitis

RECOMMENDED MONITORING

- Blood urea nitrogen, serum creatinine, electrolytes, urinalysis (baseline, 24, 48, 72 hours in acute cases)
- Serum liver enzymes and bilirubin (for hepatopathy)

PROGNOSIS AND OUTCOME

- Excellent from mild to moderate gastric irritation/ulceration with appropriate treatment
- Guarded to poor with GI tract perforation
- Renal effects of NSAIDs are reversible if discovered early and treated intensively.
- Recovery from idiosyncratic hepatic toxicity is good when NSAID is discontinued and with supportive care.

PEARLS & CONSIDERATIONS

COMMENTS

For most NSAIDs, the minimum toxic/lethal dose is unknown. Generally, a single acute ingestion of 5-10 times more than the recommended dose could cause potentially severe GI irritation/ulceration in dogs.

- Some NSAIDs (naproxen and meclofenamic acid) have a much longer half-life in the dog, owing to extensive enterohepatic recirculation (naproxen: 92 hours).

- Check baseline CBC and serum biochemistry profile in all patients before long-term use of NSAIDs.

PREVENTION

- Clinicians should inform owners to keep all NSAIDs, especially chewables, out of the reach of pets.

TECHNICIAN TIPS

Clients may ask casually about using over-the-counter NSAIDs like ibuprofen in their dog or cat. Ibuprofen is not recommended in small animals; it is the most commonly reported NSAID toxicity.

CLIENT EDUCATION

Discuss common adverse effects associated with NSAIDs. Owners should not give any medications to their pets without first consulting a veterinarian.

SUGGESTED READING

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Nodular Skin Disorders

BASIC INFORMATION

DEFINITION

A large group of diseases that manifest as solid elevated lesions of the skin of >1 cm in diameter, usually as a result of infiltration of inflammatory or neoplastic cells into the dermis or subcutis

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Seen in cats and dogs
- Neoplastic conditions are more common in mature individuals.

GENETICS & BREED PREDISPOSITION

- Familial vasculopathy and nodular dermatofibrosis of German shepherd
- Histiocytic sarcoma complex in Bernese mountain dog, Rottweiler, golden retriever (see p. 535)
- Sterile nodular panniculitis in dachshunds (see p. 824)
- Mucinosis in the shar-pei

RISK FACTORS

- Any disease or medication that causes immune compromise (e.g., feline leukemia virus [FeLV] infection, feline immunodeficiency virus [FIV] infection, hyperadrenocorticism, hypothyroidism, diabetes mellitus) predisposes animals to infections, which in turn may cause nodular dermatoses.
- Foreign-body penetration, bite wound: increased risk of infectious nodular dermatitis
- Mineralizing fat necrosis/panniculitis in dogs with pancreatitis or pancreatic carcinomas

CONTAGION & ZOONOSIS

- Dermatophytic granuloma: *Microsporum canis* and *Trichophyton mentagrophytes* are potentially contagious to human and other animals.
- Sporotrichosis: Cat-to-human transmission is extremely high. Dog-to-human transmission has not yet been described.
- Blastomycosis, coccidioidomycosis, histoplasmosis: risk of zoonosis by aerosol from culture plates; in-house culture is always contraindicated.

GEOGRAPHY AND SEASONALITY: Straelensiosis: France, Spain, Portugal; Sporotrichosis: outbreak in Brazil; See Blastomycosis, p. 138; Histoplasmosis, p. 538; Coccidioidomycosis, p. 222; Pythiosis and Lagenidiosis, p. 960; Protothecosis, p. 926.

ASSOCIATED CONDITIONS & DISORDERS: Renal cystadenocarcinoma is typically a concurrent finding with nodular dermatofibrosis.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Animals present with acute to chronic onset of single or multiple subcutaneous nodules, with or without draining tracts, and potentially accompanying systemic signs such as fever, cough, rhinitis, anorexia lethargy.

PHYSICAL EXAM FINDINGS: Lesions are elevations above the epidermal surface of 1 cm or greater in diameter. They can be solitary to multiple, localized to generalized, firm to fluctuant, draining or intact, and pruritic to nonpruritic, all depending on the underlying etiology. Depending on etiology, systemic signs such as fever and/or coughing may be noted.

ETIOLOGY AND PATHOPHYSIOLOGY

Nodules, which are larger than papules (<1 cm diameter), are usually the result of a massive infiltration of inflammatory and/or neoplastic cells into the dermis or subcutis. The inflammatory cells are in response to an infectious, antigenic, or neoplastic etiology.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Nodular skin disorders are caused by a variety of different etiologies. Biopsies for histopathologic examination and/or bacterial and fungal cultures are often required in order to obtain a diagnosis.

DIFFERENTIAL DIAGNOSIS

- Noninfectious granuloma/pyogranuloma:
  - Idiopathic sterile pyogranuloma/granuloma; sterile nodular panniculitis
  - Juvenile cellulitis (see p. 627)
  - Foreign-body reaction
  - Acral lick granuloma (see p. 22)
  - Sarcoidosis
  - Histiocytic diseases (see p. 535; histiocytoma, cutaneous or systemic histiocytosis)
  - Cutaneous xanthomatosis
- Infectious granuloma/pyogranuloma:
  - Bacterial/botryomycosis, methicillinresistant bacteria, actinomycotic
  - Systemic and subcutaneous/intermediate fungal, dermatophytic pseudomycetomas
  - Feline leprosy, atypical mycobacterial infection (see p. 737), canine leproid granuloma
  - *Rhodococcus equi* infection
  - Toxoplasmosis (see p. 1105), leishmaniasis (see p. 643)
- Lymphocytic/plasmacytic:
  - Lupus profundus (panniculitis associated with systemic lupus erythematosus [SLE]; see p. 1070)
  - Vaccine reaction, drug eruption (see p. 323), erythema nodosum
  - Plasma cell pododermatitis (see p. 891)
  - Lymphomatoid granulomatosis
  - Pseudolymphoma
  - Epitheliotropic lymphoma
  - Plasmacytoma
- Neutrophilic:
  - Deep pyoderma *(Pseudomonas. Staphylococcus;* see p. 951)
  - Familial vasculopathy of German shepherds
  - Abscess
- Eosinophilic:
  - Eosinophilic granulomas, insect-bite granulomas, straelensiosis
  - Dracunculiasis, dirofilariasis
  - Pythiosis (see p. 960)
  - Ruptured hair follicle
- Other fibrosing, dysplastic, or neoplastic cells:
  - Dermoid cyst/pilonidal cyst (see online chapter: Pilonidal Cyst)
  - Acral pruritic nodule/fibropruritic nodule
  - Calcinosis circumscripta
  - Nodular dermatofibrosis (see p. 834)
  - Mucinosis
  - Hemangioma, sebaceous gland hyperplasia/adenoma
  - Mast cell tumors (see pp. 669 and 701), cutaneous lymphoma (T-cell, B-cell; see p. 671), melanoma (see p. 711), transmissible venereal tumour (see p. 1114)

INITIAL DATABASE

- Dermatologic exam to rule out *Cuterebra* infestation, protruding foreign bodies, and any other grossly visible etiologies
- Skin scrapings to identify possible *Demodex* mites or *Dirofilaria*
- Impression smears from draining material for cytologic examination
- Fine-needle aspirate to acquire cells for cytologic examination or discover *Dracunculus* parasite
- Cytologic examination of an impression smear or fine-needle aspirate to help identify any evidence of:
  - Infectious organisms:
    - Coccal *(Staphylococcus* spp.) or rod-shaped *(Pseudomonas* spp.) bacteria
    - Gram-positive branching filamentous organisms: *Actinomyces* spp. (non-acid-fast); *Nocardia* (partially acid-fast)
    - Diff-Quik: yeast or fungal elements of systemic mycoses sometimes detectable

        - Acid-fast bacilli: atypical mycobacteria, feline lepraemurium
        - Spindle- to crescent-shaped protozoal organisms (*Toxoplasma gondii* or *Neospora caninum)*
        - Amastigotes in Giemsa-stained smears (leishmaniasis)
        - Nematodes (dracunculiasis) or microfilaria (dirofilariasis)
        - Organisms in foamy macrophages (may be noted)
    - Noninfectious findings:
        - Foamy macrophages without evidence of infectious agents often detected with sterile nodular panniculitis.
        - Eosinophils noted with eosinophilic granulomas, foreign body, or insect bite reactions.
        - Neoplastic cells: round cell tumors (e.g., histiocytes, mast cells, plasmacytoma)
- Surgical biopsies to obtain a sufficiently deep sample to incorporate the panniculus. If using a punch biopsy, clinicians should be certain to double-punch to obtain the subcutaneous fatty tissue.
- Dermatohistopathologic evaluation required to:
    - Differentiate the cellular infiltrate (neutrophils, histiocytes, plasma cells, lymphocytes, eosinophils, multinucleated giant cells, neoplastic cells)
    - Identify the presence of infectious organisms with the aid of special stains (GMS, PAS, Fite's acid-fast)
    - Help direct advanced diagnostics

ADVANCED OR CONFIRMATORY TESTING

- Clinicians should submit part of a biopsy specimen aseptically for tissue maceration and culture.
- Clinicians should also be certain to notify the laboratory of suspected organisms (adjustments to culture media selection and incubation times; precautions).
    - Bacterial culture and sensitivity testing:
        - Aerobic: *Staphylococcus* spp., *Rhodococcus equi, Nocardiosis*
        - Anaerobic: *Actinomycosis*
    - Rapid-growing atypical mycobacterial culture
    - Fungal culture (many are biohazards; clinicians should notify the laboratory and not culture these in-house): protothecosis, blastomycosis, histoplasmosis, coccidioidomycosis, cryptococcosis, pythiosis, sporotrichosis, zygomycosis, and phaeohyphomycosis, as well as dermatophytic granulomas.
    - Negative cultures support a diagnosis of sterile nodular panniculitis, lupus profundus, sterile pyogranuloma/granuloma syndrome, immune-mediated conditions and neoplasia.
- For the detection of antibody deposition (lupus) and identification of infectious agents that are at times difficult to culture or typically found low in numbers (canine sporotrichosis with direct immunofluorescence [DIF], leishmaniasis with PCR):
    - DIF
    - Fluorescent antibody testing
    - Immunoperoxidase staining
    - Immunohistochemistry
    - Immunostaining with polyclonal BCG antibody (promising method)
    - PCR
- Serologic testing:
    - *Coccidioides, Blastomyces, Cryptococcus, Histoplasma, Leishmaniasis*
- Additional laboratory tests:
    - FeLV/FIV
    - Antinuclear antibody (lupus profundus, SLE) testing
    - CBC/serum biochemistry/thyroid profile/urinalysis:
        - Rule out any metabolic disturbances resulting in immunosuppression.
        - Evidence of concurrent immune-mediated process (e.g., SLE)
        - Baseline prior to commencing any long-term medications
- Diagnostic imaging:
    - Radiographs: metastasis or infection dissemination
    - Abdominal ultrasound: clinicians should evaluate concurrent factors (pancreatitis, hyperadrenocorticism) and invasion of neoplasms (mast cell tumor, histiocytic sarcoma) into abdominal organs.

TREATMENT 

TREATMENT OVERVIEW

Because the group of nodular skin disorders encompasses such a variety of etiologies, treatment is dependent on identification of the specific cause.

PROGNOSIS AND OUTCOME 

Variable: good to poor depending on the ability to identify and specifically treat the underlying etiology

PEARLS & CONSIDERATIONS

COMMENTS

A thorough and methodical diagnostic protocol is often necessary to confirm a specific cause.

CLIENT EDUCATION

It is better to invest in a diagnostic workup to identify and treat the specific etiology rather than pursue countless therapeutic trials that often result in minimal response and maximal frustration.

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Nicotine Toxicosis

BASIC INFORMATION

DEFINITION

Intoxication in pets generally due to ingestion of tobacco or related products and manifesting with acute onset of gastrointestinal (GI) signs followed by transient, potentially severe, neurologic dysfunction.

EPIDEMIOLOGY

SPECIES, AGE, SEX: All animals of all ages and both sexes are susceptible; dogs are more likely to be involved compared to cats.

RISK FACTORS

- Availability of nicotine-containing products in pet's environment
- Dogs may be particularly attracted to chewing tobacco containing flavoring agents such as honey, molasses, licorice, syrups, or sugars.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Observation or indirect evidence of exposure to nicotine-containing products
- Clinical signs occur >1 hour after ingestion; spontaneous vomiting, salivation, and diarrhea.
- Initial central nervous system (CNS) excitation and tachypnea

PHYSICAL EXAM FINDINGS

- Hypersalivation
- Nausea
- Tenesmus
- Bradycardia (sinus); may be followed by tachycardia.
- Shallow, slow respiration, eventually leading to cyanosis, respiratory paralysis
- Neuromuscular weakness, tremors, collapse

ETIOLOGY AND PATHOPHYSIOLOGY

Source:

- Sources include cigarettes, cigars, chewing tobacco, Bidi cigarettes, nicotine gum, nicotine skin patches (Nicorette, Nicotrol), inhalers, nasal sprays, nicotinic insecticides (nicotine sulfate is available at a concentration of 0.05%-4% as insecticide dust or sprays and as a concentrated 40% solution [Black Leaf 40]; banned in the United States since 2001).
- Nicotine is a water-soluble alkaloid found primarily in cultivated tobacco *(Nicotiana tabacum)* but also in wild tobacco (*N. attenuata* and *N. trigonophylla*). Tree tobacco *(N. glauca)* contains mostly anabasine (a teratogen) but does contain some nicotine. Indian tobacco (*Lobelia inflata*) contains mostly lobeline (curare-like paralytic) and some nicotine.

Mechanism of Toxicosis:

- Nicotine mimics acetylcholine at sympathetic and parasympathetic ganglia, neuromuscular junctions of skeletal muscle, and at some synapses in the CNS. Low doses cause depolarization and stimulation of receptors similar to acetylcholine. Higher doses cause stimulation followed by blockade of autonomic ganglia and neuromuscular junctions of skeletal muscle.
- Stimulation of sympathetic cardiovascular ganglia and adrenal medulla can lead to release of catecholamines.
- GI effects: parasympathetic stimulation can lead to increased tone and motility.
- Death can result from respiratory paralysis.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A tentative diagnosis is made based on nicotine in the animal's environment and appropriate clinical signs. Confirmation with nicotine in-clinic tests is possible, especially if history of exposure is uncertain, but it is not essential.

DIFFERENTIAL DIAGNOSIS

- Other intoxications: strychnine, methylxanthines, tremorgenic mycotoxins/garbage toxicosis, organophosphates/carbamates
- The initial stages of nicotine poisoning produce physical signs that are similar to those of anticholinesterase insecticide poisoning. The latter stages produce signs that are similar to intoxication with depressants (ethanol, barbiturates, marijuana, etc.).

INITIAL DATABASE

- Serum chemistry profile: electrolyte abnormalities, azotemia (vomiting, dehydration)
- Blood gas analysis
- Electrocardiogram (ECG): sinus bradycardia or sinus tachycardia most common, ventricular arrhythmias possible

ADVANCED OR CONFIRMATORY TESTING

- Nicotine can be detected in urine, blood, GI contents, vomitus, or lavage washings. Clinicians can contact a veterinary diagnostic laboratory or a human hospital for analysis, but such confirmation should not delay initiation of treatment if nicotine toxicosis is known or suspected.
- Necropsy samples: nicotine in liver and kidney

TREATMENT

TREATMENT OVERVIEW

Treatment consists of management of severe signs first (e.g., seizures) if present, followed by decontamination of the patient (induce vomiting and give activated charcoal) in all cases not showing overt clinical signs, and enhancement of excretion of nicotine in all likely or confirmed cases.

ACUTE GENERAL TREATMENT

- Decontamination of patient:
  - Decontamination of dermal exposure consists of bathing the patient with liquid dishwashing detergent solution (wear thick rubber gloves).
  - Induction of emesis (see p. 1364) is indicated only if the patient is not showing any clinical signs (<1 hour after exposure).
  - Gastric lavage (see p. 1281) is necessary only if very large doses have been ingested and emesis cannot be induced (comatose animal).
  - Activated charcoal 1-4 g/kg PO (repeated doses may be necessary). Airway protection with a cuffed endotracheal tube is indicated if the animal is unconscious. Obtain a baseline serum sodium because some animals develop hypernatremia after activated charcoal administration.
  - Antacids are contraindicated because they will enhance absorption.
- Enhance excretion:
  - Fluid diuresis
  - Urine acidification may promote excretion of nicotine, but this should only be done if the acid-base status is monitored. Ammonium chloride (50 mg/kg PO q 6 h) or vitamin C (20-30 mg/kg IM or IV q 8 h) can be used.
- Treat sinus bradycardia with atropine, 0.04 mg/kg SQ, IM, or IV as needed.
- Supportive care:
  - Oxygen and/or artificial respiration for respiratory difficulty or paralysis
  - Diazepam for seizures (0.5-2 mg/kg IV in dogs and 0.5-1 mg/kg in cats, PRN)

RECOMMENDED MONITORING

- ECG
- Blood pressure
- Acid-base status
- CNS physical signs
- Respiratory system

PROGNOSIS AND OUTCOME

- Poor prognosis with large doses or if artificial ventilation is required
- Prognosis good if patient survives first 4 hours after ingestion

PEARLS & CONSIDERATIONS

COMMENTS

- In dogs, 10 mg/kg nicotine PO is potentially lethal. Ingestion of approximately 1 mg/kg or more should be considered serious.
- Clinically significant toxicosis has been reported in dogs at 4 mg (one cigarette in a small- to medium-sized dog).
- Most dogs vomit spontaneously after ingestion, reducing the severity of toxicosis.
- Nicotine is absorbed more in alkaline pH. In humans, the half-life is 2 hours; excretion occurs via kidneys and is pH dependent.
- Nicotine from gum has comparatively low bioavailability at about 15%.
- Nicotine content in various products:
    - Cigar: 15-40 mg/cigar
    - Cigarettes: 13-30 mg/cigarette
    - Low-yield cigarette: 3-8 mg
    - Cigarette butt: 5-7 mg
    - Snuff: 4.6-32 mg/g moist; 12.4-15.6 mg/g dry
    - Nicorette gum: 2 or 4 mg per piece (effectively 0.3-0.6 mg at bioavailability 15%)
    - Nicotrol nasal spray: 10 mg/mL
    - Transdermal patches: 8.3-114 mg/patch
    - Nicotine inhaler: 10 mg/cartridge

PREVENTION

Pet owners should keep nicotine-containing products out of their pets' reach.

SUGGESTED READING

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Neutropenia, Immune-Mediated

BASIC INFORMATION

DEFINITION

Antibody-mediated destruction of neutrophils and/or their precursors in the marrow, resulting in an absolute decrease in the number of circulating neutrophils.

SYNONYM

Steroid-responsive neutropenia

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs and cats
- Any age or gender, but female dogs <4 years old may be at increased risk.

GENETICS & BREED PREDISPOSITION

- One report involved three female giant schnauzers.
- Cats and Belgian Tervuren dogs may have physiologic neutropenia causing no clinical signs.

RISK FACTORS: None known. Drugs (phenylbutazone, griseofulvin [cats]) or infectious agents (viruses, rickettsiae) sometimes implicated.

ASSOCIATED CONDITIONS & DISORDERS: May be seen with anemia, thrombocytopenia, or pancytopenia (see p. 68)

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Lethargy or anorexia may be reported by owners.
- Signs may arise from infections, usually bacterial from invasion of normal flora.
- Clinical signs are nonspecific and usually are not helpful in localizing the infection.

PHYSICAL EXAM FINDINGS: Fever and weakness may be the only findings. Sometimes signs of opportunistic infections (e.g., diarrhea or gingivitis) may be present.

ETIOLOGY AND PATHOPHYSIOLOGY

- Idiopathic; not well studied
- Drugs or infections occasionally cause immune-mediated destruction of neutrophils.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

- Neutropenia may be the primary problem, or it may occur secondary to overwhelming infection, and determining which situation exists in a given patient is of paramount importance. A combination of physical examination, CBCs, and often diagnostic imaging and bone marrow evaluation are usually necessary to make this determination and provide appropriate treatment and an accurate prognosis.

DIFFERENTIAL DIAGNOSIS

- Immune-mediated neutropenia is more often associated with thrombocytopenia or anemia and clinical signs of variable severity.
- Secondary neutropenia is usually associated with severe clinical illness, and the count may improve within days of appropriate antibiotic treatment; conversely, primary neutropenia persists after an infection is treated.
- Primary but nonimmune-mediated neutropenia:
    - Bone marrow abnormality such as aplasia, fibrosis, dysplasia, or neoplasia. Neutropenia occurs first, then thrombocytopenia and anemia.
    - Infections such as parvovirus or ehrlichiosis in dogs, and retroviruses (feline leukemia, feline immunodeficiency) or panleukopenia virus in cats
    - Hyperestrogenism from testicular or ovarian tumors, or iatrogenic estrogen administration
- Some normal cats may have neutrophil counts between 1800 and 2500/mcL.
- Immune-mediated neutropenia is a diagnosis of exclusion. Neutrophil counts are usually <500/mcL at presentation.
- Response to treatment with corticosteroids may allow for retrospective diagnosis of immune-mediated neutropenia.

INITIAL DATABASE

- CBC: if the neutropenia is associated with other cytopenias, or if it persists for more than 2–3 days (if <1000/mcL neutrophils) or 1 week (if 1000–2000/ mcL), a bone marrow aspirate and biopsy are indicated.
- Serum biochemistry profile and possibly thoracic and abdominal radiographs can help clinicians assess for underlying disorders causing secondary (transient) neutropenia, such as neoplasia or infections.
    - Serum chemistry profile usually unremarkable, although hyperglobulinemia may be present.
    - Possible thoracic radiographic lesions (e.g., mediastinal or pulmonary disease)
- Urinalysis with bacterial culture and sensitivity (C&S) test to evaluate for urinary tract infection

ADVANCED OR CONFIRMATORY TESTING

- If relevant, abdominal ultrasonography to evaluate for evidence of neoplasia or infection
- Serologic testing for relevant infectious diseases
- No available commercial test for antineutrophil antibodies, but they have been demonstrated by flow cytometric immunofluorescence.
- Any concurrent drug therapy should be stopped if possible to rule out immune-mediated neutropenia due to adverse drug reaction.

TREATMENT

TREATMENT OVERVIEW

Assume that sepsis is present whenever fever and neutropenia are present concurrently, regardless of the cause of the neutropenia. Intensive treatment with IV bactericidal antibiotics is indicated, since sepsis may be rapidly fatal. Corticosteroids can be added later if primary immune-mediated disease remains the most likely diagnosis by exclusion.

ACUTE GENERAL TREATMENT

- It is important to weigh risks and benefits and rule out other causes of neutropenia before starting corticosteroid therapy.
- Appropriate antibiotics based on a C&S if fever is present. Empirical antibiotic treatment may be necessary initially (first few days) while bacterial cultures are underway.
    - In severely ill patients, intravenous antibiotics should be used. Options include cefoxitin, 30 mg/kg IV q 6-8 h; or ampicillin, 20 mg/kg IV q 8 h, plus enrofloxacin, 5 mg/kg (diluted 1:1 with sterile saline and given slowly IV) q 12 h (5 mg/kg q 24 h in cats).
    - In severe sepsis, consider temporary use of human G-CSF 5 mcg/kg SQ q 12 h. Development of antibodies will prevent long-term benefits.
    - In stable cases, oral trimethoprimsulfa (15 mg/kg PO q 12 h) is often suitable because it preserves normal intestinal anaerobes. Trimethoprimsulfa has rarely been implicated as a cause of neutropenia.
- Prophylactic antibiotic treatment may be warranted even for afebrile animals with severe neutropenia.
- Prevent infection by paying special attention to sterile technique with IV catheters and other invasive procedures.
- Start prednisone at 2 mg/kg PO q 24 h, which may be given after infectious causes have been ruled out or treated. Continue until neutrophil count is normal.
- If risk of ehrlichiosis (see p. 334), consider doxycycline (5 mg/kg PO q 12 h) while awaiting serologic results.

CHRONIC TREATMENT

- Neutrophil count should increase within 2 weeks of prednisone therapy.

- If there is no response, reassessment of the diagnosis is indicated. If the diagnosis is unchanged, consider human intravenous immunoglobulin (0.5 g/kg slow IV once, and a second dose may be administered after 24-48 hours if necessary; risk of anaphylaxis at either time) or cyclosporine (e.g., Neoral, Atopica: 2-5 mg/kg PO q 12 h); monitoring of serum cyclosporine levels is recommended (target: 200-500 ng/mL). It is generally best to avoid administering myelosuppressive drugs such as azathioprine or cyclophosphamide.

POSSIBLE COMPLICATIONS

Sepsis

RECOMMENDED MONITORING

Frequent assessment of body temperature and periodic reevaluation of neutrophil count

PROGNOSIS AND OUTCOME

Most dogs affected with primary immune-mediated neutropenia that are under 4 years of age recover. Older dogs or those with pancytopenia are more likely to develop complications, and their prognosis is guarded.

PEARLS & CONSIDERATIONS

COMMENTS

- The combination of fever and neutropenia should be considered to be a life-threatening emergency that warrants obtaining specimens for culture and starting IV antibiotics immediately.
- Cats tolerate neutropenia better than dogs.

TECHNICIAN TIPS

- Pay special attention to aseptic technique when placing catheters or performing any other invasive techniques in neutropenic patients.

CLIENT EDUCATION

- Clients can monitor temperature at home. If a fever develops, they must contact their veterinarian immediately for further tests and treatment.

SUGGESTED READING

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Nerve Sheath Tumors

BASIC INFORMATION

DEFINITION

A benign or malignant tumor of peripheral nerve cell origin. Nerve sheath tumors may affect peripheral nerves, spinal nerve roots, or cranial nerves. Approximately 80% of nerve sheath tumors occur in the brachial plexus region. The remaining 20% involve cranial nerves or other spinal nerve roots. The trigeminal nerve is the most common cranial nerve affected.

SYNONYMS

Peripheral nerve sheath tumor (PNST), malignant nerve sheath tumor (MNST)

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Common in dogs, less common in cats
- Reported age range is 3-13 years in dogs and 8-19 years in cats.
- Usually seen in medium- to large-breed dogs

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Nerve sheath tumors include:

- Ganglioneuroma
- Peripheral neuroblastoma
- Paraganglioma
- Peripheral nerve sheath tumors
    - Benign peripheral nerve sheath tumors
        - Schwannoma
        - Neurofibroma
    - Malignant peripheral nerve sheath tumors
        - Malignant schwannoma
        - Neurofibrosarcoma

HISTORY, CHIEF COMPLAINT

- Chronic, progressive lameness or pain
- Muscle atrophy
- Weakness
- Ataxia

PHYSICAL EXAM FINDINGS

- Varies with respect to tumor location and nerve root(s) affected
- Abnormalities *may* include:
    - Localized muscle atrophy
    - Chronic, progressive lameness (commonly in the unilateral forelimb)
    - Asymmetric paresis
    - Proprioceptive deficits
    - Hyporeflexia
    - Sensory deficits
    - Pain on palpation of tumor site (e.g., axilla)
    - Ipsilateral loss of cutaneous trunci reflex (may occur with C8-T1 spinal segments)
    - Ipsilateral Horner's syndrome (may occur with cervical or brachial plexus nerve sheath tumors)

ETIOLOGY AND PATHOPHYSIOLOGY

Undetermined; recent research suggests a point mutation in the *neu* oncogene; however, there is insufficient evidence to determine the consistency of this finding.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A presumptive diagnosis can be made with history, clinical signs, and diagnostic imaging; however, cytologic or histopathologic evaluation is required for definitive diagnosis.

DIFFERENTIAL DIAGNOSIS

- Other soft-tissue tumors may invade or compress nerves and result in similar neurologic deficits and imaging appearance (e.g., fibrosarcoma, chondrosarcoma, lymphoma).
- Abscess, granuloma
- Orthopedic abnormalities (e.g., osteoarthritis, osteochondrosis desiccans [OCD], biceps tenosynovitis)
- Other cranial neuropathies (e.g., tumors of the brainstem or cavernous sinus)
- Other neuropathies (e.g., lateralized disk herniation)
- Traumatic brachial plexus injury

INITIAL DATABASE

- Neurologic examination
- Radiographs of the affected limb may rule out orthopedic conditions.
  - Clinicians should not overinterpret presence of osteoarthritis; osteoarthritis may be a concurrent condition and not the primary cause for presentation.
- Spinal radiographs may show subtle osteolysis at the vertebral foramen.

ADVANCED OR CONFIRMATORY TESTING

- Electrophysiologic studies (see online chapter: Electromyography and Nerve Conduction Velocity):
  - Differentiate neurologic from orthopedic conditions
  - Determine specific nerve roots involved; aid in surgical planning
- Cerebrospinal fluid (CSF) evaluation (see p. 1228):
  - Occasionally, albuminocytologic dissociation (disproportionate elevation in CSF albumin concentration compared to cellularity)
- Myelography (see p. 1306):
  - May indicate local invasion into spinal canal
  - May rule out lateralized disk herniation
- Advanced imaging:
  - MRI (see p. 1302) is the preferred modality for identifying soft-tissue and intracranial lesions. However, a normal MRI does not completely rule out the presence of a small or diffuse nerve sheath tumor.
  - CT (see p. 1233) may be particularly useful in evaluating compressive spinal lesions post myelogram
- Fine-needle aspiration for cytologic examination
- Biopsy (percutaneous or surgical excision)
- Tumor staging:
  - Thoracic radiographs
  - Abdominal ultrasound
  - Lymph node aspirates

TREATMENT

TREATMENT OVERVIEW

Complete tumor excision if possible and pain relief are the desired goals; radiation therapy may be used for attempting palliation.

ACUTE GENERAL TREATMENT

- Surgical exploratory/excision:
  - Radical excision (i.e., limb amputation, ± hemilaminectomy) provides the optimal chance of complete excision and is

recommended in most cases.
- Radiation therapy:
  - Adjunctive to surgical excision
  - May be used as monotherapy in nonresectable cases
- Adjunctive chemotherapy:
  - Rarely used as monotherapy
  - Doxorubicin (dogs, cats), mitoxantrone (dogs, cats), or ifosfamide (dogs)

CHRONIC TREATMENT

- Analgesics
- Corticosteroids may help alleviate some discomfort and may reduce peritumoral inflammation; however, there is insufficient research to support or refute their use for treating this condition.

DRUG INTERACTIONS

- Concurrent administration of nonsteroidal antiinflammatory drugs (NSAIDs) and corticosteroids is *not* recommended.
- Other potential drug interactions depend on the specific therapeutic modalities chosen; clinicians should consult appropriate references.

POSSIBLE COMPLICATIONS

- Local invasion into adjacent tissues (e.g., brainstem or spinal cord)
- Metastasis:
  - Metastatic rates for nerve sheath tumors have not been established although appear to be low.

RECOMMENDED MONITORING

Clinicians should monitor for progressive/recurrent neurologic deficits and/or pain.

PROGNOSIS AND OUTCOME

- Variable; histopathologic grade, tumor location (e.g., surgical accessibility), and stage are prognostic.
- Although complete excision can be curative, often local invasion into the spinal cord or brainstem has already occurred by the time of diagnosis, making cure unlikely.
  - Median postoperative survival time is 5-6 months, with a disease-free interval of about 1 month.

PEARLS & CONSIDERATIONS

COMMENTS

- Early diagnosis increases the potential for complete excision.
- Orthopedic conditions typically do not produce neurologic deficits; if proprioceptive deficit or localized muscle atrophy is present, a nerve sheath tumor may be the cause.
- Even advanced imaging may fail to identify the tumor if it is small or diffuse.

CLIENT EDUCATION

- Clients should understand the potential for progression/recurrence.
- Clients should be counseled regarding quality-of-life issues that pertain to their pets.

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Nephrotic Syndrome

BASIC INFORMATION

DEFINITION

The presence of pathologic proteinuria, hypoalbuminemia, hypercholesterolemia, and edema. This combination is an uncommon but important complication of protein-losing nephropathy.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- More common in dogs than in cats
- More common in middle-aged to older dogs (average is about 8.5 years of age).
- For most causes, no sex predilection

GENETICS & BREED PREDISPOSITION

- Labrador and golden retrievers may be overrepresented.
- Hereditary nephritis: bull terrier, dalmatian, English cocker spaniel, Samoyed, American Eskimo, beagle, mixed breed dog (see p. 926).
- Amyloidosis: Chinese shar-pei (see pp. 926, p. 1372, and online chapter: Shar Pei Fever).

RISK FACTORS: Diseases that can cause substantial glomerular protein loss (e.g., membranous glomerulonephritis, amyloidosis) are invariably the underlying cause of nephrotic syndrome. In turn, neoplasia, infectious, and noninfectious inflammatory diseases predispose an animal to some of these glomerular diseases (see p. 450).

CONTAGION & ZOONOSIS: Some causes are zoonotic (see p. 450).

GEOGRAPHY AND SEASONALITY: Some causes are geographically and/or seasonally restricted (see p. 450).

ASSOCIATED CONDITIONS & DISORDERS

- Thromboembolic disease
- Chronic kidney disease
- Systemic hypertension
- Dyspnea from pulmonary thromboembolism or, less commonly, pleural effusion
- Ascites
- Reduced renal perfusion and possibly acute renal failure from decreased plasma oncotic pressure

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Incomplete nephrotic syndrome (edema absent): the most common form

HISTORY, CHIEF COMPLAINT: Patients may not show overt clinical signs. When present, signs may be nonspecific (e.g., weight loss, lethargy) or caused by:

- Fluid retention (e.g., edema, abdominal distension)
- Renal failure/uremia (e.g., polyuria and polydipsia [PU/PD], vomiting, halitosis)
- Thromboembolism (e.g., dyspnea, collapse)
- Systemic hypertension (e.g., blindness)
- Related to predisposing disease

PHYSICAL EXAM FINDINGS: May be unremarkable. Abnormalities may include:

- Subcutaneous edema, ascites, pleural effusion
- Evidence of thromboembolism (e.g., dyspnea, decreased peripheral pulse)
- Evidence of hypertension (e.g., choroidopathy, CNS signs, new cardiac murmur)
- Evidence of predisposing disease

- Variably sized kidneys

ETIOLOGY AND PATHOPHYSIOLOGY

- Proteinuria is due to altered glomerular capillary wall permselectivity and abnormal (inadequate) filtration of plasma proteins, primarily albumin.
- Hypoalbuminemia develops when the renal loss of plasma proteins exceeds hepatic regenerative capacity.
- The pathogenesis of hypercholesterolemia is complex and incompletely understood. Hypoalbuminemia or decreased oncotic pressure stimulates hepatic protein synthesis, including lipoprotein synthesis, leading to hypercholesterolemia. Altered lipid catabolism may contribute to the condition.
- Sodium retention and decreased plasma oncotic pressure contribute to edema formation.

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

The diagnosis of partial nephrotic syndrome is based on the combination of proteinuria, hypoalbuminuria and hypercholesterolemia; complete nephrotic syndrome includes the presence of fluid retention. Finding partial or complete nephrotic syndrome prompts further evaluation of the patient.

DIFFERENTIAL DIAGNOSIS

- The combination of proteinuria, hypoalbuminemia, hypercholesterolemia, and edema/effusion is pathognomonic for nephrotic syndrome.
- Most likely glomerular diseases that cause severe proteinuria: amyloidosis, membranous nephropathy/glomerulonephritis, membranoproliferative glomerulonephritis, hereditary nephritis, minimal change disease

INITIAL DATABASE

- CBC, biochemical profile, urinalysis: clinician should assess glomerular filtration (creatinine, blood urea nitrogen [BUN]), renal tubular function (urine specific gravity), identify evidence of predisposing disease, and rule out other causes of proteinuria (see pp. 450, p. 61, and p. 926).
- Urine protein/creatinine (UPC) ratio: confirm nephrotic range proteinuria (UPC > 2), and establish pretreatment baseline. UPC only accurate when urine sediment is inactive.
- Urine culture and susceptibility testing (C&S) to rule out infection
- Blood pressure measurement: hypertension is common. High-risk of end-organ damage if systolic >180 mm Hg.

ADVANCED OR CONFIRMATORY TESTING

- Identify predisposing diseases with abdominal ultrasound, thoracic radiographs, infectious disease testing (e.g., heartworm, ehrlichiosis), and anti-nuclear antibody (ANA) serologic analysis.
- Renal biopsy: allows definitive diagnosis of glomerular lesion; should include light, electron, and immunofluorescent microscopic evaluation. May provide prognostic information.

TREATMENT 

TREATMENT OVERVIEW

The goals of treatment are to reduce the magnitude of proteinuria, manage uremia, control systemic hypertension, and reduce patient discomfort (e.g., relief from edema, effusion).

ACUTE GENERAL TREATMENT

- Clinician should initiate angiotensinconverting enzyme (ACE) inhibitor therapy: enalapril, 0.5 mg/kg PO q 24 h to q 12 h; or benazepril, 0.25 mg/kg PO q 24 h.
- Address edema and effusion:
  - Abdominocentesis (see p. 1192) if ascites impinging on ventilation: thoracocentesis rarely required
  - Appropriate diuretic use:
    - If plasma volume is reduced (e.g., dehydration), diuretics may be ineffective and dangerous, increasing risk of renal failure or thromboembolism.

        - If plasma volume is normal, spironolactone may help delay return of third-spaced fluid and provide benefit of inhibiting aldosterone.
    - Low-level exercise may help mobilize edema.
- Address components of uremia if present (see p. 205).
- Initiate aspirin therapy as anticoagulant (0.5 mg/kg PO q 12 h) if serum albumin is <2–2.5 g/dL to reduce risk of thromboembolism.
- Add additional medications as needed to control systemic hypertension (see p. 1068).
- Address concurrent/underlying disease when possible.
- Uremic crisis may require colloid support for appropriate diuresis.

CHRONIC TREATMENT

- Disease-specific treatment indicated on basis of renal biopsy and other test results
- If proteinuria is not reduced by >50% with an ACE inhibitor, another inhibitor of the renin-angiotensin-aldosterone system (RAAS) should be added (e.g., angiotensin receptor blocker [losartan])

NUTRITION/DIET

Diet formulated for renal disease

BEHAVIOR/EXERCISE

Moderate, comfortable physical activity is encouraged; inactivity may worsen peripheral edema.

DRUG INTERACTIONS

- Hypoalbuminemia will increase the unbound (often active) fraction of highly protein-bound drugs; dosages may need to be adjusted accordingly.
- Warfarin is avoided in the face of hypoalbuminemia.
- Heparin is an ineffective anticoagulant when antithrombin is depleted.

POSSIBLE COMPLICATIONS

- Hypotension from ACE inhibitor and Ca channel blocker or severe reduction in plasma oncotic pressure
- Hyperkalemia from ACE inhibitor
- Bleeding tendency from aspirin (very rare at recommended dose)
- Worsening azotemia as a result of ACE inhibitor administration; rare
- Worsening of ascites/edema following parenteral fluid administration

RECOMMENDED MONITORING

The UPC, urinalysis, blood pressure, serum albumin and creatinine, body weight and condition score should be monitored regularly —weekly to monthly initially. Once stable, reevaluate every 3-6 months unless changes in therapy are initiated or changes are noted in clinical condition.

PROGNOSIS AND OUTCOME

- Variable but usually guarded. Prognosis improves if underlying disease causing proteinuria can be identified and corrected.
- Azotemia, systemic hypertension, and marked tubulointerstitial lesions on biopsy may be negative prognostic indicators.

PEARLS & CONSIDERATIONS

COMMENTS

- Nephrotic syndrome is a complication that can develop in animals with specific types of glomerular diseases. Nephrotic syndrome is pathognomonic for glomerular disease.
- The clinical condition can deteriorate rapidly; prompt intervention is warranted.
- Nephrotic syndrome is a predisposing factor for thromboembolic disease.

PREVENTION

- Urinalyses screening during routine health evaluations may allow early detection.
- Early intervention might prevent the development of nephrotic syndrome.

TECHNICIAN TIP

Affected dogs need frequent evaluation because they can destabilize rapidly.

CLIENT EDUCATION

Rapid deterioration is possible; frequent rechecks are necessary.

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Nephrolithiasis

BASIC INFORMATION

DEFINITION

Deposition of crystallized minerals within the kidney is less common than urolithiasis in the lower urinary tract, but incidence (or recognition) is increasing.

SYNONYMS

Kidney stones, renal urolithiasis, renolithiasis

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Feline: prevalence increases with age. Up to 47% of cats with chronic kidney disease may have upper urinary tract uroliths.
- Canine: middle-aged to older dogs

GENETICS & BREED PREDISPOSITION: (Data extrapolated from general uroliths)

- Cat: domestic short hair (DSH), domestic long hair (DLH), domestic medium-haired (DMH), Siamese, Persian, Himalayan, Manx, Maine coon
- Dog:
  - Oxalate: miniature schnauzer, Lhasa apso, Yorkshire terrier, bichon frise, Pomeranian, shih tzu, miniature poodle (see p. 1141)
  - Struvite: miniature schnauzer, shih tzu, bichon frise, miniature poodle, cocker spaniel, and Lhasa apso (see p. 1143)
  - Urate: dalmatian, English bulldog, miniature schnauzer, shih tzu, Yorkshire terrier (urate/biurate; see p. 1145)

RISK FACTORS

- Struvite: pyelonephritis
- Calcium oxalate: hyperadrenocorticism, hypercalcemia (any cause), diet
- Urate: portosystemic shunt, breed-related risk

ASSOCIATED CONDITIONS & DISORDERS

- Hydronephrosis/hydroureter
- Ureteral obstruction
- Pyelonephritis
- Renal failure

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Unilateral or bilateral
- Unobstructed or obstructed (partial or complete)
- Urolith type: calcium oxalate, struvite, urate and other purities, xanthine, silica, cystine, compound/mixed

HISTORY, CHIEF COMPLAINT: Clinical signs may be absent or may include:

- Abdominal pain
- Anorexia
- Depression
- Hematuria
- Pollakiuria
- Polyuria and polydipsia (PU/PD)

- Stranguria
- Vomiting
- Weight loss

PHYSICAL EXAM FINDINGS: Physical examination may be unremarkable or may reveal:

- Abdominal pain
- Dehydration
- Halitosis/oral ulcers (uremia)
- Renomegaly or small kidneys

ETIOLOGY AND PATHOPHYSIOLOGY

- Nephroliths are less common than cystouroliths, representing approximately l%-4% of analyzed uroliths. The actual prevalence is likely higher, since nephroliths are less frequently removed for analysis.
- The most common nephrolith types in dogs are calcium oxalate (about 40%), struvite (about 33%), and urate (about 12%). The most common nephroliths in cats are calcium oxalate.

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

Nephrolithiasis may be an incidental finding on abdominal imaging studies or may be associated with urinary obstruction, renal failure, or recurrent urinary infections.

DIFFERENTIAL DIAGNOSIS

- Radiodense renal opacities:
  - Nephrocalcinosis
  - Radiodense intestinal content
  - Calcified lymph nodes
  - Calcified adrenal glands
  - Neoplastic mineralization
  - Other ectopic calcification
- Clinical signs:
  - Urolithiasis (ureters, bladder, urethra)
  - Feline lower urinary tract signs/disease (FLUTS/D)
  - Pyelonephritis or cystitis
  - Renal failure
  - Urinary tract neoplasia
  - Prostatic disease
  - Causes of hematuria (see p. 1394)

INITIAL DATABASE

- CBC: often unremarkable
  - Normocytic, normochromic, nonregenerative anemia (if chronic kidney disease)
  - Leukocytosis ± left shift (if pyelonephritis)
- Serum biochemical profile: often unremarkable. Depending on degree of renal dysfunction and/or urinary obstruction, may reveal:
  - Azotemia
  - Hyperphosphatemia
  - Hypokalemia/hyperkalemia
  - Metabolic acidosis
- Urinalysis: may be unremarkable, or may reveal:
  - Hematuria
  - Proteinuria
  - Pyuria
  - Bacteruria
  - Crystalluria
  - Isosthenuric urine
- Urine culture and sensitivity (C&S) to rule out infection

- Blood pressure to rule out hypertension associated with chronic kidney disease
- Abdominal radiography:
  - Depending on urolith composition, radiopaque density within one or both renal pelvises
    - Radiopaque: calcium phosphate, calcium oxalate, struvite; small uroliths are difficult to detect radiographically.
    - Radiolucent: urate, cystine
  - Concunent ureteral, cystic, or urethral calculi are sometimes present.
  - Enlarged or atrophied kidneys
- Ultrasound is a sensitive means of detection but may overestimate nephrolith size:
  - Acoustic shadowing in renal pelvis
  - Concunent pyelectasia or hydronephrosis

ADVANCED OR CONFIRMATORY TESTING

- If nephroliths are recovered, quantitative urolith analysis and culture
- If definitive therapy is anticipated:
  - Nuclear scintigraphic or CT glomerular filtration rate (GFR) to determine contribution of each kidney to global GFR
  - Intravenous pyelography (IVP) or CT to confirm urolith location in kidney

TREATMENT

TREATMENT OVERVIEW

Incidentally discovered nephroliths may not require therapeutic intervention. Nephroliths may remain stationary, pass into the bladder, or become lodged in the ureter, resulting in renal dysfunction. When present, urinary obstruction (rare) should be relieved and uremia addressed directly. Whenever possible, measures to dissolve or prevent urolith growth are undertaken.

ACUTE GENERAL TREATMENT

- Complete urinary obstruction is rare, but when present, it requires interventional (surgical, endoscopic) treatment.
- Address renal failure, including electrolyte and acid-base disorders (see pp. 205, p. 207 , and p. 31).
- Address pyelonephritis (see p. 947).

CHRONIC TREATMENT

- Medical dissolution possible for some types of nephrolithiasis (see pp. 1143, p. 1145, and p. 1138).
- Invasive intervention not routinely required, and benefit must be carefully weighed against risk.
  - Indications for surgery (nephrotomy, pyelolithotomy, or nephrectomy):
    - Complete obstruction to urine flow
    - Recurrent infection (nephrolith may be nidus)
    - Marked, persistent renal hematuria
    - Progressive nephrolith enlargement (despite medical management) accompanied by reduction in renal function or in a solitary functional kidney
- Lithotripsy (extracorporeal shock wave, laser, or electrohydraulic):
  - Results in fragmentation or crushing of calculi; may require multiple treatments, depending on calculi shape, size, location, and type.
    - Indications similar to those for surgical intervention.
  - Shock wave availability limited (e.g., University of Tennessee, Pennsylvania, Purdue, Tufts, Animal Medical Center in New York City). Can cause renal damage.
  - Laser lithotripsy more readily available (several large referral centers) but technique best suited to larger animals. (see p.1297)

POSSIBLE COMPLICATIONS

- Nephrolith may lodge in ureter, causing obstructive nephropathy; particularly likely when calculi shrink (e.g., medical dissolution, lithotripsy).
- Surgical trauma of incision and transection of intrarenal vessels may further damage renal parenchyma.
- Some medical conditions may be worsened by calculolytic diets (see pp. 1143 and p. 1145).
- Recurrence rates are high, especially for calcium oxalate nephroliths.

RECOMMENDED MONITORING

- Monitoring should include imaging, urinalysis and culture, and serum biochemistry as described for urolithiasis.

- Repeated abdominal ultrasound or excretory urography (contrast is potentially nephrotoxic) should be considered in patients with radiolucent stones.

PROGNOSIS AND OUTCOME

- Dependent on urolith composition, degree of obstruction, remaining renal function, concurrent infection, and ability to identify and treat underlying cause
- Surgical intervention does not address causation; recurrence rates are high.

PEARLS & CONSIDERATIONS

COMMENTS

- Small nephroliths can be incidental findings requiring no therapy.
- Medical management of nephroliths mirrors medical management of cystoliths of identical composition.
- Nephrolithiasis does not worsen prognosis for cats with stage 2 or 3 chronic kidney disease.

PREVENTION

- Promote water consumption.
- Identify and address risk factors.

CLIENT EDUCATION

Strict adherence to dietary recommendations is crucial.

SUGGESTED READING

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Neonatal Losses

BASIC INFORMATION

DEFINITION

Life-threatening illness occurring between birth and 4 weeks of age

SYNONYMS

Fading kittens, fading puppies, stillbirth

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Canine, feline: both sexes.
- Neonatal mortality rates: 5%-30%. Greatest incidence occurs within the first week of birth.

GENETICS & BREED PREDISPOSITION

- Purebred puppies and kittens are more prone to congenital and hereditary defects.
- Cats: British shorthair, Scottish fold, Devon rex, Abyssinian, Birman, Himalayan, Persian, Somali.

RISK FACTORS

- Dam condition
- Premature labor
- Dystocia, causing fetal distress
- Prolonged labor, over 6-12 hours
- Low birth weight or failure to grow
- Lack of colostrum ingestion, immunodeficiency
- Endometritis in the dam
- Congenital anomalies (hereditary, developmental, or teratogenic)
- Malnutrition or nutritional diseases
- Assisted feeding (bottle or tube feeding, causing potential aspiration pneumonia)
- Poor environment, stress
- Parasitism
- Infectious diseases
- Inbreeding
- Tom with blood type A having mated with queen with blood type B (see p. 757)

CONTAGION & ZOONOSIS

- *Brucella cants* infection
- Herpesvirus infection
- *Bartonella* infection
- Toxoplasmosis
- Feline leukemia virus (FeLV) or feline immunodeficiency virus (FIV) infections

GEOGRAPHY AND SEASONALITY: Colder climates may negatively affect neonatal survival.

ASSOCIATED CONDITIONS & DISORDERS: Failure to thrive (weight loss), vomiting, diarrhea, respiratory distress

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Low birth weight, low weight gain, and/or failure to gain weight

- Separation from the dam or other littermates
- Sudden onset of illness characterized by depression, anorexia, hypothermia, persistent crying, abdominal distension/pain, and failure to suckle. Death can occur in 18-24 h depending on the cause.
- Primarily respiratory and gastrointestinal signs in puppies. Hemolytic or respiratory signs in kittens. With infectious causes, clinical signs vary according to the route and time of infection.
- Severity of presenting signs influences survival.

PHYSICAL EXAM FINDINGS

- General: weakness, diarrhea, gasping/panting/labored breathing/respiratory distress
- Decreased activity, decreased muscle tone, pale mucous membranes, decreased gastrointestinal sounds, dehydration, hypothermia
- Characteristics of neonatal isoerythrolysis in cats: pallor, icterus, tail tip necrosis, tachypnea, discolored urine (hemoglobinuria)

ETIOLOGY AND PATHOPHYSIOLOGY

- Mechanisms:
  - Hypoglycemia, dehydration, hypoxemia, and hypothermia are the main mechanisms for neonatal losses in both dogs and cats.
  - Hypothermia causes failure to suckle and intestinal ileus at temperatures <96°F (<35.6°C). The most common route of entry for bacterial organisms is through the umbilicus, but the oronasal route and contact with infectious vaginal fluids/discharge are also recognized portals for infection.
  - Meconium aspiration may cause pneumonia and systemic bacterial infection.
  - Neonatal isoerythrolysis (see p. 757)

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on the presence of persistent crying, anorexia, hypothermia, and abdominal pain or a combination of these in puppies and kittens under 2-3 weeks of age. Specific cause of illness can sometimes be determined by performing additional diagnostic tests.

DIFFERENTIAL DIAGNOSIS

See Etiology and Pathophysiology above.

INITIAL DATABASE

- CBC, serum chemistry profile, urinalysis:
  - Volume of blood withdrawn should be conservative owing to small body size. Do not take more than 1 mL per 100 grams of body weight. In very small patients, minimal database should consist of hematocrit, total protein, glucose, blood urea nitrogen, and urinanalysis.
  - Neonates normally have mild serum alkaline phosphatase and phosphorus elevations as well as mild blood urea nitrogen, albumin, globulin, cholesterol, and hematocrit reductions, compared to adult normal ranges.
- Compare serum gamma-glutamyl transferase (GGT) and alkaline phosphatase (ALKP) levels to assess transfer of colostrum.
  - Adequate colostral transfer should produce neonatal serum levels of these enzymes that are 30 (GGT) to 100 (ALKP) times higher during the first 1-3 days of life than normal adult values.
- FeLV/FIV test
- Fecal flotation
- Thoracic and abdominal radiographs

ADVANCED OR CONFIRMATORY TESTING

- Urine culture
- Serologic titers: *Brucella canis,* canine herpesvirus, *Toxoplasma, Neospora;* PCR test is confirmatory for herpesvirus.
- Blood typing (purebred cats)
- Virus isolation
- Pleural/abdominal fluid analysis
- Necropsy (e.g., canine herpesvirus: characteristic lesions of petechial hemorrhage in kidneys, liver, and intestinal mucosa)

TREATMENT

TREATMENT OVERVIEW

Treatment is generally supportive, based on the test results and affected body systems. Not all treatments need to be instituted at once, as it is very easy to overstress puppies and kittens of such young age. Assess organ involvement and institute/revise treatments as clinical signs dictate.

ACUTE GENERAL TREATMENT

- Management of isoerythrolysis in kittens if present (see p. 757)
- Hypothermia needs to be corrected gradually over 30 minutes to 2 hours.
- If immune compromised due to insufficient colostrum ingestion, frozen colostrum, or serum administration: serum can be given SQ at a dose of 5 mL per 100–150 grams of body weight SQ q 8 h × 24–36 h, or 15 mL/100 gram PO over 12–24 h.
- Start administering broad-spectrum bactericidal antibiotics (e.g., ceftiofur [Naxcel], 2.5 mg/kg SQ q 12 h for 5 days), which is very safe and has minimal effects on intestinal flora.
- Correct dehydration with warmed, balanced crystalloid fluids (lactated Ringer's solution or Normosol-R and 5% dextrose; 1 mL/30 g body weight IP or IO initially, then as needed based on response). See p. 1291 for Intraosseous Catheter placement.
- Correct hypoxemia by administration of oxygen at 30%–40%.
- Administer vitamin K1 once SQ (0.01–0.1 mg), as puppies <2 days old have reduced thrombin levels.
- Correct hypoglycemia if present (see p. 1571).
- Correct hypokalemia if present (see p. 377).
- Once the patient is stable, provide supportive nursing. In weaker patients with an inadequate suckle reflex, tube feeding is better than bottle feeding because it is a more reliable method to minimize possibility of aspiration. During the first week of life, feeding guidelines for kittens are 100-175 kcal/lb (220–380 kcal/kg); for puppies, requirements are 105–120 kcal/lb (230–260 kcal/kg) divided equally into 6–8 feedings daily.
- Viral replication might be inhibited by maintaining body temperature above 101°F–102°F (38.3○–38.8°C). Clinician should monitor the animal closely to avoid overheating. Incubator should be at a temperature of 85°F-95°F (29.4○–35°C) and relative humidity of 55%–65%. Acyclovir suspension can be attempted at a dose of 20 mg/kg PO every 6 hours for 7 days.

CHRONIC TREATMENT

- Supportive care
- Commercial milk replacement if mother's milk is not available. During the first week of life, neonatal caloric requirements are 133 kcal/kg/d; the requirements thereafter are 155 kcal/kg/d for week 2, 175–198 kcal/kg/d for week 3, and 220 kcal/kg/d for week 4.

NUTRITION/DIET

Supplemental feedings with milk replacer

DRUG INTERACTIONS

- Avoid drugs contraindicated for neonates (e.g., glucocorticoids, immunosuppressive agents, NSAIDs, fluoroquinolones, tetracyclines, aminoglycosides, trimethoprim-sulfa, and chloramphenicol).
- Drug absorption, metabolism, and excretion in dog or cat neonates differ from those of adult neonates and vary according to the drug; detailed drug information should be obtained prior to use in neonates.

POSSIBLE COMPLICATIONS

- Possible short-term damage to the affected organ systems (e.g., gastrointestinal, cardiovascular, respiratory) from the disease process
- Due to patient's small size, clinician needs to be careful with the amount of the administered fluid therapy so as not to create volume overload.
- Tube feeding or oral medication administration could potentially cause aspiration pneumonia.

RECOMMENDED MONITORING

Daily weighing is very important. Puppies and kittens should gain weight daily at a rate of 2–7 g per day for each kilogram of anticipated adult weight and should double their birth weight by 10 days of age.

PROGNOSIS AND OUTCOME

Supportive care is the cornerstone of successful treatment.

PEARLS & CONSIDERATIONS

COMMENTS

Instituting intensive early treatment is the key, as neonates deteriorate rapidly.

PREVENTION

Incidence of neonatal problems is reduced when clinicians:

- Avoid administering modified live vaccines during pregnancy.
- Avoid administering teratogenic drugs and chemicals.
- Avoid incompatible matings in cats and check blood type before breeding.
- Ensure that neonates have ingested colostrum within the first 24 hours to acquire passive immunity. Administer serum if immunity status is questionable.
- Administer broad-spectrum anthelmintic therapy to the dam/queen 2 weeks prior to birthing, and then to neonates every 2-3 weeks starting at 3 weeks of age and continuing until 12 weeks old.
- Administer appropriate vaccination protocols.

TECHNICIAN TIPS

- Tube feeding guidelines:
  - Use a 5-Fr or 8-Fr red rubber catheter.
  - Measure from the nose to last rib, and mark 75% of that distance.
  - Preload 6-mL syringe with milk replacer, empty all air out of the catheter by squeezing the syringe until milk starts to drip from the edge of the catheter.
  - Advance catheter along the roof of the mouth along the path of least resistance until it reaches the mark.
  - Pull back on the syringe to make sure that you have negative pressure (no air in the syringe).
  - Feed appropriate amount of milk replacer over 5-10 seconds, kink the catheter, and pull it out.
  - This technique can also be used for serum administration if colostral ingestion is questionable.

SUGGESTED READING

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Neonatal Isoerythrolysis

BASIC INFORMATION

DEFINITION

Neonatal isoerythrolysis (NI) is an immune-mediated hemolytic disease seen in newborn kittens and (rarely) puppies. NI is caused by ingestion of maternal colostrum containing antibodies to one of the neonate's blood-group antigens.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Occurs most commonly in cats

GENETICS & BREED PREDISPOSITION: Feline breeds with a high incidence of type B blood types are predisposed to NI (see p. 71)

RISK FACTORS: Any litter resulting from parents of opposite blood types is at risk of developing NI.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Patients that develop NI are normal at birth but begin to fade within 48-72 hours of birth.

ETIOLOGY AND PATHOPHYSIOLOGY

- Fetuses are not exposed to maternal antibodies in utero, as they do not cross the placenta.
- NI is caused by ingestion of maternal colostrum containing antibodies to one of the neonate's own blood-group antigens.
- Cats are unusual in that blood type B cats have naturally occurring anti-A antibodies without prior exposure: their kittens may be of blood type A, however, in which case they develop hemolysis after nursing.
- Similarly, cats with type A blood can develop anti-B antibodies, but these antibodies are weaker than anti-A antibodies in type B cats, and clinical anemia is less common.
- In dogs, the maternal antibodies may develop to a specific foreign blood group from previous transfusions.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis of NI is generally based on compatible history and/or physical exam findings within hours/days of birth. Early clinical signs of the disease are pigmenturia (dark red-brown urine), pale mucous membranes, and icterus.

DIFFERENTIAL DIAGNOSIS

Heritable red blood cell (RBC) disorders, zinc toxicosis

INITIAL DATABASE

- Packed cell volume, cytological evaluation of RBCs for evidence of agglutination and/or spherocytosis consistent with NI
- Urine: pigmenturia in fading kittens is highly suggestive of NI.

ADVANCED OR CONFIRMATORY TESTING

Blood typing of both parents. Diagnosis is confirmed by screening maternal serum, plasma, or colostrum against the paternal or neonatal RBCs (see p. 1234).

TREATMENT

TREATMENT OVERVIEW

Treatment is primarily supportive, and success depends largely on early identification and intervention.

ACUTE GENERAL TREATMENT

Kittens should be removed from the queen to terminate nursing, and all kittens in the litter should be blood typed. Type B kittens can be returned to a Type B queen. Type A kittens may require transfusion and supportive care. They should not be returned to the queen for at least 72 hours. Kittens removed from the queen need attentive bottle feeding.

PROGNOSIS AND OUTCOME 

Prevention is the preferred “treatment” for NI. Affected kittens need supportive care and blood transfusions. The prognosis remains guarded even with treatment, emphasizing the importance of prevention.

PEARLS & CONSIDERATIONS 

PREVENTION

Affected or at-risk kittens (see Epidemiology, above) should not be permitted to nurse from their mother for the first 3 days. A blood type A queen can be substituted for nursing if the natural dam was of type B, or a milk replacer can be used for the first 3 days after birth. The kittens can be returned to the dam after 3 days, because antibody-rich colostrum is generally no longer present in clinically significant quantities at that point.

CLIENT EDUCATION

Proper client education is essential, since prevention of NI is so important. Feline breeders should be counseled about making proper breeding choices and strategies for prevention.

SUGGESTED READING

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AUTHOR: SCOTT SHAW

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Necrotizing Meningoencephalitis

BASIC INFORMATION

DEFINITION

A unique nonsuppurative meningoencephalitis resulting in brain parenchymal necrosis; lesions predominate within the cerebral hemispheres.

SYNONYMS

NME, Pug or Maltese meningoencephalitis, pug dog encephalitis, Yorkshire terrier leukoencephalitis, necrotizing leukoencephalitis (NLE). Because necrotizing meningoencephalitis (NME) is not limited to pugs, clinicians often refer to the condition as *NE* (necrotizing encephalitis) or *NME* instead of pug dog encephalitis.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs of either sex, ranging in age from 6 months to 13 years; young females may be over-represented.

GENETICS & BREED PREDISPOSITION

- Many authors propose a genetic predisposition in pugs, although the exact mode of inheritance is unknown.
- Maltese dogs and Yorkshire terriers are similarly affected, although the distribution of lesions in Yorkshire terriers is different than in pug and Maltese dogs.
- The disease has been seen sporadically in other small breeds of dogs, including Chihuahuas, shih tzus, Lhasa apsos, Pekingeses, and Papillons.

GEOGRAPHY/SEASONALITY: One report found that clinical signs of NME tended to become apparent between the months of May and September.

CONTAGION AND ZOONOSIS: This disease is not transmissible between animals and poses no known threat of zoonosis. To date, attempts to isolate infectious agents including herpesvirus, adenovirus, or canine parvovirus have been unsuccessful.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Forms include acute (<2 weeks) or chronic (4 to 6 months).

HISTORY, CHIEF COMPLAINT: The majority of cases present with generalized seizures, circling, visual deficits, and head pressing. Yorkshire terriers often show signs of vestibular disturbance (ataxia, head tilt) in addition to the aforementioned signs of prosencephalic (forebrain) dysfunction.

PHYSICAL EXAM FINDINGS

- General physical examination is unremarkable
- Neurologic examination (see p. 1311) reflects the distribution of lesions in the central nervous system (CNS):
  - Deficits are often asymmetric.
  - When forebrain signs predominate, menace deficits, postural deficits (with a normal gait), nasal hypalgesia, and abnormal mentation may be present.
  - Yorkshire terriers often have signs of central vestibular disease, including abnormal nystagmus, falling, head tilt, and postural deficits.
  - Neck pain is occasionally elicited, secondary to either meningitis or forebrain disease.

ETIOLOGY AND PATHOPHYSIOLOGY

- An immune-mediated basis is strongly suspected. Autoantibodies against glial cells have been identified in the cerebrospinal fluid (CSF) and serum of affected pug dogs.
- Selective neuronal necrosis, perivascular mononuclear infiltrates, and foci of malacia and cavitation are seen in both gray and white matter.
- Many female dogs with recent pregnancy/pseudocyesis preceding clinical signs have been reported, but the role, if any, of hormonal factors in the pathogenesis of NME is poorly understood.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is based on breed, history, clinical signs typical of forebrain disease (or vestibular signs in Yorkshire terriers), characteristic cavitary changes on MRI, CSF analysis, and exclusion of other disorders such as granulomatous meningoencephalitis (GME) or infectious encephalitis.

DIFFERENTIAL DIAGNOSIS

- GME
- Infectious meningoencephalitis (e.g., protozoal, fungal, rickettsial, viral)

INITIAL DATABASE

- CBC and serum chemistry panel results are generally unremarkable.
- Infectious disease titers *(Toxoplasma, Neospora,* Rocky Mountain spotted fever, *Ehrlichia, Cryptococcus)* can rule out other potential causes of encephalitis.

ADVANCED OR CONFIRMATORY TESTING

- MRI (see p. 1302): Findings may include asymmetric ventriculomegaly, cerebral edema, noncontrast-enhancing focal or multifocal cavitating lesions, and (rarely) tentorial herniation.
- In Maltese and pug dogs, the lesions are almost exclusively supratentorial; in Yorkshire terriers, lesions may also be found in the brainstem.
- CSF analysis (see p. 1228): mild to moderate lymphocytic pleocytosis and elevated protein

TREATMENT

TREATMENT OVERVIEW

Therapeutic goals are reduction of seizure activity if present and reduction of intracranial inflammation.

ACUTE GENERAL TREATMENT

- Mannitol (1 g/kg IV) in suspected cases of cerebral edema or rapidly deteriorating neurologic status
- Anticonvulsant therapy, such as with phenobarbital or potassium bromide, is often used. These drugs, however, may cause excessive sedation in patients with structural forebrain disease.
    - Zonisamide (5–10 mg/kg PO q 12 h), levetiracetam (20 mg/kg PO q 8 h), or felbamate (15 mg/kg PO q 8 h) may be preferable choices for controlling seizures without sedative effects.
- Antiinflammatory therapy, usually prednisone at a dose of 0.5–1 mg/kg PO q 12 h, may ameliorate clinical signs.

CHRONIC TREATMENT

- Anticonvulsant therapy (as above) is required for life.
- Antiinflammatory doses of glucocorti-costeroids (e.g., prednisone 0.5–1 mg/kg PO q 12 h initially, then tapered to q 24 h or preferably q 48 h for long-term use) are required for life.
- Immunosuppression with various agents such as cyclosporine, procarbazine, cytosine arabinoside, lefluno-mide, or mycophenolate mofetil is considered a mainstay of treatment. While these medications hold promise for future treatment options, more information and long-term studies are needed before predictions can be made regarding efficacy.

POSSIBLE COMPLICATIONS

With disease progression: seizures

RECOMMENDED MONITORING

Drug monitoring of serum levels (e.g., phenobarbital, KBr) if appropriate

PROGNOSIS AND OUTCOME

Prognosis for long-term survival is grave. Despite therapy, clinical signs progress, and seizures become intractable.

PEARLS & CONSIDERATIONS

COMMENTS

The majority of dogs with NME die or are euthanized within 6 months of the onset of clinical signs. Clinicians must inform clients of the extremely guarded prognosis of NME.

PREVENTION

Unknown prevention methods.

CLIENT EDUCATION

Due to the uncertainty regarding inherit-ability of this disorder, caution should be exercised when considering breeding relatives of affected dogs.

SUGGESTED READING

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Necrotizing Fasciitis

BASIC INFORMATION

DEFINITION

Acute onset of a fulminant, rapidly progressive infection of the skin, subcutis, and fascia, causing coagulation necrosis of affected tissues, most commonly caused by β-hemolytic group G *Streptococcus.* Septic shock may be seen, either at presentation or as a later sequel.

SYNONYMS

Flesh-eating bacteria, flesh-eating disease

EPIDEMIOLOGY

SPECIES, AGE, SEX: Both dogs and cats of all ages have been reported to present with necrotizing fasciitis.

CONTAGION & ZOONOSIS: Not known to be directly transmissible to humans, but the same clinical disease occurs in humans, involving the same organisms. Therefore, strict precautions of hygiene, especially involving exposure to broken skin or mucous membranes, are warranted. Possible risk in immunocompromised humans bitten or licked by animals.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Type II (single-organism) infections of β-hemolytic group G *Streptococcus* predominate in dogs.

HISTORY, CHIEF COMPLAINT: History of recent minor trauma (e.g., minor laceration, bite) is typical but not essential. The injury may be a nonpenetrating wound (e.g., bumping, falling).

- Swelling, pain, and lameness may be noted by the owner if the disease is concentrated on a limb.
- Concurrent sepsis results in typical systemic signs, including anorexia, depression, lethargy, weakness or collapse, and diarrhea.
- The onset of clinical signs is generally acute, and the disease progression is rapid (hours).

PHYSICAL EXAM FINDINGS

- Signs include local edematous swelling, erythema, heat, and often severe pain.
  - The intensity of pain is characteristically disproportionate to the appearance of the lesion and may be excruciating.
- Overlying skin can vary in presentation, appearing from normal to soft and exudative or as a hard eschar.
- Involved muscle bellies may be hard and severely painful on palpation.
- Systemic signs include pyrexia, tachycardia, and dehydration.
- Septic shock (see p. 1591)

ETIOLOGY AND PATHOPHYSIOLOGY

- Causative organism: Lancefield group G, β-hemolytic *Streptococcus* consistent with *S. canis* is cultured in most infections.
- Bacterial exotoxins and proteases appear to cause lesions and signs.
- An extremely rapid course of progression (line of tissue inflammation/edema visibly advances over minutes to hours) is a hallmark of necrotizing fasciitis, ultimately leading to sepsis and/or the systemic inflammatory response syndrome (SIRS) (see online chapter: Systemic Inflammatory Response Syndrome).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Generally, the diagnosis is suspected based on the clinical presentation of a patient with a vague history of mild trauma who presents with disproportionately severe soft-tissue pain.

DIFFERENTIAL DIAGNOSIS

Subcutaneous abscess, seroma, or hematoma (secondary to bleeding diathesis); soft-tissue or orthopedic trauma including fractures (suspected based on intense pain) or less compatibly, blunt trauma, bites, and other such inflictions; and envenomation (insect, venomous snake)

INITIAL DATABASE

- CBC, serum biochemistry profile, urinalysis:
  - Nonspecific abnormalities consistent with severe inflammation
  - Results often not available before important treatment decisions (e.g., amputation) need to be made
- Radiographs of affected area to rule out fractures and other lesions as cause of pain
- Advanced or septic cases have clinical pathologic abnormalities of sepsis and/or disseminated intravascular coagulation (DIC).

ADVANCED OR CONFIRMATORY TESTING

- The fulminant progression of infection requires rapid intervention, which generally precludes extensive diagnostic testing.
- Presumptive diagnosis is based on history, physical exam, absence of other causative lesion (e.g., fractures), and surgical findings; subcutaneous tissue that offers little resistance to blunt (finger) dissection, and copious foul-smelling, thin, turbid subcutaneous fluid (± bacteria and degenerate neutrophils cytologically) intraoperatively offer support for the diagnosis.
- Definitive diagnosis: histopathologic confirmation of necrotizing fasciitis and bacteriologic isolation of the causative organism.

TREATMENT

TREATMENT OVERVIEW

Prompt, intensive treatment consists of wide surgical excision of affected tissue, antimicrobial therapy, aggressive pain management, and medical therapy for shock and sepsis if present.

ACUTE GENERAL TREATMENT

- Immediate aggressive treatment for SIRS and for septic shock if present (see p. 1591).
- Early aggressive surgical débridement.
  - Immediate owner consent for amputation is essential when infection is on a limb; guarded prognosis and risk of reoperation are also important consent issues.
  - Débridement of all affected and questionable tissues, followed by copious lavage with warm isotonic fluids; the addition of chlorhexidine 0.05% may be beneficial (unconfirmed).
  - Wet-to-dry bandaging until infection is controlled; the bandage should contain a thick absorptive layer and be changed daily (at least).
- Intravenous antibiotics: β-lactamase-resistant antibiotics are generally effective against *S. canis;* a broader-spectrum regime may be superior initially, because polymicrobial infections may be present.
  - Cefoxitin, 30 mg/kg IV q 6 h; *or*
  - Cefazolin or ampicillin, 22 mg/kg IV q 6 h, plus enrofloxacin, 20 mg/kg IV q 24 h (dogs) or 5 mg/kg q 24 h (cats); alternatively, cefazolin or ampicillin as above, plus amikacin, 20 mg/kg IV q 24 h (dogs and cats)
  - Aggressive analgesia (condition is usually very painful and likely refractory to analgesics).
    - Opioids (examples: morphine sulfate, 0.05-0.15 mg/kg/h IV constant rate infusion; or buprenorphine, 0.02 mg/kg IV q 6 h) combined with a nonsteroidal antiinflammatory drug (NSAID) such as carprofen, 2.2-mg/kg SQ or PO q 12 h
    - The concern that NSAIDs caused poorer outcomes in humans was unconfirmed in prospective studies.

NUTRITION/DIET

- Enteral feeding is preferred over parenteral unless contraindicated. Feed twice basal requirements.
- Placement of an esophagostomy (see p. 1267) or gastrostomy (see p. 1270) tube during surgery, using separate instrumentation and draping.

DRUG INTERACTIONS

- NSAIDs: avoid in septic shock

POSSIBLE COMPLICATIONS

Diagnostic delays allow progression of local necrosis. Further delay or inadequately aggressive early treatment increases risk of sepsis or SIRS.

RECOMMENDED MONITORING

- Monitoring of patients for septic shock and DIC and for the progression of the infection, which would indicate the need for further débridement
- Monitoring of the bandage for amount and character of exudate

PROGNOSIS AND OUTCOME

Negative prognostic factors: delay of surgery, incomplete débridement, and concurrent sepsis. Reported mortality is 17%-60% for humans and approximately 8% for dogs to date.

PEARLS & CONSIDERATIONS

CLIENT EDUCATION

Owners should be aware that treatment of these cases is drastic and should be pursued as soon as clinical suspicion arises.

SUGGESTED READING

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1ST EDITION AUTHOR: MARK W. BOHLING

Neck Ventroflexion

BASIC INFORMATION

DEFINITION

A syndrome in which the neck is continuously or intermittently maintained in a flexed position, owing to an inability or unwillingness to extend the neck dorsally or involuntary muscular flexion of the neck

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Cats are predominantly affected, but dogs may also show neck ventroflexion.
- Age and sex both vary depending on the underlying cause for the syndrome.
- Cats: hypokalemic polymyopathy, hyperthyroidism
- Young animals: inherited myopathies
- Old animals: chronic renal failure

GENETICS & BREED PREDISPOSITION

- Burmese cat: hereditary hypokalemic periodic paralysis
- Devon rex cat: hereditary myopathy
- Labrador retriever dog: hereditary myopathy

RISK FACTORS: Hypokalemia, thiamine deficiency, organophosphate toxicity, hyperthyroidism

ASSOCIATED CONDITIONS & DISORDERS: Megaesophagus, aspiration pneumonia, generalized neuromuscular weakness

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: The syndrome can be divided into three general categories:

- Neuromuscular weakness; most common in cats
- Neck guarding; more common in dogs than cats
- Active flexion; rare

HISTORY, CHIEF COMPLAINT

- Neuromuscular weakness
  - The clinician may or may not notice ventroflexion, and it may be associated with generalized weakness, reluctance or inability to walk, stiff stilted gait, and other signs of systemic illness. Signs may be transient or persistent.
- Neck guarding
  - Clinician may notice mental depression and ataxia. The neck may be held in a fixed position, with decreased movement of the head.
- Active flexion
  - The animal may experience seizure-like activity (thiamine deficiency).
  - Dietary history: Raw fish diets are high in thiaminase, causing thiamine deficiency.

PHYSICAL EXAM FINDINGS

- Neuromuscular weakness:
  - Generalized or localized neck muscle weakness is possible. Ventroflexion may be episodic or continuous. Exercise or stress may induce weakness or collapse. Muscle pain may be present.
- Neck guarding:
  - Pain on neck manipulation can occur with or without neurologic abnormalities such as ataxia, limb reflex and proprioception abnormalities, and mental depression (cervical orthopedic/neurologic disease). The animal shows resentment or resistance to neck manipulation.
- Active flexion:
  - The animal experiences seizure-like activity, and the neck is actively tucked in under sternum; the clinician may notice

increased muscle tone and encephalopathic signs (thiamine deficiency).

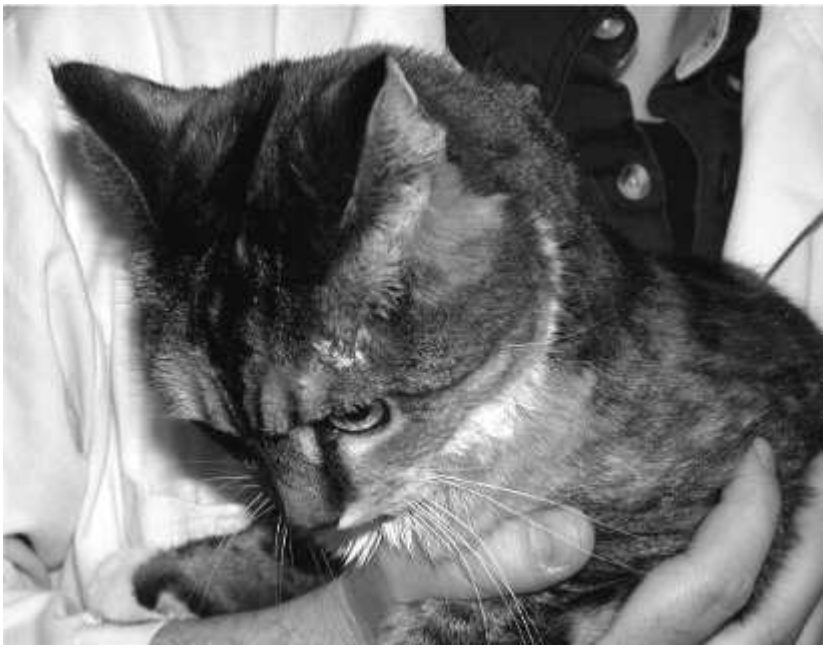
ETIOLOGY AND PATHOPHYSIOLOGY

- Weakness: muscle weakness is such that the neck muscles are unable to lift the head. Ventroflexion of the neck is a hallmark of weakness in cats.
- Neck guarding: cervical pain may cause an animal to hold the neck in a fixed flexed position (guarding) so unnecessary head and neck movement is minimized.
- The clinician may notice active contraction of the neck flexor muscles.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Neck ventroflexion is a sign, not a diagnosis. The underlying cause must be identified by a systematic diagnostic approach. Since the list of potential causes is fairly short, history, physical exam, and basic clinical blood tests are generally sufficient.



NECK VENTROFLEXION Seven-year-old female spayed domestic shorthair cat with flaccid ventroflexion of the neck due to severe hypokalemia (serum K^+ = 2.8 mEq/L).

(Courtesy Dr. Etienne Côté.)

DIFFERENTIAL DIAGNOSIS

- Neck or generalized weakness:
  - Metabolic: hypokalemia (i.e., hypokalemic polymyopathy), hypernatremic myopathy (rare), hypomagnesemia, hypoglycemia
  - Toxic (organophosphate toxicosis, botulism, tick paralysis *[Ixodes, Dermacentor],* snake bite)
  - Endocrinopathies: hyperthyroidism, hyperaldosteronism, and diabetes mellitus (hypokalemic polymyopathy)
  - Myopathies: Burmese hereditary episodic paralysis/hypokalemic periodic paralysis, Labrador retriever hereditary myopathy, Devon rex myopathy, polymyositis, myasthenia gravis, hyperkalemic periodic paralysis
  - Polyneuropathies: chronic inflammatory demyelinating polyneuropathy
- Neck pain:
  - Polyarthritis
  - Meningitis/meningoencephalitis
  - Cervical-orthopedic diseases: disk herniation, caudal cervical spondylomyelopathy, spondylitis, spinal ankylosis (hypervitaminosis A, mucopolysaccharidosis), vertebral fractures, tumors, or infections
- Active neck flexion:
  - Thiamine deficiency

INITIAL DATABASE

- Complete neurologic examination
- CBC, serum biochemistry panel (biochemistry profile to include blood glucose, creatinine, creatine kinase, sodium, potassium, calcium), urinalysis

ADVANCED OR CONFIRMATORY TESTING

- Organophosphate poisoning: serum acetylcholinesterase levels
- Myasthenia gravis: repetitive nerve stimulation, serum acetylcholine receptor antibody titer, edrophonium test
- Hyperthyroidism: serum thyroxine levels
- Other metabolic causes of weakness: serum magnesium concentration (hypomagnesemia), blood gas analysis (acid base disturbances)
- Neck pain with or without neurologic lesions localized to the neck or intracranial region: spinal survey radiographs, cerebrospinal fluid (CSF) analysis, myelogram, cervical CT, and/or MRI

Uncommon or rare:

- Polymyopathies/neuropathies: electromyography, nerve conduction velocities, nerve and muscle biopsies, preexercise and postexercise electrolyte measurements (see p. 1305 and online chapter: Electromyography and Nerve Conduction Velocity)
- Urinary fractional excretion of potassium
- Arthrocentesis (see p. 1199)

TREATMENT

TREATMENT OVERVIEW

Treatment consists of correcting the underlying problem (e.g., treat hypokalemia by potassium administration).

ACUTE AND CHRONIC TREATMENT

Depends on the underlying mechanism

POSSIBLE COMPLICATIONS

- Complications are usually associated with the underlying primary disease and not with neck ventroflexion per se.
- Megaesophagus with secondary aspiration pneumonia: myasthenia gravis, organophosphate poisoning
- Generalized weakness: decubital ulcers
- Respiratory failure: hypokalemic polymyopathy
- Dysphagia with food accumulation in larynx/pharynx, with laryngospasm and asphyxiation: Devon rex

PROGNOSIS AND OUTCOME

Depends on the underlying disease and varies from poor to good

PEARLS & CONSIDERATIONS

COMMENTS

Hypokalemic polymyopathy is probably the most common cause of ventroflexion in cats and hypokalemia must be excluded before an extensive workup is undertaken.

PREVENTION

- Appropriate amounts of potassium in food and intravenous maintenance fluids
- Appropriate thiamine levels in the diet and correct storage of food to prevent thiamine breakdown
- Correct dosage and application of organophosphate products

SUGGESTED READING

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Taboada J, Merchant S: Challenging cases in internal medicine: what's your diagnosis? Vet Med 85:932–950, 1990.

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EDITOR: ETIENNE CÔTÉ

Neck Pain

BASIC INFORMATION

DEFINITION

Sensation of discomfort or distress associated with the cervical spine or surrounding tissues

SYNONYMS

Cervical hyperesthesia or hyperpathia

EPIDEMIOLOGY

GENETICS & BREED PREDISPOSITION

- Atlantoaxial instability:
  - Toy breeds: Chihuahua, toy poodle, Pomeranian, Pekingese
- Intervertebral disk disease (IVDD): chondrodystrophoid breeds: dachshund, beagle, basset hound, Pekingese, shih tzu, other breeds
- Cervical spondylomyelopathy (CSM, Wobbler's syndrome): Great Dane, Doberman pinscher, many other breeds
- Corticosteroid responsive meningitis/arteritis: Bernese mountain dog, boxer, Nova Scotia duck tolling retriever

CONTAGION & ZOONOSIS

- Distemper viral myelitis: dog to dog
- *Brucella* canis-associated diskospondylitis: dog to dog

ASSOCIATED CONDITIONS & DISORDERS

- Horner's syndrome may be present with caudal cervical spinal lesions.
- Nerve root signature: holding up of a forelimb may be sign of nerve root pain.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Spinal disease:
  - Congenital: CSM in young Great Danes, atlantoaxial instability
  - Acquired/degenerative: IVDD, CSM in Doberman pinschers
  - Traumatic
- Infectious disease: canine distemper myelitis, systemic fungal myelitis, diskospondylitis
- Inflammatory: cranial cervical pain sometimes found with meningitis
- Traumatic: cervical fractures, instability, penetrating pharyngeal or neck wounds
- Neoplastic: spinal tumors, axial skeletal osteosarcoma, nerve sheath tumor, and other such growths

HISTORY, CHIEF COMPLAINT

- Reluctance to rise
- Reluctance to walk on stairs
- Reluctance to jump
- Crying out when changing positions, getting up, or lying down
- Shaking

PHYSICAL EXAM FINDINGS

- Abnormal head posture: holding head down, reluctant to turn head
- Arched neck or back
- Pain on manipulation of the neck

- Pain on palpation of the cervical musculature
- Reluctance to walk
- Abnormal gait if animal is neurologically impaired
- Heat and swelling in cervical tissues
- Hypersalivation, which is possible with pharyngeal injuries
- Fever associated with infections or meningitis
- Root signature (see online chapter: Root Signature [Nerve])

ETIOLOGY AND PATHOPHYSIOLOGY

- Various tissues may be the source of neck pain:
  - Epaxial musculature:
    - Traumatic muscle injury
    - Exertional rhabdomyolysis
    - Myositis from penetrating injury or foreign body (stick or grass awn migration)
    - Inflammatory myositis: immune mediated, parasitic, bacterial, or protozoal
  - Spinal column:
    - IVDD: progressive degeneration of intervertebral disk, resulting in protrusion or herniation of disk material into the spinal canal. The annulus fibrosus is the portion of the disk that contains pain receptors. Typically affects dogs 3–8 years of age but can also occur in cats.
    - Diskospondylitis: bacterial infection of vertebral body end plates; the caudal cervical region is one of the predilection sites.
    - Malformation: CSM in Great Danes, hemivertebrae, spinal canal stenosis
    - Instability: atlantoaxial instability, CSM, vertebral subluxation, traumatic fracture or luxation
    - Neoplasia: osteosarcoma, hemangiosarcoma, fibrosarcoma, chondrosarcoma, or metastatic tumors involving the vertebrae
  - Meninges:
    - Inflammatory, parasitic, protozoal, bacterial, and neoplastic lesions
  - Spinal nerves:
    - Nerve root compression, ischemia
    - Inflammation: immune mediated, infectious (protozoal, viral, parasitic)
    - Neoplasia

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis of neck pain is made by observation of the patient and physical examination. Determining the underlying cause of neck pain begins with orthopedic and neurologic examinations and a review of the history to identify duration and severity of signs and response to treatment if any (shortening the differential diagnosis list).

DIFFERENTIAL DIAGNOSIS

Neck pain is a nonspecific clinical sign. Differential diagnosis includes orthopedic, neurologic, and soft-tissue problems (see Etiology and Pathophysiology above).

INITIAL DATABASE

- Neurologic examination (see p. 1311)
- CBC
- Serum biochemistry panel
- Urinalysis
- Neck radiographs

ADVANCED OR CONFIRMATORY TESTING

- Myelogram (see p. 1306), CT (see p. 1233), or MRI (see p. 1302)
  - Very useful for spinal imaging
  - Myelogram with dynamic views may be useful for diagnosis of CSM.
  - Myelogram is also useful for IVDD and some spinal tumors.
  - MRI is best for spinal cord and nerve lesions and is becoming more widely used for IVDD.
  - MRI is more sensitive and specific than myelography or CT for identifying the location and potential cause of many

spinal lesions.
    - CT is best for evaluating bony lesions: tumors and fractures of the spine.
    - CT can be used as an adjunct to myelography.
- Cerebrospinal fluid (CSF) tap if meningitis or neoplasia is suspected (see p. 1461)
- Aspiration or biopsy of abnormal tissues
- Ultrasound of soft tissues to locate an abscess, foreign body, neoplasm, or other such abnormalities
- Surgical exploration
    - Histopathologic evaluation of tissue samples
    - Bacterial culture and sensitivity (C&S)
- Urine culture and possibly blood culture if there is a concern for diskospondylitis

TREATMENT

TREATMENT OVERVIEW

In most cases, therapeutic tenets are relief of pain, immobilization if movement is detrimental or painful, and treatment of underlying disease process.

ACUTE GENERAL TREATMENT

- Animals with acute severe neck pain are often treated with cage rest and medications such as analgesics (hydromorphone, 0.1-0.2 mg/kg SQ, IM, or IV as needed up to q 4 h; or buprenorphine, 10–15 mcg/kg IV q 6–8 h; or butorphanol, 0.1–0.2 mg/kg IV as needed up to q 4 h); and/or muscle relaxants (methocarbamol, 20–50 mg/kg PO q 8 h). Empirical glucocorticoids given prior to ruling out infectious causes can exacerbate infectious diseases.
- If spinal instability is suspected, a neck brace for immobilizing the neck can provide pain relief and prevent further tissue damage. Cage rest and exercise restriction are also important for the same purpose.

CHRONIC TREATMENT

- Nonsteroidal antiinflammatory drugs (NSAIDs; e.g., carprofen, 2 mg/kg PO q 12 h; or etodolac, 10-15 mg/kg PO q 24 h; or deracoxib, 1-2 mg/kg PO q 24 h; or firocoxib, 4-5 mg/kg PO q 24 h; or meloxicam, 0.1 mg/kg PO q 24 h)
- Low-dose corticosteroids: clinician should taper the medication during periods of improvement.
- Amantidine, 3–5 mg/kg PO q 24 h; or other agents such as tramadol, 1–4 mg/kg PO q 8–12 h; or gabapentin, 10 mg/kg PO q 8 h, can be used as adjunctive medications for pain management.
- Acupuncture
- Surgery if indicated by imaging and lack of response to conservative therapy

BEHAVIOR/EXERCISE

- Exercise restriction
- Use of a harness instead of a collar for walks
- Elevation of food and water bowls

DRUG INTERACTIONS

The clinician should never coadminister NSAIDs with corticosteroids, owing to risk of serious or life-threatening gastroenteritis and gastrointestinal ulceration.

POSSIBLE COMPLICATIONS

- Adverse reactions to the medication, especially gastrointestinal ulceration caused by taking corticosteroids and NSAIDs simultaneously, may occur.
- Pneumonia is a common complication in dogs that have tetraparesis and are recumbent.
- Respiratory obstruction is possible with a neck brace; it is important to adjust the brace so it fits properly, and the owner and clinician should monitor the animal.
- Paralysis or death is possible with acute spinal injury.

RECOMMENDED MONITORING

Any dog with signs of neck pain should be closely monitored for the development of neurologic conditions such as ataxia, paresis, paralysis, and respiratory impairment. These conditions suggest a neurologic cause and possibly warrant intensive care and further intervention.

PROGNOSIS AND OUTCOME

Highly variable depending on underlying disease process

PEARLS & CONSIDERATIONS

COMMENTS

- Neck pain in certain dog breeds is a very common problem in clinical practice.
- All dogs being considered for nonspecific supportive treatment should have cervical spinal radiographs prior to treatment.
- Cage rest, typically for at least 4 weeks is a critical component of conservative treatment.
- If a dog does not respond appropriately to nonspecific supportive therapy, the clinician should perform further diagnostic testing.

PREVENTION

- Owners should use a harness for walking their dogs.
- The clinician should inform the owner of exercise restrictions.

SUGGESTED READING

Wheeler SJ, Sharp NJ: Small animal spinal disorders: diagnosis and surgery. Baltimore, 1994, Mosby-Wolfe.

AUTHOR: DAVID A. PUERTO

EDITOR: ETIENNE CÔTÉ

Nasopharyngeal Stenosis

BASIC INFORMATION

DEFINITION

Narrowing or obliteration of the communication between the nasopharynx and oropharynx, usually involving the rostral nasopharynx

EPIDEMIOLOGY

SPECIES, AGE, SEX: Nasopharyngeal stenosis can be seen in cats and dogs of any age or gender.

GENETICS & BREED PREDISPOSITION: Smooth-haired dachshunds have been described with anomalous development of pharyngeal musculature, contributing to caudal nasopharyngeal stenosis.

RISK FACTORS: Recurrent/chronic rhinitis, nasopharyngeal surgery, reflux of gastric contents into the nasopharynx during anesthesia

ASSOCIATED CONDITIONS & DISORDERS: Chronic rhinitis and sinusitis

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Congenital stenosis of the internal nasal meatus has been described in the literature. Most cases, however, are acquired.

HISTORY, CHIEF COMPLAINT: Some or all of the following may be present:

- Upper respiratory tract disease:
  - Nasal discharge
  - Nasal stertor
  - Sneezing
  - Intermittent respiratory distress, especially cats since they are reluctant to open-mouth breathe
- Worsening of the respiratory signs during sleeping, eating or swallowing
- Poor response to empirical therapy

PHYSICAL EXAM FINDINGS

- Nasal discharge
- Nasal stridor

ETIOLOGY AND PATHOPHYSIOLOGY

- In cats, this condition is thought to result from scar formation across the rostral nasopharynx secondary to mucosal ulceration from chronic rhinitis and/or sinusitis. Therefore, the disease is usually associated with recurrent upper respiratory tract infections or allergic disease. Scar formation leads to complete or partial obstruction of the rostral nasopharynx, resulting in the accumulation of nasal secretions within the nasal cavity and consequent nasal stertor and discharge.
- Nasopharyngeal injury from surgery or contact with gastric contents or other caustic material can presumably provoke inflammation and scar tissue formation.
- Chronic inflammation from nasopharyngeal foreign bodies in dogs has also been anecdotally associated with the disease.
- Abnormal development of the muscles of the soft palate and pharynx, causing stenosis of the caudal nasopharynx, has been described in smooth-haired dachshunds.
- Nasopharyngeal tumors can also cause stenosis.
- There is a single report of choanal atresia with secondary rostral nasopharyngeal stenosis in a 20-month-old shih tzu dog.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Nasopharyngeal polyps

- Chronic rhinitis or sinusitis
- Foreign body
- Intranasal or nasopharyngeal neoplasia
- Mycotic rhinitis

INITIAL DATABASE

- CBC: usually normal
- Urinalysis: usually normal
- Serum biochemistry profile: usually normal

ADVANCED OR CONFIRMATORY TESTING

- Diagnostic imaging:
  - Nasal radiographs may be normal or show opacification of turbinate structures secondary to accumulation of nasal secretions or a mass in the nasopharynx.
  - CT scan can document the presence of a stenotic lesion or mass in the nasopharynx.
- Other diagnostic procedures:
  - Inability to pass a small catheter (3.5 Fr gauge) gently through the ventral nasal meatus into the pharynx
  - Visualization of the membrane by use of a retroflexed pediatric bronchoscope or a dental mirror
  - Histopathologic or cytologic examination of masses

TREATMENT

TREATMENT OVERVIEW

The primary aim of therapy is restoration of nasopharyngeal patency.

ACUTE GENERAL TREATMENT

Restoration of nasopharyngeal patency by:

- Surgical resection of a stenotic membrane or mass
- Dilation of the stenosis with a valvuloplasty balloon dilation catheter under endoscopic or fluoroscopic guidance
- Placement of a stent across the stenotic region:
  - Often requires CT scanning of the head, and endoscopic and fluoroscopic capabilities

CHRONIC TREATMENT

- Antiinflammatory doses of corticosteroids after surgery/dilation
- Other treatments (surgery, chemotherapy, radiation therapy) for neoplastic causes
- Stenting would be of potential palliative benefit for neoplastic stenosis not treatable by other means.

POSSIBLE COMPLICATIONS

Recurrence of the stenosis

RECOMMENDED MONITORING

Clinical signs

PROGNOSIS AND OUTCOME

Dependent on the ability to restore nasopharyngeal patency. Long-term resolution of clinical signs has been achieved with balloon dilation and stents in patients with non-neoplastic acquired stents.

PEARLS & CONSIDERATIONS

PREVENTION

Conditions that predispose to nasopharyngeal stenosis are difficult to predict, prevent, or treat, so prevention of stenosis is likewise difficult to prevent.

TECHNICIAN TIPS

- Be prepared for rapid endotracheal intubation of affected cats once anesthesia has been induced.
- Feed small frequent meals of a soft consistency, especially after surgery.

CLIENT EDUCATION

Recurrence is possible.

SUGGESTED READING

Berent AC, Weisse C, Todd K, et al: Use of a balloon-expandable metallic stent for treatment of nasopharyngeal stenosis in dogs and cats: six cases (2005-2007). J Am Vet Med Assoc 233:1432–1440, 2008.

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Nasopharyngeal Polyp

BASIC INFORMATION

DEFINITION

Non-neoplastic pedunculated mass originating from the middle ear or auditory tube epithelium. Well recognized in young adult cats; very rare in dogs.

SYNONYM

Inflammatory polyp

EPIDEMIOLOGY

SPECIES, AGE, SEX: Primarily in young adult cats

RISK FACTORS: Chronic inflammation of the upper respiratory tract or any process that obstructs middle ear drainage are proposed.

ASSOCIATED CONDITIONS & DISORDERS

- Otitis media, interna, or externa
- Horner's syndrome

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Ear (aural) polyp if mass grows into external ear canal instead of nasopharynx

HISTORY, CHIEF COMPLAINT

- Nasal discharge
- Sneezing
- Stertor
- Dyspnea
- Dysphagia
- Gagging
- Voice change
- +/− Headshaking or pawing at ears if concurrent otitis externa. Presence of concurrent nasopharyngeal and aural polyps is rare.
- +/− Vestibular signs if concurrent otitis externa progresses to otitis media/interna

PHYSICAL EXAM FINDINGS

- Increased inspiratory noise (often stertor)
- Mucoid to mucopurulent nasal discharge (unilateral or bilateral)
- Gagging
- Unilateral deafness in 35% of cats because of concurrent middle ear disease
- Uncommon signs include otitis externa, head tilt, ataxia, nystagmus, or facial nerve palsy.
- +/− Horner's syndrome: miosis, ptosis, enophthalmos, and third eyelid prolapse on affected side

ETIOLOGY AND PATHOPHYSIOLOGY

- Exact etiology is unknown, but proposed causes include inflammatory conditions and congenital persistence of branchial arches.
    - The significance of herpesvirus, calicivirus, bacteria, or fungi recovered from polyps is questionable.
- It is suspected that proliferation of the auditory (eustachian) tube or tympanic bulla mucosal epithelium obstructs drainage from the middle ear. The resulting fluid accumulation and inflammation (otitis media), which can extend into the inner ear (otitis interna) or drain through the tympanic membrane (otitis externa), provokes formation of a fibrous polyp.
- Enlarged mass fills the nasopharyngeal region, obstructing caudal nasal drainage and airflow, eventually impeding inspiration

and swallowing and causing nasal discharge.
- Alternatively, the tympanic membrane ruptures, and the mass extends into the horizontal ear canal.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The primary method of diagnosis is visualizing a firm, pink mass dorsal to the soft palate on oral examination under anesthesia. Confirmation is based on histologic analysis.

DIFFERENTIAL DIAGNOSIS

- Neoplasia (e.g., lymphoma, squamous cell carcinoma)
- Infectious rhinitis
- Nasal/nasopharyngeal foreign body
- Nasopharyngeal stenosis
- Laryngeal paralysis
- Granuloma (cryptococcosis)

INITIAL DATABASE

- Results of the CBC, biochemistry panel, and urinalysis are usually normal.
- Otoscopic examination:
  - If the patient has otitis media, bulging of tympanic membrane from fluid or mass is noted.
  - Masses extending through the tympanic membrane are visible in the external ear canal.
  - If the tympanic membrane has ruptured, the cat will have otitis externa.
- Skull radiographs:
  - Increased soft-tissue density in pharynx (lateral view)
  - Evidence of otitis media:
    - Enlarged or thickened bulla containing increased soft-tissue density

ADVANCED OR CONFIRMATORY TESTING

- Oral examination under anesthesia:
  - Palpable mass dorsal to soft palate or mass protruding into oropharynx
- CT:
  - Increased fluid and soft-tissue density in bulla
  - The bulla wall may be thickened or thin and distended.
- Histologic examination:
  - Well-vascularized fibrous tissue covered by stratified squamous or columnar epithelium
  - Inflammatory cells, primarily lymphocytes, plasma cells, and macro-phages, present within the stroma

TREATMENT

TREATMENT OVERVIEW

Nasopharyngeal polyp removal by gentle, steady traction and avulsion will cure many cats; recurrence rates are lower if removal is combined with bulla osteotomy or oral prednisolone therapy.

ACUTE GENERAL TREATMENT

- Oxygen supplementation (see p. 1318) if the patient is in respiratory distress.
- Induction of general anesthesia and removal of the polyp. Retract soft palate rostrally with spay hook, stay sutures, or Babcock forceps, and grasp the polyp gently at the base with Allis tissue forceps. Apply slow steady traction to avulse stalk of polyp from auditory tube or middle ear.
- Ventral bulla osteotomy with removal of the epithelial lining to reduce recurrence rate; culture from the bulla is also indicated at the time of surgery.

CHRONIC TREATMENT

Antibiotics if otitis media present (e.g., amoxicillin with clavulanic acid, 62.5 mg/cat PO q 12 h until culture results return).

POSSIBLE COMPLICATIONS

- Horner's syndrome is seen in approximately 80% of cases after a bulla osteotomy and can also occur with polyp traction avulsion alone; it usually resolves within 1 month.
- Otitis interna occurs in approximately 40% of cases following ventral bulla osteotomy; ataxia and head tilt can affect quality of life.

RECOMMENDED MONITORING

- Reevaluate nasopharynx, bulla, external ear canal if clinical signs recur.
- Repeat otoscopic examination and otic cytologic examination if otitis externa is present.

PROGNOSIS AND OUTCOME

- Polyp regrowth reported in 11%-50% of cats treated with traction avulsion without concurrent ventral bulla osteotomy. Recurrence lowest when postoperative prednisolone administered.
- Ventral bulla osteotomy prevents recurrence in most cats.
- Deafness in affected ear often persists after polyp removal.

PEARLS & CONSIDERATIONS

COMMENTS

- CT is more sensitive than survey skull radiographs for detecting otitis media.
- For a broad-based mass, fine-needle aspiration and cytologic evaluation are indicated to rule out lymphoma.
- The feline tympanic bulla has two chambers; the epithelial lining of both chambers should be removed during bulla osteotomy.
- Sympathetic fibers are superficial in the feline bulla; thus, development of Horner's syndrome is likely after bulla osteotomy.
- With traction alone, treatment with prednisolone (1–2 mg/kg PO q 24 h for 2 weeks after the procedure) reduces recurrence.

TECHNICIAN TIPS

- Cats with nasopharyngeal polyps can be difficult to intubate if the polyp is large. An intravenous catheter placed before induction permits administration of intravenous anesthetics.
- A laryngoscope and several sizes of cuffed endotracheal tubes should be available. Mucus and saliva may collect at the back of the throat; therefore, suction or swabs may be needed during intubation.
- The endotracheal tube may need to be tied to the lower jaw to allow soft palate retraction.
- The cuff of the endotracheal tube should be inflated, since hemorrhage is possible after polyp extraction.

CLIENT EDUCATION

Complications with bulla osteotomy are common but usually temporary.

SUGGESTED READING

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Veir JK, et al: Feline inflammatory polyps: historical, clinical, and PCR findings for feline calicivirus and feline herpes virus-1 in 28 cases. J Fel Med Surg 4:195, 2002.

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Nasal Neoplasia

BASIC INFORMATION

DEFINITION

Neoplastic growth, usually malignant, originating in the nasal passages

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Rare in cats (1% of all tumors). Older (mean age 8–10 years), neutered male cats most often affected. Has been reported as early as 2 years of age.
- In dogs, nasal tumors represent l%-2.4% of all tumors. Older dogs (mean 9-10 years; earliest reported age of 1 year) most often affected; possible male predilection.

GENETICS & BREED PREDISPOSITION: Airedale terrier, basset hound, collie, German shepherd, German short-haired pointer, keeshond, and Old English sheepdog thought to have an increased risk.

RISK FACTORS: Possible but not consistently proven risk factors include large breed, dolichocephalic breeds, urban environment, and exposure to secondhand smoke.

ASSOCIATED CONDITIONS & DISORDERS: Central nervous system signs (seizures or behavior changes) from direct tumor invasion into the brain are possible. Paraneoplastic syndromes are rare, but hypercalcemia and erythrocytosis have been reported.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Malignant tumors:
  - Epithelial:
    - Adenocarcinomas, squamous cell carcinomas, and other carcinomas account for two-thirds of nasal tumors.
  - Mesenchymal:
    - Chondrosarcoma is the most common.
    - Osteosarcoma and fibrosarcoma can occur.
    - Lymphoma is more common in cats.
  - Miscellaneous (usually rare):
    - Transmissible venereal tumors (likely to be more common where this tumor is common)
    - Olfactory neuroblastoma
    - Melanoma
- Benign tumors:
  - Epithelial or mesenchymal
  - Inflammatory polyps

HISTORY, CHIEF COMPLAINT: Average duration of clinical signs prior to diagnosis is 3–4 months:

- Epistaxis
- Bilateral or unilateral nasal discharge
- Airflow obstruction
- Sneezing or reverse sneezing
- Stertor
- Facial deformity: more common in cats
- Neurologic signs rare but may be the only clinical sign of nasal tumors

PHYSICAL EXAM FINDINGS: Same as chief complaints:

- Airflow obstruction may be detected via a mirror or glass held at the nares or from an occlusion of one nostril at a time while listening to airflow at the opening of the nares.
- Stertor

- Mandibular lymph node enlargement
- Diminished ocular retropulsion; pain with ocular retropulsion or opening mouth
- Facial deformity
- Altered mentation
- Physical exam may be unremarkable insofar as signs such as epistaxis and nasal discharge can be intermittent.

ETIOLOGY AND PATHOPHYSIOLOGY

Weak links to exposure to urban environmental pollution and secondhand smoke in the dog, and exposure to wood dust and employment in boot making and the flooring industry in people, leads to conjecture that pollutants filtered in the nasal passages initiate or promote neoplastic transformation. Upregulation of the cyclooxygenase-2 enzyme in canine nasal epithelial tumors has been recently described, but its role in tumorigenesis (if any) is unknown.

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

Nasal neoplasia is a common cause of nasal discharge, particularly in middle-aged to older dolichocephalic breeds of dogs. Be suspicious of nasal neoplasia in a dog with a history of chronic nasal discharge that is responsive to antibiotics but recurs.

DIFFERENTIAL DIAGNOSIS

- Epistaxis (see p. 357):
  - Inherited or acquired coagulopathies, including platelet and endothelial disorders
  - Infectious diseases:
    - Ehrlichiosis
    - Babesiosis
    - Leishmaniasis
    - Rocky Mountain spotted fever
  - Trauma
- Nasal discharge, obstruction, sneezing or reverse sneezing:
  - Foreign body
  - Granuloma
  - Infectious (fungal, bacterial) rhinitis or sinusitis
  - Tooth root abscess
  - Nasal mites
  - Allergic rhinitis

INITIAL DATABASE

- CBC
  - Inflammatory leukogram possible
  - Mild to moderate anemia that can be nonregenerative or microcytic
  - Erythrocytosis occasionally with fibrosarcoma
- Biochemical profile
  - Hypoproteinemia if severe hemorrhage (uncommon)
- Mandibular lymph node aspiration may show evidence of metastasis (10% of cases at diagnosis).
- Thoracic radiographs usually normal, but evidence of metastasis may be seen.

ADVANCED OR CONFIRMATORY TESTING

- Nasal imaging:
  - Plain radiographs: least sensitive, but dorsoventral intraoral and rostrocaudal frontal sinus views may identify loss of trabecular bone and increased density in the normally air-filled sinuses.
  - CT or MRI best identify and define the full extent of a tumor and can aid in distinguishing a tumor mass from fluid and surrounding tissues.
  - To avoid iatrogenic artifacts, imaging should be performed prior to biopsy whenever possible.
- Rhinoscopy may demonstrate a mass in the nasal cavity.
- Biopsy:
  - Blind transnasal core biopsy, with the location determined by previous imaging, provides the best samples.
  - Samples obtained with rhinoscopic guidance may be too small for accurate diagnosis.
  - Rarely, rhinotomy may be needed to obtain diagnostic samples.

TREATMENT

TREATMENT OVERVIEW

Because cure is usually not possible for nasal malignancies, alleviation of clinical signs becomes the focus of treatment.

ACUTE GENERAL TREATMENT

- Epistaxis:
  - Sedation
  - Packing of the nasal passages with epinephrine-soaked gauze
  - Application of cold compresses to the patient's nose
  - Ligation of the ipsilateral carotid artery (rarely needed)
- Nasal congestion, discharge:
  - Antimicrobials for secondary bacterial infections, based on a culture and sensitivity (C&S) test
  - Antiinflammatory medications (steroidal or nonsteroidal) may help but should be used cautiously.

CHRONIC TREATMENT

- External beam fractionated radiation therapy is considered definitive therapy.
  - Median survival 8-31 months depending on the report cited
  - Coarse-fractionated radiation therapy can be used for palliation.
- Chemotherapy may palliate clinical signs.
  - Carboplatin combined with piroxicam has shown the greatest response.
- Radiation therapy combined with chemotherapy does not increase survival over radiation alone.
  - Feline nasal lymphoma may be the exception.
- Surgery alone is not recommended, as it does not prolong life.
  - Surgery after accelerated radiation therapy had a reported survival of 16 months, but side effects were significant.

POSSIBLE COMPLICATIONS

- Radiation damage to the surrounding tissues will be seen acutely with mucositis, conjunctivitis, and dermatitis lasting about 2 weeks post radiation therapy. Chronic changes (late effects) can also be seen in the eye, brain, and nasal passages but are less common and should not severely affect quality of life.
- Tumor progression can cause central nervous system signs.

RECOMMENDED MONITORING

Primarily clinical signs; imaging (more than 3 months after radiation) may also be helpful.

PROGNOSIS AND OUTCOME

Varies with tumor type (animals with sarcomas generally live longer than those with carcinomas), clinical stage of tumor at time of treatment, and total dose of radiation delivered to the entire tumor. Median survival ranges from 8-31 months. Comparison of data from various reports is difficult, limiting its use to offer accurate prognoses. Feline nasal lymphoma can carry a good prognosis, with median survivals of >3 years.

PEARLS & CONSIDERATIONS

COMMENTS

- Treatment of nasal tumors with definitive curative-intent radiation therapy, with possible survival of as little as 8 months, may seem irrational. Most dogs, however, have survivals of about 1 year. Modern approaches to radiation therapy have led to decreased side effects, and most dogs tolerate therapy and have a good-quality life after therapy.
- Chemotherapy alone can also bring some relief from clinical signs, as can a more abbreviated palliative course of radiation. Even the use of piroxicam (COX-1 and COX-2 inhibitor) alone may give some relief from clinical signs for 4 months or longer (unpublished observations).
- In general, nasal tumors should be considered treatable even though they are not often curable.

PREVENTION

There is no means of preventing the development of nasal tumors.

TECHNICIAN TIPS

- While of low diagnostic yield, cytologic examination of nasal exudate can occasionally lead to a definitive diagnosis of the underlying cause of nasal disease.
- The plastic tubes that cover some IV catheters can be modified to attach a syringe and then used as a nasal biopsy instrument.

CLIENT EDUCATION

- Dogs with persistent nasal discharge may require advanced imaging to diagnose the cause of the problem.
- Acute effects of radiation therapy may not be apparent at the end of radiation therapy but can still develop within 1-2 weeks after the last dose of radiation has been administered. These acute effects often subside within an additional 1-2 weeks. Analgesics, antibiotics, and occasionally glucocorticoids can be used in animals experiencing severe acute effects of radiation therapy.

SUGGESTED READING

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Nasal Mites

BASIC INFORMATION

DEFINITION

Infection of the nasal cavity with the mite *Pneumonyssoides caninum,* an uncommonly recognized cause of nasal disease in dogs

SYNONYMS

Pneumonyssus caninum, nasal acariasis

EPIDEMIOLOGY

SPECIES, AGE, SEX: Nasal mite infection is primarily a disease of dogs; any age or gender can be affected.

GENETICS & BREED PREDISPOSITION: There are no known breed, sex, or age predilections.

RISK FACTORS: Contact with an infected animal.

CONTAGION & ZOONOSIS: *Pneumonyssoides caninum* has only been reported in dogs and foxes *(Vulpes vulpes).*

GEOGRAPHY AND SEASONALITY: Nasal mites appear to have a worldwide distribution with no seasonality.

ASSOCIATED CONDITIONS & DISORDERS: Nasal mites have been associated with gastric dilatation and volvulus.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- The most commonly reported clinical signs are reverse sneezing and sneezing.
- Other reported clinical signs include nasal discharge (typically serous), facial pruritus, head shaking, and hyposmia.
- Epistaxis and orbital cellulitis are uncommon presenting complaints.
- Many dogs have vague signs (restlessness) or are asymptomatic.

PHYSICAL EXAM FINDINGS

- Mites may or may not be observed on or around the external nares.
- ± Nasal discharge
- Epistaxis (rare)

ETIOLOGY AND PATHOPHYSIOLOGY

- *Pneumonyssoides caninum* are non-sarcoptiform mites found in the nasal and paranasal sinuses of dogs.
- Mode of transmission is currently unknown; however, it is thought to occur by direct transfer of larvae from dog to dog. Transmission has been reported between dogs housed together.
- The complete life cycle is unknown; however, adults and larvae have been identified in dogs.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis requires direct observation of the mites around the external nares or in the nares or nasal cavity.

DIFFERENTIAL DIAGNOSIS

Other causes of nasal cavity disease including foreign body, fungal rhinitis, noninfectious rhinitis, neoplasia, dental disease, coagulopathy and *Eucoleus boehmi* (nasal capillarid)

INITIAL DATABASE

- CBC:
  - Mild eosinophilia (nonspecific)
- Rhinoscopy and/or pharyngoscopy:
  - Direct visualization of nasal mites
- Retrograde nasal flushing:
  - Observation of mites in collected fluid

TREATMENT

TREATMENT OVERVIEW

Administration of drugs with acaricidal activity usually eliminates the infection.

ACUTE GENERAL TREATMENT

- Ivermectin, 300 mcg/kg PO weekly for 3 weeks
  - Ivermectin (or other macrocyclic lactones) should not be used in collies and other breeds with the MDR-1 mutation (see p. 706)
- Ivermectin, 200-400 mcg/kg SQ q 2 weeks for 3 treatments
- Selamectin (Revolution), 6-24 mg/kg applied topically q 2 weeks for 3 treatments.
- Milbemycin (Interceptor), 0.5-1 mg/kg PO q 7 days for 3 treatments. Safe for breeds sensitive to macrocyclic lactones.
- All dogs within the same household should be treated, as transmission is unknown but likely occurs by direct transfer between dogs. Cats do not require treatment, because *P. caninum* has not been reported in cats.

POSSIBLE COMPLICATIONS

Dogs with the MDR-1 mutation (ABCB1 −1Δ polymorphism) treated with macrocyclic lactones may experience ataxia, obtundation, hypersalivation, mydriasis, loss of menace, and possibly death. Alternative treatments such as milbemycin should be used for affected animals.

PROGNOSIS AND OUTCOME

Prognosis is excellent.

PEARLS & CONSIDERATIONS

COMMENTS

Nasal mites should be considered as a differential diagnosis for dogs with vague or nonspecific signs of upper respiratory tract disease in which imaging is unremarkable.

PREVENTION

Preventive measures have not been established.

TECHNICIAN TIP

Testing for the MDR-1 mutation (ABCB −1Δ polymorphism) can be accomplished by a PCR-based assay from a cheek swab. See p. 706.

CLIENT EDUCATION

Nasal mite infection is an annoyance more than a health threat to affected dogs.

SUGGESTED READING

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Nasal Discharge

BASIC INFORMATION

DEFINITION

- Fluid discharge from the external nares
- Although usually obvious, the discharge can sometimes be missed due to licking or caudal drainage.
- The underlying etiology of the discharge can be intranasal or extranasal disease.
- The type and duration of the discharge varies with the underlying cause.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Younger cats may have viral upper respiratory infections (see p. 1127) or nasopharyngeal polyps (see p. 751).
- Younger unvaccinated dogs are more likely to have canine viral respiratory infections.
- Younger animals may have congenital deformities, such as a cleft palate.
- Older animals are more likely to have neoplastic or dental-related causes of nasal discharge.
- Hunting and working dogs are more likely to have nasal foreign bodies.

GENETICS & BREED PREDISPOSITION

- Brachycephalic breeds have upper airway problems that may lead to nasal discharge.
- Dolichocephalic breeds may be more prone to nasal neoplasia.
- Several specific breeds can be affected by primary ciliary dyskinesia or cleft palate-cleft lip complex (see pp. 916 and p. 218).

RISK FACTORS

- Lack of adequate immunization against viral respiratory infections
- Exposure to unvaccinated animals and high-density husbandry/housing situations
- Geographic locations where grass awns are ubiquitous
- Dental disease and poor dental care
- Immunosuppression (fungal disease)
- Compromise of nasal mucosa (secondary bacterial infections)
- Outdoor exposure (infection, foreign bodies, trauma)

CONTAGION & ZOONOSIS: Viral upper and lower respiratory tract infections.

GEOGRAPHY AND SEASONALITY: Geographic locations where grass awns are ubiquitous (dogs) or where there is lush green grass (blade of grass foreign bodies in outdoor cats)

ASSOCIATED CONDITIONS & DISORDERS: Sneezing

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Types of nasal discharge:

- Serous: clear and watery (acellular)
- Mucoid: clear and thick (acellular with high protein content)
- Purulent: yellow-tan and thick (neutrophilic with bacteria)
- Sanguineous: red-tinged (blood mixed with another type of discharge)
- Hemorrhagic (epistaxis): frank red blood

HISTORY, CHIEF COMPLAINT: Acute onset of paroxysmal sneezing or nasal discharge may suggest nasal foreign bodies or an early viral disease. Husbandry and management practices predispose animals to certain disorders. Examples: recent boarding or exposure to new animals (viral infections); hunting and geographic location (nasal foreign bodies); pertinent medical history (dental disease, history of neoplasia, immunosuppression); exposure to irritating aerosols (hairspray, paints, etc.); vaccine history (viral respiratory tract infections). A complete history should include:

- Recent exposure to new or young animals (infectious diseases)
- Environmental risk factors such as inhaled irritants, foreign bodies, exposure to rodenticides
- Pertinent medical history such as hypertension, current medications, or a history of neoplasia
- Vaccination status
- Acute versus chronic onset (acute onset more likely to be caused by foreign bodies and early viral infection)

PHYSICAL EXAM FINDINGS

- Serous, mucopurulent, or hemorrhagic discharge that may be unilateral or bilateral
- Concurrently possible, suggesting an intranasal or local problem:
  - Facial deformity
  - Exophthalmos
  - Tooth root abscess, oronasal fistula
  - Ocular discharge (e.g., with local disorders, such as an intranasal mass obstructing the nasolacrimal duct)
  - Pawing at face
- Concurrently possible, suggesting an extranasal or systemic problem:
  - Ocular discharge (e.g., with systemic infections, such as canine distemper)
  - Petechiation, ecchymoses
  - Cough, lethargy, inappetence (pneumonia, pulmonary hemorrhage, other)

ETIOLOGY AND PATHOPHYSIOLOGY

- Serous: due to local irritation, early viral infection, allergic rhinitis, or excessive lacrimation
- Mucoid: due to chronic noninfectious irritation and overproduction of mucus by nasal epithelial cells
- Purulent: usually due to secondary bacterial infection
- Sanguineous: due to compromise of the nasal mucosa
- Hemorrhagic (epistaxis): due to local or systemic causes of bleeding

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Nasal discharge is apparent on physical exam, though its onset and volume may be underestimated, since animals lick it away. The gross appearance of the discharge guides diagnostic testing.

DIFFERENTIAL DIAGNOSIS

- Feline viral upper respiratory tract infections (feline rhinotracheitis, feline calicivirus, *Chlamydia psittaci)*
- Neoplasia (adenocarcinoma, lymphosarcoma, undifferentiated carcinoma, osteosarcoma, chondrosarcoma, fibro-sarcoma, transmissible venereal tumor)
- Foreign bodies
- Tooth root abscess, oronasal fistula
- Nasopharyngeal polyps (cats)
- Canine viral infections (canine distemper virus, canine parainfluenza virus, canine herpesvirus, canine adenovirus, types 1 and 2)
- Mycotic infection *(Aspergillus* spp. in dogs; *Cryptococcus* spp. in cats)
- Parasitic rhinitis *(Cuterebra* spp., *Pneumonyssoides caninum, Linguatula serrata)*
- Bacterial infections (usually secondary)
- Rhinitis (allergic/eosinophilic type I hypersensitivity, lymphoplasmacytic, chronic hyperplastic)
- Congenital defects (cleft palate-cleft lip complex, primary ciliary dyskinesia)
- Trauma
- Inhaled irritants (cat litter dust, aerosols, smoke)
- Epistaxis (local causes: mycotic infections, neoplasia, foreign body, trauma; systemic causes: inherited or acquired coagulopathies, thrombocytopenia, thrombocytopathia, hypertension, vasculitides)

INITIAL DATABASE

- Physical assessment for unilateral versus bilateral nasal disease performed by holding a glass microscope slide close to the external nares while holding the animal's mouth closed. When the animal exhales through the nose, steam will be present asymmetrically or unilaterally (one naris obstructed) or not at all (both nares obstructed). Neoplasia, foreign bodies, and dental disease are often causes of unilateral nasal disease and discharge, whereas other local and systemic conditions often result in bilateral disease.

- Oral examination to look for hard palate masses
- Fundic examination to look for evidence of neoplasia, fungal disease, hypertension, and associated retinal hemorrhage
- Eye globe retropulsion to assess for retrobulbar masses
- Blood pressure measurement to assess for systemic hypertension
- CBC including platelet count to look for evidence of infection, inflammation, or thrombocytopenia
- Serum biochemistry profile
- Feline leukemia and feline immunodeficiency viral testing
- Thoracic radiographs (pneumonia, metastatic disease); pneumonia commonly causes mucopurulent nasal discharge, but the reverse process (primary nasal discharge causing a secondary pneumonia) virtually never occurs.

ADVANCED OR CONFIRMATORY TESTING

Any of the following may be indicated, depending on signalment, history, and preliminary exam findings: Rocky Mountain spotted fever, *Ehrlichia,* and *Bartonella* testing; prothrombin time; partial thromboplastin time; thoracic radiographs; nasal swabs; fungal titer determinations; nasal radiography; CT; MRI; rhinoscopy; biopsy; deep tissue cultures; and exploratory rhinotomy.

TREATMENT

TREATMENT OVERVIEW

- Eliminate underlying etiology of nasal discharge.
- Restore normal nasal function.
- Reduce pain and discomfort.
- Provide supportive care.
- Relieve dyspnea, especially in cats that often will not readily breathe with an open mouth.

ACUTE GENERAL TREATMENT

- If discharge is causing dyspnea, oxygen therapy may be needed.
- Treatment for underlying coagulopathy (e.g., vitamin K1; 0.25–2.5 mg/kg for first-generation rodenticide intoxication or 2.5 mg/kg for second-generation rodenticide intoxication, SQ or PO q 12 h × 7–28 days, and fresh frozen plasma transfusion)
- Correct dehydration and electrolyte abnormalities as necessary.
- Broad-spectrum antibiotics if secondary nasal/dental infection (bacteria are rarely the primary cause of nasal disease, but secondary infection with normal nasal flora is common) or pneumonia (culture and sensitivity [C&S] test for the lower airways is essential if pneumonia is present). *Bartonella* spp. have been recently implicated as a cause of chronic rhinitis and epistaxis; azithromycin appears to be the drug of choice (5–10 mg/kg PO q 24 h; start at 5 mg/kg and, if tolerated, increase by 2.5 mg/kg each day. After 1 week, reduce to q 48 h).
- Analgesics if painful (e.g., opiates such as buprenorphine, 0.006–0.01 mg/kg IV/IM q 6-8 h; nonsteroidal antiinflammatory drugs [NSAIDs] such as deracoxib, 1–2 mg/kg PO q 24 h, can also be used). Use NSAID analgesics with caution if the animal has a history of concurrent renal, liver, gastrointestinal, or hemostatic disorders.
- Clinicians should remove the animal from environmental agents (e.g., smoke, dust); if not possible, the clinician should introduce measures to reduce exposure (e.g., air filtration systems).
- Clinicians should consider recommending surgery for treating dental disease, neoplasia, nasopharyngeal polyps, cleft palate, foreign bodies, or traumatic causes.
- Rhinoscopy for removal of a foreign body
- Radiation and/or chemotherapy for neoplasia as appropriate (based on biopsy results)
- Chemoembolization of nasal tumors may be considered when surgery, radiation, or chemotherapy is associated with excessive morbidity, cost, or a poor outcome.
- Fungal: local or systemic treatment depending on type of mycotic infection
- Parasitic rhinitis: ivermectin, 0.2 mg/kg SQ or PO, twice during a 3-week period
- Decongestants and cleaning of the nares (e.g., topical pseudoephedrine [pediatric Neo-Synephrine, 1 drop in alternating nares once daily])

CHRONIC TREATMENT

- Nutrition: cats especially may not eat if unable to smell food. Consider feeding tube (e.g., esophagostomy; see p. 1267) for nutritional support.
- Analgesics
- Antibiotics for secondary infections
- In animals with chronic rhinitis, anti-histamines, inhaled corticosteroids, and systemic NSAIDs may provide some relief (see pp. 991 and p. 993).

POSSIBLE COMPLICATIONS

- Anorexia (especially in cats with severe nasal congestion)
- Keratitis (feline herpesviral upper respiratory infections)
- Upper airway obstruction following extubation after general anesthesia
- Hemorrhage following surgery or rhinoscopy
- Dehiscence of surgical site (e.g., cleft palate)
- Progression of underlying disease

RECOMMENDED MONITORING

- Respiratory rate and effort; ventilation and oxygenation
- Appetite
- Ongoing hemorrhage
- Volume and nature of discharge
- Monitoring as normal for antimicrobials and NSAIDs
- Appropriate laboratory testing or diagnostic imaging (packed cell volume, total solids, prothrombin time/partial thromboplastin time, etc.), depending on underlying disease

PROGNOSIS AND OUTCOME 

- Dependent on etiology
- Good if the underlying problem is canine viral upper respiratory tract infection or foreign body or if the animal has undergone a successful surgery or tooth extraction
- Guarded for feline chronic viral upper respiratory tract infections; low-grade nasal congestion and discharge, with periodic flare-ups, may become persistent or lifelong.
- Guarded to good for fungal rhinitis, depending on response to therapy
- Poor if neoplasia is not amenable to surgery and radiation therapy

PEARLS & CONSIDERATIONS 

COMMENTS

Determining whether nasal discharge is unilateral or bilateral is a simple but critical first step in diagnosis. Neoplasia, foreign bodies, dental disease, and other conditions are common causes of unilateral nasal disease and discharge; other local and systemic causes often result in bilateral disease.

PREVENTION

- Isolation of cats with viral infections
- Appropriate vaccination regime and retroviral testing
- Good dental care
- Limited exposure to irritating aerosols or materials

SUGGESTED READING

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Nasal Cutaneous Disorders

BASIC INFORMATION

DEFINITION

Dermatoses affecting the bridge of the nose (haired) or the nasal planum (hairless). This distribution of lesions is relatively common in dogs and cats, and lesions can be restricted to the nasal area or be part of a more generalized condition.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Affects dogs and cats
- Diseases more likely to appear in dogs <1 year of age: demodicosis, dermatophytosis, dermatomyositis, hereditary nasal parakeratosis, juvenile cellulitis
- Epitheliotropic (cutaneous) lymphoma is more commonly seen in older dogs.

GENETICS & BREED PREDISPOSITION

- Nasal parakeratosis: Labrador retrievers
- Zinc-responsive dermatosis: Alaskan malamutes, Siberian huskies
- Dermatomyositis: collies, Shetland sheepdogs, Beauceron shepherds
- Uveodermatologic syndrome: Akitas, Samoyeds, Siberian huskies, chow chows
- Systemic lupus erythematosus (SLE) and cutaneous (discoid) lupus erythematosus (DLE): collies, Shetland sheepdogs, German shepherds
- Nasal arteritis: Saint Bernards
- Alopecia and melanoderma: Yorkshire terriers
- Familial vasculopathy: German shepherds, Scottish terriers
- Acrodermatitis: bull terriers
- Lentigo simplex: orange cats
- Ulcerative nasal dermatitis: Bengal cat

RISK FACTORS

- Sun exposure can cause or aggravate canine and feline solar dermatitis, DLE, SLE, and pemphigus erythematosus.
    - Lack of skin pigmentation can predispose the patient to sun damage.
- Immunosuppression may predispose the patient to infectious diseases.
- Susceptible dogs fed diets high in phytates (high-cereal) or in minerals such as calcium can develop zinc-responsive dermatosis.
- Outdoor animals are more susceptible to contagious diseases.

CONTAGION & ZOONOSIS

- Dermatophytosis is contagious to other animals and is a zoonotic disease.
- Sporotrichosis (especially feline) has a zoonotic potential.
- Accidental inoculation of *Blastomyces dermatitidis* has been reported in people handling specimens from affected animals.

GEOGRAPHY AND SEASONALITY

- Animals living in sunny climates more commonly develop photoaggravated dermatitis.
- Animals living in areas endemic for leishmaniasis are susceptible to the disease.

ASSOCIATED CONDITIONS & DISORDERS

- Granulomatous uveitis in uveodermatologic syndrome
- Systemic disease in SLE
- Hepatopathy or glucagon-producing pancreatic tumor in superficial necrolytic dermatitis

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Presentation depends on the underlying disease:

- Nonpruritic hair loss confined to the bridge of the nose (e.g., localized demodicosis, localized dermatophytosis) or with a generalized dermatopathy (e.g., generalized demodicosis, dermatophytosis, endocrinopathies)
- Pruritus and facial rubbing, with secondary nasal alopecia in cases of allergic disease or intranasal foreign bodies (usually accompanied by sneezing and/or nasal discharge)
- Erosions and ulcers in cases of immune-mediated diseases or nodules and plaques (e.g., neoplastic, cutaneous histiocytosis, fungal diseases)
- Signs of systemic illness may be reported concurrently with generalized disorders (e.g., systemic mycoses, SLE, systemic histiocytosis).

PHYSICAL EXAM FINDINGS: Any of the following are possible, depending on etiology and severity:

- Nasal depigmentation or hyperpigmentation
- Alopecia
- Erythema
- Papules/pustules/vesicles
- Erosions/ulcers
- Crusts
- Hyperkeratosis
- Nodules/plaques

ETIOLOGY AND PATHOPHYSIOLOGY

Nasal lesions arise following various pathomechanisms, including:

- Infectious agents, which induce an immune response from the host, resulting in tissue inflammatory cell infiltrates (folliculitis, furunculosis, granulomatous lesions, etc.)
- Altered cornification process (proliferation, differentiation, or desquamation), resulting in hyperkeratosis
- Development of antibodies or activated lymphocytes against normal body constituents (autoimmune diseases) or against inciting antigens (drugs, bacteria, viruses), which leads to tissue damage
- Defective melanin production or destruction of melanocytes, leading to pigment disorders; a disturbance at the basal epidermal cell level can cause hypopigmentation.
- Solar exposure of poorly pigmented nasal skin, resulting in a phototoxic reaction (sunburn); immune-mediated diseases, such as pemphigus erythematosus, SLE, and DLE can also be photoaggravated.

DIAGNOSIS 

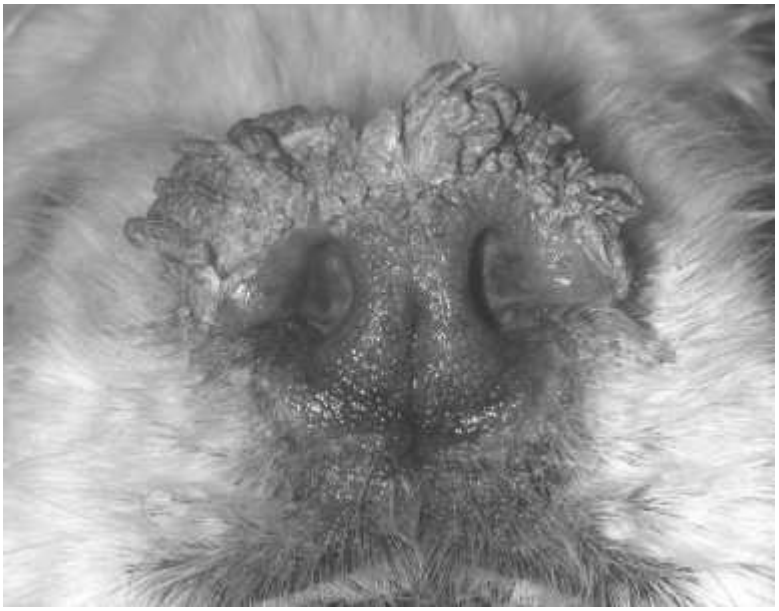
DIAGNOSTIC OVERVIEW

The presenting complaint of nasal cutaneous abnormalities warrants a dermatologic examination. Complementary testing then varies depending on the results of the dermatologic exam and resultant list of possible differential diagnoses.

DIFFERENTIAL DIAGNOSIS

- Infectious
  - Bacterial: mucocutaneous pyoderma, nasal pyoderma, feline leprosy
  - Fungal: dermatophytosis, sporotrichosis, cryptococcosis, blastomycosis, aspergillosis
  - Parasitic: demodicosis (bridge of the nose)
  - Protozoal: leishmaniasis
  - Rickettsial: canine Rocky Mountain spotted fever, canine ehrlichiosis
  - Viral: canine distemper, facial dermatitis associated with herpesvirus infection in cats
- Immune-mediated: pemphigus foliaceus and erythematosus, SLE, DLE, uveodermatologic syndrome, nasal arteritis, canine eosinophilic furunculosis of the face, feline mosquito bite hypersensitivity
- Hereditary (see Genetics and Breed Predisposition above).
- Pigmentary: nasal depigmentation (“Dudley nose”), seasonal nasal hypopigmentation (“snow nose”), vitiligo, alopecia and melanoderma, lentigo simplex
- Metabolic/endocrine: superficial necrolytic dermatitis (hepatocutaneous syndrome), canine hypothyroidism
- Nutritional: zinc-responsive dermatosis
- Environmental/traumatic: canine and feline solar dermatitis, contact dermatitis, local trauma

- Drug eruption: from topical or systemic administration
- Neoplastic: squamous cell carcinoma (SCC), basal cell carcinoma, epitheliotropic lymphoma, fibroma, feline “sarcoid,” and other such conditions
- Miscellaneous: idiopathic sterile granulomas and pyogranulomas, cutaneous and systemic histiocytosis, idiopathic nasal hyperkeratosis



NASAL CUTANEOUS DISORDERS Idiopathic nasal hyperkeratosis in a 14-year-old female cocker spaniel. Excessive keratin forms projections over the dorsal aspect of the nasal planum.

(Courtesy Dr. Nadia Pagé.)

INITIAL DATABASE

- Selection of diagnostic tests is based on history and physical examination.
- Wood's lamp (cats > dogs): dermatophytosis (fluorescent strains of *Microsporum canis)*
- Skin cytologic examination: phagocytized bacteria, inflammatory cells, acantholytic keratinocytes (pemphigus), fungal organisms
- Skin scrapings: *Demodex* spp.
- CBC/serum biochemistry profile/urinalysis (if concurrent systemic disease is suspected): results depend on underlying cause and are often normal or with nonspecific changes when cause is not systemic.
- Ocular examination (if vision loss or visible ocular lesions): uveitis (uveodermatologic syndrome). See p. 1313.
- Thoracic and abdominal imaging, if relevant, to confirm systemic disease or stage tumors

ADVANCED OR CONFIRMATORY TESTING

- Skin biopsies for histopathologic evaluation and possible immunofluorescence or irnmunohistochemical staining. Indicated when initial database is inconclusive and nasal lesions persist. Using general anesthesia, nasal planum lesions can be biopsied with a 3- or 4-mm biopsy punch. The lesion should be centered in the specimen. If possible, multiple specimens should be taken of primary lesions (e.g., pustules, papules, bullae). Crusted lesions or depigmented lesions can also be useful.
- Culture: bacterial, fungal (if evidence of bacterial/fungal infection, and if resistance to prior treatment)
- Antinuclear antibody (ANA) test: if SLE is suspected (see p. 1070)
- Endocrine or serologic testing if relevant

TREATMENT

TREATMENT OVERVIEW

- The goal of treatment is to achieve permanent cure or control of the disease. Topical treatment may be sufficient for localized and/or superficial skin disorders, whereas systemic therapy (ranging from simple to ongoing and intensive) may be needed when nasal cutaneous disorders are the first expression of a serious medical condition.

ACUTE AND CHRONIC GENERAL TREATMENT

- Treatment depends on the etiology of the lesions. Specific treatment is selected based on results of tests described above.
- If the animal has undergone prior recent treatment and a drug reaction is suspected, the animal should avoid contact with the offending medication.
- Infectious diseases may be cured with appropriate treatment. Other diseases may need chronic maintenance treatment.

PROGNOSIS AND OUTCOME

Variable, depending on the underlying disease

PEARLS & CONSIDERATIONS

COMMENTS

Skin biopsies are often needed for diagnosis of nasal cutaneous disorders.

TECHNICIAN TIP

Some nasal cutaneous disorders worsen substantially with sunlight. Be sure to take proper precautions (short walk, sunscreen, etc.) with patients with this type of problem.

PREVENTION

- Prevent sun exposure and use of sunscreens on poorly pigmented animals and/or with photoaggravated diseases.
- Discourage breeding of animals with hereditary diseases.

SUGGESTED READING

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Narcolepsy

BASIC INFORMATION

DEFINITION

- A syndrome in which abnormalities in the sleep/wake cycle are manifested as excessive sleepiness and cataplexy.
- Excessive sleepiness is characterized by waxing and waning drowsiness and abrupt onsets of falling asleep.
- Cataplexy is a brief episode of flaccid paralysis without altered consciousness, usually elicited by excitement or emotion.
- Cataplexy is the clinical sign most commonly seen in narcoleptic domestic animals, whereas excessive sleepiness is the more common sign in humans.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Narcolepsy has been reported in more than 17 canine breeds, cats, cattle, and horses.
- Age of onset of clinical signs is typically between 4 and 24 weeks of age in genetically narcoleptic dogs and between 7 weeks and 7 years in sporadically narcoleptic dogs.
- There is no apparent sex predisposition.

GENETICS & BREED PREDISPOSITION: Narcolepsy is inherited with autosomal recessive transmission in the Doberman pinscher, Labrador retriever, and dachshund and occurs sporadically in other breeds of dogs. Clinical signs are often most severe in small dog breeds.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Cataplexy is the most common clinical sign and is manifested by partial to complete paralysis that may involve all muscles or may be restricted to certain limbs or the head and trunk.
    - Consciousness is maintained at the onset of the attack; however, prolonged episodes may lead to rapid eye movement (REM) sleep.
    - The episodes typically occur spontaneously and are usually elicited by excitement, food, or play.
    - There is an abrupt onset as well as termination of the attack, and the attack may be disrupted by a loud noise or stimulation of the animal.
    - Episodes may last a few seconds to more than 30 minutes.
- Excessive sleepiness is characterized by prolonged periods of sleep, difficulty arousing the dog during sleep, and apparent drowsiness throughout the day.

PHYSICAL EXAM FINDINGS: Physical examination and neurologic examination are typically within normal limits.

ETIOLOGY AND PATHOPHYSIOLOGY

- The narcolepsy syndrome is associated with a deficit in hypocretin (orexin) neurotransmission.
- Hypocretin is an excitatory peptide neurotransmitter produced in the hypothalamus.
- Canine narcoleptics have normal amounts of hypocretin but lack the receptor to which it binds.
- Mutations in hypocretin-receptor-2 gene were found in the familial form (canarc-1), and losses of hypocretin ligand have been associated with sporadic canine narcolepsy.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is achieved by observing the cataplectic attack. The food-elicited cataplexy test and pharmacologic testing are helpful tools in eliciting the attacks.

DIFFERENTIAL DIAGNOSIS

Narcolepsy must be distinguished from other paroxysmal disorders such as epilepsy, syncope, myasthenia gravis, and metabolic disorders (hypoglycemia, hypocalcemia, etc.).

INITIAL DATABASE

Basic clinical pathologic and imaging studies are typically within normal limits.

ADVANCED OR CONFIRMATORY TESTING

- Cerebrospinal fluid may contain a decreased hypocretin-1 concentration (<80 pg/mL; the normal range is 250-350 pg/mL).
- The food-elicited cataplexy test (FECT) is performed by placing pieces of food at set intervals apart and timing the animal while it consumes the food.
    - A normal animal should be able to consume the food in a short period of time (<45 sec).
    - Narcoleptic animals may need more time (more than 2 min) to consume the food because of partial to complete cataplexy, which is evident on observation of the test.
- Mildly affected animals may need pharmacologic testing to confirm a cataplectic attack.
    - Physostigmine salicylate, a cholinesterase inhibitor that crosses the blood-brain barrier, is given (0.025-0.1 mg/kg IV). Physostigmine increases the chances of spontaneous or elicited cataplectic attacks within 5-15 min in susceptible animals. The side effects of this drug are excessive salivation and diarrhea.

TREATMENT

TREATMENT OVERVIEW

The goal of treatment is controlling cataplexy, because the impact of excessive sleepiness is less in dogs than it is in humans. This is achieved through the use of tricyclic antidepressants.

CHRONIC TREATMENT

- Cataplexy is treated with tricyclic antidepressants that act by blocking cellular norepinephrine reuptake in the central nervous system (CNS).
    - Imipramine (1 mg/kg PO q 8 h) has been used successfully in the long-term treatment of cataplexy. Imipramine also blocks serotonin reuptake.
    - Other tricyclic antidepressants used include amitriptyline (2.2-4.4 mg/kg PO q 24 h), desipramine, and protriptyline.
- Excessive sleepiness is treated with stimulant sympathomimetics such as methylphenidate (0.1 mg/kg PO q 24 h) or dextroamphetamine.
- Selegiline (2 mg/kg PO q 24 h) is a monoamine oxidase B inhibitor that has been an effective anticataplectic drug through its metabolism to amphetamine and methamphetamine and by increasing dopamine levels in the CNS.

RECOMMENDED MONITORING

Routine blood screening and cardiovascular evaluation prior to and periodically after the initiation of therapy with tricyclic antidepressants.

PROGNOSIS AND OUTCOME

- Cataplectic attacks are generally not life threatening, and although there is no cure, the clinical signs are usually successfully minimized with treatment.
- Some animals may improve with no treatment.

PEARLS & CONSIDERATIONS

COMMENTS

Abrupt withdrawal of medication can lead to increased cataplexy, so clinicians should warn clients not to discontinue medications quickly.

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Ovarian Tumors

BASIC INFORMATION

DEFINITION

Ovarian tumors are uncommon, benign or malignant neoplasms arising from specific tissue in the female gonad. Tumor classification includes epithelial (adenoma, adenocarcinoma, carcinoma, cyst adenoma, cyst adenocarcinoma), germ cell (dysgerminoma, teratoma, teratocarcinoma), and sex cord (granulosa cell tumor, Sertoli, Sertoli-Leydig).

EPIDEMIOLOGY

SPECIES, AGE, SEX: Canine, intact females:

- Epithelial tumors: median age 9.6 years (adenomas, 10.5 years; adenocarcinomas, 9.3 years)
- Sex cord tumors: median age 8 years (granulosa cell tumor, 7 years; Sertoli, 5 years; Sertoli-Leydig, 12 years)
- Germ cell tumors: median age *6.4* years (dysgerminoma, 9 years; teratoma, 5 years; teratocarcinoma, 5 years)

Feline, intact females:

- Epithelial tumors: median age 10 years (cystadenoma, 10 years)
- Germ cell tumors: median age 6 years (dysgerminoma, 6 years; teratoma, 8 years)
- Sex cord tumors: median age 9 years (granulosa, 10 years)
- Epithelial tumors: 5% of all pathologic examination reports, no case reports
- Germ cell tumors: 15% of all pathologic examination reports, 50% of case reports
- Sex cord tumors: 31% of all pathologic examination reports, 50% of case reports

RISK FACTORS

- Intact reproductive status (presence of ovaries)
- Age

ASSOCIATED CONDITIONS & DISORDERS: Persistent estrus, hyperestrogenism (anemia and thrombocytopenia), pyometra and/or cystic endometrial hyperplasia are sometimes seen in association with epithelial and sex cord tumors.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Epithelial tumors (adenoma, adenocarcinoma, carcinoma, cystadenoma, cystadenocarcinoma)
- Sex cord tumors (granulosa cell tumor, Sertoli, Sertoli-Leydig)
- Germ cell tumors (dysgerminoma, teratoma, teratocarcinoma)

HISTORY, CHIEF COMPLAINT: Dog:

- Abdominal enlargement (adenomas, adenocarcinoma, granulosa cell tumor, dysgerminoma, teratoma, teratocarcinoma)
- Depression (dysgerminoma, teratocarcinoma)
- Estrous cycle abnormalities such as prolonged estrus (adenocarcinoma, granulosa cell tumor)
- Vaginal discharge and vulvar enlargement (adenocarcinoma, granulosa cell tumor)
- Incidental finding during ovariohysterectomy or necropsy (adenomas, teratoma)
- No common findings (Sertoli and Sertoli-Leydig cell tumors)
- Fever, pallor, weakness, and heart murmurs if pancytopenia secondary to estrogen myelotoxicity

Cat:

- Estrous cycle abnormalities such as persistent estrus (granulosa cell tumor)
- Depression (granulosa cell tumor)
- Incidental finding during ovariohysterectomy or necropsy (cystadenoma, dysgerminoma, teratoma)
- Fever, pallor, weakness, and heart murmurs if pancytopenia secondary to estrogen myelotoxicity

PHYSICAL EXAM FINDINGS

- Estrus (vaginal smear for cytologic examination)
- Vaginal discharge
- Abdominal enlargement/effusion
- Fever, pallor, weakness, and heart murmurs if pancytopenia secondary to estrogen myelotoxicity

ETIOLOGY AND PATHOPHYSIOLOGY

Clinical signs can be related to hormone production by sex cord tumors; the signs can also be related to organ impingement by space-occupying masses or metastasis for other types. Abdominal distension can occur secondary to carcinomatosis (abdominal effusion).

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

The diagnosis is expected if an older intact animal has persistent estrus, vaginal discharge, or abdominal enlargement. The diagnosis is aided by diagnostic imaging and is confirmed via surgery.

DIFFERENTIAL DIAGNOSIS

- Estrus
- Pyometra
- Gastrointestinal or other intraabdominal disease

INITIAL DATABASE

- Routine lab tests (CBC including platelet count, urinalysis, serum chemistry panel): generally unremarkable unless estrogen toxicity is present
- Vaginal cytologic examination
    - Confirmation of estrus
    - Assessment for pyometra or other infection

ADVANCED OR CONFIRMATORY TESTING

- Abdominal radiographs
- Abdominal ultrasound
- Abdominocentesis and fluid analysis
- Thoracic radiography for metastasis
- Exploratory surgery
- Histopathologic examination of tissue

TREATMENT 

TREATMENT OVERVIEW

Surgical excision is the most common treatment; however, chemotherapy has been used in some patients.

ACUTE GENERAL TREATMENT

Ovariohysterectomy. A unilateral ovariectomy has been reported, with a subsequent small litter resulting.

CHRONIC TREATMENT

- Chemotherapy should be considered if there is histologic evidence of vascular or lymphatic invasion or evidence of metastasis in the peritoneal cavity during surgery (carcinomatosis).
    - Cisplatin (not in cats) or cyclophosphamide and chlorambucil and nitrosourea have been used for treating metastatic carcinomas in a few dogs, resulting in a median 9-month survival.
    - Additional chemotherapeutics that can be considered include doxorubicin, carboplatin, and 5-fluorouracil. If effusions

are present, intracavitary chemotherapy may be indicated.

POSSIBLE COMPLICATIONS

- Metastasis
- Canine:
  - Epithelial tumors: adenomas and adenocarcinoma in 50% of cases according to pathologic examination reports
  - Germ cell tumors: dysgerminoma is rare; teratoma resulted at a rate of 50% in one study; teratocarcinoma is common
  - Sex cord tumors: granulosa in 30% of case reports
- Feline sex cord: granulosa, lung, liver, and spleen reported

RECOMMENDED MONITORING

- In dogs, enlargement of the abdomen and estrous cycle abnormalities (e.g., prolonged estrus, vaginal discharge, vulvar enlargement) should be monitored. The presence of fever, pallor, weakness, or heart murmurs may indicate pancytopenia secondary to estrogen myelotoxicity.
- In cats, estrous cycle abnormalities (e.g., persistent estrus) should be monitored. The presence of fever, pallor, weakness, or heart murmurs may indicate pancytopenia secondary to estrogen myelotoxicity.

PROGNOSIS AND OUTCOME

- Excellent if benign and no metastasis has occurred
- Unknown, but likely poor if distant metastasis or carcinomatosis is present at the time of diagnosis

PEARLS & CONSIDERATIONS

COMMENTS

May be unilateral or bilateral

PREVENTION

Ovariectomy or ovariohysterectomy

CLIENT EDUCATION

Ovariohysterectomy will eliminate risks of ovarian as well as uterine tumors.

SUGGESTED READING

Jergens AE, Shaw DP: Tumors of the canine ovary. Compend Contin Educ Pract Vet 9:489, 1987.

Johnston S, Root-Kustritz MV, Olson PNS: Disorders of the canine ovary. In Johnston S, Root-Kustritz MV, Olson PNS, editors: Canine and feline theriogenology. Philadelphia, 2001, WB Saunders, pp 193–205.

Smith CA: Ovarian disorders of the bitch and queen. In Root-Kustritz MV, editor: Small animal theriogenology. St Louis, 2003, Butterworth Heinemann, pp 331–365.

AUTHOR: BRUCE E. EILTS

EDITOR: MICHELLE KUTZLER

Otodectic Mange

BASIC INFORMATION

DEFINITION

A contagious, primarily aural infestation caused by the mite, *Otodectes cynotis*

SYNONYMS

Otodectic acariasis, otoacariasis, ear mite infestation

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Very common in cats. Common in dogs.
- More commonly seen in puppies and kittens. May occur at any age.

RISK FACTORS: Contact with stray animals, shelter, boarding or grooming facility

CONTAGION & ZOONOSIS: Very contagious disease. Transmission by direct contact and via fomites. Very low zoonotic risk.

GEOGRAPHY AND SEASONALITY: Worldwide, nonseasonal

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Aural/periaural pruritus evidenced by head shaking and ear scratching. Asymptomatic carriage occurs.

PHYSICAL EXAM FINDINGS

- Otitis externa characterized by erythema and dark brown, ceruminous otic exudate (“coffee grounds”)
- Erosions, ulcers, crusts found on the inner pinna and the entrance of the external ear canal
- Occasional “ectopic” infestations evidenced by alopecia, erythema, papules and crusts of the periaural region, head, neck, feet and tail occur when mites escape from the ears.
- Cats may present with one or a combination of cutaneous patterns: erosive and crusting dermatosis of the head and neck, miliary dermatitis, symmetric alopecia, eosinophilic granuloma complex.
- Positive ear-pedal reflex is possible, particularly in cats: the animal scratches with ipsilateral hindlimb when ear canal is swabbed.
- Ear mites can be visualized by otoscopic examination, appearing as moving white specks.

OTODECTIC MANGE Gross appearance of a young cat with otoacariasis (otodectic mange) demonstrating the specs of characteristic exudate (“coffee grounds”) in the external ear canal.

OTODECTIC MANGE Microscopic appearance of ear mites from a cat *(Otodectes cynotis).*

ETIOLOGY AND PATHOPHYSIOLOGY

These psoroptiform, non-host-specific, nonburrowing mites can cause a hyper-sensitivity reaction by feeding on epidermal debris and tissue fluids on the surface of the external ear canal lining.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is established through historical and physical examination findings AND the visualization of mites and/or eggs on direct otoscopic or microscopic examination. If mites/eggs cannot be found, a positive response to treatment can be used for tentatively confirming the diagnosis.

DIFFERENTIAL DIAGNOSIS

- Hypersensitivities (atopic dermatitis, flea bite allergy, food allergy, contact allergic dermatitis, adverse drug reaction)
- Ectoparasites *(Sarcoptes,* fleas, lice)
- Otodemodicosis
- Bacterial and fungal otitis externa
- Neoplasia, polyps

INITIAL DATABASE

Microscopic examination of ear swab samples placed in mineral oil is the most effective method for identifying ear mites and eggs. Adult stages have four pairs of long legs. Males have suckers on short pedicles on all legs. Females have them only on the first and second pairs of legs. If the skin is involved, collect a minimum of three broad, superficial skin scrapings as well. Crusts and papules represent the best areas to scrape but mites may be hard to find.

TREATMENT

TREATMENT OVERVIEW

Treatment is achieved by cleaning the external ear canal with a ceruminolytic ear cleanser followed by the application of traditional topical (otic) products or more convenient systemic acaricidal products to the affected animal(s) as well as to all in-contact dog, cats, and ferrets.

ACUTE AND CHRONIC TREATMENT

- Topical (otic) acaricidal products
  - Thiabendazole (Tresaderm [Merial]) applied in affected ears q 12 h for up to 7 days. Off-label use (7 days on, 7 days off, and 7 days on) is more likely to effectively eradicate the mite infestation.
  - Ivermectin (Acarexx [Boehringer Ingelheim Vetmedica]) applied in affected ears in cats as young as 4 weeks of age. Single application as labeled may be suboptimal *(labeled in cat only).*
  - Milbemycin oxime (MilbeMite [Novartis]) applied in affected ears in cats as young as 4 weeks of age. Single application as label may be suboptimal *(labeled in cat only).*
  - Fipronil (Frontline Spot-on [Merial]): 2 drops applied in affected ears once or twice, 1 month apart (off-label)
- Any of the above topical otic treatments should be used in conjunction with an appropriate whole-body acaricide to eliminate ectopic mites.
- Systemic acaricidal treatment
  - Selamectin (Revolution/Stronghold [Pfizer]) and moxidectin (Advantage Multi/Advocate [Bayer]) are approved as topical (spot-on) products for ear mite treatment and prevention in dogs and cats; 2-3 doses administered 15-30 days apart may be necessary for optimal control.
  - Ivermectin (Ivomec [Merial]) or moxidectin (Cydectin [Wyeth]): 200-300 mcg/kg PO or SQ every 1-2 weeks for up to 4 treatments can be used (off label).
  - Whole-body acaricide treatments are not required when spot-on, PO, or SQ macrocyclic lactones (selamectin, ivermectin, moxidectin) are used.

DRUG INTERACTIONS

Off-label doses of ivermectin or moxidectin should not be used in sensitive canine breeds unless the MDR1 mutation is confirmed to be absent (seep. 706).

POSSIBLE COMPLICATIONS

Otitis media

RECOMMENDED MONITORING

Repeat ear swab and physical examination 1 month after first treatment if clinical signs persist.

PROGNOSIS AND OUTCOME

Excellent

PEARLS & CONSIDERATIONS

COMMENTS

- Other household pets such as ferrets can become infested.
- Ear mites can only be eradicated if all animals in contact are treated simultaneously.

PREVENTION

- Ear mites have a 3-week life cycle, a 2-month life span, and can live off the host for weeks. The environment may require thorough cleaning and treatment in cattery or kennel situations.
- When Revolution/Stronghold or Advantage Multi/Advocate is/are used as flea control, they have the added benefit of ongoing ear mite prevention.

TECHNICIAN TIPS

- The diagnosis may be falsely based on the typical appearance of the otic exudate alone, without visualization of parasites on microscopy. This is often misleading. It is important to distinguish an ear infected with yeast or bacteria from one infested with mites by performing a cytologic examination of swabbed ear exudate.
- Tresaderm should be refrigerated in the veterinary office for efficacy. Once given to owner, it can remain at room temperature for up to 7 days (cold drops are uncomfortable in a pet's ears). If treatment is prescribed for more than 7 days, dispense two bottles. Tell owners to keep one bottle out for 7 days, with the other bottle refrigerated until the first is discarded after 7 days.

CLIENT EDUCATION

Most pet owners have heard of ear mites and know they are common parasites. There is a tendency in the general public to see inflamed ears with discharge and assume it is an ear mite infestation, often leading to weeks of inappropriate treatment with over-the-counter treatments. These treatments have largely been replaced by far simpler veterinary products.

SUGGESTED READING

Curtis CF: Current trends in the treatment of *Sarcoptes, Cheyletiella and Otodectes* mite infestations in dogs and cats. Vet Dermatol 15:108, 2004.

AUTHOR: VINCENT DEFALQUE

EDITOR: MANON PARADIS

Otitis Media/Interna

BASIC INFORMATION

DEFINITION

- Otitis media: inflammation of the middle ear
- Otitis interna: inflammation of the inner ear
- Otitis media/interna may be acute or chronic, may be unilateral or bilateral

SYNONYM

Glue ear = primary secretory otitis media

EPIDEMIOLOGY

SPECIES, AGE, SEX

- More common in dogs than cats
- Any age or breed, either sex

GENETICS & BREED PREDISPOSITION

- Breeds of dogs predisposed to developing otitis externa (e.g., cocker spaniels) may be predisposed to developing otitis media/interna.
- Cavalier King Charles spaniels: presumed inherited primary secretory otitis media

RISK FACTORS

- Dogs, otitis media/interna with otitis externa; three general categories of contributing factors for developing otitis externa: (1) morphologic and environmental (e.g., external ear conformation and high humidity); (2) primary causes (e.g., atopic dermatitis, disorders of keratinization, aural neoplasia, parasitic infection); (3) perpetuating factors (e.g., secondary infections, endocrinopathies)
- Cats, parasitic otitis externa (e.g., *Otodectes* sp.); feline immunodeficiency virus (FIV) infection (predisposes to dermatologic disease); feline leukemia virus (FeLV) infection (predisposes to neoplasia); nasopharyngeal polyps, upper respiratory tract disease

ASSOCIATED CONDITIONS & DISORDERS

- Facial nerve paresis/paralysis: common, otitis media
- Horner's syndrome: common, otitis media
- Peripheral vestibular disease: common, otitis interna
- Keratoconjunctivitis sicca: uncommon, otitis media
- Otitis externa: common in dogs, uncommon in cats
- Deafness or hearing impairment (see p. 280)
- Hypersensitivity disorders
- Neoplasia
- Sinonasal disease: more common than originally believed
- Nasopharyngeal polyps (dogs and especially cats): common in cats, rare in dogs
- Aural cholesteatoma: uncommon
- Meningitis/meningoencephalitis: uncommon
- Congenital palatine anomalies: rare

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: One or more may be present:

- Signs of otitis externa if concurrent otitis externa present (see p. 804)
- Vestibular signs: up to two-thirds of peripheral vestibular disorders can be attributed to otitis media/interna

- Deafness
- History and/or signs of upper respiratory disease (e.g., ocular and nasal discharge)
- Scratching of the head and upper neck region
- Head shaking
- Pain when opening mouth/reluctance to eat

PHYSICAL EXAM FINDINGS: One or combination of several:

- Distant examination:
  - General physical signs of systemic disease (e.g., lethargy, inappropriate body condition, etc.) if underlying systemic disease (e.g., lymphoma)
  - Focal aural or generalized dermatologic signs
  - Horner's syndrome if otitis media
  - Signs of vestibular disease if otitis interna
  - Facial asymmetry (otitis media)
- Otoscopic examination: see p. 804 and p. 1316
  - Abnormalities of the external ear canal if concurrent otitis externa
  - Abnormalities of the tympanic membrane on otoscopic examination (e.g., tympanic membrane rupture (many do not have obvious ruptured membrane), inward or outward bulging of the tympanic membrane, opaque and thickened tympanic membrane
- Neurologic and electrophysiologic examination:
  - Findings consistent with peripheral vestibular disease, facial nerve paralysis, and/or Horner's syndrome
  - Deafness (absent startle response [Preyer response]) unilaterally or bilaterally; abnormalities of the brainstem auditory evoked response (see p. 1216) (otitis media and/or interna)

ETIOLOGY AND PATHOPHYSIOLOGY

- Otitis media and interna often, though not always, occur together.
- Otitis media may develop through one of three different mechanisms:
  - Extension from otitis externa via the tympanic membrane: common (16% of acute otitis externa cases; up to 80% of chronic otitis externa cases)
  - Retrograde migration of infectious agents via the auditory (eustachian) tube
  - Hematogenous origin
- Otitis interna develops principally from extension of otitis externa/media

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A thorough history and clinical and neurologic examinations are important for differentiating otitis media/interna from other causes of peripheral vestibular disease, Horner's syndrome, and facial nerve paresis/paralysis. Confirmation is obtained with diagnostic imaging and during surgical intervention.

DIFFERENTIAL DIAGNOSIS

- Peripheral vestibular disease:
  - Strongly consider idiopathic vestibular disease if no signs of concurrent facial nerve paresis/paralysis and Horner's syndrome.
  - Nasopharyngeal polyps (cats ≫ dogs)
  - Ototoxicosis (to inner ear): when history of ototoxic drug exposure
  - Neoplasia (generalized with metastasis to middle/inner ear or focal within middle/inner ear)
  - Trauma
  - Syringomyelia may result in head shaking, neck and ear itching as only presenting sign and has been observed concurrently with secretory otitis media in Cavalier King Charles spaniels (seep. 184).
- Horner's syndrome (see p. 543)
- Facial nerve paresis/paralysis (see p. 376)

INITIAL DATABASE

- Distant and proximal, otoscopic, and neurologic examinations
- CBC, serum biochemistry, urinalysis (initial screen for systemic disease and for preanesthetic workup)

ADVANCED OR CONFIRMATORY TESTING

- Skin scrapings and ear swabs for determining if concurrent otitis externa present
- Myringotomy (tympanum puncture) with middle ear aspirates/swabs for Cytologie examination and bacterial and fungal culture and antimicrobial sensitivities
- Bulla radiography
- CT (seep. 1233) and/or MRI (seep. 1302) of the middle and inner ear

TREATMENT

TREATMENT OVERVIEW

Treatment should be aimed at treating the underlying cause of the disease (e.g., surgical removal of polyp or neoplasia).

ACUTE GENERAL TREATMENT

- In cases of acute otitis media/interna: identify inciting cause (e.g., migrating foreign body), and then treat the primary cause appropriately.
- If fluid/material present within the middle ear:
  - Medical:
    - Appropriate systemic, nonototoxic, antimicrobial therapy
    - Myringotomy will help relieve pressure and associated pain.
    - +/− Flushing the otic bulla (otitis media) with sterile saline solution to remove material, then instillation of appropriate nontoxic antimicrobials, and repeated weekly until ear canal and bulla is non-exudative on otoscopic examination
    - Appropriate systemic or topical nontoxic corticosteroids (reduce inflammation)
  - Surgical:
    - Ventral or lateral bulla osteotomy + appropriate antimicrobial therapy (cases where bulla effusion and/or masses are present)
    - +/− Total ear canal ablation when otitis media/interna concurrent chronic otitis externa

POSSIBLE COMPLICATIONS

- If underlying/concurrent disease not treated appropriately, chronic relapsing otitis media/interna may result.
- Extension of otitis media/interna may extend to involve the central nervous system.

RECOMMENDED MONITORING

Frequent reexamination to tailor therapy appropriately

PROGNOSIS AND OUTCOME

- Good to poor depending upon the cause and chronicity of the disease process before instituting treatment
- Hearing loss and neurologic signs may be permanent.

PEARLS & CONSIDERATIONS

COMMENTS

- Ensure patient is examined for underlying systemic disease.
- Treatment will only be successful after identifying and appropriately treating underlying cause.
- For patients that are deaf: these patients should not be off leash and may pose risk for biting unsuspecting person (i.e., from being afraid, startled, etc.).
- Dogs and cats with otitis media/interna may resent being handled around the head, especially with long-standing aural treatments; consider sedation or anesthesia for aural examinations.

PREVENTION

- Selective breeding
- Aural hygiene

CLIENT EDUCATION

- Clients should be informed that hearing loss and neurologic signs may be permanent.
- For deaf animals, ensure client knows animal should not be allowed to roam freely (hit by car) and that they may bite/injure unsuspecting people or dogs that startle them.

SUGGESTED READING

Gotthelf LN: Diagnosis and treatment of otitis media in dogs and cats. Vet Clin North Am Small Anim Pract 34:469–487, 2004.

Palmero BS, Morris DO, Wiemelt SP, et al: Evaluation of outcome of otitis media after lavage of the tympanic bulla and long-term antimicrobial drug treatment in dogs: 44 cases (1998-2002). J Am Vet Med Assoc 225:548–553, 2004.

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EDITOR: CURTIS DEWEY

Otitis Externa

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

An acute or chronic inflammatory condition affecting the external ear canal

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Common in dogs, uncommon in cats
- Dogs: no sex or age predisposition

GENETICS & BREED PREDISPOSITION

- Idiopathic glandular hyperplasia: cocker spaniels, springer spaniels
- Hair within ear canal: poodles
- Pendulous pinnae: cocker spaniels, springer spaniels, Brittany spaniels, basset hounds, beagles
- Stenotic ear canals: English bulldogs, chow chows, shar-peis
- Cats: young cats may have ear mites, nasopharyngeal polyps; elderly cats may have neoplasia.

RISK FACTORS

- Frequent swimming
- Excessive ear care (including plucking hair)

CONTAGION AND ZOONOSIS

- Ear mites *(Otodectes cynotis* [see page 808]): primary cause of 50% feline otitis cases, 5%-10% in dogs. Commonly contagious between animals.
- Ear mites are rarely zoonotic, although close contact may cause pruritus on the arms or signs of otic discomfort.

GEOGRAPHY AND SEASONALITY

- May be more common in humid environments
- More common in summer months when associated with seasonal environmental allergies (atopic dermatitis), swimming, humidity.

ASSOCIATED CONDITIONS & DISORDERS

- Pyotraumatic dermatitis (seep. 30).
- Aural hematoma (seep. 120).
- Allergic disorders (see p. 106).
- Otitis media may be present in 16% and 82%, respectively, of acute and chronic otitis externa cases in dogs. The tympanum appears intact in about 70% of dogs with proven otitis media.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Head rubbing, ear scratching, or headshaking: common
- Unilateral otitis should raise suspicion for foreign object, polyp, or neoplasm.
- Owners may report odor or discharge from one or both ear canals.
- Head tilt if severe or if otitis media
- Hearing deficit
- Evidence of generalized skin disease possible. Foot chewing, face rubbing, or an obvious seasonality may suggest an underlying environmental or food allergy.

PHYSICAL EXAM FINDINGS

- Otic pruritus or headshaking
- Erythema and edema of the ear canal wall
- Otic discharge: brown-black coffee grounds (ear mites), brown or gray (complicated by *Malassezia),* white-yellow (ceruminous), yellow-green (complicated by bacterial infection)
- Abnormal otic odor
- Erosions and ulcers (most commonly associated with *Pseudomonas* infection, inappropriate cleaning/sampling, or reaction to topicals)
- Alopecia and excoriations on the pinna
- Chronicity: hyperplasia of the ear canal wall, and ceruminous and sebaceous glands leading to stenosis; thickened, nonpliable ear canals indicating mineralization, fibrosis, and stenosis
- Hearing deficits
- Pain when opening the mouth, facial nerve paralysis, hemifacial spasm, head tilt, nystagmus, and/or Horner's syndrome: suggest otitis media
- ± Mass within the ear canal
- ± Signs of generalized skin disease

ETIOLOGY AND PATHOPHYSIOLOGY

Otitis externa is a multifactorial problem. Its severity depends on the interaction of predisposing, primary, and perpetuating factors:

- Predisposing factors: increase the risk of developing otitis externa, such as conformation (congenital stenosis: shar-pei; excessive hair: poodles), lifestyle (grooming, swimming, excessive ear care), obstructive lesions (neoplasms, polyps), and systemic disease (fever, immune suppression, viruses, debilitation).
- Primary factors: incite the condition, such as foreign bodies, allergic disorders (atopic dermatitis, adverse cutaneous food or drug reaction), immune-mediated factors (pemphigus complex), parasites *(Otodectes,* chiggers, ticks), cornification disorders (idiopathic primary seborrhea), and glandular disorders (excessive cerumen/sebum accumulation, sebaceous adenitis).
- Perpetuating factors: prevent the resolution of the problem, such as organism overgrowth (bacteria, yeast), pathologic change (epidermal/glandular hyperplasia, stenosis, mineralization, otitis media), and overtreatment with topical ear medications.
- Pathologic changes permanently alter the microclimate within the canal, promoting colonization by opportunistic microorganisms that may produce further inflammation. As the inflammation progresses, dermal fibrosis followed by mineralization of the auditory cartilages and osseous metaplasia may be noted, leading to decreased flexibility, progressive stenosis, and finally obstructive ear disease.

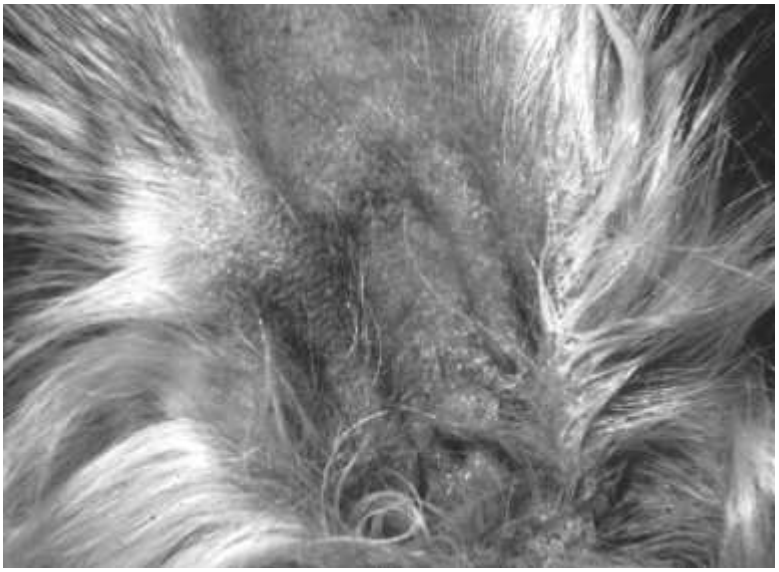
DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis of otitis externa and assessment of severity are based on a thorough history, clinical examination findings, cytologic examination, and if indicated, the results of bacterial culture and susceptibility testing. Advanced diagnostic tests are selected for individual cases with evidence of otitis media, hearing loss, a mass lesion, systemic manifestations of allergic disease, or other complicating factor(s).

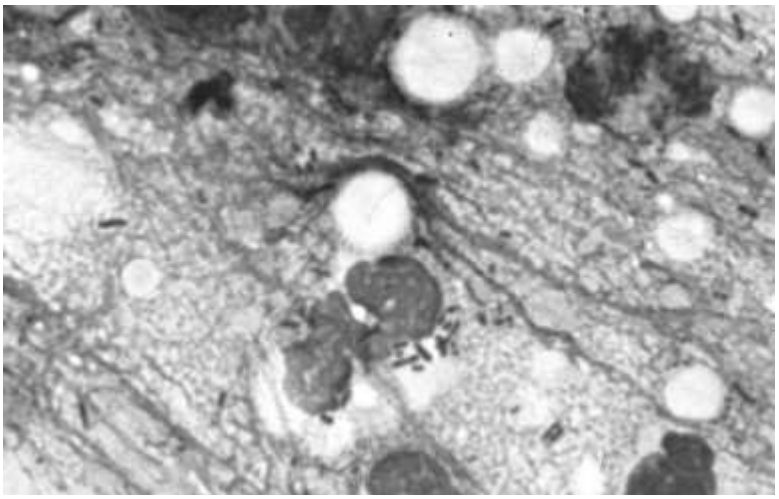
INITIAL DATABASE

- History and clinical examination of the ear canals and skin. A history of otic pruritus that precedes odor and discharge is suggestive of allergy. Examination of the vertical and horizontal canal for evidence of ulceration, hyperplasia, thickening, nonpliability, or discharge/debris. Examination of the tympanic membrane if possible (may require sedation/analgesia or general anesthesia).
- Ear canal cytologic examination (vertical canal/horizontal canal junction) for bacteria, yeast, inflammatory cells, and epithelial cells (acantholytic keratinocytes in pemphigus). Inflammatory cells are an important prognostic indicator and should be assessed at each recheck; considered abnormal, per high-power dry microscopic field (400x magnification): >5 *Malassezia* yeast and/or >25 bacteria (dogs), >12 yeast, and/or >15 bacteria (cats). In fall and winter (low humidity) in the northeastern United States, median numbers of cocci and yeast/HPF were <1 in normal dogs and cats. Rods were not seen.
- Bacteria or yeast in the cerumen or on epithelial cells with no inflammatory cells present indicates colonization, not infection, and specific antibiotic or antifungal treatment may not be appropriate.
- Bacterial culture, susceptibility, and minimum inhibitory concentrations (MIC): if bacterial rods are noted on a Cytologie examination or if antimicrobial resistance is suspected.
- The significance of culture and susceptibility testing results are difficult to assess without concurrent cytology.



OTITIS EXTERNA Pinna in a 9-year-old dog, showing the effects of otitis externa due to food allergy. The dog had a 5-year history of bilaterally symmetrical erythematous otitis externa and pinnitis.

(Courtesy Dr. D.W. Scott.)



OTITIS EXTERNA Cytologie examination of the ear canal in a 7-year-old American cocker spaniel with severe, suppurative otitis externa. Note nuclear streaming, degenerative neutrophils, and phagocytosed rods. *Pseudomonas aeruginosa* was isolated in culture.

(Courtesy Dr. D.W. Scott.)

ADVANCED OR CONFIRMATORY TESTING

- Video otoscopy (seep. 1310 : facilitates examination of the horizontal canal and tympanic membrane.
- Biopsy of the ear canal for histopathologic examination: rarely done and of minimal diagnostic value in chronic cases unless a neoplasm is suspected (e.g., visible mass)
- Radiography: fails to diagnose otitis media in 25% of proven cases
- CT (seep. 1233) and MRI (see p. 1302) are both superior to radiography for detecting polyps and neoplasms, distinguishing between fluid and tissue in the middle ear, and detecting otitis interna.
- Neurologic examination
- Brainstem auditory-evoked response (BAER) testing (hearing examination) (see p. 1216)
- Allergy testing: elimination diet trial: intradermal or serum allergy testing

TREATMENT

TREATMENT OVERVIEW

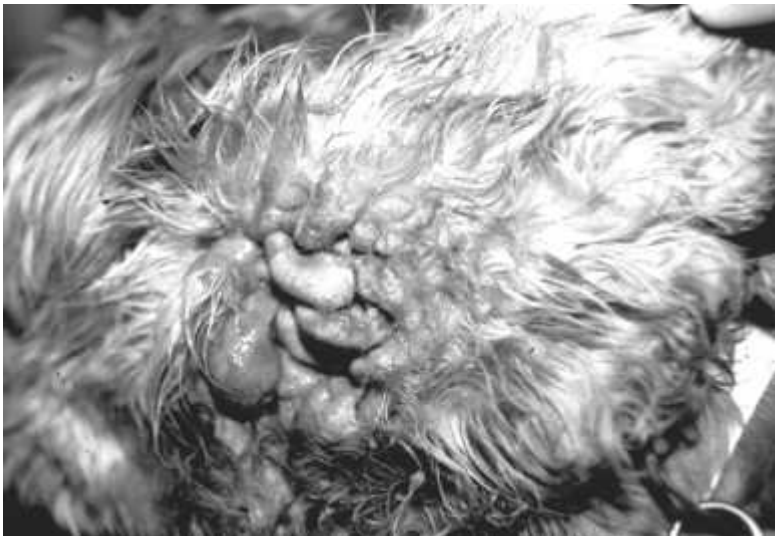
- The primary goal is reduction of ear canal inflammation (provides comfort for the patient, may help eliminate secondary organism involvement, and allows owner to clean and treat effectively). Treatment should be sufficiently thorough to avoid the development of chronic pathologic change. Clinicians should identify and treat all predisposing and perpetuating factors.

ACUTE GENERAL TREATMENT

- Inflammation, ulceration, and ear canal stenosis may preclude a thorough otoscopic examination even under general anesthesia. In such cases, supportive topical and/or systemic therapy is rendered on the basis of cytological findings. Otoscopic examination may then be accomplished on the recheck visit in 2 weeks.
- Polypharmaceutical products (antibacterial, antifungal, glucocorticoid combinations) are very useful in acute, uncomplicated cases: e.g., Animax, Otomax, Surolan.
- When strict antibacterial topical therapy is desired, chlorhexidine (Chlorhexiderm flush), gentamicin (Gentamicin Ophthalmic drops), and enrofloxacin-silver sulfadiazine (Baytril Otic) are useful: 5-20 drops, q 24 h to q 12 h, depending on patient size and disease severity.
- When strict antifungal topical therapy is desired, miconazole (Conofite) and chlorhexidine-miconazole (Malaseb flush) are useful options: 5-20 drops; q 24 h to q 12 h, depending on patient size and disease severity.
- Systemic antibacterial or antifungal therapy is indicated when marked inflammation, ulceration, stenosis, and/or pain are present. Systemic antibiotics are best chosen on the basis of culture and susceptibility testing. Systemic antifungals most often used are ketoconazole (10 mg/kg PO q 24 h with food) or fluconazole (10 mg/kg PO q 24 h with food).
- Antimicrobial therapy is continued for 1-2 weeks beyond cytological cure. In general, clinical cure precedes cytological cure by 1 to 2 weeks. Cytological examination every 2 weeks is a key to successful therapy.
    - Tris-EDTA (T8 solution) may increase the susceptibility of *Pseudomonas* and other gram-negative rods to topical antibacterials. The Tris-EDTA is typically instilled into the ear canal 15 minutes prior to the topical antibiotic.
- Glucocorticoids:
    - Systemic glucocorticoids (e.g., prednisone or prednisolone, 1 mg/kg q 24 h PO [dog] or prednisolone, 2 mg/kg q 24 h PO [cat]) may be necessary for the first 10-14 days of treatment when severe pain/pruritus are welfare issues or create pet/client compliance difficulties, or stenosis is preventing appropriate therapy or otoscopic examination.
    - Topical glucocorticoids are useful in the chronic management of otic allergies and ceruminous otitis: examples are HydroB 1020 (hydro-cortisone and aluminium acetate) or Synotic (fluocinolone and DMSO). Topical glucocorticoids must be administered no more frequently than q 48 h.
- Ear cleaning:
    - Flushing debris from the ear canal can be of great benefit. It should not be attempted in the face of severe inflammation, as it may lead to increased discomfort, erosion, and ulceration.
    - Ear cleansers can be detergent and ceruminolytic (Epi-Otic, Oti-Clens, Alo-Cetic, Routeen) or antimicrobial (Chlorhexiderm, Malaseb).
    - In general, ear cleaning is performed once or twice daily until no more debris is visible (typically 3-7 days). Cleaning is then performed once or twice weekly until terminated.
    - Excessive cleaning is a common *cause* of ear disease! All cleansers are liquids and keep the ear canal moist, macerated, and prone to microbial overgrowth and infection.
- Discouraging recurrent bacterial/yeast infections:
    - Recurrent bacterial (especially *Pseudomonas)* and yeast infections can be frustrating. In some instances, these are triggered by swimming (“swimmer's ear”).
    - The use of an astringent, acidifying, and antimicrobial topical such as acetic acid (1 part vinegar to 2-3 parts water) can be very useful. This solution can be applied after a day of swimming or once/twice weekly as needed. Do not use if erosions/ulcers present.

CHRONIC TREATMENT

- Once an ear has reached the obstructive or “end” stage, with palpable mineralization and complete occlusion of the external ear canal by hyperplastic tissue, surgical intervention and a total ear canal ablation (TECA) and bulla osteotomy may be indicated.
- In patients with medically resistant otitis externa, lateral ear resection may be useful if the horizontal canal is normal.



OTITIS EXTERNA Pinna in an American cocker spaniel showing end-stage otitis externa. Note the nodular proliferation of inflammatory tissue obliterating the ear canal.

(Courtesy Dr. D.W. Scott.)

POSSIBLE COMPLICATIONS

Paraaural abscesses and draining tracts, otitis media, and otitis interna may develop if otitis externa is not resolved.

RECOMMENDED MONITORING

Clinicians should reevaluate the patient every 2 weeks; the purpose is to assess response to therapy by noting improvement in clinical findings and performing ear cytologic examination.

PEARLS & CONSIDERATIONS

COMMENTS

- Since many ear problems are part of a generalized dermatologic disease, a full dermatologic examination is indicated as part of the evaluation.
- Complete resolution of ear problems is very unlikely unless predisposing, primary, and perpetuating factors are identified.
- Dogs and cats with atopic dermatitis or food allergy may present with signs of otitis externa only.
- Response to therapy should be based on degree of clinical improvement and cytologic examination results.

TECHNICIAN TIPS

- Samples for analysis (e.g., swabs for cytologic exam, bacterial culture) should be obtained prior to ear cleaning/medication, which otherwise dilutes and washes away the material of interest.
- Severe inflammation and signs of pain are contraindications to ear cleaning and should be brought to the veterinarian's attention first if ear cleaning was prescribed. Ear cleaning should not hurt.

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Osteosarcoma

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Osteosarcoma (OSA) is a primary malignant tumor of mesenchymal tissue that always includes the production of bone (osteoid) by malignant osteoblasts. Appendicular OSA involves the limbs; axial OSA involves the remainder of the skeleton.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- In dogs, OSA accounts for up to 85% of all primary bone tumors:
  - Median age is 7-9 years, with a smaller peak incidence at 1.5-2 years of age.
  - There is no obvious gender predilection.
- In cats, primary bone tumors are uncommon, but OSA accounts for 70%-80% of those seen. OSA also rarely can occur in the soft tissues at sites of previous vaccinations.

GENETICS & BREED PREDISPOSITION

- Large- and giant-breed dogs are predisposed.
- Body size (height and weight) is a more important predictor than breed.
- Compared to small-breed dogs (weighing <10 kg [22 lbs]), the risk of OSA is 60 times higher in dogs weighing > 30 kg *[66* lbs], and 8 times higher in dogs weighing 20-30 kg (44-66 lbs).
- Appendicular OSA accounts for almost 95% of all cases in dogs weighing >40 kg but only 40%-50% of all cases in dogs weighing <15 kg.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Approximately 75% of OSA arises from the appendicular skeleton and 25% from the axial skeleton. Rarely, OSA can arise in the soft tissues (called *extraskeletal OSA).*
- Appendicular: in the forelimb, the distal radius and proximal humerus are most commonly affected. In the hind limb, lesions are evenly distributed between the distal femur, proximal tibia, and distal tibia.
- Axial: in the axial skeleton, the mandible, maxilla, vertebra, and ribs are most commonly affected.

HISTORY, CHIEF COMPLAINT

- Appendicular OSA usually is associated with progressive lameness. Lameness is less commonly acute and severe due to a pathologic fracture. A palpable swelling may or may not be present.
- Axial OSA can present with a variety of signs. Localized swelling with or without pain is common. Tumors arising from the mandible or maxilla can be associated with halitosis, dysphagia, pain on opening the mouth, or nasal discharge. Vertebral tumors may induce neurologic deficits. Rarely, rib tumors are associated with respiratory signs.
- If pulmonary metastasis is present, the first clinical signs usually are vague, including lethargy and anorexia. The animal may cough, but overt respiratory distress is uncommon. Rarely, lameness develops in one or more limbs secondary to hypertrophic osteopathy.

PHYSICAL EXAM FINDINGS

- Dogs with appendicular OSA exhibit lameness of variable severity, ranging from minimal to non-weight-bearing. A palpable swelling may or may not be present.
- Dogs with axial OSA can have variable physical examination findings (see History above). Signs of pain or discomfort are not as consistent as with appendicular tumors. Depending on the size and location of the tumor, a mass may or may not be visible or palpable.

ETIOLOGY AND PATHOPHYSIOLOGY

- Etiology is largely unknown, but it is often hypothesized that minor traumatic events incurred by weight-bearing bones induce mitogenic signals, increasing the probability of mutation and malignant transformation.
- OSA has also been associated with fractures, metallic orthopedic implants, chronic osteomyelitis, bone infarction, osteochondromatosis, and ionizing radiation.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is strongly suspected based on patient signalment, history, physical examination findings, and radiographic evidence of an aggressive bone lesion. Cytology can help further support the diagnosis, but confirmation requires histopathologic examination.

DIFFERENTIAL DIAGNOSIS

- Other primary bone tumors (chondrosarcoma, fibrosarcoma, hemangiosarcoma)
- Metastatic bone tumors (transitional cell, prostatic, mammary, thyroid, anal sac carcinomas)
- Tumors that locally invade adjacent bone (synovial cell sarcoma; histiocytic sarcoma; oral squamous cell carcinoma [SCC], melanoma, fibrosarcoma, ameloblastoma; digital SCC, melanoma)
- Hematopoietic tumors (myeloma, lymphoma). Radiographic lesions typically are purely lytic.
- Bacterial or fungal osteomyelitis

INITIAL DATABASE

- Radiographic imaging of OSA:
  - Aggressive bone lesions are associated with neoplasia and infection, and they are characterized by one or more of the following radiographic signs:
    - Presence of bone disruption, particularly involving the cortex
    - Bone lysis; permeative and moth-eaten patterns always are aggressive; geographic lysis can be aggressive or benign.
    - Nonhomogeneous, interrupted periosteal bone formation, or amorphous new bone deposited haphazardly in the soft tissues surrounding the bone
    - Ill-defined or indistinct transition zone between normal and abnormal bone
  - Appendicular OSA is usually located in the metaphyseal region of long bones. Extension across joints is uncommon.
- Following a radiographic or histologic diagnosis, animals should be completely staged.
  - CBC, serum biochemistry panel, urinalysis
  - Three-view thoracic radiographs:
    - <10% of animals will have visible pulmonary metastatic lesions at initial diagnosis.
    - Most dogs with OSA ultimately develop visible metastatic disease, even if the primary tumor is surgically removed, indicating metastasis has occurred prior to initial presentation.
  - <5% of dogs will have lymph node metastasis. Any enlarged regional lymph nodes should be evaluated with cytologic examination and/or histopathologic examination.

ADVANCED OR CONFIRMATORY TESTING

- Fine-needle aspiration (FNA) and cytologic analysis is a minimally invasive diagnostic that can help support a diagnosis of OSA.
  - FNA can be considered for lesions with associated cortical destruction. Ultrasound guidance can be used to aid sample collection.
  - cytologic analysis can distinguish between malignant and nonmalignant lesions with an accuracy of 70%-85%. In samples diagnostic for cancer, staining for alkaline phosphatase can help distinguish OSA from other bone tumors.
- Histopathologic examination is required to confirm the diagnosis of OSA.
  - An incisional biopsy can be performed using a Jamshidi bone marrow biopsy needle. Tumors are distinguished from benign lesions with an accuracy of 90%; the specific tumor type is diagnosed with an overall accuracy of 80%.
    - Based on radiographic images, biopsy core(s) should be taken from the lesion's center. Samples taken from the periphery are likely to be nondiagnostic, containing only reactive bone.
  - If signalment, history, and initial database all support a diagnosis of OSA, and if the owners are willing to treat aggressively, it is reasonable to surgically remove the local disease (limb spare or amputation), with biopsy submission following surgery.
- CT imaging is recommended for axial tumors to more accurately stage local disease and help with planning surgery and/or radiation therapy. If a patient is undergoing CT, concurrent imaging of the lungs is recommended as a more sensitive way to screen for pulmonary metastasis.
- Whole-body bone survey radiography and nuclear scintigraphy (i.e., bone scan) are not routinely recommended; however,

any suspicious lesions or painful areas should be imaged.

TREATMENT

TREATMENT OVERVIEW

Definitive treatment includes surgical removal of the primary tumor followed by adjuvant chemotherapy to help delay the onset of visible metastasis. Palliative therapy, which focuses primarily on pain control, is indicated when patients present with metastatic disease or when owners decline definitive therapy.

ACUTE GENERAL TREATMENT

- Surgical removal of the primary tumor:
  - Amputation is the standard treatment for appendicular OSA. Most animals function well after surgery; osteoarthritis is rarely a contraindication.
  - Several limb-salvage techniques exist, where the neoplastic portion of the affected bone is excised while sparing the remainder of the limb. Candidates should have tumors arising from the distal radius, distal ulna, or proximal femur, and the tumor should involve <50% of the bone, with minimal extension into the surrounding soft tissues.
    - Compared to amputation, limb-salvage techniques result in similar survival times but have much higher complication rates (infection, implant failure, local tumor recurrence).
  - For animals with axial OSA, wide surgical excision is recommended whenever possible. Complete excision is often more difficult because of the tumor's proximity to vital structures. When excision is incomplete, adjuvant radiation therapy may help improve local control.
- In the adjuvant setting, IV treatment with cisplatin (50-70 mg/m^2 every 3 weeks along with saline diuresis), carboplatin (250-300 mg/m^2 every 3 weeks), and/or doxorubicin (30 mg/m^2 every 2 weeks) extends disease-free interval and survival. Special handling requirements and potentially severe or life-threatening adverse effects for animals exist with all chemotherapeutic drugs; these concerns and rapid evolution of protocols warrant consultation with/referral to an oncologist.
  - Platinum drugs are more efficacious than doxorubicin.
  - Combinations of cisplatin/doxorubicin and carboplatin/doxorubicin have also been evaluated. There is no clear evidence that combination chemotherapy is superior to single-agent platinum therapy.
- A variety of palliative treatments can be used to help control the pain associated with the primary tumor. In general, multimodality therapy is more effective. Also, pain is easier to prevent than it is to reverse.
  - Nonsteroidal antiinflammatory (NSAID) choices include: aspirin (10-25 mg/kg PO q 8-24 h), carprofen (2 mg/kg PO q 12 h), deracoxib (1-2 mg/kg PO q 24 h; may use 3-4 mg/kg PO q 24 h for first 7 days only), meloxicam (0.1 mg/kg PO q 24 h), firocoxib (5 mg/kg PO q 24 h)
  - Other oral analgesic drugs include acetaminophen with codeine (Tylenol #4 [300 mg acetaminophen, 60 mg codeine]).
  - Pamidronate (1-2 mg/kg IV in saline over 2 h, q 3-4 weeks) decreases bone resorption, increases bone mineral density, and in 30% of dogs, decreases pain.
  - Palliative radiation therapy very effectively controls the pain associated with bone tumors. For animals with appendicular OSA, 75%-90% of animals have a noticeable improvement in lameness, with analgesia persisting for a median of 2-3 months.
  - Animals with pulmonary metastasis often benefit from oral glucocorticoids at antiinflammatory doses, such as prednisone, 0.5-1 mg/kg PO q 24 h (do not combine with NSAIDs).

RECOMMENDED MONITORING

Clinicians should evaluate animals every 2-3 months for evidence of local recurrence and metastatic disease. At a minimum, this includes a thorough physical examination and three-view thoracic radiographs. Imaging of the site of the primary tumor may be indicated as well, depending on location, completeness of excision, and clinical signs.

PROGNOSIS AND OUTCOME

- Most animals with OSA ultimately succumb to the effects of the primary tumor and/or metastatic disease.
- The lungs are the most common site for metastasis, followed by other bones and then various soft tissues.
- For animals with appendicular OSA:
  - With amputation alone, median survival is 4-5 months; the 1-year survival rate is 10%, and the 2-year survival rate is 2%.
  - When amputation or limb salvage is combined with adjuvant platinum-based chemotherapy, median survival improves to 10-12 months, and the 2-year survival rate improves to 15%-25%. When surgery is combined with single-agent doxorubicin, median survival is 8 months; the 1-year survival rate is 35%, and the 2-year survival rate is 17%.

        - Elevated serum alkaline phosphatase is associated with a poor prognosis. In addition, the prognosis may be even more guarded if alkaline phosphatase remains elevated in the postoperative period.
    - With palliative care alone, survival times are up to 4-5 months, depending on how well the pain associated with the primary tumor can be controlled.
    - Once metastatic disease is visible, survival times typically are <2-3 months regardless of therapy (palliative or aggressive).
- For most animals with axial OSA, prognosis is similar or more guarded depending on whether the primary tumor can be completely removed surgically.
- Mandibular OSA carries a better prognosis. With mandibulectomy alone, metastatic rate is around 30%, and median survival is around 17 months. There is no evidence that chemotherapy improves outcome.
- Nasal and digital OSA may also have a lower metastatic rate, but information is limited.

PEARLS & CONSIDERATIONS

COMMENTS

- Animals who are non-weight-bearing lame on a limb affected by OSA have already demonstrated the degree to which they will be able to ambulate after amputation.

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Osteomyelitis

BASIC INFORMATION

DEFINITION

An acute or chronic inflammatory process of bone secondary to hematogenous or traumatic infection with pyogenic organisms

SYNONYM

Bone infection

EPIDEMIOLOGY

SPECIES, AGE, SEX: Young male dogs for traumatic osteomyelitis

GENETICS & BREED PREDISPOSITION: German shepherds for *Aspergillus*

RISK FACTORS

- Open fractures secondary to trauma, bite wounds, gunshot wounds
- Closed fractures or elective orthopedic procedures with direct or hematogenous contamination
- Extension of soft-tissue infections
- Immune system is compromised, allowing hematogenous dissemination

GEOGRAPHY AND SEASONALITY

- Blastomycosis and histoplasmosis: mid-Atlantic states, south of the Ohio River and east of the Mississippi
- Coccidioidomycosis in the southwestern United States and Central and South Americas
- Actinomycosis associated with migrating grass awns in summer in California and Florida

ASSOCIATED CONDITIONS & DISORDERS: Periodontitis, bulla osteitis, disco-spondylitis, and paronychia, depending on location of infected bone

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Orthopedic surgery, trauma, or travel (systemic fungal infection) may be in the recent history.
- Owner may have noted lethargy, anorexia, lameness, swelling, signs of pain, and cutaneous draining tracts.

PHYSICAL EXAM FINDINGS

- Acute osteomyelitis: fever, lethargy, anorexia, limb or joint swelling/pain, lameness
- Chronic osteomyelitis: draining tracts or fistulas, normothermia, disuse muscle atrophy, lameness, limb deformity

ETIOLOGY AND PATHOPHYSIOLOGY

- Neonatal osteomyelitis may originate from the umbilicus.
- Acute postoperative osteomyelitis presents with clinical signs 2-7 days after the surgery.
- Radiographic changes evident 2 weeks after trauma or surgery.
- Glycocalyx (biofilm) is formed on surgical implants after combining with bacteria. This produces a barrier that protects bacteria from antibodies and drugs.
- Between 50% and 60% of cases are monomicrobial, with *Staphylococcus* spp. most common (50%).
- Between 40% and 50% of cases are polymicrobial, with a mixture of aerobes and anaerobes.
- Up to 70% of cases are positive for anaerobes, including *Actinomyces, Clostridium, Bacteroides, Fusobacterium,* and *Peptostreptococcus* spp.
- Other common isolates are *Streptococcus, Escherichia colt, Pasteurella, Pseudomonas, Proteus,* and *Klebstella* spp.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

- Diagnosis is suspected based on history, clinical and radiographic findings, and is confirmed with direct bacterial or fungal cultures.

DIFFERENTIAL DIAGNOSIS

- Bone infarct, neoplasia, cellulitis

INITIAL DATABASE

- CBC, serum biochemistry panel
- Craniocaudal and mediolateral radiographs of affected bone
- Thorax and abdominal radiographs if fungal etiology suspected
- Arthrocentesis (seep.1199) with cytologic examination; culture and sensitivity (C&S) test if joint involvement
- Aerobic and anaerobic C&S tests of deep fine-needle aspirates of tissues
- Fungal titers

ADVANCED OR CONFIRMATORY TESTING

- Ultrasound may reveal soft-tissue abscess or periosteal elevation
- Contrast fistulogram to localize source or sequestrum
- CT and/or MRI
- Radionuclide bone scan with technetium-99m will detect inflammatory lesions; more specific if performed with leukocytes labeled with gallium-67 or indium-lll, and best if animal has a confirmed leukocytosis
- Blood and/or urine cultures if systemic infection suspected

TREATMENT

TREATMENT OVERVIEW

- Treatment is based on identification and elimination of the source of infection. Infected fractures must be stabilized for healing to occur, and removal of infected bone may be necessary.

ACUTE GENERAL TREATMENT

- Acute osteomyelitis requires 4-6 weeks of antimicrobials based on C&S results.
- Initial antibiotics may be given IV.
- Since *Staphylococcus* spp. are most common, initial therapy can involve:
  - Clavulanic acid/amoxicillin: 10-20 mg/kg PO q 12h, *or*
  - Cefazolin: 10-30 mg/kg SQ, IM, or IV q 8 h; *or*
  - Clindamycin: 5-10 mg/kg PO q 12 h; *or*
  - Cloxacillin: 20-40 mg/kg PO q 8 h
- Definitive (medium- and long-term) antibiotic selection will depend on results of bacterial C&S.
- Choices for fungal osteomyelitis include itraconazole, ketoconazole, amphotericin B, and fluconazole

CHRONIC TREATMENT

- May require surgical exploration and removal of sequestrum (dead bone) with curettage of surrounding bone.
- Removal of loose implants, retention of stable implants, and possibly external fixation if additional stability is needed.
  - Fracture-associated infection will not clear unless fracture is stable.
- A cancellous bone graft may be indicated once the infection has subsided.
- Open drainage with lavage or closed drainage with ingress/egress
- Antibiotic-impregnated polymethylmethacrylate beads
- Animals should continue antibiotics for minimum of 6-8 weeks.

DRUG INTERACTIONS

- Clinicians should avoid administering aminoglycosides to animals with renal disease.
- Clinicians should avoid administering quinolones to skeletally immature dogs (risk of cartilage defects).
- Monitor renal values if on amphotericin B.
- Monitor hepatic values if on itraconazole or ketoconazole.

POSSIBLE COMPLICATIONS

- Bone abscess
- Bacteremia
- Fracture/limb deformity
- Implant failure(s)
- Cellulitis
- Draining tracts
- Delayed/nonunion
- Sequestra formation

RECOMMENDED MONITORING

- Radiographs at 4-6 week intervals to evaluate healing
- Clinicians can aspirate and reculture if animal shows signs of recurrence.

PROGNOSIS AND OUTCOME

- Acute osteomyelitis can be eradicated with early aggressive treatment.
- Chronic osteomyelitis can recur within weeks to years after the initial treatment.
- Fungal osteomyelitis may require several months of treatment, and outcome is guarded to poor.
- Involvement of joints may result in osteoarthrosis and limb disuse.

PEARLS & CONSIDERATIONS

COMMENTS

- Obtaining a culture only from the drainage tract can be confusing because contaminants (skin organisms and gram-negative bacteria) are common.
- Leukocytosis is common with acute disease; typically it is absent with chronic conditions.
- Antibiotic-coated implants are being used for prevention and treatment.

PREVENTION

- Aseptic surgical technique
- Appropriate antimicrobial prophylaxis and therapy

CLIENT EDUCATION

- Treatment of chronic osteomyelitis can be costly and lengthy.

TECHNICIAN TIPS

- Animals with active draining infections should be isolated to reduce possibility of cross-contamination of other surgical patients.

SUGGESTED READING

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AUTHOR: MARY E. SOMERVILLE

EDITOR: JOSEPH HARARI

Osteochondrosis

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

- Osteochondrosis is an abnormality of endochondral ossification, producing thickened cartilage that is susceptible to injury.
- Osteochondrosis produces a nonpainful thickening of cartilage, which may tear and loosen and thus develop into the painful and clinically overt osteochondritis dissecans (OCD).
- In turn, OCD may lead to osteoarthritis (see p. 796; also called *degenerative joint disease* [DJD]), a deterioration of articular cartilage and joint capsule tissues that leads to decreased joint function.
- It is a common heritable/developmental disorder in canines.

SYNONYMS

Osteochondritis, osteochondritis dissecans (OCD)

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Fast-growing large-and giant-breed dogs
- More frequent in males
- First signs may appear at maximum growth rate (4-8 months of age)

GENETICS & BREED PREDISPOSITION: Predisposition within these breeds is seen in certain blood lines, but the mode of inheritance is unknown:

- Border collie, German shepherd, golden retriever, Great Danes, Irish wolfhound, Labrador retriever, Newfoundland, rottweiler, Saint Bernard, Bernese Mountain dogs, others

RISK FACTORS

- Genetic
- Rapid growth rate
- Excessive intake of calcium (Ca) with or without excess of phosphorus (P) and vitamin D and/or excessive intake of food
- Hormonal effects (i.e., male dogs, calcitonin)
- Increased joint loading and trauma from intense exercise

ASSOCIATED CONDITIONS & DISORDERS

- Hip dysplasia also occurs in dogs that eat an excessive amount of food.
- Disturbances in endochondral ossification also are seen in the radius curvus syndrome (elbow incongruity) and ununited bone protuberances (anconeal, coronoid, and supraglenoid processes, ununited medial epicondyle).

HISTORY, CHIEF COMPLAINT

- Young dogs with good general health (typically)
- Chief complaint is lameness:
  - Can be unilateral or bilateral
  - Variable degree of lameness
  - Variable duration of lameness
  - May become clinically overt after skeletal maturity
- History may include use of homemade diet or supplemented commercial dog food during the preweaning or postweaning period.

PHYSICAL EXAM FINDINGS

- Lameness as previously described; may manifest as a short-stepping gait if bilateral

- Joint pain, swelling, crepitus, decreased range of motion during flexion and extension
- Muscle atrophy of the affected limb(s).

ETIOLOGY AND PATHOPHYSIOLOGY

- Excessive intake of food with normal content of Ca, P, and vitamin D, increased Ca intake (with or without increased P intake with normal Ca:P ratio), or increased intake of vitamin D with normal Ca and P intake causes disturbed endochondral ossification in fast-growing (not miniature) dogs.
    - Increased protein intake (as in puppy food) does not disturb endochondral ossification.
- Disturbed endochondral ossification leads to cartilage thickening and retention of cartilage in the physis and articular epiphysis.
- The thickened cartilage impedes the diffusion of nutrients from the synovium.
- Tissue malnutrition, ischemia, and chondrocyte necrosis occur.
- Clefts develop at the junction of viable and nonviable layers.
- During normal joint motion and loading, vertical fissures develop in the articular cartilage and result in the formation of a cartilage flap.
- The flap may remain attached to the remaining cartilage tissue or may completely detach (“joint mouse”).
- Inflammatory mediators are released into the synovium, and DJD results.
- Osteochondrosis most commonly affects:
    - Shoulder: caudal humeral head
    - Elbow: medial humeral condyle
    - Hock (tibiotarsal joint): medial or lateral trochlear ridges of the talus
    - Stifle: lateral or medial femoral condyle
    - Also identified in the vertebral articular processes

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on the age (juvenile), breed (large/giant), history, diet, unilateral or bilateral lameness, and radiographic signs of subchondral bone erosion in typical locations.

DIFFERENTIAL DIAGNOSIS

- Shoulder joint: humeral or scapular fracture; biceps tenosynovitis, scapulohumeral luxation
- Elbow joint: fragmented coronoid process, ununited anconeal process, ununited medial epicondyle, incongruity, collateral ligament injury
- Stifle joint: cranial cruciate ligament rupture or avulsion, meniscal injury, collateral ligament injury, extensor tendon avulsion, patella luxation, femoral or tibial fracture
- Hock joint: collateral ligament rupture, fracture
- Radius curvus syndrome: shortening of antebrachium as in chondrodystrophy, curvature due to physeal (Salter type V) fracture

INITIAL DATABASE

- Radiographs of the affected and contralateral joints:
    - Indentation (flattening or saucer shape of the subchondral bone) at the lesion
    - Mineralized density within the joint may be present.
    - Varying degrees of osteoarthrosis
    - Subchondral sclerosis in advanced cases
    - Multiple orthogonal views may be required for accurate visualization.
- Dietary history including food intake and body condition score
- Blood Ca, P, and vitamin D concentrations at the time of clinical signs are not diagnostic.

ADVANCED OR CONFIRMATORY TESTING

- Contrast radiography or CT imaging may be necessary. Scintigraphy and MRI are uncommonly indicated.
- Arthrocentesis for synovial fluid analysis when joint swelling or effusion is present may be indicated. Mild increase in mononuclear cell counts with OCD and DJD.
- Arthroscopy (see p. 1200) can be used for direct visualization of lesion if radiography inconclusive; can also be used for treatment.

TREATMENT

TREATMENT OVERVIEW

- Treatment mainly consists of surgery (arthroscopy or arthrotomy) to débride the devitalized cartilage and stimulate new cartilage formation at the subchondral bone defect. Recent reports have described successful use of autogenous osteochondral grafts (plugs) in treating elbow and stifle joint lesions.
- Restoration of joint health
- Elimination of discomfort and lameness
- Education of clients to provide satisfactory nutrient intake in growing animals to prevent other joints from developing OCD
- Modify excessive activity in large juvenile breeds.

ACUTE GENERAL TREATMENT

- Conservative management:
  - Exercise restriction for 6 weeks
  - Clinicians can choose from the following NSAIDs (never give more than one at a time):
    - Aspirin: 10-25 mg/kg PO q 12 h
    - Carprofen: 2 mg/kg PO q 12 h
    - Etodolac: 10-15 mg/kg PO q 24 h
    - Deracoxib: 1-2 mg/kg PO q 24 h
    - Firocoxib: 5 mg/kg PO q 24 h
    - Ketoprofen 0.25 mg/kg PO q 24 h
    - Meloxicam: 0.1 mg/kg PO q 24 h
    - Tepoxalin: 10 mg/kg PO q 24 h (new product, objective data pending)
- Arthrotomy or arthroscopy to remove loose, discolored, thickened, or devitalized cartilage, cartilage flaps, and intraarticular osteochondral fragments
  - The ridge of the talus is NOT curetted, to avoid creating further joint instability.
  - Curettage and forage (drilling) of the subchondral bone lesion to optimize healing through stimulation of fibro-cartilage formation.

CHRONIC TREATMENT

- DJD (also degenerative osteoarthrosis) may occur at a later age; clinicians can treat the condition by preventing overload of the joint (by limiting activity and body weight gain) and administering NSAIDs as listed above.
- Nutraceutical agents:
  - Glucosamine hydrochloride, chondroitin sulphate, manganese ascorbate, and avocado/soybean unsaponifiables (Dasuquin [Nutramax Laboratories, Edgewood, Md]).
  - Glucosamine (clinicians should follow label instructions for oral dosing).
  - Chondroitin sulfate (clinicians should follow label instructions for oral dosing).
- Chondroprotective agents:
  - Polysulfated glycosaminoglycans (PSGAG): 4.4 mg/kg IM, twice a week for up to 4 weeks (maximum of 8 injections)
  - Pentosan polysulfate: intraarticular (5-10 mg/joint weekly); IM or SQ (3 mg/kg once weekly for 4 weeks); or oral (10 mg/kg weekly for 4 weeks, repeated every 3 months)
  - Hyaluronan: 3-5 mg intraarticular, once a week
- Nutraceutical agents, chondroprotective agents, and intraarticular hyaluronic acid should be considered because they help relieve discomfort, reduce degradative and inflammatory enzyme levels, and stimulate production of synovial fluid, proteoglycan, and collagen.
- Limitation/control activity to low impact.

NUTRITION/DIET

- Animals should avoid excessive intake of food, calcium (bones, bone meal, milk, tablets, powder), or vitamin D (drops, tablets, fish diets).
- Owners should avoid ad libitum feeding:
  - Volume of food should be based on the animal's body condition score.
- During growth, owners should feed their pets a commercially available dog food with a calcium content of <3.5 g/1000 kcal and energy density <4 kcal/g (<17% fat).
- Optimal calcium levels are found in purpose-made large-/giant-breed puppy foods; owners should not feed adult dog food to puppies.
  - Owners should not add supplements.
  - These feeding guidelines are especially important in the preweaning and postweaning periods.

- The lowest risk of diet-induced disease is found in animals whose body condition score is maintained at 2/5 during the period of growth.
- Owners should only use calculated energy requirements and manufacturer's recommendations as initial starting points for feeding, with amounts adjusted to maintain the desired body condition score.

DRUG INTERACTIONS

Intraarticular corticosteroid injections increase lesion severity and are contraindicated.

POSSIBLE COMPLICATIONS

- Untreated cartilage flaps irritate the joint and thus cause more DJD. In OCD of the shoulder joint, the flap can loosen and migrate into the biceps tendon sheath.
- Perioperative and postoperative:
  - Seroma formation due to excessive postoperative physical activity occurs commonly after arthrotomy.
  - Swelling from irrigating fluid leaking into the periarticular soft tissue may occur after arthroscopy.
  - Infection (uncommon)
  - Failure to remove all the osteochondral fragments
  - Tibiotarsal joint instability, not only due to aggressive curettage

RECOMMENDED MONITORING

- Multiple joints, including contralateral, may be affected and should be clinically and radiographically evaluated.
- If lameness persists, synovial fluid analysis, radiographs, arthroscopy, CT, or MRI may be indicated.

PROGNOSIS AND OUTCOME 

- Shoulder: good after treatment, even in cases with DJD. Most dogs become sound 4-8 weeks after surgery.
- Elbow: fair to good when cartilage damage is small in young animals and DJD is minimal. Fair to poor when combined with fragmented coronoid process and/or severe cartilage damage.
- Stifle: variable; a large lesion in a young animal may have a poor prognosis.
- Hock: fair; joint capsule thickening helps stabilize the joint, although residual instability will remain, and DJD should be anticipated.

PEARLS & CONSIDERATIONS 

COMMENTS

- Although the lameness may be unilateral, osteochondrosis often occurs bilaterally. Radiographs of the contralateral joint are indicated.
- Clinicians should make sure surgical curettage of the tibiotarsal joint is kept to a minimum to prevent further joint instability.

PREVENTION

- Owners should only breed animals screened for OCD (and other hereditary diseases); affected dogs and their relatives (parents and siblings) should not be bred.
- Diet management (see above)

TECHNICIAN TIPS

- Application of cold compress immediately after surgery and continued for the first 2-3 days will minimize swelling and inflammation.
- Application of heat compress is recommended after swelling and inflammation have subsided.
- Massage, physical, and hydrotherapy should be considered.

CLIENT EDUCATION

- Before purchasing a puppy, owners should become familiar with the weaker points of the breed in question.
- When a veterinarian knows that an animal's OCD occurs in high incidence, the veterinarian should inform the owner to buy a puppy of screened parents and preferably from a family with previously screened puppies that do not have any hereditary

bone diseases.
- Dietary management (see Nutrition/Diet above)
- Owners should give the puppy the time to grow and should not train their dog too heavily or too early.

SUGGESTED READING

Fitzpatrick N, et al: Early clinical experience with osteochondral autograft transfer for treatment of osteochondritis dissecans of the medial humeral condyle in dogs. Vet Surg 38:246, 2009.

Schulz K: Diseases of the joints. In Fossum T, editor: Small animal surgery, ed 3, St Louis, 2007, Mosby Elsevier, pp 1143–1315.

AUTHOR: JOSEPH C. GLENNON

EDITORS: JOSEPH HARARI, KATHRYN E. MICHEL

Osteoarthritis

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Progressive, noninflammatory, irreversible deterioration of articular cartilage

SYNONYMS

Degenerative joint disease, osteoarthrosis

EPIDEMIOLOGY

SPECIES, AGE, SEX: Increasing prevalence with age

GENETICS & BREED PREDISPOSITION: Secondary to:

- Elbow osteochondrosis and dysplasia (rottweilers, Labrador retrievers, Bernese mountain dogs)
- Hip dysplasia (many breeds)
- Cranial cruciate ligament rupture (many breeds)
- Patellar luxation (toy breed dogs)
- Arthropathy in Scottish fold cats

RISK FACTORS

- Joint instability (hip dysplasia, cranial cruciate ligament rupture, trauma)
- Joint incongruity (elbow dysplasia, trauma)
- Obesity
- Work duty (dogs)
- Athletics (dogs)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Primary (idiopathic) osteoarthritis: unknown cause; not common in animals
- Secondary osteoarthritis: commonly results from trauma, joint instability, incongruity, immobilization, or osteochondrosis

HISTORY, CHIEF COMPLAINT

- Reluctance to ambulate
- Lameness and stiffness after excessive exercise or prolonged rest
- Irritable behavior when approached or touched

PHYSICAL EXAM FINDINGS

- Stiff or altered gait (e.g., bunny hopping)
- Lameness
- Abnormalities during joint manipulation (flexion and extension): joint pain, crepitus, instability, and/or decreased range of motion
- Joint effusion
- Joint thickening
- Muscle atrophy

ETIOLOGY AND PATHOPHYSIOLOGY

- Joint homeostasis is disrupted by abnormal cartilage and membrane cell functions, nutrition, or joint biomechanics.
- A catabolic imbalance results, with chondrocytes unable to replace degraded extracellular matrix (degradation via cytokines

and other inflammatory mediators).
- This cycle progresses irreversibly as the weakened biomechanical integrity of articular cartilage potentiates further dysfunction and disease.
- Periarticular fibrosis is a secondary process directed toward stabilizing the joint.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on signalment, history, and especially physical examination (lameness; thickened, painful joint); confirmation requires imaging, primarily radiographs.

DIFFERENTIAL DIAGNOSIS

- Infectious arthritis (bacterial, spirochetal, bacterial L-forms, mycoplasmal, rickettsial and ehrlichial, viral, fungal, and protozoal)
- Immune-mediated arthritis (erosive arthritis, nonerosive arthritis)
- Neoplasia (synovial cell sarcoma, osteosarcoma)

INITIAL DATABASE

- Clinical examination localizing joint pain
- Radiography: subchondral sclerosis, joint space narrowing, osteophytosis, enthesiophytosis, joint capsule thickening, subchondral bone attrition, intraarticular calcified bodies, soft-tissue calcification or subchondral cysts, bone remodeling, joint effusion

ADVANCED OR CONFIRMATORY TESTING

- Arthrocentesis and synovial fluid analysis:
  - Total cell count <5000 nucleated cells/mcL; mononuclear cells/macrophages predominate, <10% polymorphonuclear cells; fluid is clear, hazy, or pale yellow with normal to decreased viscosity.
- Arthroscopy to visualize articular cartilage
- CT may confirm joint incongruity.
- MRI may identify morphologic cartilage changes.
- Nuclear scintigraphy may help localize osteoarthritis.

TREATMENT

TREATMENT OVERVIEW

- The goal of treatment is to alleviate pain, improve function, limit disease progression, and facilitate joint reparative processes. Treatment is aimed at surgical correction of primary cause of osteoarthritis (CCLR, FCP, OCD); non-surgical management includes pain medication, exercise modification, and weight management.

ACUTE GENERAL TREATMENT

- Surgical treatment for cause of joint degeneration: repair of an articular fracture, removal of osteochondral lesion, stabilization of joint
- A nonsteroidal antiinflammatory drug (NSAID) to reduce inflammatory mediators and pain; one of the following NSAIDs (dogs):
  - Carprofen: 2 mg/kg PO, q 12 h
  - Deracoxib: 1-2 mg/kg PO, q 24 h (may use 3-4 mg/kg PO, q 24 h for first 7 days only)
  - Firocoxib: 5 mg/kg PO, q 24 h
  - Meloxicam: 0.1 mg/kg PO, q 24 h
  - Etodolac: 10-15 mg/kg PO, q 24 h
  - Aspirin: 10-25 mg/kg PO, q 8-24 h
  - Tepoxalin: 10 mg/kg PO, q 24 h
  - Meclofenamic acid: 1.1 mg/kg PO, q 24 h after eating, for 5 days maximum
- A chondroprotective agent:
  - Polysulfated glycosaminoglycan: 5 mg/kg IM once weekly for 4-6 weeks (dogs)
  - Pentosan polysulfate (from beech-wood hemicellulose): 3 mg/kg SQ once weekly (dogs)
  - Oral formulations (glucosamine, chondroitin sulphate, hyaluronan): according to formulation/labeled instructions

- Opioids (e.g., butorphanol, 0.5-1 mg/kg PO q 6-8 h) or synthetic opiate agonist (e.g., tramadol, 1-4 mg/kg PO q 8-12 h) if necessary to decrease pain
- NMDA receptor antagonist: amantadine, 3-5 mg/kg PO q 24 h given along with an NSAID

CHRONIC TREATMENT

- NSAIDs
- Cartilage modifiers
- Joint arthroplasty in severely affected hips, knees, and elbows
- Joint arthrodesis in severely affected joints
- Acupuncture

NUTRITION/DIET

Weight control to maintain a thin or non-obese body condition score

BEHAVIOR/EXERCISE

Exercise modification including low-impact activity such as leash walks and swimming, rather than unrestricted off-leash activity

DRUG INTERACTIONS

- Gastrointestinal irritation, hemorrhage, gastric ulceration, and perforation with NSAIDs
- NSAID-induced nephrotoxicity possible with hypovolemia or preexisting renal disease
- Hepatotoxicity with carprofen
- Decreased platelet aggregation with aspirin therapy

POSSIBLE COMPLICATIONS

Polysulfated glycosaminoglycan is a heparin analog; caution if given with NSAIDs to an animal with a bleeding disorder.

RECOMMENDED MONITORING

Clinicians should:

- Quantify muscle mass with palpation and tape measure.
- Measure range of motion with a goniometer during examination.
- Palpate joint effusion and for periarticular fibrosis.
- Monitor joint pain and gait during examination or with force plate analysis.
- Assess serial radiographs.
- Assess animal's attitude, appetite, body condition score, body weight, and activity level.

PROGNOSIS AND OUTCOME 

- Osteoarthritis is typically an irreversible, slowly progressive disease.
- Medical and/or surgical treatment may permit a good quality of life.

PEARLS & CONSIDERATIONS 

COMMENTS

- Radiographic signs of osteoarthritis may not correlate with clinical signs. Treatment decisions cannot be made on the basis of radiographic findings alone.
- Efficacy of cartilage modifiers is not as well documented as NSAIDs.
- Comparative efficacy of NSAIDs is debatable.
- Use of corticosteroids in place of NSAIDs is controversial; using both together is contraindicated because of severe, potentially life-threatening gastrointestinal ulceration.
- In cats, low-dosing regimens of mono-therapy with ketoprofen, meloxicam, or butorphanol have been described.

PREVENTION

Prompt recognition and early intervention may delay progression of disease.

TECHNICIAN TIPS

Slow leash walks with slings to support body weight (especially during rising) may improve dogs' comfort.

CLIENT EDUCATION

- Treatment is palliative (no “magic bullet”); disease will likely progress.
- Client participation is necessary for long-term management.

SUGGESTED READING

Aragon CL, et al: Systematic review of clinical trials of treatments for osteoarthritis in dogs. J Am Vet Med Assoc 230:514–521, 2007.

Mathews KA: Nonsteroidal anti-inflammatory analgesics. In Ettinger SJ, Feldman EC, editors: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Elsevier Saunders, pp 518–521.

Todhunter RJ, Johnston SA: Osteoarthritis. In Slatter D, editor: Textbook of small animal surgery, ed 3, Philadelphia, 2003, WB Saunders, pp 2208–2246.

AUTHORS: WESLEY J. ROACH, SPENCER A. JOHNSTON

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1ST EDITION AUTHOR: DEONNA WORLEY

Oronasal Fistula

BASIC INFORMATION

DEFINITION

A connection between the oral and nasal cavities, usually resulting from severe periodontal disease. In dogs, this condition is almost invariably the result of oral disease extending dorsally and is virtually never caused by nasal disease extending ventrally.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Older small dogs, typically with narrow muzzles. Either sex.

GENETICS & BREED PREDISPOSITION

- Conformation of skull and predisposition to development of periodontal disease
- Breeds: miniature poodles, Chihuahuas, Yorkshire terriers, miniature schnauzers, dachshunds

RISK FACTORS: See Periodontal disease, p. 860.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Area of the maxillary canine tooth is most often affected. Oronasal fistulas are occasionally seen in the premolar area. A fistula may be present even though the tooth is still in place.

HISTORY, CHIEF COMPLAINT

- Acute: epistaxis after tooth extraction
- Chronic: nasal discharge, sneezing, halitosis

PHYSICAL EXAM FINDINGS

- Mucopurulent nasal discharge
- Typically, the canine tooth has been lost or was previously extracted.
- A defect is seen at the junction of the palate and mucosa of the lip, with oral epithelium connected to the nasal epithelium.
- In the occasional case in which the tooth is still present, the tooth typically is mobile and has severe plaque as well as calculus accumulation and deep pockets on periodontal probing.

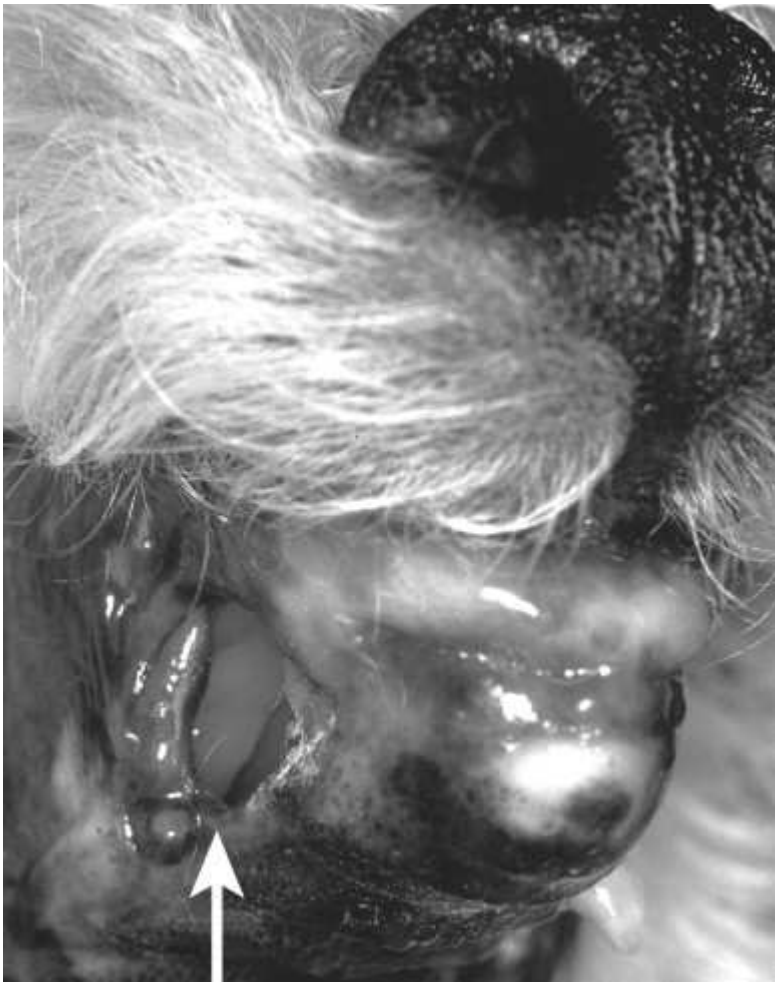
ETIOLOGY AND PATHOPHYSIOLOGY

Periodontitis results in alveolar bone loss and loss of nasal epithelium separating the oral and nasal cavities.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is purely visual on physical examination. If uncertainty exists, oronasal communication can be demonstrated with injection of water into the fistula while the patient is intubated and under general anesthesia.



ORONASAL FISTULA Upper lip retracted to show a chronic oronasal fistula in the area of a missing right maxillary canine tooth in a dog *(arrow).* The maxillary incisors and most other maxillary teeth also are missing in this dog.

(Copyright Dr. Alexander M. Reiter.)

DIFFERENTIAL DIAGNOSIS

Other causes of chronic nasal discharge. Clinicians should ALWAYS remember to thoroughly examine the mouth and teeth of animals with nasal discharge.

INITIAL DATABASE

- CBC, serum chemistry profile, urinalysis (preanesthetic): generally unremarkable
- Thoracic radiographs: if the chief complaint, history, and physical examination findings raise the possibility of metastatic disease or of pneumonia

ADVANCED OR CONFIRMATORY TESTING

- Periodontal probing and dental radiographs (seep. 1246) will demonstrate the severity of alveolar bone loss.
- If the diagnosis of an oronasal fistula is uncertain, clinicians can inject water (via a syringe nozzle, not by needle) into the questionable area in the mouth while the dog is anesthetized (and while the nose is lower than the cranium) to look for flow of water from the naris.
- Clinicians should check other areas of the mouth, because periodontal disease is likely to be generalized and severe.

TREATMENT

TREATMENT OVERVIEW

Treatment consists of closing the oronasal fistula to prevent continued entry of food or fluid into the nasal cavity.

ACUTE GENERAL TREATMENT

- Under general anesthesia (and after tooth extraction in the area of the oronasal fistula if the tooth is still present), the first step is gentle irrigation of the tissue lining of the fistula to remove debris.
- Single buccal-based flap technique: creation of a flap of buccal mucosa sutured over the defect. The edges of the flap must be gently apposed to freshly incised edges of epithelium and be under no tension following closure. This requires dissection of the labial mucosa (epithelium and supporting connective tissue) from its maxillary attachments and also requires resection of the epithelium lining the oronasal fistula on the palatal side.
- Double flap technique: initially, a full-thickness mucoperiosteal palatal flap is raised but remains hinged at the medial margin of the defect. The flap should be transposed to cover the defect (palatine epithelium becomes “nasal” epithelium). Then a labial-based flap is raised, advanced, and sutured over the connective tissue side of the first flap.
- Treatment of periodontal disease in other areas of the mouth is important. This will often require extraction of other maxillary teeth on the same side; closure of these extraction sites can be combined with closure of the flap covering the oronasal fistula.

POSSIBLE COMPLICATIONS

Dehiscence: avoid tension as previously described.

PROGNOSIS AND OUTCOME

Excellent

PEARLS & CONSIDERATIONS

COMMENTS

- Clinicians should always examine the mouth and teeth of animals with nasal discharge.
- Gentle tissue handling will improve healing chances.

PREVENTION

See Periodontal Disease, p. 860.

CLIENT EDUCATION

See Periodontal Disease, p. 860.

SUGGESTED READING

Harvey CE, Emily PP: Small animal dentistry. St Louis, 1993, Mosby, pp 345–348.

AUTHOR: COLIN E. HARVEY

EDITOR: ALEXANDER M. REITER

Organophosphate and Carbamate Insecticide Toxicosis

BASIC INFORMATION

DEFINITION

Organophosphate (OP) and carbamate insecticides are used for controlling insects in agriculture, around the home, and on or around animals (e.g., for controlling fleas and ticks). Toxicosis results from dermal or oral exposure and is characterized by any combination of increased salivation, lacrimation, urinary incontinence, diarrhea, dyspnea, emesis (SLUDDE), bradycardia, tremors, shaking, ataxia, and seizures, and may be fatal.

SYNONYM

Acetylcholinesterase = cholinesterase

EPIDEMIOLOGY

SPECIES, AGE, SEX

- All breeds and both sexes susceptible
- Very young, elderly, or debilitated animals are more susceptible than healthy adult animals.
- Cats are particularly sensitive to chlorpyrifos; the onset of clinical signs is usually delayed (1-5 days) after exposure, and signs can last 2 to 4 weeks.

RISK FACTORS: Exposure to other acetylcholinesterase inhibitors

GEOGRAPHY AND SEASONALITY: Toxicosis more common in summer months (insecticide use); can occur year-round in areas where insects flourish throughout the year

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Known dermal or oral exposure to an OP or carbamate
- Recent history (usually within 24 hours prior to onset of clinical signs) of using an OP or carbamate insecticide in the yard or in the house
- Rapid onset of clinical signs (minutes to hours after exposure)
- Salivation, vomiting, diarrhea, lacrimation, dyspnea
- Tremors, muscle weakness, ataxia, seizures; acute death possible
- Cats may not show typical OP toxicosis signs from chlorpyrifos intoxication. Clinical signs, which begin 1-5 days after exposure, can consist of anorexia, depression, vomiting, tremors, salivation, ataxia, seizures, and ventroflexion of the neck.

PHYSICAL EXAM FINDINGS

- Muscarinic signs: SLUDDE, miosis, and bradycardia
- Nicotinic signs: muscle tremors, weakness, and paresis progressing to paralysis
- Central nervous system (CNS) signs: hyperactivity, depressed respiration, and seizures
- Note that muscarinic signs may be overridden by sympathetic stimulation, resulting in opposite effects (mydriasis, tachycardia, etc.).

ETIOLOGY AND PATHOPHYSIOLOGY

Source:

- Organophosphates (OPs) are aliphatic carbon, cyclic, or heterocyclic phosphate esters. Carbamates are cyclic or aliphatic derivatives of carbamic acid.
    - Commonly used carbamates are aldicarb, carbofuran, methomyl, propoxur, and carbaryl (Sevin).
    - Commonly used OPs are disulfoton, acephate, terbufos, phorate, parathion, chlorpyrifos (Dursban), fenthion (Spotton), diazinon, and malathion

Mechanism of Toxicosis:

- OPs and carbamates competitively inhibit AChE by binding to its esteric site. Acetylcholine (ACh) then accumulates in the synapse and causes excessive synaptic neurotransmitter activity, leading to muscarinic, nicotinic, or CNS effects. Competitive inhibition of AChE explains the result of confirmatory testing with OP or carbamate toxicosis (low blood AChE level).
- Some OPs undergo "aging," rendering the phosphorylated (inactivated) cholinesterase enzyme very stable so that recovery of AChE activity occurs only through the synthesis of new enzyme. In general, inhibition of AChE by the OPs tends to be irreversible, while inhibition by the carbamates is reversible, which allows a spontaneous regeneration of the enzyme. Therefore, both carbamates and OPs respond initially to atropine, but only carbamates continue to do so. OPs become refractory to atropine treatment when they age.
- Atropine blocks the effects of the excess ACh at the neuromuscular junction. Atropine can only control the muscarinic signs (not the nicotinic signs).
- Death from either OPs or carbamates occurs secondary to respiratory failure from excessive bronchial secretions, bronchiolar constriction, paralysis of intercostal muscles or diaphragm, or respiratory paralysis (CNS effects).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A tentative diagnosis is based on history of exposure (recent use of pesticide on the animal or in the environment) and presence of one or several SLUDDE signs. Serum AChE levels are the clinical confirmatory test of choice, but treatment generally needs to be initiated prior to availability of results.

DIFFERENTIAL DIAGNOSIS

- Some *Solanaceae* family plants; anatoxin-a(s) found in some blue-green algae
- Muscarinic signs: muscarinic mushrooms, tremorgenic mycotoxins
- Nicotinic signs: nicotine, pyrethrins/pyrethroids, organochlorine-type pesticides, caffeine, strychnine, fluoroacetate (1080), 4-aminopyridine, metaldehyde, zinc phosphide, lead
- CNS signs: any disorder that can cause seizures (see p. 1009)

INITIAL DATABASE

- CBC, urinalysis (usually within normal range)
- Serum biochemistry profile: possible increase in liver and pancreatic enzymes with exposure to some OPs (disulfoton)

ADVANCED OR CONFIRMATORY TESTING

- AChE levels: serum, plasma, whole blood (preferred), brain, or retina:
  - An AChE result that is <50% of normal indicates significant exposure likely, whereas an AChE activity <25% of normal indicates toxicosis.
  - AChE activity can remain depressed for 6-8 weeks (with OPs).
  - Since carbamates are reversible inhibitors of AChE, the results may be normal even in the face of carbamate toxicosis. In such cases, the diagnosis rests on history of exposure and physical exam findings, although carbamate levels also may be measured.
- AChE insecticide screen: liver, kidney, gastrointestinal tract contents, and source material to look for specific insecticide.

TREATMENT

TREATMENT OVERVIEW

Triage identifies cases with life-threatening clinical effects on presentation, which are treated with atropine and pralidoxime (for OPs), ventilator support if hypoventilation, seizure control if needed, and supportive care. Decontamination (bathing, emesis, charcoal, gastric lavage) and other treatment measures are then carried out after the animal has been stabilized.

ACUTE GENERAL TREATMENT

- Clinicians should treat life-threatening signs if present:
  - Atropine sulfate (dogs/cats): 0.1-0.2 mg/kg; one-fourth dose IV and rest of dose IM or SQ to reduce muscarinic signs. The dose can be repeated as needed to control bradycardia and bronchial secretions.

    - Pralidoxime chloride (2-PAM; Protopam) (dogs/cats): 20 mg/kg IM, SQ, or very slow IV q 12 h is used for controlling the nicotinic signs, although some benefit also may be seen with controlling muscarinic and CNS signs. 2-PAM should not be used with carbamates, since it would not be beneficial; oximes reverse binding of toxin to AChE, but carbamate binding to AChE is inherently reversible. If the animal shows no response after 3 doses, the clinician should discontinue treatment with 2-PAM. Oximes such as pralidoxime are ineffective once OP "aging" has occurred. However, the time of aging varies with the compound, so pralidoxime may be effective even days after exposure.
- Seizure control:
    - Diazepam: 1-2 mg/kg IV, repeat as needed; *or*
    - Phenobarbital: 2-5 mg/kg IV bolus, repeated in 20 minutes up to two times. Clinicians can consider pentobarbital if this is ineffective.
    - Pentobarbital to reach desired effect; repeat as needed.
    - Controlling tremors: methocarbamol, 50-100 mg/kg IV. Clinicians can repeat as needed without exceeding more than 330 mg/kg/d.
- Oxygen supplementation and ventilatory support as needed for animals in respiratory distress.
- Decontamination of the animal: indicated once any potentially life-threatening hemodynamic, neurologic, and respiratory abnormalities have been addressed.
    - Dermal exposure: Consists of bathing the animal with a mild dishwashing liquid, then rinsing the coat thoroughly, and drying and keeping the patient warm.
- Emesis only in patients not showing clinical signs; usually effective within a few hours of ingestion (see p. 1364):
    - Apomorphine (0.03-0.04 mg/kg IV or IM; clinicians can instead administer a crushed tablet portion with water, instill into conjunctival sac, and rinse following emesis).
    - Hydrogen peroxide 3% (2 mL/kg, max 45 mL PO; repeat in 10-15 minutes if no vomiting).
- Gastric lavage:
    - Should be considered where a large amount of poison has been ingested or when emesis is contraindicated (comatose) and emesis has not occurred. Clinicians can anesthetize with a short-acting barbiturate and use a cuffed endotracheal tube to protect airway (see p. 1281).
- Activated charcoal:
    - 1-4 g/kg PO or labeled dosage of commercial product. In animals showing overt clinical signs, repeat in 8 hours (half the original dose).
- Supportive care: IV fluids as needed

NUTRITION/DIET

Tube feeding (see p. 1267) or other nutritional support may be necessary for cats who may be anorectic for days to weeks after being exposed to chlorpyrifos.

DRUG INTERACTIONS

Clinicians should avoid:

- Enhancing toxicity: phenothiazine tranquilizers (e.g., acepramazine), opiates, aminoglycoside antibiotics, theophylline
- Administering neuromuscular blocking agents: levamaisole, succinylcholine, nicotine, and curare can enhance the nicotinic effects of OPs.

POSSIBLE COMPLICATIONS

- Pancreatitis and hepatic disease have occurred in some animals after OP toxicosis.
- Certain OPs can cause a delayed neuropathy 2-3 weeks after acute poisoning. This complication is characterized by hind limb ataxia, hypermetria, and proprioceptive deficits. Chlorpyrifos (experimentally at high doses) is possibly associated with this neuropathy in cats.
- There are usually no long-term effects in animals that recover from acute OP or carbamate toxicosis unless there have been prolonged seizures.

RECOMMENDED MONITORING

- Heart rate
- Respiratory rate and effort, and lung sounds
- CNS signs

PROGNOSIS AND OUTCOME 

- Prognosis good unless the animal suffers from respiratory distress (excessive bronchial secretions, aspiration pneumonia) or

seizures
- Duration of signs depends on treatment, dose, compound, and species of animal

PEARLS & CONSIDERATIONS

COMMENTS

- The main difference of clinical importance between carbamates and OPs is that AChE inhibition is generally irreversible in cases of OP toxicity but reversible in cases of carbamate toxicity:
  - Pralidoxime (2-PAM, protopam) is indicated for treatment of OP toxicosis but not carbamate toxicosis (ineffective).
  - Carbamates are generally short-acting.
- SLUDDE signs can occur from several causes. If history of exposure to an anticholinesterase insecticide is not known, a test dose of atropine can be given to determine whether the signs are caused by an anticholinesterase (OP or carbamate) insecticide:
  - Record baseline heart rate.
  - Administer preanesthetic-level dose of atropine (i.e., 0.02 mg/kg IV for dogs and cats), and monitor the animal's response for 15 to 30 minutes.
  - If the heart rate increases and mydriasis occurs, then the muscarinic signs are not due to OP or carbamate toxicosis (it takes approximately 10 times the preanesthetic dose of atropine to resolve signs caused by cholinesterase inhibitor insecticides).
- For dead animals, the clinician can submit half the brain (sagittal section, frozen) to the lab (put the other half in formalin for histopathologic examination) but only if rabies is definitively ruled out (otherwise, the material could be hazardous to personnel during opening of skull and handling of tissue).
- With the availability of safer insecticides for controlling insects, the incidence of OP and carbamate toxicoses in animals has decreased
- See table for toxicity ratings:

LD50: dose that is lethal to 50% of exposed individuals.

Toxicity Ratings

Toxicity Rating	LD50	Substances
Highly toxic	<50 mg/kg	Disulfoton, coumaphos, famphur, phorate, terbufos, methomyl, aldicarb
Moderately toxic	50-1000 mg/kg	Acephate, chlorpyrifos, diazinon, carbaryl, phosmet, propoxur
Lower toxicity	>1000 mg/kg	Malathion, tetrachlorvinphos

CLIENT EDUCATION

Pet owners should use insecticides according to label directions and keep all insecticides away from pets.

SUGGESTED READING

Blodgett DJ: Organophosphate and carbamate insecticides. In Peterson ME, Talcott PA, editors: Small animal toxicology, ed 2, St Louis, 2006, Elsevier Saunders, p. 941.

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Orbital Diseases

BASIC INFORMATION

DEFINITION

Orbital diseases encompass several conditions that frequently lead to an abnormal position of the eye within the orbit. These abnormal positions include exophthalmos (a forward displacement of the eye), enophthalmos (a caudal displacement of the eye), and strabismus (a deviation of axis of the resting eye position). Orbital diseases can be congenital or acquired.

SYNONYMS

Exophthalmia, enophthalmia, retrobulbar disease, orbital or retrobulbar abscess and/or cellulitis, orbital or retrobulbar neoplasia

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs and cats
- Orbital abscess and/or cellulitis are more common in younger animals.
- Orbital neoplasia is more common in older animals.

GENETICS & BREED PREDISPOSITION

- Ocular proptosis (see p. 918) is more common in brachycephalic breeds.
- Myositis is more common in German shepherds, weimaraners, golden retrievers, and Labrador retrievers (masticatory myositis); extraocular polymyositis is more common in golden retrievers (seep. 704).
- Craniomandibular osteopathy is more common in West Highland white terriers.
- Congenital strabismus may be seen in shar-pei dogs as well as in Siamese and some shorthair cats.

RISK FACTORS: Chewing on sticks or other foreign material (orbital abscess)

ASSOCIATED CONDITIONS & DISORDERS

- Pharyngeal abscess (see p. 14)
- Masticatory myositis (seep. 704)
- Systemic mycoses (seep. 138)
- Nasal neoplasms (exophthalmia and/or strabismus) (see p. 749)
- Emaciation (enophthalmos)
- Dehydration (enophthalmos)

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Sudden, progressive, or congenital change in position of the eye

PHYSICAL EXAM FINDINGS: Bilateral or unilateral:

- Exophthalmos with any or all of the following:
  - Reduced ability or inability to retropulse the globe within the orbit
  - Lagophthalmos (incomplete closure of the eyelids) with or without corneal ulceration (seep. 250)
  - Third eyelid protrusion (see p. 1089)
  - Conjunctival hyperemia, chemosis
  - Periocular swelling
  - Pain on opening the mouth (orbital abscess/cellulitis; myositis)
- Enophthalmos with any or all of the following:
  - Third eyelid protrusion (see p. 1089)
  - Ptosis (drooping upper eyelid)
  - Extraocular and/or masticatory muscle atrophy
  - Entropion
  - Emaciation may be noted, a component of which (the loss of orbital fat) may be the cause of enophthalmos.

- Strabismus:
  - Deviation of the eye(s): dorsal, ventral, medial, lateral, or a combination of these eye positions
  - ± Exophthalmos or enophthalmos
- Variable systemic signs depending on underlying cause
- Inflamed oral mucosa or draining fistula behind the last upper molar with orbital abscess

ETIOLOGY AND PATHOPHYSIOLOGY

- Exophthalmos: caused by space-occupying orbital lesion caudal to the eye:
  - Congenital:
    - Orbital varix, arterial to venous shunts: rare
    - Orbital cysts and dermoids: uncommon
  - Acquired:
    - Ocular proptosis: usually unilateral, peracute, trauma-associated (seep. 918)
    - Orbital abscess/cellulitis: usually unilateral, peracute to acute, painful resistance to ocular retropulsion and mouth manipulation
    - Orbital hemorrhage: secondary to coagulopathy or head trauma.
    - Orbital neoplasia: usually unilateral, progressive, typically not painful, primary or secondary, predominantly malignant
    - Orbital pseudotumor (cats): rare, progressive, fibrosing disease; restricts eye's mobility; may become bilateral condition
    - Mucocele: unilateral, progressive, arising from zygomatic salivary gland
    - Myositis: bilateral, enophthalmia occurring in late stages
- Enophthalmos: caused by loss of orbital volume or space-occupying lesion rostral to the eye:
  - Congenital: microphthalmos (see p. 778)
  - Acquired:
    - Phthisis bulbi (see p. 778)
    - Loss of orbital fat (older animals with weight loss) or muscle
    - Ocular pain
    - Dehydration
    - Horner's syndrome (seep. 1396)
    - Neoplasia anterior to the eye (e.g., rostral orbit)
- Strabismus; typically caused by lesions restricting extraocular muscle mobility or affecting their innervation:
  - Congenital:
    - Unilateral or bilateral, progressive juvenile fibrosis of the medial rectus muscle seen in Chinese shar-pei dogs
    - Bilateral medial strabismus (esotropia) in Siamese cats
  - Acquired:
    - Trauma-induced extraocular muscle avulsion or scarring
    - Extraocular muscle scarring from previous inflammation
    - Abnormal innervation of extraocular muscle(s) (e.g., cranial nerve [CN] III, IV, and/or VI lesions)

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on the time frame of clinical signs, signalment, and clinical appearance of the affected eye. Orbital imaging may be necessary for a definitive diagnosis if the ocular globe is normal.

DIFFERENTIAL DIAGNOSIS

- Exophthalmos:
  - Buphthalmos, which is enlargement of the eye (seep. 448 or 1559)
  - Episcleritis/scleritis (see p. 356)
- Enophthalmos: ruptured globe (see p. 249)

INITIAL DATABASE

- Complete ophthalmic examination (seep. 1313)
- Complete neurologic examination if strabismus (see p. 1311)
- Oral examination if orbital abscess (buccal pain and/or purulent drainage)
- CBC, serum biochemistry profile, urinalysis, skull radiographs, chest radiographs, fine-needle aspirates of submandibular lymph nodes if enlarged, abdominal ultrasound if orbital neoplasia suspected

- CBC may reveal evidence of inflammation (bands, toxic changes in neutrophils) with orbital abscess
- Pharmacologic testing (topical 10% phenylephrine) for Horner's syndrome (see p. 1396)

ADVANCED OR CONFIRMATORY TESTING

- Ocular/orbital ultrasound if exophthalmos (assess for orbital abscesses or masses)
- CT or MRI if orbital masses suspected
- General anesthesia and ultrasound-guided fine-needle aspirates or biopsies of orbital mass, abscess, or mucocele
- Masticatory or extraocular muscle biopsies (see p. 1305) under general anesthesia (e.g., myositis; referable procedure)

TREATMENT

TREATMENT OVERVIEW

Although treatment of orbital abscesses and myositis may not require referral, treatment options for orbital neoplasia are likely to require referral to a veterinary ophthalmologist, surgeon, and oncologist.

- If possible, return the eye to its normal position.
- Alleviate pain.
- Preserve vision (optic neuropathy and/or retinal detachment may occur with space-occupying orbital lesions).

ACUTE AND CHRONIC TREATMENT

Treat underlying cause:

- Ocular proptosis (see p. 918)
- Orbital abscess:
  - Suspected if the oral mucosa caudal to last upper molar is abnormal; in such cases, medical stabilization (e.g., rehydration) is warranted if necessary, followed by surgical drainage via blunt dissection under general anesthesia; samples should be obtained for aerobic & anaerobic culture and sensitivity (C&S).
  - Systemic nonsteroidal antiinflammatory drugs (NSAIDs) for 7 days; may require longer depending on resolution of pain and inflammation.
    - Dogs: carprofen, 2.2 mg/kg PO q 12 h (may use single loading dose of 4 mg/kg SQ once) or meloxicam, 0.1 mg/kg PO q 24 h (may use single loading dose of 0.2 mg/kg SQ or PO once) for 5 days
    - Cats: tolfenamic acid, 4 mg/kg SQ, IM, PO q 24 h for 3-5 days
  - Broad-spectrum oral antibiotics for 14-21 days (amoxicillin-clavulanic acid, 13.5 mg/kg PO q 12 h [dogs] or 62.5 mg PO q 12 h [cats]). Amoxicillin-clavulanic acid is the first-choice antibiotic for this condition.
  - Hospitalization with supportive treatment for first postoperative 24-48 hours (if necessary)
- Orbital neoplasia:
  - Surgical excision (exenteration, orbitotomy, or orbitectomy); may require referral to a veterinary ophthalmologist or surgeon
  - Adjunctive radiation therapy or chemotherapy depending on type of neoplasm (consult veterinary oncologist or ophthalmologist).
  - Orbital pseudotumor:
  - Immunosuppressive therapy (e.g., corticosteroids; azathioprine) or radiation therapy
- Mucocele: surgical excision (typically curative); may require referral to a veterinary ophthalmologist or surgeon
- Myositis: prednisone, 1-2 mg/kg PO q 12 h, tapered gradually once response to treatment is noted (see p. 704). This is long-term therapy that should be tapered every 2-4 weeks pending response to treatment. Additional immunosuppressive drugs may be required if response to treatment is not seen within 1-2 weeks.

POSSIBLE COMPLICATIONS

- Permanent strabismus or third eyelid protrusion
- Blindness
- Loss of the eye
- Systemic complications possible (potentially severe), depending on extent of disease process

RECOMMENDED MONITORING

Weekly or bimonthly reexamination for inflammatory diseases

PROGNOSIS AND OUTCOME

- Favorable with orbital abscess if treated adequately
- Guarded with myositis
- Poor with orbital neoplasia

PEARLS & CONSIDERATIONS

COMMENTS

Orbital disease should be investigated in a timely fashion to alleviate discomfort and potentially preserve vision.

CLIENT EDUCATION

- Consult a veterinarian as soon as an alteration in position of the eye(s) is noted.
- Relapses can occur with myositis or when an orbital foreign body persists.

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Oral Tumors, Malignant

Additional Images Available on Website

BASIC INFORMATION

DEFINITION

Neoplastic oral disease that is locally invasive and may metastasize to distant sites. Oral tumors comprise approximately 6% of all tumors in dogs and 10% of all tumors in cats.

SYNONYM

Malignant oral neoplasia

EPIDEMIOLOGY

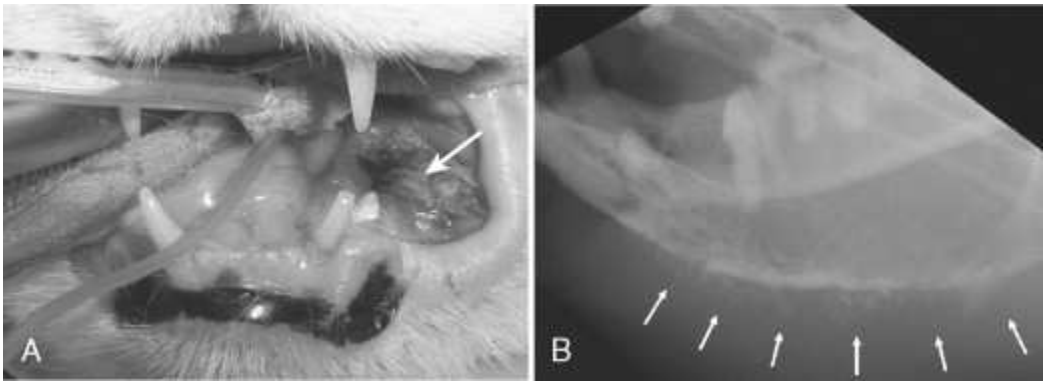
SPECIES, AGE, SEX

- Malignant oral tumors can occur at any age, but middle-aged and geriatric pets are overrepresented.
- Canine papillary squamous cell carcinoma (SCC) occurs most commonly in adolescent and young adult dogs.
- The most common canine malignant oral tumor is malignant melanoma (melanosarcoma;), seen most often in dogs >10 years of age.
- The most common feline malignant oral tumor is SCC (see p. 1045), representing 70% of oral tumors in cats. Average age of onset is 10 years, but cats as young as 5 months have been affected.

GENETICS & BREED PREDISPOSITION: Breeds with pigmented oral mucosa may be predisposed to malignant melanoma.

RISK FACTORS: Factors that increase the risk of feline SCC 3- to 5-fold:

- Exposure to flea collars
- High intake of canned cat food
- Regular ingestion of canned tuna



ORAL TUMORS, MALIGNANT A, Clinical photograph of a cat with squamous cell carcinoma affecting the left lower jaw *(arrow).***B**, Radiograph obtained with dental film of same patient (extraoral lateral oblique technique), showing severe lysis of left mandible and sunburst pattern at ventral mandibular border *(arrows).*

(Copyright Dr. Alexander M. Reiter.)

CONTAGION & ZOONOSIS: Canine transmissible venereal tumor (seep. 1114) can manifest as a primary or metastatic tumor on the lips, buccal mucosa, and tonsils.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Dogs: malignant melanoma, SCC, fibrosarcoma, osteosarcoma, osteochondrosarcoma (multilobular tumor of bone), mast cell

tumor, hemangiosarcoma, peripheral nerve sheath tumor, lymphosarcoma (epitheliotropic lymphoma)
- Cats: SCC, fibrosarcoma, osteosarcoma, hemangiosarcoma, malignant melanoma

HISTORY, CHIEF COMPLAINT

- Swelling of mandible or maxilla
- Oral bleeding, halitosis
- Dysphagia if the mass is large enough to affect masticatory function
- Appetite and activity level are often unaffected

PHYSICAL EXAM FINDINGS

- Specifics may vary with tumor type:
  - Malignant melanoma is pigmented (melanotic) or nonpigmented (amelanotic) and often lobulated, ulcerative, and friable; necrosis may be present when the tumor outgrows its blood supply.
  - Fibrosarcoma is often smooth and firm and may cause generalized disfigurement but rarely bleeds spontaneously.
  - Peripheral nerve sheath tumor tends to grow along larger nerves (e.g., infraorbital nerve into infraorbital canal and inferior alveolar nerve into mandibular canal).
  - SCC is pink, friable, often verrucous (cauliflower-like), and may be either proliferative or ulcerative. Desmoplasia (formation of fibrous tissue) secondary to SCC development may result in a firm tumor on palpation.
  - Osteosarcoma can manifest as a diffuse swelling of the maxilla or mandible but often also exhibits a fleshy, pink or red proliferative component that bleeds easily.
  - Osteochondrosarcoma is locally invasive but slow to metastasize and usually located at mandibular ramus, caudal maxilla, zygomatic arch, or calvarium.
- Halitosis, oral bleeding, facial/oral swelling
- Enlarged mandibular lymph nodes possible
- Maxillary, retroorbital and caudal pharyngeal masses: decreased ability to retropulse the eye globes and decreased range of jaw opening if rostral movement of the mandibular coronoid process is prevented by the tumor or if the tumor involves the temporomandibular joint.

ETIOLOGY AND PATHOPHYSIOLOGY

Etiology is unknown, but genetic predisposition may play a role.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis of malignant oral masses usually requires histopathologic analysis of a biopsy, since many oral masses do not exfoliate well on fine-needle aspirates. Incisional (rather than excisional) biopsy is the preferred initial step for suspected malignancies in order to provide the clinician and client with further information prior to deciding on radical surgery and/or radiation therapy.

DIFFERENTIAL DIAGNOSIS

As for benign oral tumors (see p. 786)

INITIAL DATABASE

CBC, serum biochemistry profile, urinalysis, and thoracic radiographs: to assess for metastases, concurrent illnesses

ADVANCED OR CONFIRMATORY TESTING

- Anesthetized oral examination
- Dental radiography
- CT: particularly helpful for maxillary and caudal mandibular masses
- Cytologic examination of oral masses (fine-needle aspiration, “woodpecker” technique, or scraping from tumor cut surface)
- Cytologic examination of aspirated material or histopathologic examination of resected lymph nodes
- Histopathologic evaluation of incisional or excisional biopsy

TREATMENT

TREATMENT OVERVIEW

- Merely debulking aggressive tumors is rarely helpful. Once a diagnosis is obtained, the mass together with a margin of normal surrounding tissue should be removed comprehensively to prevent local recurrence.
- If complete removal is not an option, radiation or chemotherapy may decrease the rate of growth, depending on tumor type.

ACUTE GENERAL TREATMENT

- Removal of a circumscribed mass to the normal level of the surrounding gingiva will often serve as an adequate biopsy but may not prevent local recurrence. Incisional biopsies of large masses are warranted to provide information prior to performing a radical maxillectomy or mandibulectomy.
- Aspiration and/or removal of head and neck lymph nodes are warranted for staging of animals with malignant oral tumors.

CHRONIC TREATMENT

- Depending on biopsy results and tumor extent, radical surgery and/or radiation therapy may be treatment options. Even when surgery is an option, consult with a medical oncologist and/or radiation oncologist regarding the need for adjuvant or postoperative treatment. Chemotherapy may be used as an adjunctive therapy but is rarely effective by itself against most oral tumors. Immunotherapy of certain tumors shows great promise, and a commercially available melanoma vaccine is available through oncologists (see p. 711).
- Radiation therapy offers good long-term control for treatment of microscopic disease, but bulky tumors rarely respond well.
- Piroxicam, 0.3 mg/kg PO q 24 h in dogs may slow the progression of some carcinomas. Short-term (10 days) use of piroxicam in cats appears to be safe at 0.3 mg/kg PO q 24 h. Further studies are necessary to determine long-term gastrointestinal safety in cats. If prescribed long-term for cancer palliation, the author prescribes 0.3 mg/kg q 48 h.

NUTRITION/DIET

Soft food/esophagostomy tube if necessary because of inability to prehend or chew food

DRUG INTERACTIONS

Piroxicam and other NSAIDs may cause significant gastric ulceration; clinicians should avoid concurrent use of corticosteroids and consider gastric protectants such as misoprostol.

POSSIBLE COMPLICATIONS

- Recurrence of primary tumor. Surgeons should remove at least 1 cm of clinically and radiographically healthy tissue surrounding malignant tumors. Many locally aggressive tumors (fibrosarcoma, peripheral nerve sheath tumor, malignant melanoma) require even wider margins.
- Intraoperative or postoperative bleeding: having blood products available is important with mandibulectomy and maxillectomy procedures.
- Dehiscence of the surgical site: avoid using electrocautery on mucosal edges because it can obscure histologic examination of margins of excised tissue and increases the likelihood of wound dehiscence, which may result in the need for further surgical intervention (such as repair of an oronasal fistula).
- Sublingual or cervical mucoceles may occur if transection of salivary ducts is necessary; these ducts should be ligated if transected.

RECOMMENDED MONITORING

- Oral examination to monitor for local recurrence 1 month after surgery and at a maximum of 6-month intervals thereafter.
- Thoracic radiographs and lymph node palpation should be performed every 6 months.

PROGNOSIS AND OUTCOME

- Median survival time for most malignant oral tumors after surgical excision has been 7-12 months. However, when surgeons obtain clean surgical margins in the absence of microscopic metastasis, patients can be cured.
- Prognosis with SCC is good if found while still surgically resectable.
- Malignant melanomas >8 cm^3 (2 × 2 × 2 cm) have a high incidence of microscopic metastasis at the time of diagnosis.
- Mandibular osteosarcoma has been reported to have a lower metastatic rate and better prognosis than appendicular osteosarcoma.
- Tonsillar SCC in dogs commonly metastisizes to regional lymph nodes, with 85% having regional metastasis at necropsy.

PEARLS & CONSIDERATIONS

COMMENTS

- Incisional biopsy should be performed for larger oral masses. Excisional biopsy may be curative but carries the risk of inadequate tumor removal. When submitting excisional biopsies, clinicians should request that the pathologist evaluate margins for the presence of neoplastic cells. Clean margins according to histologic examination do not rule out the possibility of recurrence, but animals with clean margins have a better long-term prognosis.
- Dental radiography (see p. 1246) is invaluable in providing diagnostic and treatment planning information for oral tumors. Benign tumors tend to displace teeth that often remain firmly seated, whereas more aggressive tumors will cause root and alveolar bone resorption, which may manifest as very mobile (floating) teeth. Benign tumors may have a smooth layer of reactive bone surrounding the neoplastic tissue, whereas a malignant tumor often exhibits destruction of cortical bone, with formation of a classic radiographic "sunburst" appearance (see figure).
- Right or left total mandibulectomy (previously referred to as *hemimandibulectomy)* and maxillectomy surgeries carry with them the potential for profuse bleeding. Blood type and cross matching may be warranted preoperatively.
- Sublingual edema seen within 48 hours after mandibulectomy should not be confused with a sublingual mucocele (ranula). Edema will usually resolve without treatment.
- Pigmentation is not a reliable indicator of tumor type. About 40% of oral malignant melanomas may be amelanotic (unpigmented). Malignant tumors other than melanoma may be partially pigmented if the patient's oral mucosa is normally pigmented.
- Removal of regional lymph nodes may be beneficial at the time of oral surgery. A single surgical approach to parotid, mandibular, and retropharyngeal lymph nodes has been described.
- If the biological behavior of a tumor does not match histopathologic results, clinicians should have the biopsy reread or retaken. A type of fibrosarcoma exists which appears histologically benign but is biologically (clinically) very aggressive.
- Nonhealing dental extraction sites, particularly in cats, may be a clinical manifestation of SCC; clinicians should biopsy any suspicious tissues at the time of extraction.
- Dehiscence and inappropriate healing often occur when oral surgery is performed on irradiated sites.

TECHNICIAN TIPS

- Technicians are on the front line of identifying oral tumors during professional dental cleanings. Do a complete oral examination on each anesthetized patient, including the sublingual area, palate, and tonsils. Bring all identified oral masses to the attention of the clinician for possible biopsy under the same episode of general anesthesia.
- Provide as much information as possible on histopathology forms. Include size (in three dimensions), surface characteristics (ulcerated, smooth, verrucous), complete history, and specific location of tumors. When an excisional biopsy is performed, ask the pathologist to evaluate the specimen for evidence of "clean" or "dirty" margins.

CLIENT EDUCATION

- Complete surgical removal of oral tumors provides the best long-term prognosis. Tumors that are detected early are likely to be operable. Clinicians should advise new pet owners to socialize puppies and kittens and allow them to feel comfortable with periodic examination of the oral cavity.
- Animals adapt remarkably well after radical resection of oral tumors (mandibulectomy or maxillectomy), though one study noted that 12% of cats did not regain the ability to eat on their own. Altered cosmesis is usually well accepted by owners if masticatory function can be restored. Clients should be shown before-and-after pictures of similar surgical cases to ensure their understanding of cosmetic changes (see online version of this chapter).
- Lymph node aspirates and thoracic radiographs are important for preoperative animal staging, but microscopic metastasis cannot be totally ruled out by these tests.

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Oral Tumors, Benign

BASIC INFORMATION

DEFINITION

Tumor generally refers to a swollen or distended area. A second definition refers more specifically to a benign or malignant neoplastic disease. Benign and malignant oral tumors are common in dogs, whereas oral tumors in cats tend to be malignant. Benign tumors may be locally invasive but do not metastasize to distant sites.

SYNONYMS

- Benign oral neoplasia
- "Epulis" (plural = "epulides") is a nonspecific clinical descriptive term referring to a local exophytic growth on the gingiva (e.g., focal fibrous hyperplasia, peripheral odontogenic fibroma [fibromatous epulis and ossifying epulis], acanthomatous ameloblastoma [acanthomatous epulis], nonodontogenic tumors). See p. 359 .

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs: usually gingival hyperplasia, peripheral odontogenic fibroma, acanthomatous ameloblastoma; occasionally pyogenic granuloma, dentigerous cyst, odontoma, papilloma, osteoma, plasmacytoma; rarely giant cell epulis, amyloid-producing odontogenic tumor
- Cats: usually gingival hyperplasia; occasionally giant cell epulis, osteoma, plasmacytoma; rarely peripheral odontogenic fibroma, acanthomatous ameloblastoma, inductive ameloblastoma (feline inductive odontogenic tumor), amyloid-producing odontogenic tumor, odontoma
- Benign oral tumors can occur at any age.
- Oral papillomas (see p. 830) usually occur in dogs <2 years old.
- Inductive fibroameloblastomas usually occur in cats <2 years old.
- Odontogenic tumors (those arising from tooth-forming tissue) can occur at any age, but tumors in young pets are more likely to be of odontogenic origin.

GENETICS & PREDISPOSITION

- Peripheral odontogenic fibroma: more common in brachycephalic dog breeds
- Oral tumors in cats are rarely benign.

CONTAGION & ZOONOSIS: Oral papillomas in young dogs are caused by species-specific papillomavirus.

ASSOCIATED CONDITIONS & DISORDERS

- Gingival hyperplasia
- Malignant oral tumors

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Gingival hyperplasia: abnormal increase in the number of normal cells in a normal arrangement, resulting in clinical enlargement or thickening of gingiva
- Pyogenic granuloma: usually developing on the gingival margin and consisting of markedly vascular granulation tissue with endothelial proliferation, generally ulcerated and inflamed, commonly with hemosiderin deposits
- Dentigerous (tooth-containing) cyst (follicular cyst): develops around the crown of an unerupted tooth
- Odontoma: not a true tumor, but considered to be a hamartoma (accumulation of normal epithelial and mesenchymal odontogenic cells arranged in an abnormal manner, but allowing for induction of dental hard tissues)
    - Compound odontoma: hard tissues produced in a relatively organized manner, resulting in tooth-like structures
    - Complex odontoma: dental hard tissue bearing no resemblance to a tooth
- Peripheral odontogenic fibroma: historically classified as fibromatous and ossifying epulides (ossifying epulides may contain bone-, dentin- or cementum-like tissue within the soft tissue swelling); minimally invasive
- Giant cell epulis (giant cell tumor, giant cell granuloma): rare; rapid growth with inflammatory and ulcerative changes, osteoid and woven bone formation; multinucleated giant cell is main component in mass; rapid recurrence after incomplete excision; thought to be a variant of the peripheral odontogenic fibroma.
- Ameloblastoma: central (intraosseous) or peripheral (extraosseous); both locally invasive, but central ameloblastoma often exhibiting cystic bony changes; acanthomatous ameloblastoma in dogs historically classified as acanthomatous epulis but probably similar to peripheral ameloblastoma
- Inductive fibroameloblastoma (feline inductive odontogenic tumor): rare; occurs most commonly in the rostral maxilla of cats <2 years of age; may be locally invasive but does not metastasize
- Amyloid-producing odontogenic tumor: rare; previously referred to as *calcifying epithelial odontogenic tumor;* may be locally invasive in both dogs and cats but does not metastasize

- Plasmacytoma (plasma cell tumor): extramedullary variant at nasal, pharyngeal, and oral mucosa that has no apparent primary bone involvement; sessile or polypoid sessile and usually solitary oral masses appear to remain localized.
- Osteoma: slow-growing; composed of well-differentiated, densely sclerotic, compact bone

HISTORY, CHIEF COMPLAINT

- Focal swelling of gingiva and/or alveolar mucosa commonly noted as an incidental finding by the client or the veterinarian during routine physical examination
- Benign oral tumors rarely present with oral bleeding or halitosis unless they are large enough to be traumatized by opposing teeth upon closure of the mouth. Bleeding at the lesion site is a common complaint in dogs with a large acanthomatous ameloblastoma.

PHYSICAL EXAM FINDINGS

- Focal swelling of gingiva and/or alveolar mucosa, often circumscribed and rarely ulcerated
- Benign tumors that are locally invasive (e.g., canine acanthomatous ameloblastoma) may cause disfigurement secondary to invasion of the maxilla or mandible.
- Displaced but often firmly seated teeth
- Mandibular lymph nodes are often within normal limits.
- Appetite and activity level are usually unaffected.

ETIOLOGY AND PATHOPHYSIOLOGY

- Etiology is unknown, but genetic predisposition may play a role.
- Some benign masses have been suspected to undergo malignant transformation, though this seems to be rare.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis of benign oral masses usually requires histopathologic examination of an incisional or excisional biopsy specimen, because many oral masses do not exfoliate well upon cytologic sampling.

DIFFERENTIAL DIAGNOSIS

- Normal anatomy (e.g., incisive papilla caudal to maxillary incisors in dogs and cats; lingual molar gland caudolingual to mandibular first molar teeth in cats): if the mass is located directly on the midline or bilateral, consult an anatomy textbook to rule out normal structures before performing a biopsy
- Scar tissue (chewing lesions from traumatizing buccal or sublingual mucosa)
- Eosinophilic granuloma (see p. 351): occurring in dogs and cats on tongue, lips, and palate
- Inflammatory swelling due to foreign body
- Apical abscess (see p. 10)
- Osteomyelitis/bone sequestrum: usually seen in the incisive bone or bilaterally in the caudal mandible or maxilla; often appears as bony swelling with gingival recession, erosion, and ulceration; exposed bone; and fetid odor. Cocker spaniels and dachshunds may be overrepresented.
- Gingival hyperplasia
- Dentigerous cyst: arising in area of a tooth that has not erupted
- Craniomandibular osteopathy (CMO): most commonly seen in West Highland white, Scottish, Cairn terriers; mandibular swellings associated with CMO are often bilateral.
- Malignant oral tumors (see p. 788)

INITIAL DATABASE

- CBC, serum biochemistry profile, and urinalysis: generally unremarkable
- Thoracic radiographs (often unremarkable if oral tumor is benign)

ADVANCED OR CONFIRMATORY TESTING

- Anesthetized oral examination
- Dental radiography: variable bony changes
- CT scan (particularly helpful for maxillary masses)
- Cytologic examination of aspirated oral masses and lymph nodes
- Histopathologic evaluation of incisional or excisional biopsy

TREATMENT

TREATMENT OVERVIEW

- Marginal resection (removal of the mass and a small amount of unaffected surrounding tissue) will usually prevent local recurrence of benign mass lesions. For such tumors as acanthomatous ameloblastoma, wide resection (removal of the mass and 1-2 cm of surrounding tissue) is indicated.

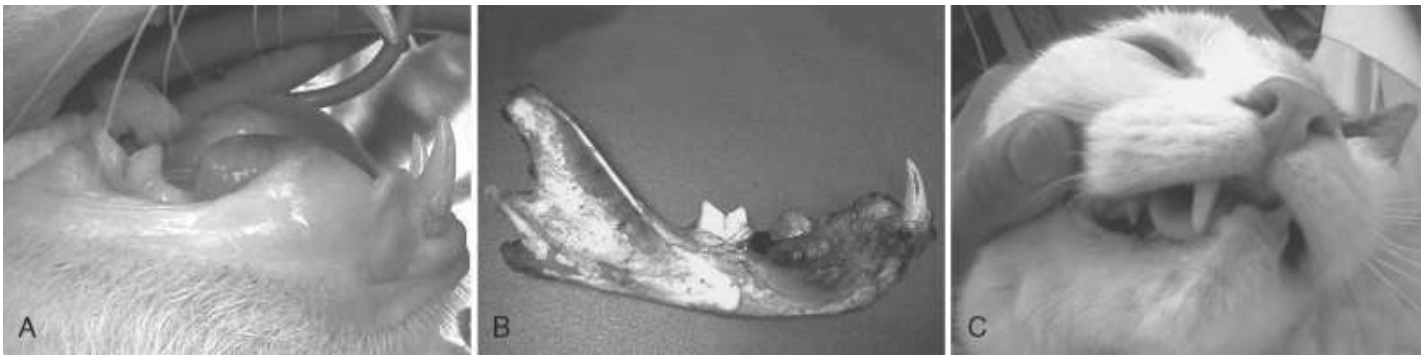
- When surgical excision is not an option, efforts should be made to decrease the rate of growth (such as radiation therapy) and provide relief from discomfort (extraction of teeth impinging on the tumor, administration of pain medications).

ACUTE GENERAL TREATMENT

- Removal of a circumscribed mass to the normal level of the surrounding gingiva will often serve as an adequate biopsy but may not prevent local recurrence. Peripheral odontogenic fibromas will likely recur without removal of the tooth and the periodontal ligament lining the alveolar socket (s).
- Incisional biopsies of large masses are warranted to provide information prior to considering radical surgery.

CHRONIC TREATMENT

- Depending on biopsy result and tumor extent, surgery or radiation therapy may be good long-term options.
- Intralesional chemotherapy has been reported to be successful for treatment of some benign tumors (e.g., acanthomatous ameloblastoma). Systemic chemotherapy may be used as an adjunctive therapy but is rarely effective by itself against most oral tumors.
- Radiation therapy offers excellent long-term control for treatment of acanthomatous ameloblastoma, but malignant tumors may develop in the irradiated area in 3.5%-12.5% of dogs.



ORAL TUMORS, BENIGN A, Total mandibulectomy: preoperative image of a cat with a right mandibular amyloid-producing odontogenic tumor (APOT), which is a benign but locally aggressive neoplasm. **B**, Total mandibulectomy: intraoperative image of resected right mandible from same cat shown in A. **C**, Total mandibulectomy: postoperative image of same cat presenting several months later for a recheck; excellent healing of the surgical site; no tumor recurrence.

(Copyright Dr. Alexander M. Reiter.)

POSSIBLE COMPLICATIONS

- Recurrence of primary tumor
- Intraoperative or postoperative bleeding
- Dehiscence of the surgical site: use of electrocautery may obscure histologic examination of margins of excised tissue and increase the likelihood of wound dehiscence in oral surgery.

RECOMMENDED MONITORING

Repeat oral examination, including head/neck lymph node palpation, to monitor for recurrence at 6-month intervals.

PROGNOSIS AND OUTCOME

- Prognosis is excellent with benign tumors if they are amenable to complete surgical resection or respond to radiation therapy.
- When clients are reluctant to pursue surgery, radiation therapy has been documented to provide a good long-term clinical outcome for treatment of canine acanthomatous ameloblastoma.

PEARLS & CONSIDERATIONS

COMMENTS

- For larger oral masses, start with an incisional biopsy to obtain more information prior to definitive resection; biopsy results will help determine the required extent of definitive surgical resection, and other treatment options. When submitting excisional biopsies, clinicians should request that the pathologist evaluate margins for presence of neoplastic cells. Clean margins according to histologic examination do not rule out the possibility of recurrence, but animals with clean margins do have a better long-term prognosis.
- Dental radiography is invaluable in providing diagnostic and treatment planning information for oral tumors. Benign tumors tend to displace teeth that often remain firmly seated, whereas aggressive tumors will cause root and alveolar bone resorption, which may manifest as very mobile (floating) teeth. Benign tumors may have a smooth layer of reactive bone surrounding the neoplastic tissue, whereas a malignant tumor often exhibits destruction of cortical bone with formation of a classic “sunburst” appearance.
- Right or left total mandibulectomy (previously referred to as *hemimandibulectomy)* and maxillectomy surgeries carry with them the potential for

profuse bleeding. Blood type and cross matching may be warranted preoperatively.

TECHNICIAN TIPS

- Technicians are on the frontline of identifying oral tumors during professional dental cleanings. Do a complete oral examination on each anesthetized patient, including the sublingual area and tonsils. Bring all identified oral masses to the attention of the clinician for possible biopsy during the same anesthetic episode.
- Provide as much information as possible on histopathologic evaluation forms. Include size (in three dimensions), surface characteristics (ulcerated, smooth, verrucous), complete history, and specific location of tumors.

CLIENT EDUCATION

- Complete surgical removal of oral tumors provides the best long-term prognosis. Clinicians should advise new pet owners to socialize puppies and kittens and allow them to feel comfortable with periodic examination of the oral cavity.
- Animals adapt remarkably well after radical resection of oral tumors, and altered cosmesis is usually well accepted by owners if enough function can be restored to allow for independent eating and drinking. Clients should be shown before-and-after pictures of similar surgical cases to ensure their understanding of cosmetic changes.

SUGGESTED READING

Gardner DG: Epulides in the dog: a review. J Oral Pathol Med 25:32, 1996.

Verstraete FJM: Self-assessment colour review of veterinary dentistry, London, 1999,Manson Publishing.

AUTHOR: JOHN R. LEWIS

EDITOR: ALEXANDER M. REITER

Optic Neuritis

BASIC INFORMATION

DEFINITION

Inflammation of one or both optic nerves, leading to loss of vision. This is an acquired condition that may be primary or secondary to systemic central nervous system (CNS) disease. The optic nerve is surrounded by dura mater and communicates with the subarachnoid space.

SYNONYM

Papillitis (inflammation of the optic disk)

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs and cats; more commonly seen in middle-aged dogs

ASSOCIATED CONDITIONS & DISORDERS

- Granulomatous meningoencephalitis (GME) (see p. 457)
- Systemic infectious diseases, including:
  - Systemic mycoses in dogs and cats
  - Feline infectious peritonitis (FIP; seep. 383)
  - Canine distemper (see p. 317)
  - Toxoplasmosis in dogs and cats (see p. 1105)
  - Neosporosis in dogs (seep. 1105)
- Neoplasia: primary or secondary

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Intraocular: inflammation of the optic disk; detected with ophthalmic examination
- Orbital: inflammation of the retrobulbar/orbital portion of the optic nerve; not detectable with ophthalmic examination
- Intracranial: inflammation of the portion of the optic nerve following its exit from the orbit at the optic foramen and to the level of the optic chiasm; not detectable with ophthalmic examination but may be associated with neurologic deficits

HISTORY, CHIEF COMPLAINT: Sudden blindness of one or both eyes

PHYSICAL EXAM FINDINGS

- Blindness if bilateral
- Absent unilateral or bilateral menace response(s), pupillary light and dazzle reflexes
- Fixed and dilated pupil (mydriasis; unilateral or bilateral)
- Swollen, edematous, and hyperemic optic disk with possible peripheral retinal edema and/or hemorrhages if intraocular portion of optic nerve (i.e., optic disk) is affected
- Normal-appearing optic disk if the inflammation is limited to the orbital and/or intracranial portions of the optic nerve
- Small, pale optic disk (i.e., optic disk atrophy) in advanced cases
- Depending on the cause (see Etiology, below), systemic abnormalities also may be present.

ETIOLOGY AND PATHOPHYSIOLOGY

- Infectious:
  - Canine: viral (canine distemper [seep. 317]), systemic mycoses (seepp. 138 , 266, and538), protozoal *(Toxoplasma gondii; Neospora caninum.* seep. 1105)
  - Feline: viral (FIP), systemic mycoses (cryptococcosis [seep. 266], histoplasmosis [seep. 538]), protozoal *(Toxoplasma gondii)*
- Neoplastic: feline lymphoma, orbital neoplasia

- Immune-mediated: GME
- Traumatic: leading to orbital cellulitis or abscess
- Nutritional: vitamin A deficiency (rare in dogs and cats)
- Secondary to orbital inflammation, meningitis, scleritis, retinitis, posterior uveitis
- Idiopathic

DIAGNOSIS

DIAGNOSIS OVERVIEW

The diagnosis is suspected with loss of vision, fixed and dilated pupil(s), and abnormal appearance of the optic disk(s). A normal electroretinogram further supports the diagnosis; evidence of sterile inflammation in cerebrospinal fluid is consistent but not required. To confirm orbital/intracranial optic neuritis, advanced imaging such as MRI is required. Since treatment (corticosteroids) may alter the results of advanced diagnostic tests, prompt referral to a veterinary ophthalmologist should be considered for optic neuritis suspects.

DIFFERENTIAL DIAGNOSIS

- Unilateral:
  - Acute primary glaucoma (elevated intraocular pressure [IOP] > 30 mm Hg) and signs of glaucoma (see pp. 448 and 1559)
- Bilateral:
  - Sudden acquired retinal degeneration (SARD) in dogs (seep. 983): normal fundic (i.e., posterior segment) examination early on with flatline electroretinogram (ERG; see p. 1255), meaning no retinal function, versus ERG waveforms confirming retinal function in acute optic neuritis.
  - Immune-mediated retinitis in dogs: uncommon to rare; normal fundic exam possible early on; low retinal function on ERG, vision may return with oral prednisone (1 mg/kg PO q 24 h) in combination with oral doxycycline (5 mg/kg PO q 24 h)
  - Enrofloxacin toxicosis in cats: retinal degeneration noted on fundic examination versus normal-appearing retina with optic neuritis. Exception: if the intraocular portion of optic nerve (i.e., optic disk) is affected with optic neuritis, the clinician may detect peripheral retinal edema and/or hemorrhages.
  - Neoplasm at the optic chiasm (advanced imaging such as MRI to differentiate from bilateral orbital/intracranial optic neuritis)
  - Cortical (central) blindness (normal pupillary light reflexes; normal fundic examination; possibly additional neurologic abnormalities)
  - Papilledema: edema of the optic nerve head (no blindness)

INITIAL DATABASE

- Complete ophthalmic examination (seep. 1313), including:
  - Menace response and dazzle reflex (absent in affected one or both eyes)
  - Pupillary light reflexes (PLRs): if bilateral optic neuritis, pupils typically are fixed and dilated, thus producing negative direct and consensual PLRs; if unilateral, direct PLR absent in affected eye and consensual PLR absent in contralateral eye. NOTE: *Consensual PLR* refers to reaction of contralateral eye. For example, an absent consensual PLR in the right eye describes the lack of constriction of the right pupil in response to light shone into the left eye.
  - Assessment of IOP; rule out acute primary glaucoma (IOP > 30 mm Hg; seepp. 448 and 1559).
  - Examine posterior segment of eye (i.e., fundus) using direct and/or indirect ophthalmoscopy.
- Neurologic examination (seech p. 1311)

ADVANCED OR CONFIRMATORY TESTING

- ERG to assess retinal function; normal in optic neuritis
- MRI (seep. 1302) or CT (seep. 1233):
  - Advanced imaging can help detect neoplastic processes along the optic nerve and optic chiasm. If a mass is detected in the retrobulbar optic nerve, exenteration (removal of the globe and all of the orbital contents) could be curative.
- Cerebrospinal fluid (CSF) analysis (see p. 1228); may be abnormal, depending on the cause of optic neuritis
- Visual-evoked potentials to assess optic nerve function; severely diminished with optic neuritis

TREATMENT

TREATMENT OVERVIEW

Prompt antiinflammatory therapy is warranted with this condition, but prognosis for return of vision remains poor.

ACUTE GENERAL TREATMENT

- Treat the underlying cause if determined.
- Idiopathic or traumatic (i.e., noninfectious) etiology: prednisone, 1-2 mg/kg PO q 12 h for 7-14 days; then 0.5-1 mg/kg PO q 12 h for 7-14 days; then gradual decrease to reach a maintenance dosage

CHRONIC TREATMENT

GME: possible lifelong immunosuppressive therapy (see p. 457)

RECOMMENDED MONITORING

Monitor clinical signs (i.e., vision and optic disk with or without secondary retinal lesions if intraocular optic neuritis) within 24 hours of the animal commencing medical treatment(s) and at least weekly for the first month (reassessment intervals will vary depending on the cause and response to treatments)

PROGNOSIS AND OUTCOME 

- Prognosis depends on underlying cause.
- Prognosis for return of vision is generally poor, and blindness is usually permanent.
- In cases that do respond to treatment, recurrences may occur if medication is decreased too rapidly or if duration of therapy is inadequate.
- If the animal is untreated or unresponsive to treatment, optic disk atrophy and attenuation of retinal blood vessels will occur.

PEARLS & CONSIDERATIONS 

COMMENTS

- Suspicion or confirmation of optic neuritis warrants referral to a veterinary ophthalmologist.
- Early diagnosis and appropriate, aggressive medical therapy are paramount to limit damage to the optic nerve(s).
- GME is the leading cause of optic neuritis in dogs.

CLIENT EDUCATION

Counsel clients on the high probability of living with a blind dog.

SUGGESTED READING

Nafe LA, Carter JD: Canine optic neuritis.Compend Contin Educ Pract Vet 3:978,1981.

Nell B: Optic neuritis in dogs and cats. Vet Clin North Am Small Anim Pract 38:403–415,2008.

AUTHOR: CHANTALE L. PINARD
EDITOR: CHERYL L. CULLEN

Opiates/Opioids Toxicosis

BASIC INFORMATION

DEFINITION

- Adverse effects including CNS depression, ataxia, weakness, hypersalivation, vocalization, disorientation, coma, hypothermia, hypotension, bradycardia and possible respiratory depression seen at the recommended dose or from acute overdose of medications containing opiates/opioids
- The term *opiate* refers to alkaloids such as morphine or codeine obtained from the sap of poppy plant (natural); *opioids* are synthetic and natural morphine-like medications which work through the opioid receptors.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs and cats of all breeds, ages, and both sexes susceptible. Dogs more likely to get into owner's medications by accident compared to cats.

GENETICS & BREED PREDISPOSITION: Cats and MDR1-deficient dogs are more sensitive to the effects of opioids (see p. 706).

RISK FACTORS: Concurrent administration of other CNS depressants or preexisting hepatic damage may increase the risk of toxicosis.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Toxicosis is generally acute.

HISTORY, CHIEF COMPLAINT

- Evidence of exposure (owner administration, chewed bottle)
- Presence of CNS depression, vocalization, ataxia, weakness within a few hours after exposure

PHYSICAL EXAM FINDINGS

- CNS depression, sedation, ataxia, weakness, vomiting (gastrointestinal [GI] stasis)
- Bradycardia, hypotension
- Idiosyncratic agitation/excitation (cats and young animals)
- Coma, hypothermia, respiratory depression (rare)

ETIOLOGY AND PATHOPHYSIOLOGY

- Opioids are used as analgesics, antidiarrheals, cough suppressants, and as sedatives before surgery.
- Buprenorphine, butorphanol, fentanyl, hydromorphone, tramadol, and loperamide are commonly used opioids in veterinary medicine.
- Opioids work through interaction with opiate receptors (mu, delta, kappa, sigma, epsilon, nociceptin). Opioids act in the central nervous system to elevate the pain threshold and alter the psychological response to pain. The receptors are found in the limbic system, spinal cord, thalamus, hypothalamus, striatum, and midbrain. Opioids may be agonists, mixed agonist-antagonists, or antagonists at these receptors.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Exposure is suspected or certain from history of ingestion and presence of typical clinical signs (depression, ataxia, sedation, weakness). Over-the-counter urine drug tests (illicit drug test kits) may be used for confirming exposure.

DIFFERENTIAL DIAGNOSIS

- Differentiate from other CNS depression-causing toxicoses such as barbiturate overdose, benzodiazepines, phenothiazines,

alcohol, ivermectin, antifreeze, marijuana.
- Nontoxicologic rule outs include hypoglycemia, meningoencephalitis, intracranial neoplasia, and uremic or hepatic encephalopathy.

INITIAL DATABASE

- Heart rate (increased or decreased), respiratory rate (may be depressed)
- Blood pressure
- Blood gas (respiratory acidosis if hypo-ventilation), oxygen saturation
- Body temperature (normal or below normal)

ADVANCED OR CONFIRMATORY TESTING

- Urine drug screen (antemortem)
- Blood, urine, tissues (postmortem)

TREATMENT

TREATMENT OVERVIEW

Severe intoxications affecting respirations and heart rate require stabilization: intubation and positive-pressure ventilation if the patient is apneic and drugs to address cardiac arrhythmias. Naloxone and supportive care are indicated for reversal of opiate effects in all confirmed or strongly suspected cases showing clinical signs. Induction of vomiting and administration of activated charcoal are warranted in exposed patients not showing any clinical signs.

ACUTE GENERAL TREATMENT

- Provide ventilatory support in a comatose animal with respiratory compromise.
- Naloxone (0.002-0.04 mg/kg IV, IM, SQ); repeat as needed depending on the opioid involved.
- Fluid diuresis depending on severity of signs
- Diazepam (0.25-1 mg/kg slow IV) for dysphoric reactions (vocalization, excitation)
- Cyproheptadine (1.1 mg/kg PO or per rectum) can be used for serotonin syndrome-like effects (muscle rigidity, disorientation). See p. 1427 .

BEHAVIOR/EXERCISE

Restrict/confine activity at home until resolution of signs.

DRUG INTERACTIONS

- Erythromycin, cimetidine, ketoconazole, itraconazole, fluconazole, diltiazem will decrease clearance and increase half-life of opioids owing to decreased metabolism.
- Benzodiazepines, barbiturates, centrally acting muscle relaxants, and phenothiazines will increase CNS depression and risk of respiratory depression.

RECOMMENDED MONITORING

- Heart rate, respiration
- Blood pressure,
- Oxygen saturation
- Body temperature
- CBC, and serum biochemistry profile (no significant changes expected)

PROGNOSIS AND OUTCOME

Good for most exposures, because dogs and cats tolerate higher doses of opioids compared to humans. Animals do not seem to develop severe respiratory depression as readily as humans do from opioid overdose.

PEARLS & CONSIDERATIONS

COMMENTS

- Fentanyl lozenges or suckers contain a sucrose and liquid glucose base and are attractive to pets. There is usually enough fentanyl left on the stick of a used sucker or in a used fentanyl patch to cause overt clinical signs if ingested by a pet. The plastic stick or patch can be retained as a foreign body, causing prolonged exposure and intoxication.
- Due to first pass effect, there is low bioavailability of some opioids when given orally. Opioids are metabolized in liver, and some undergo glucuronide conjugation before being excreted. Cats are deficient in glucuronidation process, and therefore half-life of some opioids in cats is prolonged.

PREVENTION

Keep all medications away from pets.

TECHNICIAN TIPS

Owners/clients may not readily admit presence of any opioids/opiates in pet's environment. Therefore, any mention of this information should be relayed to the attending veterinarian for optimal treatment of the patient.

CLIENT EDUCATION

Keep all medications, used patches, and sucker sticks away from pets.

SUGGESTED READING

Kahan CM, editor: Toxicities from illicit and abused drugs. In: The merck veterinary manual, ed 9, White House Station, NJ, 2005, Merck & Co, Inc, pp 2537–2541.

AUTHOR: TINA WISMER

EDITOR: SAFDAR KHAN

Onion or Garlic Toxicosis

BASIC INFORMATION

DEFINITION

Intoxication results from consumption of a plant in the genus *Allium,* which includes garlic, onions, leeks, scallions, shallots, and chives. Most of these plants are perennial, rhizomatous, or bulbous herbs. Most have a distinctive odor.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Cats are more susceptible than dogs.

GENETICS & BREED PREDISPOSITION: Japanese breeds such as the Akita, Shiba Inu, and Tosa are more susceptible to oxidative damage to the red blood cell (RBC).

RISK FACTORS

- Dogs' indiscriminate feeding behavior increases the risk of ingestion.
- Cats are more likely to be exposed from ingesting foods like baby food with onion or garlic powder as a flavoring (chronically), although some cats can be as indiscriminate as dogs.

ASSOCIATED CONDITIONS & DISORDERS: Any cause of oxidative RBC damage, Heinz body anemia (seep. 1487), hemolytic anemia (see), hemoglobinuria, and methemoglobinemia

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- History of exposure to raw, cooked, dried, or powdered chives, onions, garlic, leeks, shallots, or scallions
- Common physical signs: weakness, lethargy, pale mucous membranes, discolored urine
- Less common: halitosis, hypersalivation, vomiting, and/or diarrhea
- The owner of any dog with hemolytic anemia should be asked about exposure to onions/garlic.

PHYSICAL EXAM FINDINGS

- Lethargy, weakness, and/or ataxia
- Mild hypersalivation, vomiting, and/or diarrhea
- Pale mucous membranes (anemia), tachypnea, tachycardia
- Discolored (red to brown) urine (hemoglobinuria)

ETIOLOGY AND PATHOPHYSIOLOGY

Source:

These plants grow wild and are widely cultivated.

Mechanism of Toxicosis:

- *Allium* spp. contain sulfoxides (which provide the characteristic odor) that are hydrolyzed to thiosulfinates. Thiosulfinates decompose to dipropyl sulfide. Dipropyl sulfides oxidize RBC membranes, resulting in hemolysis, Heinz bodies, anemia, and less commonly methemoglobinemia.
- Poisoning can result from ingesting raw, dried, powdered, or cooked onions and garlic: cooking or drying does not inactivate the toxic principle.
- Dogs fed onion soup equivalent to 30 g of raw onion/kg q 24 h for 3 days developed marked Heinz body anemia. Similarly, a significant increase in Heinz bodies was seen 12 hours after feeding dogs 200 g (½ lb) of boiled onions (approximate dose of 17 g onions/kg).
- Dogs given an extract equivalent to 5 g of whole garlic/kg PO q 24 h for 7 days developed anemia 9-11 days after dosing.
- Generally, most dogs need to eat at least 0.5% (5 g/kg) body weight to develop onion toxicosis, unless the dog is of a sensitive breed (see Genetics & Breed Predisposition above; Suggested Reading below).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is based on historical evidence of *Allium* species ingestion and the delayed onset (usually 2-5 days) of compatible signs (anemia, pale mucous membrane color, hemoglobinuria, hemolysis).

DIFFERENTIAL DIAGNOSIS

Toxicologic:

- Other agents known to cause hemolysis, anemia, or hemoglobinuria such as zinc, benzocaine and other local anesthetics, acetaminophen, naphthalene mothballs, propylene glycol, methylene blue, phenols

Spontaneous, Nontoxicologic:

- Parasites such as *Mycoplasma (Haemobartonella) felis, Babesia canis, Cytauxzoon felis,* and *Ehrlichia* spp.
- Immune-mediated hemolytic anemia
- Severe hypophosphatemia
- Ruptured hemangiosarcoma
- Hereditary RBC fragility syndromes
- Feline leukemia virus infection, feline immunodeficiency virus infection, feline infectious peritonitis
- Myelophthisic neoplasia
- Severe hookworm infestation

INITIAL DATABASE

- CBC, serum biochemistry profile:
  - Decreased hematocrit, elevated white blood cell count, methemoglobinemia, and Heinz bodies are possible.
  - Smears should be examined for Heinz bodies, evidence of regeneration.
- With methemoglobinemia (see p. 1501), serum may be brown and/or blood may fail to turn red when exposed to air.
- Hematologic changes (e.g., hemolysis, Heinz body anemia, methemoglobinemia) may occur as early as 12 hours post ingestion but generally take 2-5 days to develop.
- Urinalysis:
  - Reddish-brown color suggests hemoglobinuria (rule out hematuria, myoglobinuria).
  - Urine dipstick will be positive for blood with hemoglobinuria or hematuria.
  - Centrifuged urine will remain reddish brown with hemoglobinuria, whereas the supernatant of centrifuged urine will clear with hematuria.
- Specific assay for serum methemoglobin is available in central laboratories.

ADVANCED OR CONFIRMATORY TESTING

Cooximetry (measures percentage of methemoglobin) and methemoglobin assays exist but are not typically useful in the limited time frame of an intoxication.

TREATMENT

TREATMENT OVERVIEW

If no clinical signs are present, treatment consists of immediate decontamination of the patient (induction of vomiting and administration of activated charcoal). If the patient is showing overt signs compatible with toxicosis, care may include improving tissue oxygenation (packed RBC or whole blood transfusion) and general supportive care.

ACUTE GENERAL TREATMENT

- No clinical signs apparent:
  - Induction of vomiting (seep. 1364) with recent ingestion.
  - Activated charcoal 1-2 g/kg PO (dose according to packaging label of product; e.g., 10 mL of activated charcoal suspension PO made from 2 g activated charcoal suspended in 10 mL tap water). Repeat dosing may be indicated with large ingestions (caution: monitor for hypernatremia if repeatedly giving charcoal-cathartic combination, e.g.,

Toxiban).
- Patient showing clinical signs:
  - Packed RBC or whole blood transfusion if necessary (NOTE: new RBCs remain at risk for hemolytic damage if toxicant is still in the blood). See p. 1347.
  - IV fluids to treat shock and promote fluid diuresis; caution regarding hemodilution with anemia
  - Management of vomiting and diarrhea as needed
  - Oxygen supplementation of limited benefit, since oxygen saturation of intact hemoglobin remains high, and methemoglobin binds oxygen poorly even with supplementation.

CHRONIC TREATMENT

Generally not indicated; recovery is expected with appropriate acute treatment.

BEHAVIOR/EXERCISE

Exercise restriction pending resolution of anemia

DRUG INTERACTIONS

Garlic has an antithrombotic effect, and concomitant use of garlic and drugs that alter platelet function (e.g., aspirin, clopidogrel) may produce additive antithrombotic effects.

POSSIBLE COMPLICATIONS

- Hemoglobinuria-associated renal tubular damage possible in severe cases
- Abortions can occur secondary to severe hypoxemia if a pronounced anemia is present.

RECOMMENDED MONITORING

- CBC/hematocrit/blood smear
- Renal function

PROGNOSIS AND OUTCOME

- Generally good with prompt veterinary care of patients showing overt clinical signs
- Guarded with severe anemia or secondary renal damage

PEARLS & CONSIDERATIONS

COMMENTS

- Many commercial garlic or onion powder products will list the conversion for a clove of garlic (e.g., 1 tsp of garlic powder equals one clove of garlic).
- One pearl onion weighs about 14 g, a small onion (2 in/5 cm diameter) weighs about 56-85 g, a medium onion (3 in/7.5 cm diameter) weighs about 226-255 g, and a large onion (4 in/10 cm diameter) weighs about 425-450 g.
- A medium onion yields about 1 cup of coarsely chopped onion.

TECHNICIAN TIP

When recommending baby food to stimulate appetite, it is important to remind clients to avoid products with garlic or onion powder, especially for cats.

PREVENTION

Owners should keep foods with onion or garlic ingredients out of their pets' reach.

CLIENT EDUCATION

Garlic supplementation for the prevention of heartworm disease is unsubstantiated and contraindicated.

SUGGESTED READING

Tang X, Xia Z, Yu J: An experimental study of hemolysis induced by onion (Allium cepa) poisoning in dogs. J Vet Pharmacol Ther 31:143–149, 2008.

AUTHOR: DONNA MENSCHING

EDITOR: SAFDAR A. KHAN

1ST EDITION AUTHOR: CHARLOTTE MEANS

Oleander Toxicosis

BASIC INFORMATION

DEFINITION

An acute poisoning that occurs following ingestion of dried or fresh parts of an oleander plant (genus *Nerium* or *Thevitia).* Clinical manifestations are similar to those of digoxin toxicity: gastrointestinal (GI) signs initially, with possible subsequent cardiac arrhythmias.

SYNONYMS

- *Nerium oleander:* oleander
- *Thevitia nerifolia:* yellow oleander

EPIDEMIOLOGY

SPECIES, AGE, SEX: Animals of all ages, breeds, and both sexes susceptible; dogs are more commonly affected.

RISK FACTORS: Availability of oleander plant in pet's environment

GEOGRAPHY AND SEASONALITY: Oleander is an ornamental evergreen shrub widely cultivated all over the world and most of the southern United States, notably California and Florida.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Observed or suspected exposure to plant
- Vomiting, with plant material in the vomitus
- Owners may note lethargy, salivation, signs of abdominal pain, diarrhea, weakness, and tremors.

PHYSICAL EXAM FINDINGS

- See History, Chief Complaint above.
- Cardiac arrhythmias, either tachycardias (premature beats or runs of tachycardia) or bradycardias; a pattern of bradycardia, initially present for 24 hours, followed by tachycardia and ventricular arrhythmia, has been described.
- Central (seizures) and peripheral (tremors, weakness) nervous system effects. Severe intoxications can lead to coma and death.

ETIOLOGY AND PATHOPHYSIOLOGY

- Clinical signs usually appear within 6 hours of ingestion, depending on the amount ingested.
- Oleander contains cardiac glycosides (oleandrin, neriine, etc.) that inhibit the sodium/potassium (Na^+/K^+) ATPase enzyme, which is essential for normal cellular function in multiple body systems, notably the cardiovascular and nervous systems.
- Inhibition of Na^+/K^+ ATPase leads to an abnormal accumulation of potassium outside the cell and sodium inside the cell, producing a cascade of calcium release that results in cardiac arrhythmia and myocardial ischemia or necrosis (in severe cases).
- The toxic effects are indistinguishable from those of digoxin toxicosis in pets receiving digoxin therapeutically.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A functional diagnosis is made when a pet with appropriate clinical signs and possibility of exposure (e.g., unmonitored in garden) is seen in areas where oleanders are accessible, and general decontamination of the patient is warranted based on these findings alone. New cardiac arrhythmias increase the index of suspicion. Diagnosis can be confirmed (generally retrospectively and therefore

for preventative, group health, or medicolegal reasons) by showing presence of oleandrin in body fluids by thin-layer chromatography (TLC) or high-performance liquid chromatography (HPLC).

OLEANDER TOXICOSIS Oleander plant, showing characteristic long, oval, robust leaves and ornamental flowers.

DIFFERENTIAL DIAGNOSIS

- Advanced primary heart disease (cardiomyopathy, valvular heart disease, traumatic myocarditis if hit by car, etc.)
- Primary bradycardias (third-degree atrioventricular block, sick sinus syndrome, atrial standstill/hyperkalemia)
- Systemic causes of ventricular arrhythmias (seep. 1165)
- Exposure to other plants that contain cardiac glycosides (seep. 175)

INITIAL DATABASE

- CBC: no significant changes likely
- Serum chemistry profile: hypokalemia or hyperkalemia possible. Hypokalemia may be particularly detrimental: it fosters ventricular arrhythmia and also makes animals refractory to antiarrhythmics (lidocaine, quinidine, mexiletine, etc.).
- Electrocardiogram (ECG) to determine type of cardiac arrhythmia if present.

ADVANCED OR CONFIRMATORY TESTING

- Confirmation of oleandrin in body fluids, stomach, and intestinal contents by using TLC and HPLC techniques (available in some veterinary diagnostic laboratories).
- Postmortem examination may reveal oleander plant material in the GI tract, pericardial effusion, possibly pulmonary edema, and varying degrees of thrombi and hemorrhages in epicardial surfaces.
- Histologic examination of the heart tissue may reveal evidence of myocardial inflammation, degeneration, and necrosis.

TREATMENT

TREATMENT OVERVIEW

When exposure is known or suspected but no clinical signs are present, induction of vomiting is indicated, followed by administration of activated charcoal. If overt signs are present (or emerge) or physical exam abnormalities lead to identification of consequences of toxicosis (e.g., cardiac arrhythmias), treatment is directed at both decontamination and palliation of consequences (e.g., antiarrhythmic therapy) while also addressing any potentially complicating factors (e.g., hypokalemia, retention of plant material). Antidigitalis antibodies are indicated in critical cases with severe signs when not cost-prohibitive.

ACUTE GENERAL TREATMENT

- These guidelines are appropriate for an average adult dog.
- Decontamination of patient:
    - Induction of emesis if appropriate and within 1-2 hours after ingestion (seep. 1364)

- Activated charcoal: administration of activated charcoal after inducing emesis or if few hours have elapsed after exposure; 1-4 g/kg with a cathartic such as 70% sorbitol (3 ml/kg) PO

- Treating cardiac arrhythmias:
  - Sinus bradycardia (see online chapter: Sinus Bradycardia) that occurs within 24 hours of exposure: clinicians should treat the condition if severe (e.g., heart rate <60-80 beats/min in an awake and standing large- to small-breed dog, respectively) or if the condition is associated with overt signs (e.g., lethargy).
  - Ventricular arrhythmias (see p. 1165)
  - Supraventricular arrhythmias (see p. lll): extremely rapid, persistent supraventricular tachycardias may need to be controlled (e.g., with propranolol, 0.1-0.5 mg IV total dose per bolus; no more frequently than 1 bolus q 1-3 min to 5 mg maximum for large dogs). The goal is to lower heart rate to acceptable level (e.g., by 20%) and not cause an overly rapid suppression.
- Use of specific fluorescent antibodies (FAB, Digibind) in severe cases:
  - IV antidigitalis antibodies; inactivate significant proportion of circulating cardiac glycoside
  - Extremely expensive (several thousand dollars per dose); reserved for cases in which animals are profoundly ill or manifesting severe arrhythmias and in which cost of treatment is unimportant to the owner (for dosage and details, see online chapter: Digitalis Toxicosis)
- For supportive care, clinicians should:
  - Administer IV fluids as needed.
  - Treat diarrhea, severe vomiting, and abdominal pain as needed.
  - Correct electrolytes (potassium) if needed.

RECOMMENDED MONITORING

- ECG
- Serum chemistry profile, especially electrolytes

PROGNOSIS AND OUTCOME

- Poor prognosis with severe cardiac arrhythmias; animals are often found dead.
- Clinical signs of toxicosis may persist for 24 hours or longer in animals that ultimately survive; hospitalization for >24 hours is appropriate, and outcome can be successful.

PEARLS & CONSIDERATIONS

COMMENTS

- Animals that survive may have no permanent sequelae or may have sustained myocardial infarcts, causing some degree of permanent cardiac damage (severe intoxications).
- Oleander leaves can be identified by a characteristic venation pattern and stromata; they have a prominent midrib with parallel veins extending to the periphery.
- All parts of oleander are toxic; ingestion of dry leaves/clippings is the most common cause of poisoning in animals.
- As little as 0.005% of an animal's body weight in oleander leaves (e.g., 10-12 leaves) may be lethal to an animal.
- Intoxication can occur by drinking water in which oleander was soaked.

PREVENTION

Owners should use extreme caution when growing oleander close to animal housing or on premises.

SUGGESTED READING

Galey FD: Cardiac glycosides. In Plumlee KH, editor: Clinical veterinary toxicology, Philadelphia, 2004, Elsevier (Health Sciences Division), pp 386–388.

Gwaltney-Brant SM, Rumbeiha WK: Newer antidotal therapies. Vet Clin North Am Small Anim Pract 32:323–339, 2002.

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Ocular Size Abnormalities

BASIC INFORMATION

DEFINITION

- Buphthalmos: a larger than normal globe; may be congenital or acquired and is a result of current or past glaucoma
- Microphthalmos: a smaller than normal globe; a congenital condition sometimes associated with other ocular anomalies
- Phthisis bulbi: a shrunken globe; a condition acquired as a result of chronic ocular inflammation (e.g., uveitis or severe ocular trauma)
- May occur in one or both eyes

SYNONYMS

Buphthalmia (buphthalmos), microphthalmia (microphthalmos)

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Buphthalmos may occur, and microphthalmos does occur, congenitally.
- Phthisis bulbi: no age predisposition

GENETICS & BREED PREDISPOSITION

- Buphthalmos secondary to glaucoma (see p. 448) is inherited in several breeds.
- Microphthalmos is inherited in miniature schnauzers, Australian shepherds, collies, Shetland sheepdogs, and Doberman pinschers.

ASSOCIATED CONDITIONS & DISORDERS

- Buphthalmos can be associated with:
  - Lagophthalmos (incomplete closure of the eyelids) with or without secondary corneal ulceration (see p. 250)
  - Lens subluxation/luxation (see p. 644)
  - Intraocular neoplasia (seep. 620)
- Microphthalmos is associated with:
  - Other congenital ocular anomalies, including cataracts (seep. 181) and retinal dysplasia/folds
  - Collie eye anomaly, including choroidal hypoplasia with or without optic nerve coloboma, staphyloma, retinal detachment, and intraocular hemorrhage
- Phthisis bulbi is associated with:
  - Untreated or poorly responsive ocular inflammation (e.g., uveitis or severe ocular trauma)
  - Variable systemic abnormalities depending on cause of uveitis (see p. 1151)

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Condition is most likely unilateral but can also occur bilaterally.

- Buphthalmos: enlargement of globe during first few months of life (i.e., congenital glaucoma); progressive enlargement of globe and “red eye” (seep. 448)
- Microphthalmos: small eye from birth
- Phthisis bulbi: progressive shrinkage of globe following a “red eye” (seep. 967)

PHYSICAL EXAM FINDINGS

- Buphthalmos: larger globe and signs of glaucoma, including:
  - Red eye (congested conjunctival and scleral blood vessels)
  - Diffuse corneal edema with possible striae (white streaks in the cornea from breaks in Descemet's membrane)
  - Corneal vascularization if eyelids cannot close over the enlarged globe (i.e., lagophthalmos)
  - Fixed and dilated pupil

    - Lens subluxation/luxation (see p. 644)
    - Blindness
- Microphthalmos: smaller globe and the following:
    - Enophthalmos (caudal displacement of the eye) (see p. 790)
    - Prolapsed third eyelid (seep. 1089)
    - Other intraocular abnormalities (cataracts, retinal folds/dysplasia)
    - ± Small palpebral fissure (i.e., small opening between the eyelids) or entropion and/or conjunctivitis if eyelids are normal length despite small eye
    - Vision may be normal, reduced, or absent.
- Phthisis bulbi: shrunken globe and the following:
    - Enophthalmos (caudal displacement of the eye; see p. 790)
    - Prolapsed third eyelid
    - Corneal edema; deep corneal vascularization
    - ± Entropion, conjunctivitis, posterior synechiae, cataract, iris atrophy
    - Vision typically reduced or absent

ETIOLOGY AND PATHOPHYSIOLOGY

- Buphthalmos: result of untreated or poorly managed glaucoma
- Microphthalmos: congenital deficiency of optic vesicle or failure of normal growth and expansion of optic cup; inherited condition
- Phthisis bulbi: acquired condition that possibly follows chronic intraocular inflammation (see pp. 1151, 448, and 249)

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The definitive diagnosis depends on the general appearance of the ocular globe and signalment of the patient.

DIFFERENTIAL DIAGNOSIS

- Buphthalmos: exophthalmos (forward displacement of the globe; see p. 790)
- Microphthalmos, phthisis bulbi: ruptured globe (seep. 249)

INITIAL DATABASE

- Complete ophthalmic examination, including:
    - Measurement of intraocular pressure (IOP): may be elevated (>30 mm Hg, indicating uncontrolled glaucoma), or normal (chronic glaucoma) with buphthalmos; typically low (<10-15 mm Hg) with phthisis bulbi.
    - Fluorescein dye application with buphthalmos (there may be positive dye retention, such as with a corneal ulcer)
    - Neuroophthalmic exam (seep. 1313) to assess vision (e.g., menace response)
- Additional tests vary depending on underlying cause

ADVANCED OR CONFIRMATORY TESTING

- Buphthalmos: ocular ultrasound if corneal or ocular media opacification precludes evaluation of intraocular structures (e.g., assess lens for cataracts and globe for intraocular mass)
- Ocular histopathologic examination if enucleation is performed due to blindness and ocular pain (common with buphthalmos)

TREATMENT

THERAPEUTIC OVERVIEW

The management of ocular pain is paramount, independent of the appearance of the globe. Unfortunately, pain control may require enucleation for several patients. No treatment may be required if ocular size abnormalities are not accompanied by evidence of discomfort, inflammation, or elevated IOP.

ACUTE GENERAL TREATMENT

- For buphthalmos (for treatment options, see Glaucoma,p. 1151); if the animal's globe is blind and if glaucoma remains

medically uncontrolled, options include:
  - Enucleation, evisceration with intraocular prosthesis, or chemical ablation of blind eyes with chronic primary glaucoma (seep. 115); chemical ablation is not recommended in cats
  - Enucleation of eyes with intraocular neoplasia
  - Enucleation of eyes with congenital glaucoma
- For microphthalmos: enucleation is warranted if eye is blind and entropion or chronic conjunctivitis occurs.
- For phthisis bulbi: treatment of underlying uveitis and advise enucleation if eye is blind and entropion or chronic conjunctivitis occurs.

PROGNOSIS AND OUTCOME

- Prognosis for vision is grave in cases of buphthalmos and advanced phthisis bulbi.
- Depending on the degree of microphthalmos and the presence of other ocular anomalies, the prognosis for vision varies for microphthalmos.

PEARLS & CONSIDERATIONS

COMMENTS

- Measure the corneal horizontal diameter of each eye to document buphthalmos or microphthalmos/phthisis bulbi.
- Recommend against breeding animals affected with buphthalmos or microphthalmos if the condition is deemed to be breed-related or inherited in nature.
- Abnormal ocular size requires prompt evaluation and may or may not indicate an immediate need to treat; a proper and complete clinical ophthalmic exam determines the need for intervention (or lack thereof).

CLIENT EDUCATION

Clinicians should advise clients to seek veterinary care for their pets as soon as the eye becomes “red” and/or the eye changes in appearance.

SUGGESTED READING

Moore PA: Examination techniques and interpretation of ophthalmic findings. Clin Tech Small Anim Pract 16:1, 2001.

AUTHOR: CHANTALE L. PINARD

EDITOR: CHERYL L. CULLEN

Ocular Discharge

BASIC INFORMATION

DEFINITION

- Abnormal secretions on or around the eye(s)
- These secretions can be watery (serous), contain mucus (mucoid), or contain white blood cells, mucus, and bacterial/fungal agents (mucopurulent).
- An abnormal overflow of tears down the face is termed *epiphora.*

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs and cats; variable age of onset depending on cause

GENETICS & BREED PREDISPOSITION: Depends on cause; examples:

- Brachycephalic breeds with medial entropion (seep. 348)
- Breeds predisposed to distichia, ectopic cilia, and trichiasis (see p. 319)
- Breeds predisposed to congenital atresia, ectopia, and/or imperforated lacrimal puncta
- Breeds predisposed to entropion and/or ectropion (seep. 348)
- Dolichocephalic breeds of dogs with narrow skull conformation and deep medial canthal areas (i.e., medial canthal pocket syndrome)

RISK FACTORS: Outdoor animals prone to infectious causes of conjunctivitis (see pp. 237and239) and ocular trauma (seep. 249)

CONTAGION & ZOONOSIS: Certain infectious causes of conjunctivitis are contagious (e.g., feline herpesvirus type-1 [FHV-1]) and/or zoonotic (e.g., *Chlamydophila* spp.).

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Clear, white, to grey mucoid or green-yellow secretions on the eye(s) or eyelids
- Sudden, progressive, or persistent in nature

PHYSICAL EXAM FINDINGS: Unilateral or bilateral serous, mucoid, or mucopurulent ocular secretions with one or more of the following:

- Blepharitis: inflammation of the eyelids (see p. 966)
- Conjunctivitis (see pp. 237 and239)
- Corneal ulceration (seep. 250)
- Keratoconjunctivitis sicca (KCS; seep. 628)
- Qualitative tear film abnormality (e.g., mucin and/or lipid deficiency; see p. 1076)
- Entropion and/or ectropion
- Distichiasis/ectopic cilia/trichiasis (see p. 319)
- Anterior uveitis (see p. 1151)
- Glaucoma (see p. 448)
- Ocular size abnormalities (see p. 778)
- Orbital disease (see p. 790)
- Congenital anomalies or infection of nasolacrimal system (e.g., dacryocystitis; see online chapter: Dacryocystitis)

ETIOLOGY AND PATHOPHYSIOLOGY

- Serous discharge:
  - Corneal mechanical irritation:
    - Distichiasis/ectopic cilia/trichiasis (see p. 319)
    - Entropion (seep. 348)
    - Eyelid agenesis (partial more common than complete): more common in cats

        - Eyelid neoplasia
    - Blockage of nasolacrimal system, congenital:
        - Imperforate lacrimal punctum (dorsal and/or ventral lacrimal puncta/punctum not open; common)
        - Micropunctum (small ventral lacrimal punctum; common)
        - Nasolacrimal aplasia (lack of opening into nasal cavity; rare)
        - Obstruction of nasolacrimal duct in dogs by dacryops (cysts originating from lacrimal tissue) or nasal cyst (rare)
    - Blockage of nasolacrimal system, acquired:
        - Dacryocystitis (inflammation of the nasolacrimal system; see online chapter: Dacryocystitis)
        - Neoplasia (primary, rare; secondary, more common; e.g., nasal; maxillary sinus)
        - Foreign body
        - Trauma to medial canthus/eyelid, involving lacrimal punctum/puncta and/or canaliculus/canaliculi
    - Ocular pain:
        - Conjunctivitis (see pp. 237, 239)
        - Simple or indolent corneal ulceration (see p. 250)
        - Qualitative tear film abnormality (e.g., mucin and/or lipid deficiency; see)
        - Anterior uveitis (seep. 1151)
        - Glaucoma (seep. 1559)
- Mucoid to mucopurulent discharge:
    - Blepharitis (see p. 966)
    - Conjunctivitis (see pp. 237, 239)
    - KCS (seep. 628)
    - Melting/infected corneal ulceration (see p. 250)
    - Orbital abscess/cellulitis (see p. 790)
    - Dacryocystitis (seep. 280)
    - Nasolacrimal foreign body (e.g., grass awn; parasite)

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Ocular discharge is apparent on physical examination. The underlying cause should be investigated with a review of the history and physical examination and an ophthalmic examination initially. If the cause is not elucidated, specific ocular tests (some requiring referral) may be warranted.

DIFFERENTIAL DIAGNOSIS

- Ocular discharge with “red eye(s)” is often associated with overproduction of tears (i.e., linked with causes of corneal mechanical irritation, infection or ocular pain).
- Ocular discharge with “quiet eye(s)” (no evidence of ocular pain or eyelid conditions) is often associated with impaired drainage of tears (e.g., congenital or acquired blockage of nasolacrimal system).

INITIAL DATABASE

- Complete ophthalmic examination (seep. 1313), including:
    - Careful examination with magnification of the eyelids
    - Schirmer tear test (dogs: low with KCS; normal 15-25 mm/min; equivocal if 8-15 mm/min)
    - Fluorescein dye application (corneal dye retention with corneal ulceration; dye exiting nares helps confirm patent nasolacrimal system)
    - Intraocular pressure (IOP) (pressures at >30 mm Hg with glaucoma; may be low at <10-15 mm Hg with uveitis; both painful conditions)
- Conjunctival and/or corneal (if infected corneal ulcer) swabs for:
    - Cytologic examination to determine cell type and possible etiology
    - Culture and sensitivity (C&S): aerobic; if needed, anaerobic and fungal
    - PCR: FHV-I, *Chlamydophila* spp., and *Mycoplasma* spp.

ADVANCED OR CONFIRMATORY TESTING

- Varies depending on underlying cause
- Blockage of nasolacrimal system can be investigated with nasolacrimal system flush (see online chapter: Dacryocystitis), if no fluorescein dye exits, nares and blockage is suspected. If results are unclear, confirmation is possible with nasal radiographs and a contrast study of the nasolacrimal system. Contrast CT scanning can accurately assess the integrity of the

nasolacrimal system.

TREATMENT

TREATMENT OVERVIEW

Treatment is directed at the underlying cause. If discharge persists, referral to a veterinary ophthalmologist should be considered.

ACUTE GENERAL TREATMENT

- Treat the underlying cause (see Etiology and Pathophysiology section above).
- Blockage of nasolacrimal system: treat the primary lesion causing the obstruction (may be difficult to diagnose; if so, consult a veterinary ophthalmologist).

CHRONIC TREATMENT

May be required with certain diseases (e.g., KCS)

POSSIBLE COMPLICATIONS

- Conjunctivitis due to FHV-1 may lead to symblepharon (adhesions of conjunctiva to surrounding tissues), KCS, ulcerative keratitis, and stromal keratitis (seep. 524,).
- Chronic epiphora can lead to localized facial dermatitis at the medial canthus.

RECOMMENDED MONITORING

Varies depending on the underlying

PROGNOSIS AND OUTCOME

Prognosis is guarded to excellent depending on the underlying cause.

PEARLS & CONSIDERATIONS

COMMENTS

- Clinicians should perform routine aerobic bacterial C&S tests and submit them in cases of mucopurulent discharge to identify the implicated bacterium or fungus.
- Fungal infections are rare causes of ocular discharge in cats and dogs.
- Serous ocular discharge in cats is common with FHV-1.
- A thorough examination of the ENTIRE conjunctival sac, including dorsally throughout the dorsal surface of the globe and ventrally on both sides of the third eyelid, is necessary to identify any retained foreign material.

CLIENT EDUCATION

At the first sign of abnormal ocular discharge in their pets, owners should consult their veterinarian.

SUGGESTED READING

Gerding PA, Kakoma I: Microbiology of the canine and feline eye. Vet Clin North Am Small Anim Pract 20:615, 1990.

Pena MT, Leiva M: Canine conjunctivitis and blepharitis. Vet Clin North Am Small Anim Pract 38:233–249, 2008.

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Obsessive-Compulsive Disorder (OCD)

BASIC INFORMATION

DEFINITION

Mood/behavioral disorders characterized by repetitive, invariant, patterned behaviors which are exaggerated in intensity, frequency, and duration given the inciting stimuli (i.e., expressed out of context). The behavior interferes with health and well-being.

SYNONYMS

Compulsive disorders, stereotypies; include star gazing, air or fly snapping, spinning/tail chasing, and self-mutilation

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs and cats of any age

GENETICS & BREED PREDISPOSITION: Dogs: Genetic predisposition is suspected. Anecdotally, certain syndromes are more commonly associated with some breeds:

- Acral lick dermatitis: large and giant dog breeds
- Air/fly snapping, checking (hind quarter area), star gazing: miniature schnauzer
- Flank sucking: Doberman pinscher
- Spinning/tail chasing: German shepherd dog, bull terrier, Parson Russell and Jack Russell terrier

Cats: fabric chewing or ingestion is anecdotally associated with so-called Asian breeds (e.g., Siamese, Tonkanese, Burmese).

RISK FACTORS: Stressful or traumatic event. Lack of a daily routine.

CONTAGION & ZOONOSIS: Characteristically, OCD is not induced in conspecifics (e.g., housemates) by affected individuals.

ASSOCIATED CONDITIONS & DISORDERS: The patient may have multiple diagnoses of other impulsive or anxiety-based disorders.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Repetitive behavior that is out of context (may have exacerbated over time or begun suddenly).
- Inciting triggers may be identifiable, or the behavior may occur spontaneously.
- Earlier in the course, the owners may have been able to stop the behavior, but that may not be the case at the time of presentation, and the pet may not stop until exhausted.
- The pet may hide (to perform the behavior) or become aggressive when the owners try to stop the behavior or may begin avoiding the owners.
- Distress vocalizations (whining, crying, yowling, or growling) may occur before, during, or after performance of the compulsive behavior.
- When owners do not identify the behavior as abnormal, the chief complaint may refer to damage to self (alopecia, granuloma, weight loss, change in voice, recurring gastrointestinal obstruction due to pica), damage to the home, or altered social interactions.
- Chief complaint may suggest partial seizures or dysphoria.
- With chronicity, some owners may not consider the behavior problematic or abnormal.

PHYSICAL EXAM FINDINGS

- Often unremarkable
- Skin lesions possible with overgrooming/self-mutilation
- Weight loss if near-constant

ETIOLOGY AND PATHOPHYSIOLOGY

- A genetic contribution is suspected.
- In humans, the current hypothesis of OCD involves dysfunction in a neuronal circuit traversing from the orbital frontal cortex to the cingulate gyrus, caudate nucleus and putamen (the striatum), the globus pallidus, thalamus, and back to the frontal cortex.
- Dysfunction involving glutamate and/or gamma-aminobutyric acid (GABA) is a new focus for research.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

History is the cornerstone of diagnosis: occurrence of repetitive, invariant behaviors that are spontaneous or triggered are difficult or impossible to interrupt and interfere with normal maintenance and social behaviors.

DIFFERENTIAL DIAGNOSIS

- Attention-seeking (behavior occurs only when the owner is present).
- Separation anxiety (behavior occurs only when the owners are absent).
- Cognitive dysfunction (middle aged/geriatric animals that pace or stare)
- Hyperthyroidism (primarily cats)
- Neuropathic pain disorders (e.g., feline hyperesthesia, neck and shoulder hyperesthesia in syringomyelia in the Cavalier King Charles spaniel)
- Degenerative joint disease, anal sac disease, cystitis (excessive licking or hindquarter checking)
- Circling, spinning, and air snapping patients should be evaluated for peripheral or central vestibular disease, psychomotor seizures, or other central nervous system lesions.

INITIAL DATABASE

- CBC, urinalysis, and serum chemistry profile: usually within normal limits (assess for systemic disorders; prior to initiation of medications).
- Dermatologic diagnostic tests (see p. 1248) if skin lesions are a feature.

TREATMENT

TREATMENT OVERVIEW

- All cases of OCD warrant intervention, which is individualized and based on frequency and severity of clinical signs.
- Treatment usually is a combination of behavioral and environmental modification and psychotropic medication.
- The goal is to minimize—and if possible eliminate—bouts of compulsive behavior and the concomitant anxious states that accompany them.

ACUTE AND CHRONIC TREATMENT

- Owner: identify and eliminate trigger events/situations.
- No punishment should ever be used, since it can heighten anxiety and worsen, not improve, the problem.
- If possible, the pet can be redirected to an alternative and incompatible behavior—such as licking food from a toy instead of licking the skin—if the redirection does not make the pet more anxious.
- The pet should be calmly rewarded for any spontaneous calm behavior.
- Keeping a structured daily routine helps decrease anxiety.
- The most successful medications used in the treatment of OCD in people include a number of selective serotonin reuptake inhibitors (SSRIs) and clornipramine, a tricyclic antidepressant (TCA). In dogs and cats, the most commonly used are:
    - Clornipramine (Clomicalm): dogs, 2-3 mg/kg PO q 12 h for a minimum of 16 weeks; cats, 0.5 mg/kg PO q 24 h for a minimum of 16 weeks
    - SSRI drugs (fluoxetine [Prozac, Reconcile]): dogs, 1 mg/kg PO q 24 h for 16 weeks minimum; cats, 0.5 mg/kg PO q 24 h for 16 weeks minimum. Paroxetine (Paxil); dogs, 1 mg/kg PO q 24 h for 16 weeks minimum; cats, 0.25-0.5 mg/kg PO q 24 h for 16 weeks minimum. Sertraline (Zoloft); dogs, 1 mg/kg PO q 24 h for 16 weeks minimum; cats, 0.5 mg/kg PO q 24 h for 16 weeks minimum.
- Very distressed pets may need concomitant use of benzodiazepines (anxiolytic, faster onset of action).
    - Diazepam or oxazepam (oxazepam for cats, obese patients, liver disease), 0.2-0.4 mg/kg PO q 12-24 h; or alprazolam, 0.01-0.025 mg/kg PO q 8-24 h; or clonazepam (dogs), 0.01-0.05 mg/kg PO q 12-24 h for the first 2-3 weeks of treatment. Adjust to ideal dose based on response and lack of adverse (e.g., hepatic) effects. May also be used

preemptively when stress or change in routine is anticipated.
- *N*-methyl-D-aspartate (NMDA) antagonists hold promise as a potential treatment of OCD as single pharmacologic agents or as an adjunct to SSRIs.
- Typically, TCA or SSRI therapy is necessary for longer periods of time than other anxiety-based disorders (months to years, depending upon severity and how long the disorder has been ongoing). Lifelong medication use is not unusual in severe cases.

BEHAVIOR/EXERCISE

Some patients benefit from activities that serve as a controlled outlet for the compulsive behavior (e.g., retrieving, herding, agility, flyball), although they can be too arousing for others; tailor treatment to the individual.

DRUG INTERACTIONS

- TCAs and SSRIs should not be given with monoamine oxidase inhibitors (MAOIs), which are found in many flea and tick collars and dips and in some medications to treat cognitive dysfunction.
- TCAs: use with caution if cardiac arrhythmias, liver or thyroid disorders.
- Use of SSRIs with tramadol, which has a weak serotonin reuptake inhibiting effect, may increase the risk of serotonin syndrome (see p. 1427). Coadministration of fluoxetine, paroxetine, and possibly sertraline may result in decreased plasma concentrations of tramadol's active demethylated metabolite via inhibition of hepatic P450 enzymes. If their use together is necessary, starting both at reduced doses, titrating each to effect and keeping watch for signs of serotonin syndrome reduces but does not eliminate the risk; the client should be informed and should learn to monitor heart rate for profound increases as one way of assaying an early sign of serotonin syndrome.

POSSIBLE COMPLICATIONS

Paroxetine: avoid in renal disease; anecdotal reports of constipation in cats.

RECOMMENDED MONITORING

- Cats receiving paroxetine: monitor stool consistency (reports of diarrhea)
- Animals that take BZDs require a physical exam every 6 months in most U.S. states. The potential for human abuse of the drugs warrants vigilance regarding refill requests.
- Performing a yearly physical exam, CBC, serum chemistry profile, urinalysis, and thyroid screen (twice yearly in senior and geriatric pets) should be a minimum for animals taking other psychotropic medications.

PROGNOSIS AND OUTCOME

- Prognosis is highly variable from guarded to very good for management of the clinical signs of OCD, and is contingent upon a number of variables:
  - Time at which treatment is first instituted (the earlier, the better the prognosis)
  - Owner compliance with all (and not just portions) of the treatment recommendations
  - Frequent communication and follow-up between the owner and the clinician, as the treatment plan will need adjustment based on the pet's response and changing life circumstances
  - Untreated OCD seldom improves and very commonly worsens over time.

PEARLS & CONSIDERATIONS

COMMENTS

Repetitive behaviors are commonly thought of by clients as entertaining or as “quirks” in their pet's personality and seldom understood to be potential early markers of this disease. Many such pets go through their lives suffering greatly while their owners are ignorant of the distress associated with OCDs. Early intervention is a significant factor in the successful treatment of OCDs, but owners seldom talk about behavior during a veterinary visit unless prompted. It is extremely important to incorporate questions about behavior into all wellness and sick exams. “Any behavior that is new, different or peculiar since the last veterinary exam?” is sufficient to open the door and encourage owners to talk about their pet's behavior.

PREVENTION

- Consider temperament when selecting breeding stock.

- At the onset of any repetitive behaviors, the owners should be instructed to watch for a worsening of signs or any specific triggers that may initiate the behavior. Keeping a diary, written or preferably on video media, is helpful to track onset and progression.

TECHNICIAN TIPS

OCD may create a home situation that is very different and disrupted compared to an owner's expectations. Support from the entire veterinary staff for identifying and treating this disorder correctly can be rewarding for all and lifesaving for the pet.

CLIENT EDUCATION

Treatment of OCD is never static, often lifelong, and subject to adjustment based on changing conditions. Relapses may occur with treatment discontinuation. Planning in advance of added stressors can help minimize their effect on an OCD patient.

SUGGESTED READING

Overall KL, Dunham AE: Clinical features and outcome in dogs and cats with obsessivecompulsive disorder: 126 cases (1989-2000). J Am Vet Med Assoc 221:1445−1452, 2002.

AUTHOR: SONYA JUARBE-DIAZ

EDITOR: KAREN OVERALL

Obesity

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

A chronic relapsing disorder associated with excessive accumulation of body fat, resulting in an increase in body weight beyond the limitation of skeletal and physical requirements. Animals with an accumulation of body fat of more than 20% of their moderate body weight for that species and breed are considered obese.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Any species, both sexes, any age (3 months of age until the end of life)

GENETICS & BREED PREDISPOSITION: Between 30% and 70% of the risk for obesity in dogs is attributable to breed; breeds that are reportedly at increased risk include Labrador retrievers, cairn terriers, cocker spaniels, dachshunds, Shetland sheepdogs, basset hounds, beagles, and cavalier King Charles spaniels.

RISK FACTORS: Genetic predisposition, neutering, multiple pet households, indoor housing, overfeeding, sedentary lifestyle, metabolic disorders

ASSOCIATED CONDITIONS & DISORDERS: Some obese animals may be at increased risk for diabetes, joint problems, muscle tears, hip dysplasia, tracheal collapse, skin and heart disorders, complications during anesthesia and surgery, and reduced life expectancy.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- The most common history collected is of a pet that has gradually been gaining weight over a period of years, and the owner has been unaware of the increase.
- Another common history is of acute weight gain over a period of a few months after the animal was switched to a different diet or started on a new medication; the animal could also have gone through a stressful period or could have developed a metabolic disorder.

PHYSICAL EXAM FINDINGS: A body condition score (BCS) of 5/5 is characterized by the following:

- Ribs and other skeletal prominences are difficult to feel under thick fat cover.
- Fat hangs from the abdomen.
- The tail base is thickened.
- The animal does not have an apparent waist when it is viewed from the side or above.
- The animal is markedly broadened when it is viewed from above.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis should include identification of conditions that can predispose to or be mistaken for weight gain.

DIFFERENTIAL DIAGNOSIS

- Hypothalamic disorders, hypothyroidism, hyperadrenocorticism (Cushing's disease), insulinoma, chronic corticosteroid use, and chronic use of some epileptic drugs (phenobarbital) can cause obesity.
- Tumors, edema, and ascites may be confused for obesity.

INITIAL DATABASE

- CBC, serum chemistry panel, urinalysis: clinicians should assess for metabolic diseases that could affect the animal's weight,

such as diabetes mellitus, hyperlipidemia, or hypothyroidism.
- Thyroid function studies (TSH, free T4) are used for evaluating the role of hypothyroidism as a cause of obesity (prevalence of hypothyroidism is less than 1% in dogs; rare in cats).

ADVANCED OR CONFIRMATORY TESTING

Radiographic imaging studies are not specific in the diagnosis of obesity but may provide evidence of the extent of fat accumulation in the periphery and in the abdominal and thoracic compartments.

TREATMENT 

THERAPEUTIC OVERVIEW

The therapeutic goal is to return the animal to a healthy status and resolve complaints. A 10% decrease in body weight reduces the risk of obesity-related diseases in humans and a 1%-2% weight loss per week is a reasonable initial goal for animals.

ACUTE GENERAL TREATMENT

Treatment is aimed at weight reduction and risk-factor modification.

- Clinicians should take an accurate diet history; it provides essential information about the food intake of the pet as well as information about the food itself and the related bond between a pet and owner. An accurate diet history can take 30-60 minutes to collect.
- The clinician should calculate caloric intake from all sources. Caloric content of human foods is available at the U.S. Department of Agriculture's Web site (http://nal.usda.gov).
- Clinicians should determine weight reduction goal and calories. An initial goal of a 10% weight loss usually is reasonable and can be attained by prescribing an energy deficit of 10 kcal per kilogram of body weight per day through a combination of decreased intake (about 8 kcal/kg/d) and increased activity-induced expenditure (about 2 kcal/kg/d).
- The clinician should make sure the animal completes the dietary plan.
    - The clinician should create the plan with the owner to increase compliance for completion of the plan.
    - Once the owner and clinician agree to a plan, a schedule of follow-ups must be established to provide coaching and monitor progress.

NUTRITION/DIET

- Therapeutic and over-the-counter (OTC) diets are available that have been formulated to have a low-caloric density and may aid in restricting calories.
- Cases that require a large amount of weight loss may require a therapeutic diet versus an OTC to attain the protein/calorie ratio needed for success.
- In all cases, it is crucial to determine the protein, mineral, and vitamin intake of the diet to ensure that changes will not result in nutrient depletion.

BEHAVIOR/EXERCISE

- The owner should encourage the animal to be active 30 minutes every day if the animal can tolerate this comfortably. This can be achieved with gradual increased increments of 10 minutes of activity per day. The clinician and owner can adjust the time and intensity of the activity according to weight loss and the animal's enjoyment.
- There are many behavioral solutions that may be presented to the owner and should be a part of every recommendation. See Suggested Reading below.

DRUG INTERACTIONS

Glucocorticoids, phenobarbital

POSSIBLE COMPLICATIONS

Nutrient depletion, increased anesthetic risk, slower wound healing, hepatic lipidosis (cats)

RECOMMENDED MONITORING

The clinician's first contact with the client occurs 1 week after initial recommendations are made, followed by repeat “check-ins” at 6 weeks, 3 months, 6 months, and 1 year. These appointments permit the clinician to monitor the animal's BCS and weight progress,

make adjustments as needed, and continue to support and motivate the client.

PROGNOSIS AND OUTCOME

Very good, depending on compliance of owner

PEARLS & CONSIDERATIONS

COMMENTS

- According to veterinary experience, the critical key to successful obesity therapy is ongoing follow-up and support of the animal and owner's progress.
- Many clinics are opting to create a “clinic within a clinic“ that is run by the staff and entails a weight management program similar to Weight Watchers for their clients' pets.

PREVENTION

Starts with puppies/kittens; clinicians should recommend adjusting feeding after spaying/neutering if needed.

TECHNICIAN TIPS

- Assign a “weight loss consultant” to each client. Each time the client calls or comes in, there is consistency in care.
- Provide measuring cups with a line or marker drawn on the cup for desired amount to help with compliance.
- Create a contest to spread the enthusiasm to keep the clients interested.

CLIENT EDUCATION

- Clients should be able to assess and feed according to their pet's appropriate BCS.
- Every client should know how many kilocalories a pet food cup or can contains.

SUGGESTED READING

Buffington CAT, Holloway C, Abood S: Manual of veterinary dietetics, St Louis, 2004, WB Saunders, pp 109−116.

Nestle Purina Weight Management Program, Nestle Purina Veterinary Resource Center at 1-800-222 VETS (8387).

www.nssvet.org

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Pythiosis and Lagenidiosis

BASIC INFORMATION

DEFINITION

Pythiosis and lagenidiosis are oomycotic infections of the gastrointestinal (GI) tract *(Pythium)* or skin *(Pythium* and *Lagenidium)* of dogs and cats caused by *Pythium insidiosum* and *Lagenidium* spp.

SYNONYMS

Phycomycosis, swamp cancer

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs are affected more often than cats. Dogs (young to middle-aged adults); cats (any age but often less than 1 year old).

GENETICS & BREED PREDISPOSITION

Dogs: large breeds, especially outdoor working breeds such as Labrador retriever

RISK FACTORS

Recurrent exposure to warm freshwater lakes, swamps, and ponds that may contain *Pythium* or *Lagenidium* zoospores, but disease in house pets without such exposure has been reported.

CONTAGION & ZOONOSIS

Motile zoospores found in warm freshwater habitats cause infections in mammalian species including humans; no direct contagion or zoonotic potential.

GEOGRAPHY AND SEASONALITY

Endemic in warm, humid regions such as the southern United States and the Gulf Coast of Texas, southeast Asia, and eastern Coastal Australia. Infections are most often diagnosed in fall, winter, and early spring.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Pythiosis: GI disease, cutaneous disease
- Lagenidiosis: cutaneous disease initially, usually progressing to systemic involvement by the time the diagnosis is established; often affecting large vessels

HISTORY, CHIEF COMPLAINT

- GI infection: weight loss with chronic vomiting and/or diarrhea; large-bowel diarrhea seen commonly; dogs usually continue to feel well and have a good appetite despite significant weight loss.
- Cutaneous infection: nonhealing wounds and invasive skin masses containing ulcerated nodules and draining tracts

PHYSICAL EXAM FINDINGS

Dog:

- GI infection: chronic severe weight loss in an otherwise active, alert dog; abdominal mass often palpable
- Cutaneous infection: chronic nonhealing wounds and invasive masses that contain ulcerated nodules and draining tracts, most often involving the extremities, tailhead, ventral neck, or perineum

Cat:

- Nasopharyngeal infection: chronic nasal discharge and upper respiratory signs
- Cutaneous infection: invasive subcutaneous masses (especially in inguinal, tailhead, and periorbital regions) or ulcerated plaquelike lesions on the extremities
- GI infection: occasionally seen

ETIOLOGY AND PATHOPHYSIOLOGY

- Infection follows exposure of the immunocompetent host to motile zoospores in warm freshwater environments.
- Hyphal growth within affected tissues causes massive inflammation resulting in masses, draining lesions, and regional lymphadenopathy. In the GI tract, transmural thickening may result in GI obstruction.
- Dogs with *Pythium* infection may have any portion of the GI tract affected; pylorus, proximal duodenum, and ileocolic junction are affected most often. Mesenteric lymphadenopathy is common. Esophagus is affected less often.
- Dogs with *Lagenidium* spp. infection have progressive cutaneous or subcutaneous lesions (often multifocal) involving the extremities, mammary region, perineum, or trunk.
- In contrast to *Pythium* infection, dogs with lagenidiosis have lesions in distant sites, including great vessels, sublum-bar and inguinal lymph nodes, lung, pulmonary hilus, and cranial mediastinum.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected in one of two contexts: chronic diarrhea (where marked intestinal thickening/mass raises the differential diagnosis of neoplasia) or chronic, invasive, often ulcerated subcutaneous masses. Confirmation is either via serum titers or histologic demonstration of the organism on biopsy.

DIFFERENTIAL DIAGNOSIS

- GI neoplasia
- Pyloric outflow obstruction due to hypertrophy, intussusception
- Zygomycosis and other hyphal fungal infections
- Mycobacterial, nocardial, and actino-mycotic infections of skin

INITIAL DATABASE

- CBC: eosinophilia and nonregenerative anemia may be seen.
- Serum biochemistry panel: hyperglobulinemia is common. Hypercalcemia has been reported.
- Abdominal radiographs: abdominal mass effect; evidence of intestinal obstruction
- Abdominal ultrasound: severe segmental thickening of the GI tract, mesenteric lymphadenopathy

ADVANCED OR CONFIRMATORY TESTING

- Histopathologic examination of tissue: eosinophilic pyogranulomatous inflammation; *Pythium* hyphae are difficult to visualize on H&E stained sections, whereas *Lagenidium* hyphae are easier to see.
    - Broad, rarely septate, occasionally branching hyphae seen on silver stains. *Lagenidium* hyphae are much wider than *Pythium* hyphae.
    - Immunohistochemical stains can be used for confirming the diagnosis.
- Culture using fungal media
- Serologic testing: ELISA and immuno-blot assays available from the *Pythium* laboratory at Louisiana State University —sensitive and specific for diagnosis of pythiosis and lagenidiosis and for monitoring response to therapy (titers may decrease to normal in months following successful treatment).

TREATMENT

TREATMENT OVERVIEW

Complete surgical resection is indicated whenever possible; otherwise disease will progress.

ACUTE GENERAL TREATMENT

Complete surgical resection is treatment of choice: segmental GI lesions are occasionally completely resectable, especially in cats or if diagnosed early in dogs; if cutaneous lesions are limited to a single extremity, amputation is recommended. Local postoperative recurrence is common. Resection of *Lagenidium* lesions is less likely to be curative.

CHRONIC TREATMENT

- Medical therapy with itraconazole (10 mg/kg PO q 24 h) and terbinafine (5-10 mg/kg PO q 24 h) is recommended for at least 2-3 months after surgery. Some animals (fewer than 20%) will respond to long-term medical therapy alone. Medical therapy for lagenidiosis is typically ineffective.
- Treatment with a *Pythium* vaccine has been recommended but has not been well evaluated, and inconsistent results have been noted.

POSSIBLE COMPLICATIONS

Sudden death associated with *Pythium* infarction or invasion of mesenteric vessels or rupture of a *Legenidium*-induced aneurysm of the aorta or vena cava

RECOMMENDED MONITORING

ELISA serology should be used for monitoring response to medical therapy or recurrence after surgical resection.

PROGNOSIS AND OUTCOME

- Pythiosis: fair to guarded if lesions appear surgically resectable; guarded to poor if medical therapy alone is used
- Lagenidiosis: grave

PEARLS & CONSIDERATIONS

COMMENTS

- GI pythiosis is often mistaken diffuse neoplasia at surgery.
- Aggressive surgery with wide surgical margins is critical to surgical cure.
- ELISA testing can result in a noninvasive diagnosis and can be used to monitor treatment.

CLIENT EDUCATION

Chronic vomiting and weight loss in a dog that spends time in the water in endemic areas should prompt early evaluation for *Pythium* infection.

SUGGESTED READING

Grooters AM: Pythiosis, lagenidiosis, and zygomycosis in small animals. Vet Clin North Am Small Anim Pract 33:695, 2003.

AUTHOR: JOSEPH TABOADA

EDITOR: DEBRA L. ZORAN

Pyrethrins/Pyrethroids Toxicosis

BASIC INFORMATION

DEFINITION

Pyrethrin (natural) and pyrethroid (synthetic) insecticides are used in numerous household and garden insecticide products and many flea-control formulations (aerosols, dusts, granules, sprays, collars, dips, shampoos, and once-a-month spot-on products). Adverse reactions and toxicosis vary in severity depending on the agent involved, animal type, and route of administration. Signs can include hypersalivation and restlessness, behavior changes (hiding), vomiting, ataxia, agitation, tremor, and seizures.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Cats are more sensitive than dogs, especially to concentrated synthetic pyrethroids such as permethrin (present at 45%-65% in many dog topical products).
- No breed or sex predisposition

RISK FACTORS

Very young, aged, anemic, or debilitated animals may be at risk for greater toxic effects.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Route:

- Accidental, inadvertent oral exposure can result in acute-onset hypersalivation and vomiting.
- Dermal application may result in acute-onset dermal paresthesia or tingling effect due to stimulation of sensory nerve endings; some dermal-only exposures result in hypersalivation.

Type:

- Pyrethrins (in concentrated amounts) and type I pyrethroids can cause acute-onset tremor, ataxia, hyperexcit-ability, and hyperthermia.
- Type II pyrethroids can cause acute hypersalivation, tremors, rigidity, seizures, ataxia, and coma.

HISTORY, CHIEF COMPLAINT

- History of product use on the animal or another family animal (relay toxicosis), in the yard, or in the house
- Hypersalivation, vomiting; agitation, constant restless or irritable behavior
- Muscle tremors, twitching, ataxia, or seizures

PHYSICAL EXAM FINDINGS

- Hypersalivation
- Muscle tremors (partial to full body), seizure (primarily in cats exposed to permethrin)
- Hyperthermia (if significant neuromuscular signs) followed by hypothermia

ETIOLOGY AND PATHOPHYSIOLOGY

Source:

- Pyrethrins are obtained naturally from *Chrysanthemum* flowers
  - Examples: pyrethrin I and II, pyrethrum, cinerin I and II, jasmolin I and II
  - Pyrethrins are generally safer than pyrethroids.
- Pyrethroids are synthetic analogs of the pyrethrin base and of two basic types:

- Type I: lacks an alpha-cyano group
- Type II: possesses an alphacyano group. Type II is more toxic than type I.
  - Examples, type I: allethrin, bar-thrin, bifenthrin, bioresmethrin, cismethrin, dimethrin, permethrin, phenothrin, resmethrin, tefluthrin, tetramethrin
  - Examples, type II: acrinathrin, cyfluthrin, cyhalothrin, cyperme-thrin, cyphenothrin, deltamethrin, esfenvalerate, fenpropathrin, fen-valerate, flumethrin, fluvalinate, lamda-cyhalothrin, tralomethrin
  - Agents are sold under numerous trade names.
  - Different formulations may be combined with an insect growth regulator (e.g., methoprene, pyriproxyfen) and one or more synergists (e.g., piperonyl but oxide, MGK-264).

Mechanism of Toxicosis:

- Pyrethrin and pyrethroid agents delay opening and closing of sodium channels, resulting in repetitive nerve discharges.
- Type I pyrethroids and pyrethrins cause repetitive discharges and tend to cause tremors and seizures.
- Type II pyrethroids cause longer duration of the sodium current in the axon than type I pyrethroids and pyrethrins. Type II pyrethroids can cause conduction blockage, typically causing weakness and paralysis.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is based on history (known recent use of a pyrethrin or pyrethroid agent either on the patient or in the patient's environment), physical signs (hypersalivation, tremors, twitching, ataxia), and often both. Widely promoted “plant-based” nature of pyrethrins/pyrethroids may mean clients do not consider exposure, and the diagnosis can depend on the clinician's recognition of signs as a reason for asking the owner specifically about exposure to “natural” insecticides.

DIFFERENTIAL DIAGNOSIS

Toxicologic:

- Tremorgenic mycotoxins (see p. 434)
- Organophosphate/carbamate (see p. 792)
- Metaldehyde toxicosis (see p. 720)
- Caffeine (methylxanthine) toxicosis (seep. 194)
- Nicotine toxicosis (see p. 766)
- Prescription, nonprescription drug (serotonergics, dopaminergics, sympa-thomimetics) overdose
- Strychnine toxicosis (see online chapter: Strychnine Toxicosis)
- Organochlorine toxicosis

Spontaneous, Nontoxicologic:

- Intracranial disorders (neoplasia, encephalitis, trauma, idiopathic epilepsy)
- Metabolic disorders (hypocalcemia, portosystemic shunt, etc.)

INITIAL DATABASE

- Body temperature (elevated initially due to muscle tremors followed by hypothermia)
- Serum renal profile and urinalysis (for myoglobinuria, renal compromise due to pigment nephropathy, if severe tremors are present)
- CBC, serum biochemistry profile: no significant changes are expected in routine cases.
- Neurologic examination

ADVANCED OR CONFIRMATORY TESTING

Pyrethrins/pyrethroids can be detected in hair, stomach contents, fat, liver, brain, serum, and urine. Hair samples can be submitted to a veterinary diagnostic laboratory; presence of insecticide only confirms exposure.

TREATMENT

TREATMENT OVERVIEW

Successful management generally involves treatment and resolution of neuromuscular signs, followed by dermal decontamination (bathing with a dilute dishwashing detergent solution as appropriate for the case) once the patient is stable, to prevent reexposure through grooming/licking. Supportive care is indicated until recovery (typically 1-3 days).

ACUTE GENERAL TREATMENT

- In mild cases (excessive hypersalivation following a labeled application), wipe the patient down with a soft, clean, damp washcloth to remove any excess/residual product from the application site. Clean the muzzle area of saliva, and provide small amount of a tasty treat to dilute any small traces of ingested toxicant.
- In more severe cases (tremor or seizure), treatment requires stabilization of neuromuscular signs:
  - Severe tremor or convulsive activity is best controlled with methocarbamol (consider 100-150 mg/kg IV as loading dose, onset is immediate; labeled dose range is 55-220 mg/kg IV); in this range, methocarbamol is a relatively very safe drug. Can use orally (60-130 mg/kg PO), but has a 30-min onset by this route.
    - Repeat PRN to effect, but do not exceed 330 mg/kg per day (labeled ceiling).
  - Diazepam, 0.5-1 mg/kg IV, for mild tremor or paresthesia. Diazepam is generally not effective for controlling severe tremors.
  - If necessary for refractory seizures, may consider phenobarbital (dog, cat, 2-5 mg/kg slow IV, not more than 60 mg/min to avoid respiratory depression, especially in cats; onset 5 minutes); propofol (dog, cat, 3-6 mg/kg slow IV, avoid respiratory depression/apnea; then IV constant rate infusion 0.1-0.6 mg/kg/min), or isoflurane.
- Decontamination of severely-affected patient:
  - Bathe patient (following stabilization; see Pearls) in a dilute solution of liquid dishwashing detergent in lukewarm tap water for dermal exposures, and repeat if needed. Dry thoroughly to prevent chilling.
  - Induction of vomiting rarely indicated; only in patients not showing any clinical signs following accidental ingestion of large amounts of product (seep. 1364)
- Activated charcoal: as above for induction of vomiting (rarely used, only with large ingestions in the absence of any clinical signs). Dose according to charcoal product labeled instructions.
- Supportive care:
  - IV fluids (e.g., lactated Ringer's solution to correct dehydration or volume loss, plus maintenance to maintain adequate perfusion; forced diuresis not indicated).
  - Atropine can be considered for severe hypersalivation, 0.01-0.02 mg/kg IV/IM. Atropine is not antidotal and provides no beneficial effect for other signs.
  - Regulation of body temperature (cool water bathing if hyperthermia; avoid reducing temperature too rapidly).

DRUG INTERACTIONS

Concurrent exposure to other pesticides may increase risk of toxicosis.

POSSIBLE COMPLICATIONS

- Myoglobinuria and acute renal failure due to severe tremors (uncommon)
- Disseminated intravascular coagulation secondary to prolonged hyperthermia (uncommon)

PROGNOSIS AND OUTCOME

- Generally good; recovery in 1 to 3 days
- Guarded if tremors are not controlled or if seizures are prolonged and/or intractable

PEARLS & CONSIDERATIONS

COMMENTS

- In general, flea products will not cause systemic CNS signs if used according to label.
- Cats are very sensitive to concentrated permethrin-based dog-only topical products.
- Systemic CNS effects unlikely if animals access a sprayed area after it has dried.
- Tremors may last for 3 days. After patient stabilization, oral methocarbamol (50-100 mg/kg PO q 6-8 h) can be started, and the animal can be discharged for home observation.

PREVENTION

- Separate permethrin-treated dogs from dog-friendly family cats for several days to avoid relay toxicosis in the cat.

- Keep pets out of areas being treated with insecticides until the product has dried.

TECHNICIAN TIPS

- Note of caution: attempting to bathe a cat that is already tremoring or convulsing, and prior to stabilizing the patient, may further stress the patient and complicate successful treatment. It is essential to control these severe signs first, then proceed to bathing procedure (common sense, but this error has been made repeatedly by veterinarians and technicians alike).
- Whether in response to a client's question or during in-hospital use, it is important to avoid using pyrethrin/pyrethroid products formulated for dogs on cats, which is a significant risk.

CLIENT EDUCATION

Observation of labeled and veterinary instructions for safe applications to reduce accidents at home; ensure cats in the home are not casually coming into contact with dogs being treated with synthetic pyrethroids.

SUGGESTED READING

Volmer PA: Pyrethrins and pyrethroids. In Plumlee KH, editor: Clinical veterinary toxicology. St Louis, 2004, Mosby, pp 188–190.

Hansen SR: Pyrethrins and pyrethroids. In Peterson ME, Talcott PA: Small animal toxicology, ed 2, St Louis, 2006, Saunders Elsevier.

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Pyothorax

BASIC INFORMATION

DEFINITION

Accumulation of purulent exúdate within the pleural space; associated with significant pleural inflammation

SYNONYM

Pleural empyema

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs and cats:

- Medium and large breeds of dogs ovenepresented
- Males of both species ovenepresented
- Median age of occurrence = 4 years

GENETICS & BREED PREDISPOSITION

- Dog: hunting breeds subject to increased risk of inhaled foreign (plant) material
- Cat: higher risk if from multicat household and if young; no difference if indoor versus outdoor

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Slowly progressive onset of dyspnea, inappetence, weight loss
- Acute decompensation with dyspnea/tachypnea/collapse from pleural effusion

PHYSICAL EXAM FINDINGS

- Respiratory: dyspnea, tachypnea; muffled heart and lung sounds on auscultation (unilateral/bilateral)
- Systemic: depression, weight loss, ± pyrexia, ± pale mucous membranes
- Cats: possibly decreased compressibility of cranial thorax on palpation

ETIOLOGY AND PATHOPHYSIOLOGY

- Septic pyothorax (most common): potential causes of infection of the pleural space include:
  - Penetrating/migrating plant material
  - Inhaled plant material
  - Penetrating injury:
    - Bite, stab, gunshot wounds
  - Esophageal perforation:
    - Foreign body
    - *Spirocerca lupi* infection
  - Hematogenous spread
  - Extension from diskospondylitis
  - Pneumonia or lung abscess
  - Pulmonary or intrathoracic neoplasia
- Pleuritis (and nonseptic pyothorax) can be associated with canine hepatitis, leptospirosis, canine distemper, feline infectious peritonitis, or feline upper respiratory tract infection.
- Cats: role of feline immunodeficiency virus (FIV) or feline leukemia virus (FeLV) in development of pyothorax not proven

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on patient signalment, presenting history, and physical examination findings. Confirmation requires demonstration of pleural fluid by diagnostic imaging and appropriate analysis of the fluid. Cytologie examination provides a working clinical diagnosis.

DIFFERENTIAL DIAGNOSIS

- Pulmonary disease:
  - Pneumonia
  - Abscess
- Pleural effusion:
  - Chylothorax
  - Heart failure
  - Hemothorax
  - Idiopathic
- Diaphragmatic hernia
- Intrathoracic neoplasia

INITIAL DATABASE

- CBC:
  - Usually: neutrophilic leukocytosis with or without a left shift
  - Possible: leukopenia, thrombocyto-penia if sepsis
- Serum biochemistry profile:
  - Multiple abnormalities (hepatic and renal parameters, electrolytes, hypo-albuminemia, etc.) can occur secondary to sepsis.
- Pleural fluid evaluation (see p. 1338):
  - Diagnostic: obtain fluid for analysis; typically blood-tinged fluid, which may be opaque and often has a foul odor (anaerobes). Macroscopic yellow clumps (“sulfur granules”) strongly suggest presence of *Actinomyces* (see p. 26).
- Analysis of pleural fluid:
  - Fluid analysis/cytologic examination; exúdate (by definition):
    - Protein >3 g/dL
    - Nucleated cell count >7 10^9/L, often >30 × 10^9/L
    - Degenerate neutrophils predominate, with macrophages and activated mesothelial cells also present. Intraleukocytic bacteria are diagnostic (septic pyothorax).
  - Gram stain:
    - Guides initial empirical antimicrobial therapy:
      - Oropharyngeal bacteria (e.g., *Pasteurella* spp., *Bacteroides* spp., *Fusobacterium* spp.) common in cats; *Escherichia coli* in dogs (both gramnegative rods)
      - *Actinomyces* (anaerobe) and *Nocardia* (aerobe): both grampositive short rods and filaments; important potential pathogens in dogs from regions where grass awn endemic
  - Anaerobic and aerobic bacterial culture and susceptibility (C&S):
    - Test of choice for planning long-term antimicrobial therapy
- Survey thoracic radiographs:
  - Initially to identify pleural effusion
  - After therapeutic thoracocentesis, to evaluate pleural space, mediastinum, and pulmonary parenchyma for potential primary cause of pyothorax
- Thoracic ultrasound examination:
  - Identify masses and evaluate their internal structure.
  - Identify site of greatest pleural effusion for centesis (if overall small volume of effusion).
  - Identify foreign material in the pleural space if possible (may be very challenging).

ADVANCED OR CONFIRMATORY TESTING

CT scan:

- Potentially identify cause of pyothorax.
- Evaluate mass(es) in thoracic cavity and determine if resectable.

TREATMENT

TREATMENT OVERVIEW

Patient stabilization, pleural drainage (thoracostomy tubes for pleural lavage), +/− surgical exploration and débridement of the thoracic cavity and long-term antimicrobial therapy are the standard of care. Long-term antimicrobial therapy is based on results of microbiologic C&S testing.

ACUTE GENERAL TREATMENT

- Stabilization of respiratory compromise:
  - Therapeutic (and diagnostic) thoracocentesis (see p. 1338)
  - Oxygen administration (seep. 1318)
  - Intensive care monitoring
- Correction of fluid and electrolyte deficits
- Antimicrobial therapy:
  - Empirical therapy active against both aerobic and anaerobic bacteria:
    - Gram stain results (as previously described)
    - Amoxicillin/ampicillin, 22 mg/kg IV or PO q 8 h, if *Actinomyces* suspected
    - Trimethoprim-sulfa, 15 mg/kg PO q 12 h, if *Nocardia, E. coli,* or *Pasteurella* suspected
- Medical management:
  - Bilateral thoracostomy tube placement
  - Thoracic lavage every 6-8 hours with body-temperature warmed sterile saline
  - Serial cytologic evaluation of pleural fluid to assess success of lavage therapy:
    - Improvement includes change from degenerate neutrophils with intracellular or extracellular bacteria to nondegenerate neutrophils without bacteria.
- Surgical management:
  - Indicated if:
    - Definitive cause identified and retained in thoracic cavity (foreign body, lung lobe abscess)
    - Fluid loculated within the pleural space (lavage cannot access portions of fluid accumulation)
    - Patient fails to respond to intensive medical therapy (4-5 days of pleural lavage and antibiotics)
    - *Actinomyces* present (in dogs, notoriously poor response to medical management alone)
  - Consists of aggressive débridement of the pleural space, removal of underlying cause if identified, thorough intraoperative lavage, and postoperative intermittent pleural aspiration, lavage, and antimicrobial therapy.

CHRONIC TREATMENT

- Thoracostomy tube removal based on overt clinical and cytologic resolution of infection
- Long-term antibiotic therapy in all cases:
  - Based on accurate identification of organism(s) involved
  - Up to 3 months of therapy may be required.

POSSIBLE COMPLICATIONS

Failure to resolve/recurrence of pyothorax:

- Cause not removed
- Failure of medical management:
  - Ineffective pleural lavage
  - Ineffective/inappropriate antibiotic therapy

RECOMMENDED MONITORING

Survey thoracic radiographs:

- At completion of antibiotic therapy
- Periodically (every 3 months)

PROGNOSIS AND OUTCOME

- Surgical management is associated with a better prognosis than medical management in dogs with pyothorax: disease-free at 1 year: 78% (surgical) versus 25% (medical).
- Development of fibrosing pleuritis is associated with poor outcome.
- Lower heart rate and hypersalivation are both associated with poorer outcomes in cats.
- Overall, *66%* of cats and 80% of dogs can survive if treated appropriately.

PEARLS & CONSIDERATIONS

COMMENTS

- Intensive therapy should start immediately upon diagnosis. Undertreatment is thought to be a major contributor to morbidity/mortality.
- Surgical treatment has been associated with a better outcome than medical treatment alone.
- Bilateral thoracostomy tubes are helpful in aspiration and lavage of the pleural space.
- Antimicrobial therapy should be guided by culture and susceptibility, with attention paid to *Actinomyces* and *Nocardia.*
- Obligate anaerobes are common in pyothorax and are present in combination with aerobes; antimicrobial treatment should be aimed at both types of bacteria until culture results are available.

TECHNICIAN TIPS

Knowledge of and experience in working with thoracostomy tubes is important in the management of patients with pyothorax:

- Used as the primary treatment modality for nonsurgical thoracic drainage and lavage
- Used in the postoperative period for continued thoracic drainage +/− lavage.

SUGGESTED READING

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Johnson MS, Martin MWS: Successful medical treatment of 15 dogs with pyothorax. J Small Anim Pract 48:12, 2007.

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Pyometra

BASIC INFORMATION

DEFINITION

Very common uterine disease of middle-aged to older female dog or cat; characterized by an accumulation of purulent material in the uterine lumen or uterine stump

SYNONYMS

Purulent endometritis, purulent metritis, pyo, pyometritis

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Female canine or feline (more common in bitches than queens)
- Any age after puberty (more common after 5-6 years of age)

RISK FACTORS

- In dogs, age, hormonal (estrogen and/or progestin) treatments and estrous cycle irregularities are proposed risk factors.
- In cats, pseudopregnancy and ovarian diseases (e.g., granulosa cell tumor) are risk factors.

ASSOCIATED CONDITIONS & DISORDERS

- Sepsis
- Septic shock
- Systemic inflammatory response syndrome (SIRS)
- Multiple organs dysfunction syndrome (MODS)
- Disseminated intravascular coagulation (DIC)
- Acute renal failure
- Acute hepatic injury
- Vaginitis and UTI
- Peritonitis

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Open pyometra: mucoid, purulent, mucopurulent or hemorrhagic vulvar discharge
- Closed pyometra: no (or minimal) vulvar discharge

HISTORY, CHIEF COMPLAINT

- Diestrus or anestrus (from a few weeks following the end of estrus up to a few months)
- Anorexia, vomiting
- Lethargy, depression
- Polyuria and polydipsia (PU/PD)
- Abdominal distension (less common)
- Vulvar discharge may be noted by owner.
- Intact female or history of incomplete ovariohysterectomy
- Previous treatment to induce abortion or parturition
- In the queen, the disease is generally more subacute or chronic and associated with few clinical signs but irregular cycles, vaginal discharge, and/or abdominal distension.

PHYSICAL EXAM FINDINGS

- Purulent vulvar discharge is common and should always prompt the consideration of pyometra:
  - Absence of vulvar discharge does not rule out pyometra.
- Abdominal palpation:
  - Signs of abdominal pain
  - Enlarged uterus (may be difficult to palpate if only a moderate enlargement and/or the abdomen is tense)
  - Abdominal distension
- Dehydration
- Fever (or hypothermia if severe, such as in septic shock)
- Red mucous membranes (hyperdynamic stage of sepsis) or pale mucous membranes (septic shock)
- Normal pulse and cardiac auscultation or tachycardia, weak pulse, and cool extremities possible with septic shock
- Normal respiration or hyperpnea

ETIOLOGY AND PATHOPHYSIOLOGY

Two proposed pathways:

- Chronic degenerative uterine process associated with progesterone and bacterial contamination and proliferation; in older animals, often associated with cystic endometrial hyperplasia (CEH):
  - Excessive diestrous endometrial hyperplasia (progesterone-induced), causing cyst formation, decrease myometrial activity, local immune suppression.
  - Pyometra results when bacteria colonize the uterus via ascension through the cervix, or hematogenously.
  - The bacterium most commonly isolated from pyometra is *Escherichia coli,* but *Staphylococcus* spp., *Streptococcus* spp., *Pseudomonas* spp., and *Proteus* spp. also reported.
  - In the queen, the pathogenesis is most likely associated with prolonged progesterone impregnation during pseudopregnancy.
- Pyometra not associated with CEH; trophoblastic reaction:
  - Subclinical bacterial infection in early to mid-diestrus induces uterine endometrial hypertrophy followed by a trophoblastic like hyperplasia of the endometrium and endometrial glands.
  - Increase in glandular secretions exacerbates the infection. This mechanism may explain the occurrence of pyometra in younger bitches.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Pyometra may be strongly (open pyometra) or weakly (closed pyometra) suspected on physical exam; noting that the patient is an intact female is a critical element of the initial suspicion. Leukocytosis on CBC further supports the diagnosis but is not always present. Clinical confirmation justifying treatment (most commonly ovariohysterectomy) comes from abdominal ultrasound.

DIFFERENTIAL DIAGNOSIS

- Mucometra (uterine lumen filled with mucoid endometrial gland secretions without infection; no systemic signs or leukocytosis expected)
- CEH
- Pregnancy
- Vaginitis and purulent UTI
- Reproductive tract tumors
- Uterine torsion
- Postpartum metritis
- Other systemic diseases resulting in an acute abdomen

INITIAL DATABASE

- CBC:
  - Mild to moderate normocytic, normochromic anemia (packed cell volume 30%-35%)
  - Leukocytosis with left shift and/or toxic changes
  - Approximately 25% of leukograms are within normal range in pyometra cases.
- Serum biochemistry profile: elevated hepatic and renal values possible
- A vaginal swab, particularly if it is collected near the external cervical os, may allow detection of a purulent exudate in closed pyometra.
- Vaginal cytologic exam: presence of numerous degenerate neutrophils
- Urinalysis:

- Cystocentesis is contraindicated in suspected or confirmed pyometra cases.
- Catheterized or free-catch samples may show evidence of infection, either as a real finding (bacterial cystitis is often concurrent with pyometra) or as an artifact of collection.

- Abdominal radiographs:
  - Distended viscus consistent with enlarged, fluid-filled uterus:
    - Note: Abdominal radiographs will not differentiate between pyometra and pregnancy of less than 45 days of gestation or mucometra.
    - Abdominal radiographs may not detect slightly enlarged uterus.
- Ultrasonographic examination:
  - Enlarged fluid-filled uterus:
    - Note: easily differentiates from pregnancy; abdominal ultrasound is the method of choice for establishing a diagnosis of pyometra.

ADVANCED OR CONFIRMATORY TESTING

- Open pyometra: cranial vaginal (near external cervical os) culture and sensitivity (C&S)
- Closed pyometra: transcervical endoscopy with uterine sample for C&S
- Gross and histopathologic examination of the surgically removed uterus

TREATMENT

TREATMENT OVERVIEW

- Supportive care followed by ovariohysterectomy (majority of cases) or medical management (bitches with reproductive value)
- Queens: same approach; more resistant to luteolytic treatments and require higher doses

ACUTE GENERAL TREATMENT

- General systemic treatment:
  - Stabilization and treatment of acute renal failure if identified (seep. 1591)
  - IV fluid therapy: typically to correct dehydration, using replacement fluids such as lactated Ringer's solution or 0.9% NaCl, with or without colloids. Rate is calculated based on dehydration and ongoing fluid losses.
  - Treatment/prophylaxis for disseminated intravascular coagulation (DIC; see p. 315)
  - Broad-spectrum antibiotic therapy: oral route is indicated for stable patients; individuals showing systemic signs of illness should receive antibiotics parenterally:
    - Amoxicillin with clavulanic acid, 20 mg/kg PO q 8-12 h; *or*
    - Enrofloxacin, 5 mg/kg PO or diluted 1:1 with saline and given slowly (over 5 minutes) IV q 6-12 h as needed (maximum 5 mg/kg q 24 h in cats); *or*
    - Cephalexin, 22-30 mg/kg PO q 8 h
  - Pain management (e.g., buprenorphine, 0.01-0.03 mg/kg SQ, IM, or IV q 6-12 h as needed based on pain parameters)
- Surgical pyometra treatment: ovariohysterectomy
- Medical pyometra treatment:
  - Prostaglandin F-2alpha (PGF2α, dino-prost [Lutalyse])
    - When used alone, high doses are required (>0.1 mg/kg SQ), which can be associated with significant, sometimes life-threatening, side effects (hypersalivation, emesis, diarrhea, tremor, ataxia, tachypnea, tachycardia, hypovolemic shock).
    - PGF2α alone cannot be used for treating a closed pyometra because of the potential of uterine rupture.
    - Synthetic PGF2α (e.g., cloprostenol [Estrumate] 0.001-0.005 mg/kg SQ from once a day to every 3 days) will produce similar results but more side effects.
    - Low, increasing doses of $PGF^{2\alpha}$ (0.01-0.05 mg/kg SQ q 5-8 h for 7-10 days or until uterine evacuation is complete as assessed by ultrasonography) are not associated with clinical side effects but must be combined with either a dopamine agonist or a progesterone receptor antagonist.
    - Dopamine agonists are used for hastening luteolysis via prolactin inhibition:
      - Cabergoline (Dostinex), 0.005 mg/kg PO q 24 h for 8-10 days; *or*
      - Bromocriptine (Parlodel), 0.03 mg/kg PO q 8-12 h for 10 days; given orally, adverse effects are uncommon at this dose.
    - Progesterone receptor antagonists are used for mimicking luteolysis through progesterone antagonism:
      - Mifepristone (Mifeprex), 2.5 mg/kg PO q 24 h for 5 days; *or*
      - Aglepristone (Alizine), 10 mg/kg SQ twice at 24 hours apart
  - Closed pyometra can safely be treated with PGF2α, starting at 0.01 mg/kg SQ q 5-8 h on day 1, then 0.025 mg/kg SQ q 5-8 h on day 2, then 0.05 mg/kg q 5-8 h the following days in association with dopamine agonists or progesterone antagonists. This treatment will first induce cervical opening before uterine contractions.

- Queens should receive higher natural prostaglandin (dinoprostum [Dynolytic; Upjohn]) doses (generally ranging from 0.05-0.1 mg/kg SQ q 5-8 h for 7-10 days or until uterine evacuation is complete) associated with dopamine agonists.
- Medical management of dogs with transcervical endoscopic catheterization technique (TECT) hastens uterine emptying time.
- Treatment efficacy is evaluated using transabdominal ultrasonography. At least 50% reduction of the uterine luminal diameter should be observed in less than 5-7 days after treatment initiation; complete by 5-10 days.
- Antimicrobial treatment should be continued for at least 2 weeks after the cessation of PGF2α and other specific treatments.

CHRONIC TREATMENT

If necessary, for chronic kidney disease (antigen/antibody complex-induced glomerulonephritis). Seepp. 205 and 450.

DRUG INTERACTIONS

Antiemetic drugs should not be used, as they stimulate prolactin release which would delay luteolysis and prolong medical pyometra treatment.

POSSIBLE COMPLICATIONS

- Peritonitis (resulting from uterine rupture)
- Stump pyometra (resulting from incomplete ovariohysterectomy)
- Bacterial cystitis (often concurrent with pyometra)
- Abdominal abscesses (resulting from bacteremia)
- DIC, SIRS, MODS
- Septic shock

RECOMMENDED MONITORING

- Intensive/critical care
- Cardiovascular support with IV fluid therapy
- Pain management
- Monitor for DIC (CBC, platelet count, coagulation profile, D-dimer test)
- Monitor for liver and kidney failure with a chemistry profile
- Ultrasonographic examination of the uterus every other day during treatment to monitor response

PROGNOSIS AND OUTCOME 

- Always guarded depending on presence of sepsis and liver or renal failure; otherwise good
- In medically managed dogs, is generally advised to breed during the first subsequent cycle
- No difference in the incidence of recurrent pyometra in medically treated dogs compared to intact dogs of the same age that did not previously have pyometra

PEARLS & CONSIDERATIONS 

COMMENTS

- Clinical signs are not related to the size of the distended uterus.
- Pyometra should always be included as a differential diagnosis in a female dog with clinical signs of an acute abdomen or with nonspecific clinical signs.
- A closed pyometra can be a life-threatening condition. Treatment, particularly general, should not be delayed even if the animal appears to be healthy.

PREVENTION

- Ovariohysterectomy in females that are not going to be bred and in females that have retired from breeding
- Avoid prophylactic antibiotic treatment, as this is often associated with progressive development of bacterial resistance and virulence.

CLIENT EDUCATION

- If the animal is not to be used for reproduction, a complete ovariohysterectomy will prevent the development of pyometra.
- Contact the veterinarian immediately if any of the above clinical signs is observed in a post estrus, intact aging female.

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Johnston S, et al: Disorders of the canine uterus and uterine tubes. In Johnston SD, Root-Kustritz MV, Olson PNS, editors: Canine and feline theriogenology. Philadelphia, 2000, WB Saunders, pp 206–224.

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Pyoderma

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Pyoderma is a bacterial infection of the skin. It is one of the most common diseases of dogs.

SYNONYM

Bacterial dermatitis

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Common in dogs, rare in cats.
- Impetigo (superficial form of pyoderma, typically in juvenile patients): noted in puppies sometimes in conjunction with immunosuppression, poor nutrition, endoparasitism, or poor hygiene.
- Acne is a type of pyoderma that occurs more commonly in young dogs.
- Feline: deep bacterial infections (cellulitis, abscess) are more common in outdoor animals.

GENETICS & BREED PREDISPOSITION

- Intertrigo (skin fold pyoderma): English bulldogs
- Mucocutaneous pyoderma: German shepherd, Bichon frise, poodle
- Familial idiopathic deep pyoderma: German shepherd
- Acne: short-coated breeds such as boxers, Doberman pinschers, bulldogs, Great Danes, mastiffs, rottweilers, and German short-haired pointers

RISK FACTORS

- Some forms of pyoderma, particularly superficial bacterial folliculitis (SBF) and bacterial overgrowth syndrome (BOGS) are often secondary to underlying etiologies such as hypersensitiv-ity skin disease (atopic dermatitis, food allergy, flea bite hypersensitivity), endocrinopathies (hypothyroidism, hyperadrenocorticism), parasitic skin disease *(Sarcoptes, Demodex* spp.), immune-mediated diseases, or cornification disorders.
- Deep pyoderma may be associated with underlying immunoincompe-tence.

CONTAGION & ZOONOSIS

Staphylococcus pseudintermedius, the cause of 90% of canine pyoderma cases, is considered nonpathogenic to humans.
GEOGRAPHY AND SEASONALITY Warm and humid environments predispose animals to pyoderma.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Surface pyoderma: infection restricted to the surface layer of the epidermis:
  - Dog: intertrigo (skin fold pyoderma), acute moist dermatitis (pyotraumatic dermatitis, hot spots), BOGS
- Superficial pyoderma: infection involving the epidermis and the infundibular portion of the hair follicle:
  - Dog: impetigo, SBF, superficial spreading pyoderma, mucocutaneous pyoderma
- Deep pyoderma: bacterial infection extending beyond the hair follicle to involve the dermis and subcutis, which may lead to cellulitis:
  - Dog: acne, pyotraumatic furunculosis, nasal folliculitis (inflammation of the hair follicle) and furunculosis (simultaneous occurrence of many furuncles, which are inflamed hair follicles that have ruptured, triggering pyogranulomatous dermal inflammation), interdigital furunculosis/pododermatitis, infected aerai lick dermatitis (lick granuloma), callus pyoderma, and postgrooming furunculosis; German shepherd pyoderma
  - Cat: bite wounds, cellulitis, abscess, feline acne

HISTORY, CHIEF COMPLAINT

Animals typically are presented for evaluation of skin changes: pustules, crusts, epidermal collarettes, hair loss and/or pruritus. Animals with deep pyoderma may show signs of pain.

PHYSICAL EXAM FINDINGS

- Impetigo: small nonfollicular pustules and crusts on the ventral abdomen
- BOGS: pruritus, greasy coat, offensive odor, erythema, lichenification, hyper-pigmentation, excoriations and alopecia
- SBF: papules, pustules, and epidermal collarettes with patchy alopecia, producing a “moth-eaten” appearance of the haircoat over the trunk. Resolving lesions may show central hyperpig-mentation (“bull's-eye” lesion).
- Superficial spreading pyoderma: large epidermal collarettes with an erythematous leading edge noted over the trunk; associated exúdate may form crusts.
- Canine acne: deep furunculosis and folliculitis, with crusting and possible scarring on the lips and chin of young dogs
- Mucocutaneous pyoderma: crusts and erosions affecting the lip margin, nasal planum, eyelid margin, vulva, prepuce, and perianal area
- Pyotraumatic folliculitis and furunculosis: may occur anywhere on the body depending on underlying cause; atypical acute moist dermatitis with superficial ulceration but also a component of deep folliculitis and occasional furunculosis. Clinically, this lesion may be thickened and plaque-like and have satellite papules and pustules.
- Nasal folliculitis and furunculosis: initially a papular/pustular eruption on the bridge of the nose that progresses to ulceration, crusting, and hemorrhage
- Interdigital folliculitis/pododermatitis: lesions of the feet; interdigital papulonodules, pustules, and ulceration with draining tracts and fibrosis; alopecia secondary to licking
- Callus pyoderma: develops over pressure points. Skin is thickened, fibrotic, and hyperpigmented with foci of papules, pustules, and ulceration.
- Postgrooming folliculitis/furunculosis: papular/pustular rash, crust formation, self-induced alopecia
- German shepherd pyoderma: lesions include ulcerations and draining tracts on the lateral thighs, trunk, and groin ± lips.
- Infected feline acne: comedones, papules, pustules, and alopecia confined to the mandibular and perilabial areas
- Feline bite wounds/abscess/cellulitis: swelling, pain, and alopecia in the affected area; possible dermal and cutaneous necrosis with ulceration, purulent exudate, and hemorrhage

PYODERMA Epidermal collarettes on ventral abdomen of a dog with pyoderma.

ETIOLOGY AND PATHOPHYSIOLOGY

- Canine skin is characterized by a relatively thin *stratum corneum,* a paucity of intercellular lipids, lack of a follicular plug, and a higher pH than that of humans and other domestic species. This predisposes the dog to overgrowth of commensal flora and colonization by potentially pathogenic bacteria.
- Superficial infection may occur if the integrity of the skin is weakened by trauma or there are changes in surface immunity.
- Deep bacterial infections are generally an extension of a superficial pyoderma. As infection progresses deeper into the hair follicle, rupture of the follicle (furuncles) occurs. This leads to a pyogranulomatous endogenous foreign-body reaction on the part of the host. This reaction occurs initially in the dermis and is an inflammatory response to keratin, bacterial organisms, and cellular debris.

- Approximately 90% of cases in dogs are caused by coagulase-positive *S. pseudintermedius,* a normal component of canine skin flora. A small number of cases are caused by *Staphylococcus aureus,* the most common human pathogen.
  - *Staphylococcus intermedius* was reclassified as *S. pseudintermedius* in 2007.
- The gram-negative organisms, *Proteus* spp., *Escherichia coli,* and *Pseudomonas* spp. may act as secondary invaders. Deep pyoderma is occasionally associated with *Actinomyces, Nocardia,* mycobacteria, and *Actinobacillus* spp.
- In cats, *Pasteurella multocida* and beta-hemolytic *Streptococcus* are routinely involved.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The dermatological exam alone may provide a strong suspicion of pyoderma (see signs listed above). With clinical signs of deep pyoderma, systemic signs, or recurrence despite therapy, additional tests beyond basic dermatologic testing are often indicated to rule out predisposing causes.

DIFFERENTIAL DIAGNOSIS

- Demodicosis
- Dermatophytosis
- Pemphigus foliaceus
- Cutaneous epitheliotropic lymphoma
- Subcutaneous mycoses (deep pyoderma)
- Atypical mycobacterial infections (deep pyoderma)
- Hookworm (deep pedal pyoderma)
- Foreign-body granulomas (deep pyoderma)

INITIAL DATABASE

- Skin scrapings to confirm or rule out *Demodex* and *Sarcoptes*
- Skin cytologic examination: direct smear from pustule reveals bacteria, neutrophils in varying stages of degeneration, and active bacterial phagocytosis.
- Fungal culture (for dermatophytes and possibly for deep mycosis if draining tracts are present)

ADVANCED OR CONFIRMATORY TESTING

- Culture and sensitivity (C&S): not normally employed in superficial pyoderma cases unless there has been a failure to respond to rational antibiotic therapy or bacilli are noted on skin cytologic examination.
- Skin biopsy and histopathologic exam: normally not performed unless cases are not responding to appropriate antibiotic therapy. Findings include intraepidermal neutrophilic pustules, folliculitis, or furunculosis ± underlying cause (e.g., *Demodex,* pemphigus foliaceus, epitheliotrophic lymphoma).
- Endocrine status: thyroid function and adrenal function tests
- Allergy testing: intradermal or serum allergy testing for environmental allergies, and elimination diet trial for food allergy

TREATMENT

TREATMENT OVERVIEW

The main goals are to treat the infection and determine the underlying cause(s).

ACUTE GENERAL TREATMENT

Topical Therapy:

- Most commonly used: mupirocin (Bactroderm) and fusidic acid (Fucidin). Silver sulfadiazine and benzoyl peroxide 5% gels are also available.
- Shampoo therapy very effectively decreases bacterial skin colonization (adjunctive therapy). Shampoo therapy (10-15 minutes contact time) with products containing benzoyl peroxide, chlorhexidine, ethyl lactate, and povidone-iodine may improve the condition.
- Clip the fur off affected areas.
- Deep pyoderma: bathe animal or soak lesion with Epsom salts solution (magnesium sulfate, 2 tablespoons/liter of lukewarm

water) or Burow's solution (magnesium sulfate-aluminum acetate solution) daily.

Systemic Antibiotic Therapy:

- Bactericidal antibiotics are generally recommended for skin infections; however, bacteriostatic drugs may be effective in an immunocompetent animal. The chosen drug should have a narrow spectrum to limit the effects on the normal flora of both the skin and gastrointestinal (GI) tract.
- Cases should be treated for a minimum duration of 3-4 weeks, or 7-14 days beyond clinical cure. Deep pyoderma may take as long as 12 weeks to resolve.
- The most commonly used antibiotics include (generally monotherapy):
  - Cephalexin, 22-30 mg/kg PO q 12 h (most common choice in dogs)
  - Clavulanic acid-potentiated amoxicillin, 12.5-25 mg/kg PO q 12 h
  - Clindamycin, 5.5-11 mg/kg PO q 12 h
  - Cefovecin injectable, 8 mg/kg SQ q 14 days
- Other suggested drugs/dosages include (generally monotherapy; all PO): cefpodoxime, 5-10 mg/kg q 24 h; cefadroxil, 22 mg/kg q 12 h; oxacillin, 22 mg/kg q 8 h; erythromycin, 10-20/ kg q 8 h (vomiting and diarrhea common); lincomycin, 15-25 mg/kg q 12 h; azithromycin, 5 mg/kg q 24 h; tylosin, 10-20 mg/kg q 12 h; trimeth-oprim-sulfa, 15-30 mg/kg q 12 h; difloxacin, 5-10 mg/kg q 12 h (not in immature animals); enrofloxacin, 5-20 mg/kg q 24 h (not in immature animals); marbofloxacin, 2.75-5.5 mg/kg q 24 h (not in immature animals); orbifloxacin, 2.5 mg/kg q 24 h (not in immature animals); doxycycline, 5 mg/kg (day 1), then 2.5 mg/kg q 12 h
- Appropriate pain management

CHRONIC TREATMENT

- In face of an idiopathic recurrent pyoderma (generally SBF) that recurs less than three or four times a year, it is often more economical and reasonable to treat each event with an appropriate course of antibiotics. Moreover, when an antibiotic (e.g., cephalexin) is effective in treating an episode of pyoderma, there is no need to change for another antibiotic when the pyoderma recurs later on.
- In cases of idiopathic recurrent pyoderma where several episodes occur annually and/or when total annual antibiotic administration is more than 12 weeks, adjunctive immunomodulatory therapy or extended antibiotic regimens (both controversial in veterinary dermatology) may be needed to maintain clinical remission.
- Immunomodulatory therapy: Staphage Lysate (SPL [Delmont Laboratories]) may help decrease recurrences of pyoderma in up to 35% of dogs. The dog should initially receive a 4- to 6-week course of oral antibiotic in conjunction with a 20- to 30-week course of SPL (0.5 mL twice weekly SQ). If the pyoderma does not recur during that period of time, the frequency of injections is gradually reduced to once weekly, then every other week.
- Extended regimens of antibiotic therapy (or pulse therapy). Pyoderma has to be eliminated by standard appropriate, safe, bactericidal antibiotic therapy (e.g., cephalexin) before extended regimen is used. Many different treatment regimens have been recommended. Pulse therapy implies using full therapeutic doses on an intermittent basis. One proposed regimen involves 1 week at full recommended daily dose, followed by 1 week off medication, and so on. If recurrence is prevented, the duration of the time off the antibiotic can be extended to up to 3 weeks. Two days per week dosing (at full daily dose) is another popular regimen. A third recommended regimen involves once-daily to once-every-other-day dosing.
- Antimicrobial shampoo or lotions used on a regular basis may assist in the prevention of relapses by limiting the bacterial surface flora.

POSSIBLE COMPLICATIONS

- Many antibiotics occasionally cause vomiting and diarrhea.
- Fluoroquinolones: cartilage damage in growing puppies
- Potentiated sulfonamides: keratoconjunctivitis sicca, arthritis, uveitis, immune-mediated dermatitis, hepatobiliary disease, drug interaction, decreased thyroid function (possible hypothyroidism at high dose)
- Benzoyl peroxide gel has to be used with care because it may be irritating with repeated use and causes fabric and hair discoloration.
- Drug-induced pemphigus foliaceus (cephalosporins)

RECOMMENDED MONITORING

It is important to assess response to therapy before the antibiotic course is completed in order to determine the appropriate duration of antibiotic administration and also to determine if there is residual pruritus, which would suggest underlying allergy or ectoparasite or concurrent *Malassezia* dermatitis.

PROGNOSIS AND OUTCOME 

- Superficial pyoderma: good prognosis as long as underlying factors are addressed adequately
- Deep pyoderma: some cases of deep pyoderma will result in scarring.
- Affected animals are often immuno-suppressed or have other intercurrent diseases.

PEARLS & CONSIDERATIONS

COMMENTS

- Epidermal collarettes are extremely useful secondary skin lesions to look for (clip some hair if needed); they are strongly suggestive of a superficial pyoderma.
- Any therapeutic plan for controlling pyoderma without considering underlying predisposing factors is destined to fail.
- Most dermatologists use cephalexin as their first drug choice because it has been shown to be a very effective drug against *S. pseudintermedius,* with minimal change in resistance pattern over the years.
- Both pemphigus foliaceus and epitheliotrophic lymphoma may present as pyodermas that fail to respond to appropriate antibiotic therapy. Skin biopsy is indicated.
- The use of immunomodulating therapy and extended antibiotic regimen should be limited to veterinary dermatologists.

TECHNICIAN TIPS

- Whenever medicated shampoos are used, it is important to respect the contact time, typically 10-15 minutes. Using a timer will aid in providing sufficient contact time.
- Clipping the hair coat may facilitate topical treatment and accelerate healing. However, one needs the client's permission first.

CLIENT EDUCATION

Counsel clients concerning the potential chronicity of the disease, owing to underlying predisposing factors. The need of long antibiotic therapy regimens, the importance of treating for 1-2 weeks beyond cure, and the need for recheck must be explained thoroughly.

SUGGESTED READING

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AUTHOR: MICHAEL HANNIGAN

EDITOR: MANON PARADIS

Pyloric Hypertrophy Syndrome

BASIC INFORMATION

DEFINITION

Stenosis of the gastric outflow tract secondary to one of the following: hypertrophy of the circular muscle of the pylorus, hyperplasia of the mucosa of the pyloric antrum, or combination of muscular and mucosal thickening

SYNONYMS

Acquired antral pyloric hypertrophy, chronic hypertrophic pyloric gastropathy, gastric antral mucosal hypertrophy, hypertrophy of the muscular layer of the pylorus, pyloric stenosis

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Congenital: dogs and cats, identified sometime after animal starts eating solid food, usually at 4-12 months of age
- Acquired: canine, middle-aged (4-7 years) and older

GENETICS & BREED PREDISPOSITION

- Congenital: brachycephalic breeds including Boston terriers, English bulldogs, boxers, and Siamese cats
- Acquired: small, often Asian-breed dogs including Lhasa apso, shih tzu, Pekingese, and Maltese

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Congenital: selective hypertrophy of the circular pyloric muscle
- Acquired: mucosal hypertrophy or combination of mucosal and muscular hypertrophy; mucosal hypertrophy may be focal (polyp) or more generalized involving entire pyloric antrum

HISTORY, CHIEF COMPLAINT

- Chronic vomiting, usually of food several hours after eating; may be projectile
- In congenital form, vomiting begins after animal starts eating solid foods
- Anorexia
- Mild weight loss
- Regurgitation

PHYSICAL EXAM FINDINGS

- Generally unremarkable
- Thin body condition is possible

ETIOLOGY AND PATHOPHYSIOLOGY

- Cause is unknown, and genetics of congenital form are not described.
- Excessive secretion of gastrin may stimulate growth of gastric smooth muscle and mucosa of gastric body.
- Some cases of “acquired” form may be slow progression of congenital form.
- Regurgitation can develop secondary to reflux esophagitis or persistent vomiting.
- Metabolic alkalosis (hypochloremic, hypokalemic) may develop, although only with severe luminal obstruction as fluid typically passes to the duodenum in most cases. In those cases with hypochloremic, hypokalemia, metabolic alkalosis, paradoxic aciduria is possible, although this is not clinically significant.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Chronic vomiting is the main historical clue to this disorder, particularly if it is projectile in nature and/or in a brachycephalic dog. Suspicion may be increased with characteristic contrast radiographic findings, but confirmation requires direct visualization (endoscopic or via laparotomy).

DIFFERENTIAL DIAGNOSIS

- For clinical presentation: other causes of chronic vomiting such as parasitism or viral, bacterial, fungal, or protozoal infection, inflammatory bowel disease, food allergy or intolerance, neoplasia, obstruction, systemic disease (liver disease, kidney disease), central nervous system disease, and drugs must be ruled out by a systematic evaluation.
- For imaging findings: infiltrative diseases such as neoplasia, pythiosis, or other fungal diseases

INITIAL DATABASE

- CBC, serum biochemistry profile, and urinalysis: often unremarkable but hyponatremic, hypochloremic metabolic alkalosis and paradoxic aciduria may be present due to vomiting of gastric contents only. May have prerenal azotemia without concentrated urine secondary to inability to concentrate urine because of hypokalemia.
- Radiographs: usually unremarkable. Stomach may be distended with fluid, uncommonly with air. Severe pyloric hypertrophy may occasionally be noted on plain films.
- Ultrasound: mucosal or muscular thickening of pylorus

ADVANCED OR CONFIRMATORY TESTING

- Contrast radiographs using barium sulfate: delayed gastric emptying, thickening of the pylorus, abrupt narrowing of the pyloric canal filled with contrast (beaklike appearance), or a narrow band of contrast filling the pylorus.
- Endoscopy (see p. 1284): the mucosa appears normal in color, but abundant antral folds or polyps with or without erosive lesions may be seen. Muscular hypertrophy can be more difficult to appreciate, but the pylorus will not distend with air. Either lesion may create a narrowed pyloric lumen through which it is difficult to pass an endoscope.
- Celiotomy: thickened pylorus and abundant mucosal folds in the antrum and pylorus
- Histopathologic evaluation of tissue: mucosa normal or thickened with erosions, edema, and hyperplasia or cystic changes in gastric glands; increased numbers and prominent branching pattern of surface gastric pits; erosions may have lymphocyte and plasma cell infiltration; *Campylobacter-like* organisms have been reported.

TREATMENT

TREATMENT OVERVIEW

The treatment goal is elimination of pyloric canal obstruction caused by the exuberant tissue, which is achieved surgically.

ACUTE GENERAL TREATMENT

- Surgery is indicated for all forms of pyloric hypertrophy syndrome.
- Y-U pyloroplasty is the most common procedure, allows for resection of hypertrophied mucosa, and is recommended in most cases.
- Gastroduodenal anastomosis (Billroth I) for cases with extensive mucosal involvement, particularly when thickening results in loss of normal pliability
- Pyloromyotomy is often ineffective and is not recommended for any type of pyloric hypertrophy.
- Short-term postoperative compromise of gastrointestinal motility may be treated with metoclopramide (0.2-0.4 mg/kg q 8-12 h PO, SQ; or constant rate infusion IV 1-2 mg/kg/d).

POSSIBLE COMPLICATIONS

- Potential complications of surgery include infection, leakage, and dehiscence. The risk of dehiscence is greater with the Billroth I procedure.
- Gastrointestinal motility may be temporarily compromised after surgery.

PROGNOSIS AND OUTCOME

Prognosis is excellent if no postoperative complications occur.

PEARLS & CONSIDERATIONS

COMMENTS

- Should be suspected in brachycephalic breeds with chronic vomiting
- Some cases of “pyloric stenosis” may be functional defects rather than anatomic defects.
- Surgery may not improve measured gastric transit time.
- Hypertrophic gastritis is distinct from this syndrome in that it typically spares the pylorus despite remarkable mucosal hypertrophy of the body and fundus. Seen primarily as a familial disorder as part of immunoproliferative enteropathy of Basenji dogs and familial stomatocytosis-hypertrophic gastritis of Drentse Patrijshond dogs. Reported in a single Old English sheepdog.
- The author has seen pyloric hypertrophy syndrome present as acute gastric dilatation without volvulus in older (8-10 years old) Labrador retrievers.

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Pyelonephritis

BASIC INFORMATION

DEFINITION

Pyelonephritis describes inflammation of the renal pelvis and interstitium typically associated with or originating from ascending bacterial infection. Acute pyelonephritis is uncommon; chronic pyelonephritis is more common but often clinically inapparent.

SYNONYM

Pyelitis

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs and cats are susceptible, with females predisposed; most common in older animals or in younger animals with predisposing cause (e.g., congenital urinary malformations, uroliths).

RISK FACTORS

Dogs and cats:

- Anatomic abnormalities:
  - Ectopic ureter(s)
  - Urethral/ureteral obstruction
  - Hydroureter/hydronephrosis
  - Perineal urethrostomy
  - Urolithiasis
  - Vulvar conformational abnormalities
- Functional abnormalities:
  - Urine retention (>0.25 mL/kg following complete voiding)
  - Urine reflux due to increased intra-vesicular pressure
  - Isosthenuria or hyposthenuria from any cause
  - Immunocompromise
  - Indwelling urinary catheter or repeated catheterization
- Lower genitourinary tract infection:
  - Dogs and cats: various bacteria; *Escherichia coli* most common isolate in urinary infections o Fungal and yeast pyelonephritis possible, especially in immunocompromised animals
  - Bacterial prostatitis: intact male dogs CONTAGION & ZOONOSIS Rarely, shared clones of bacteria involved in urinary tract infections (UTI) have been found in people and their dogs.

ASSOCIATED CONDITIONS & DISORDERS

- Acute renal failure
- Chronic kidney disease
- Hypokalemia (cats)
- Bacterial cystitis
- Urolithiasis

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Ascending pyelonephritis
- Hematogenous pyelonephritis: rare; may be associated with septicemia

HISTORY, CHIEF COMPLAINT

Clinical signs may be absent; chronic pyelonephritis is a common complicating factor in chronic kidney disease. When present, clinical signs may include:

- Polyuria and polydipsia (PU/PD; acute or chronic pyelonephritis)
- Malaise (uncommon)
- Hematuria
- Pollakiuria, stranguria (if concurrent lower urinary tract disorder)
- Abdominal, lumbar, or general discomfort (usually associated with acute pyelonephritis)
- Recurrent lower urinary infections (chronic pyelonephritis)
- History of predisposing cause may be present (e.g., urinary catheterization, uroliths)

PHYSICAL EXAM FINDINGS

Exam may be normal, especially in the more common chronic form of infection. Abnormalities, when present, may include:

- Fever (more often associated with acute pyelonephritis)
- Dehydration
- Renomegaly (acute pyelonephritis)
- Renal asymmetry (chronic pyelonephritis)
- Abdominal/renal/lumbar pain
- Oral ulcerations/halitosis (uremia)
- Debris or secretions in the oral cavity (vomitus, saliva)
- Bladder discomfort (if concurrent lower urinary infection)

ETIOLOGY AND PATHOPHYSIOLOGY

- Infectious agent (bacteria, fungus, yeast) usually ascends to renal pelvis from lower urinary tract. The agent rarely infects the kidneys hematogenously.
- Onset may be acute (less common) or insidious (more common).
- Renal response to injury causes clinical signs:
  - Acute infection results in nephritis (renal inflammation), causing renomegaly and renal pain.
  - Acute or chronic infection causes nephrogenic diabetes insipidus via bacterial toxin actions on antidiuretic hormone receptors.
  - Chronic infection results in renal scarring, resulting in smaller than normal kidneys.
- Infection may result in acute renal failure, overt chronic kidney disease, or exacerbation of preexisting chronic kidney disease.

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

The diagnosis of pyelonephritis should be considered in any animal with pyuria and/or bacteriuria (especially in absence of lower urinary tract signs), polyuria/polydipsia, kidney disease, chronic lower urinary tract infection, or immunocom-promise. Although acute pyelonephritis may cause dramatic illness, chronic pyelonephritis with obscure clinical signs occurs more commonly.

DIFFERENTIAL DIAGNOSIS

- PU/PD (see p. 902)
  - PD from psychogenic causes, hyperosmolarity, or alteration of the thirst center (e.g., central nervous system [CNS] neoplasia)
  - Osmotic diuresis (e.g., diabetes mellitus, renal glucosuria, drug or toxin)
  - Nephrogenic diabetes insipidus (e.g., congenital, electrolyte abnormalities, hormonal abnormalities, renal failure)
  - Deficient interstitial concentrating gradient (e.g., medullary washout, hyponatremia, portosystemic shunt)
  - Lack of antidiuretic hormone (i.e., central diabetes insipidus)
- Bacteria (see pp. 276 and)
- Pyelectasia (seep. 547)

INITIAL DATABASE

- CBC: may be normal (chronic pyelonephritis) or may show leukocytosis with left shift (acute pyelonephritis); normocytic, normochromic nonregenerative anemia is possible with concurrent chronic kidney disease.
- Serum biochemical profile: often normal, but when acute or chronic renal disease is present, azotemia (elevated blood urea nitrogen [BUN], creatinine), hyperphosphatemia, hypokalemia, or hyperkalemia, and/or metabolic acidosis are often identified.

- Urinalysis: isosthenuria is common; bacteria is inconsistent and often absent; occasionally leukocyte casts (acute pyelonephritis), pyuria, hematuria, and/or crystalluria.
- Abdominal radiographs: variable renal shadow (normal, large, or small and irregular). Radiopaque urinary (upper or lower) calculi (suspect struvite) are sometimes present.
- Abdominal ultrasound: renal pelvic dilation is common; renomegaly or small and irregular kidneys, alterations in renal parenchymal echogenicity also can be present.
- Urine culture prior to treatment whenever suspicion of pyelonephritis exists (even if urine sediment inactive):
    - In occult pyelonephritis, urine culture can be negative.

ADVANCED OR CONFIRMATORY TESTING

- Pyelocentesis (ultrasound guided) to obtain urine directly from the renal pelvis for culture; this procedure is uncommonly used. Begin with routine cystocentesis instead and choose pyelocentesis if trying to pinpoint source of infection to one kidney (rarely clinically necessary).
- Excretory urogram and/or cystourethrogram to rule out anatomic abnormalities. Abdominal ultrasound is the preferred first choice instead.
- If clinical signs are compatible, rule out hyperadrenocorticism as a predisposing cause.
- Renal cortex biopsy: typically not helpful to diagnose pyelonephritis, owing to localization of disease (renal pelvis and interstitium).

TREATMENT

TREATMENT OVERVIEW

The mainstay of treatment is long-term therapy with appropriate type and dose of antimicrobial drugs. It is often a challenge to obtain a positive urine culture, despite renal infection. Since pyelonephritis often occurs secondary to another disease process, recurrence is common unless the predisposing condition can be addressed. Renal failure is addressed as needed (see pp. 31, , and).

ACUTE GENERAL TREATMENT

- Antimicrobial therapy:
    - Antibiotic selection is based on culture and antimicrobial susceptibility (C&S) results whenever possible.
    - Pending results, or if culture is negative despite clinical suspicion of pyelonephritis, therapy is indicated using an antibiotic with gram-negative spectrum that is renally excreted (fluoroquinolone, augmented penicillin, trimethoprim-sulfa) to reach adequate tissue concentrations. Examples:
        - Fluoroquinolone, such as enrofloxacin, 5-20 mg/kg q 12-24 h (dogs), or 5 mg/kg q 24 h (cats) PO, IM, or diluted 1:1 with sterile saline and given slowly IV (oral therapy instituted when practical)
        - Amoxicillin with clavulanic acid, 22 mg/kg PO q 8-12 h
    - For intact male dogs, it is preferable to select an antimicrobial that will penetrate the blood-prostate barrier (e.g., fluoroquinolone, trimethoprim-sulfa).
    - Due to the sluggish rate of renal medullary blood flow, duration of antibiotic therapy should be greater than that for a simple lower urinary tract infection. Therapy typically lasts 3-6 weeks depending on clinical improvement, underlying disease, and follow-up test results.
    - If initial urine sediment was active, a repeat urinalysis about 1 week after starting antibiotic therapy is recommended to ensure resolution of bacteruria and pyuria.
    - If predisposing cause cannot be resolved, urine cultures should be repeated regularly to address future infections.
    - Fungal pyelonephritis may be more difficult to eradicate than bacterial pyelonephritis (see online chapter: Cystitis, Fungal/Algal).
- Treatment of uremic renal failure starts with isotonic crystalloid fluid therapy (see pp. 31 and).
- Medical therapy for hypokalemia:
    - Occurs commonly in cats with chronic PU/PD
    - Potassium chloride (KCl) supplementation of IV fluids used for diuresis, based on sliding scale (see table):
    - Do not exceed a rate of 0.5 mEq KCl/kg per hour for potassium replacement.
    - Recheck potassium levels are indicated at least daily during fluid therapy.
    - When the patient is eating, oral potassium gluconate replacement can be initiated at a starting dose of 2 mEq per cat q 12 h, adjusted as needed based on serial serum potassium measurements.
- Uremic signs are managed as for acute renal failure and chronic kidney disease (see pp. 31 and 207).
- Maintain fluid balance:
    - Hospitalization is not indicated if the patient is drinking and eating enough to maintain hydration.
    - If the patient is hospitalized for IV fluid therapy, fluids should be tapered slowly over 2-3 days and discontinued once hydration is maintained by oral intake.

Administer as constant rate infusion via infusion pump to minimize risk of overly rapid delivery, and adjust supplementation as needed

based on repeated assessments of serum potassium concentrations. Not for oliguric/anuric patients.

Potassium Supplementation in Intravenous Fluid Therapy

Serum Potassium Concentration	Potassium Supplementation to IV Fluids
Potassium 3.5–5.5 mEq/L	Add 20 mEq KCl/L crystalloid
Potassium 3–3.4 mEq/L	Add 30 mEq KCl/L crystalloid
Potassium 2.5–2.9 mEq/L	Add 40 mEq KCl/L crystalloid
Potassium 2–2.4 mEq/L	Add 60 mEq KCl/L crystalloid
Potassium < 2 mEq/L	Add 80 mEq KCl/L crystalloid

- ○ In cats and small dogs, the ability to maintain hydration might require a period of adaptation. Following hospital discharge, SQ crystalloid fluid therapy might be indicated q 12-48 h (seepp. 31 and).

CHRONIC TREATMENT

- Identification, treatment, or cure of predisposing cause if possible (e.g., hyperadrenocorticism, ectopic ureter, urolithiasis)
- Other treatments for chronic kidney disease as necessary (see pp. 205 and 207)

NUTRITION/DIET

Recommend diets appropriate for management of renal failure if it exists. A diet restricted/optimized in protein and phosphorus is ideal. Regardless, ensure the availability of fresh drinking water at all times.

DRUG INTERACTIONS

Cats should be treated cautiously with enrofloxacin, since acute retinal degeneration can occur. Avoid trimethoprim-sulfa antibiotics in Doberman pinschers or dogs with keratoconjunctivitis sicca.

POSSIBLE COMPLICATIONS

- Failure to resolve infection. Bacterial resistance is common if there is infection secondary to an underlying process or a structural lesion.
- Urolithiasis (nephrolithiasis), ureteral obstruction due to urolithiasis

RECOMMENDED MONITORING

- A repeat urine culture 1-2 weeks after completion of antibiotics and approximately 1 and 2 months later are indicated to ensure negative culture.
- If predisposing cause cannot be resolved (e.g., chronic kidney disease), monitoring should include urinalysis and urine culture every 3-6 months to identify recurrence.
- When initial urine culture is negative despite clinical suspicion of pyelonephritis, monitoring should include water consumption daily before and after initiation of antibiotics to assess efficacy of therapy. If water consumption decreases within 2 weeks of antimicrobial therapy, treatment should be continued for a total of 3-6 weeks.

PROGNOSIS AND OUTCOME

- Guarded to good depending on ability to correct predisposing cause and antimicrobial susceptibility of pathogen
- Prognosis for recurrent pyelonephritis is guarded, since infections can cause chronic or acute renal failure, and recurrent infections tend to develop multiple antimicrobial resistance over time.

PEARLS & CONSIDERATIONS

COMMENTS

- Pyelonephritis is often difficult to confirm, especially after antimicrobial therapy has been initiated.

- Evidence of renal pelvic dilation (pyelectasia) on ultrasound, without other supportive clinical findings, might indicate a past infection with permanent renal injury instead of active infection. Vigorous IV fluid therapy can also cause pyelectasia and should be considered an ultrasonographic differential diagnosis for pyelonephritis.
- Chronic pyelonephritis can occur without producing any overt clinical signs and without changes on CBC, serum biochemical profile, or urine sediment exam.
- A urine C&S is warranted in the management of any chronic renal disorder, because pyelonephritis may be clinically silent and difficult to detect (e.g., diluted urine may give the mistaken appearance of an inactive sediment); however, the condition is treatable, potentially resulting in a reversal of renal tubular damage.

PREVENTION

- Address anatomic or functional abnormalities directly.
- Treatment of infections with the appropriate antimicrobial therapy at the correct dose for at least 3-6 weeks
- Regular follow-up visits to identify recurrent infections as early as possible

TECHNICIAN TIPS

- Urinary catheterization can introduce bacteria; therefore, strict aseptic technique should be used.
- Animals that are hospitalized should be allowed to empty their bladder on a regular basis. Dogs that are particularly well housetrained can retain urine when kenneled, which can predispose to ascending pyelonephritis. Cats may have preferences for the type of cat litter used. Monitoring frequency and volume of urine output in hospitalized animals is vitally important.

CLIENT EDUCATION

- Owner education regarding signs of lower and upper urinary tract infection before pyelonephritis develops
- Treatment of resistant strains of bacteria causing pyelonephritis may be costly and require prolonged therapy.
- Chronic kidney disease may predispose animals (especially cats) to recurrent renal infections.

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Pustular and Crusting Skin Disorders

BASIC INFORMATION

DEFINITION

Pustules and crusts are common skin lesions. Pustules are small, circumscribed elevations of the skin filled with pus. Healing or ruptured pustules may form crusts, the dried accumulation of exúdate (blood, pus, serum) over a lost or damaged epidermis.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs and cats
- In dogs, impetigo, demodicosis, juvenile cellulitis and dermatophytosis are typically seen in young animals. Pemphigus is more common in middle-age adults.
- Hereditary mechanobullous disease: epidermolysis bullosa develops shortly after birth.
- Drug eruptions may occur at any age.

GENETICS & BREED PREDISPOSITION

- Juvenile cellulitis (seep. 627): dachshund, golden and Labrador retrievers, Gordon setters, pointers. More than one puppy can be affected in a litter.
- Subcorneal pustular dermatosis and superficial suppurative necrolytic dermatitis: miniature schnauzer
- Pemphigus foliaceus: Akita, chow chow, dachshund
- Drug eruption (especially sulfon-amides): Doberman pinscher
- Canine linear immunoglobulin A (IgA) pustular dermatosis: dachshund

RISK FACTORS

- Pyoderma, the most common cause of pustular and crusting dermatitis in dogs, is often secondary to a predisposing skin disease (atopic dermatitis, food allergy, demodicosis, end ocrinopathies).
- With the exception of abscesses, pyoderma is uncommon in cats.
- Cats affected with feline immunodeficiency virus (FIV) are more susceptible to dermatophytosis.

CONTAGION & ZOONOSIS

Dermatophytosis is contagious to other animals and is zoonotic.

GEOGRAPHY AND SEASONALITY

- Pemphigus foliaceus and pemphigus erythematosus (see p. 850) can be aggravated by exposure to sunlight.
- Pyodermas associated with underlying atopic dermatitis may have a seasonal occunence.

ASSOCIATED CONDITIONS & DISORDERS

Bullous impetigo in adult dogs is often associated with immunosuppression (e.g., hyperadrenocorticism, diabetes mellitus, hypothyroidism).

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Pustules are usually short-lived and may go unnoticed. Scaling and crusting are often the dominant presentation.
- Pruritus varies with the skin disorder. It can be a major presenting complaint in pyodermas, with or without underlying allergies or ectoparasitism.
- A variable degree of hair loss may accompany follicular damage.
- Systemic signs of lethargy and anorexia can be part of the presenting picture with pemphigus foliaceus, cutaneous drug eruptions, or superficial suppurative necrolytic dermatitis of the miniature schnauzer.

PHYSICAL EXAM FINDINGS

- Pustules are most commonly yellow. Green pustules may indicate the presence of gram-negative bacteria or marked toxic change. Larger flaccid pustules are more common in the pemphigus complex and bullous impetigo.
- Scales, epidermal collarettes, crusts of various color (brown, honey-colored) and texture (adherent, flaky), alopecia, erythema, and focal areas of hyperpig-mentation or hyperkeratosis may be noted. Depending on the condition and severity, the extent and location of lesions may be variable.

ETIOLOGY AND PATHOPHYSIOLOGY

Pustules result from a loss of epidermal intercellular cohesion (edema, degeneration, inflammation, autoantibody formation, etc.), causing epidermal or subepidermal cavities that eventually fill with inflammatory cells.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The combined presence of crusts and pustules restricts the differential diagnosis, but pustules can be short lived, and the clinician should perform a careful examination before confirming their absence. Cytologic examination of the content of an intact pustule or from the exudates under a crust is an important step to orient the diagnosis. When pustules or crusts are present in dogs, skin scrapings should always be performed to rule out demodicosis. Skin biopsies are recommended in most cases presenting with pustules and crusts once pyoderma, demodicosis, and dermatophytosis have been ruled out.

DIFFERENTIAL DIAGNOSIS

- Infectious: pustules most often have a follicular orientation.
  - Bacterial: pyoderma (bacterial folliculitis*, impetigo*, furunculosis), dermatophilosis
  - Fungal: dermatophytosis
  - Parasitic: demodicosis*, *Pelodera* dermatitis
  - Protozoal: leishmaniasis
- Immune mediated: juvenile cellulitis, pemphigus complex (especially pemphigus foliaceus*), canine eosinophilic folliculitis* and furunculosis, canine sterile eosinophilic pustulosis*, subcorneal pustular dermatosis*, and canine linear IgA pustular dermatosis*
- Drug eruption: superficial suppurative necrolytic dermatitis of schnauzers (associated with shampoo therapy), drug-induced pemphigus foliaceus, and eosinophilic pustulosis (subcorneal to follicular neutrophilic pustulosis)

*Intact pustules are often present

INITIAL DATABASE

- The medical history of the animal is important in determining etiology: age of onset, breed, presence or absence of pruritus, previous medications, other animals affected, progression, chronicity, and seasonality.
- Lesion distribution is important to orient the diagnosis:
  - Face (lips, muzzle, eyelids, ear pinnae): juvenile cellulitis, pemphigus erythematosus, demodicosis, eosinophilic folliculitis and furunculosis, nasal pyoderma, mucocutaneous pyoderma, drug eruption
  - Feet: pyoderma, dermatophytosis, demodicosis, pemphigus foliaceus
  - Trunk: superficial pyoderma, demodicosis, subcorneal pustular dermatosis, pemphigus foliaceus, drug eruption, impetigo (abdomen)
- Cytologic examination of pustular contents:
  - Bacteria: phagocytized bacteria (often cocci, because staphylococcal organisms are the primary isolates from dogs and cats with pyoderma).
  - Neutrophils: pyoderma, pemphigus complex, subcorneal pustular dermatosis, and canine linear IgA pustular dermatosis
  - Eosinophils: abundant eosinophils with eosinophilic folliculitis/furunculosis and sterile eosinophilic pustulosis; eosinophils are also associated with superficial pyodermas with parasitic or allergic disorders, deep pyodermas (furunculosis), drug eruptions, and pemphigus foliaceus.
  - Acantholytic keratinocytes: seen in pemphigus complex in conjunction with numerous intact neutrophils and/or eosinophils
- Skin scrapings: *Demodex* spp.
- Fungal culture: dermatophytosis
- CBC, serum biochemistry profile, and urinalysis if systemic disease is suspected; results often unremarkable besides

mild/moderate neutrophilic or eosinophilic leukocytosis.

ADVANCED OR CONFIRMATORY TESTING

- Skin biopsies for histopathologic evaluation
- Bacterial culture and sensitivity (C&S) indicated if bacilliform bacteria are noted on cytologic examination or if poor response to previous appropriate antibiotic therapy.
- Endocrine tests if history and physical exam suggest underlying endocrinopathy.
- Serologie testing for FIV, feline leukemia virus (FeLV), leishmaniasis, based on history and environment

TREATMENT 

TREATMENT OVERVIEW

Pyoderma is the most common cause of pustules and crust formation in dogs. Most pyodermas are successfully addressed with antibiotic therapy. Because etiologies of crusting and pustular skin diseases are often infectious or parasitic, glucocorticoids should not be used until a final diagnosis has been reached.

ACUTE AND CHRONIC TREATMENT

Depends on etiology of the disorder:

- Antibiotic therapy: common empirical choices include cephalexin, 22-30 mg/kg PO q 12 h; or amoxicillin-clavulanate, 15-20 mg/kg PO q 12 h, usually for 1-2 weeks beyond resolution of lesions. A more specific selection can be made based on results of C&S.
- Antifungal therapy: itraconazole, 5 mg/kg PO q 24 h for 3-6 weeks (pulse or continuous) is a good first-choice therapy in cats with dermatophytosis.
- Antiparasitics: choice depends on the parasite identified.
- Glucocorticoids for immune-mediated disorders such as juvenile cellulitis, pemphigus complex, eosinophilic folliculitis/furunculosis, eosinophilic pustulosis
    - Prednisone/prednisolone is a common first choice in dogs, usually for 10-14 days at high induction dosage (2-4 mg/kg PO q 24 h) then gradually tapered according to clinical response. Prednisolone (specifically) is preferred in cats.

PROGNOSIS AND OUTCOME 

- Varies according to the disease
- Excellent for most parasitic and infectious skin diseases
- Excellent for some immune-mediated skin diseases such as juvenile cellulitis, sterile eosinophilic folliculitis, and furunculosis

PEARLS & CONSIDERATIONS 

COMMENTS

- Crusts alone are noted in certain diseases, such as in cornification disorders or zinc-responsive dermatosis.
- Crusts secondary to excoriations are frequently seen in atopic dermatitis, food intolerance, and flea bite dermatitis.
- Treat and rule out the presence of pyoderma before taking biopsies.

CLIENT EDUCATION

- In lay terms, pustules are “pimples” and crusts are “scabs.”

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Pupil Abnormalities

BASIC INFORMATION

DEFINITION

Abnormalities include pupils that are inappropriately dilated or constricted as well as pupils with distorted shape.

SYNONYMS

Anisocoria: unequal or asymmetric pupils

Dyscoria: misshapen/distorted pupil

Miosis: constricted pupil

Mydriasis: dilated pupil

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs and cats
- Iris atrophy is a normal aging change and is therefore seen in older animals.
- Iris coloboma (absence of or defect in iris) is a developmental/heritable condition that is usually noticed initially in young animals, most frequently dogs.

GENETICS & BREED PREDISPOSITION

- Distorted pupil: A distorted pupil, such as iris coloboma, may be breed-related in dogs. Australian shepherds and dal-matians are overrepresented.
- Dilated pupil:
  - Glaucoma, primary (predisposed breeds)
  - Toy and miniature poodles are predisposed to optic nerve hypoplasia.
  - Heritable retinal degeneration in many breeds of dogs (see p. 983)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Conditions that lead to pupil abnormalities can be divided into those that cause:

- Pupillary dilation (mydriasis)
- Pupillary constriction (miosis)
- Abnormal pupil shape (dyscoria)

HISTORY, CHIEF COMPLAINT

The pet's owner may notice abnormalities in pupil size and shape. More likely, veterinarians notice the pupil abnormalities in animals presenting for painful, red, or blind eyes.

PHYSICAL EXAM FINDINGS

- Dilated pupil and the following:
  - Scalloping at pupillary margin:
    - Iris coloboma: focal; young animal
    - Iris atrophy: typically multifocal and/or “moth-eaten” effect in iris stroma; typically age-related change (i.e., older animals)
  - Blindness (negative menace response):
    - See Retinal Degeneration, p. 983; Retinal Detachment, p. 985.

        - Optic nerve lesion (e.g., optic nerve hypoplasia, congenital, glaucoma [seep. 1559], optic neuritis (seep. 784)
        - Optic chiasmal lesion (see p. 784)
    - "Quiet" (i.e., nonred) sighted (visual) eye:
        - Internal ophthalmoplegia (paralysis of the iris and ciliary muscles) caused by:
            - Pharmacologic pupillary dilation (e.g., parasympatholytics such as atropine and topical tropicamide)
            - Iris atrophy
            - Lesions involving the parasympathetic fibers of the oculomotor nerve (cranial nerve [CN] III); relatively rare
        - Fearful animal (i.e., sympathetic stimulation): transient mydriasis; resolves once animal becomes calm
- Constricted pupil and the following:
    - Red eye with or without vision impairment:
        - See Uveitis, .
        - Corneal ulceration (seep. 250) and "axon reflex" miosis through trigeminal and oculomotor nerves (CNs V and III)
        - Pharmacologic pupillary constriction (e.g., parasympathomimetic, such as topical pilocarpine, dem-ecarium, or synthetic prostaglan-dins; such analogs include latanoprost, bimatoprost, and tra-voprost; may cause conjunctival hyperemia).
    - Quiet eye with or without vision impairment:
        - Horner's syndrome (see p. 543): other signs include ptosis (drooping of upper eyelid), enophthal-mos (caudal displacement of the eye), and third eyelid protrusion.
- Distorted pupil and the following:
    - Scalloping at pupillary margin:
        - Iris coloboma: focal; young animal
        - Iris atrophy: typically multifocal and/or "moth-eaten" effect in iris stroma; typically age-related change (i.e., older animals)
    - Red eye with or without vision impairment:
        - Adhesions of iris to lens and/or iris to cornea (posterior and anterior synechiae, respectively) from current or past anterior uveitis (see p. 1151)
        - Iris prolapse through full-thickness corneal lesion (see p. 249)
        - Iridodonesis (tremulousness of the iris on movement of the eye) noted, with loss of iris support subsequent to lens subluxation/luxation (see pp. 644 and)
- Anisocoria:
    - Primary iridal disease (age-related atrophy); heritable or developmental coloboma, active inflammatory process causing miosis; chronic inflammation leading to degeneration and/or posterior synechia
    - Primary neurologic cause (CN III abnormality, Horner's syndrome, fright response)
    - Pharmacologic agents (miotics such as pilocarpine, mydriatics such as atropine and tropicamide)
- Unresponsive pupil(s):
    - Retinal disease (seep. 141)
    - Optic nerve disease
    - Iridal disease (see p. 141)
    - Pharmacologic agents
    - Posterior synechia secondary to anterior uveitis

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis of pupil abnormalities requires consideration of the entire eye as well as the orbit and the brain. Pupil abnormalities are frequently indicative of serious but nonocular problems.

INITIAL DATABASE

Complete ophthalmic examination (seep. 1313), including:

- Neuro-ophthalmic examination (seep. 1311) (i.e., menace response; dazzle, palpebral, pupillary light, and vestibulo-ocular reflexes)
- Fluorescein stain application (miosis commonly occurs in animals with corneal ulceration)
- Intraocular pressures (>30 mm Hg with glaucoma; often low [< 10-15 mm Hg] with uveitis)

ADVANCED OR CONFIRMATORY TESTING

Variable depending on underlying condition:

- Pharmacologic testing (e.g., 10% phen-ylephrine) for Horner's syndrome
- CT scans, MRIs, and other imaging procedures; cerebrospinal fluid tap for diseases of the neurologic system (e.g., optic neuritis; optic chiasmal lesions) or orbital disorders
- Electroretinogram (see p. 1255) to assess retinal function (also see p. 983)

TREATMENT

TREATMENT OVERVIEW

If a specific systemic cause of oculomotor neuropathy, optic neuropathy, anterior uveitis, or Horner's syndrome can be identified, treatment should address the specific cause. Treatment is either not indicated or not available for iris atrophy, iris coloboma, optic nerve hypoplasia, retinal degeneration, and optic nerve atrophy/degeneration.

ACUTE AND CHRONIC TREATMENT

Directed at underlying cause

PROGNOSIS AND OUTCOME

- Prognosis varies widely depending on underlying condition and cause.
- Many causes of pupil abnormalities are completely innocuous, while others may be life threatening.

PEARLS & CONSIDERATIONS

COMMENTS

Many pupil abnormalities can be diagnosed with careful consideration of the signalment and the presence or absence of other ophthalmic signs.

CLIENT EDUCATION

- Pupil abnormalities can be an early sign of serious disease.
- Early detection may improve prognosis

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Pulse Abnormalities

BASIC INFORMATION

DEFINITION

The arterial pulse is produced by the fluctuation between diastolic and systolic arterial pressure and can be palpated as an impulse in superficial arteries, such as the femoral artery. *Pulse deficit* refers to a heartbeat that is heard on auscultation or felt on the chest wall but does not generate a palpable arterial pulse.

SYNONYMS

- Hyperkinetic pulse: strong, bounding, or “water-hammer” pulse
- Hypokinetic pulse: weak or “thready” pulse

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs and cats of either sex and any age

ASSOCIATED CONDITIONS & DISORDERS

- Reduced pulse amplitude (hypokinetic pulse):
  - Decreased cardiac output (hypovo-lemia, systolic dysfunction)
  - Left ventricular outflow tract obstruction (aortic stenosis, systolic anterior motion of the mitral valve). The pulse is not transmitted normally to the peripheral arteries; with aortic stenosis, it may be decreased and delayed *(pulsus parvus et tardus).*
- Increased pulse amplitude (hyperkinetic pulse):
  - Increased stroke volume (anemia, pregnancy, increased sympathetic tone, hyperthyroidism, bradyarrhythmias)
  - Decreased diastolic arterial pressure (patent ductus arteriosus, aortic insufficiency). Diastolic runoff through the ductus arteriosus or aortic valve, respectively, causes a greater difference between systolic and diastolic pressures (greater pulse pressure) and a correspondingly stronger pulse.
- Variation in pulse amplitude:
  - Exaggerated effect of respiration: *pulsus paradoxus* (pericardial effusion with cardiac tamponade). The pulse is stronger during expiration and weaker during inspiration.
  - Tachyarrhythmias (atrial fibrillation, ventricular and atrial premature complexes, ventricular tachycardia). Generally, in a given animal with one of these arrhythmias, the pulse becomes weaker with higher heart rates or beats that are more premature.
  - Severe myocardial failure *(pulsus alternans).* The pulse amplitude alternates between a strong pulse and a weak (or absent) pulse.
- Regional variation in pulse amplitude:
  - Arterial thromboembolism (feline myocardial disease, infective endocarditis, hypercoagulable states)
- Variation in pulse rhythm:
  - Tachyarrhythmias (atrial fibrillation, premature atrial and ventricular complexes)
  - Bradyarrhythmias (second-degree atrioventricular block)

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

Highly variable and dependent on underlying cause

PHYSICAL EXAM FINDINGS

- Systemic or primary cardiac problems may alter the pulse; therefore, a complete physical exam is necessary.
- Femoral pulses are easiest to palpate in cats and dogs.
- The dorsal metatarsal pulse can also be palpated.
- Auscultate heart sounds simultaneously (by definition, a pulse deficit exists when a heart sound does not have a

corresponding palpable peripheral pulse).
- Pulse quality relates mainly to pulse amplitude (also affected by rate of rise of arterial pressure in systole and affected by pulse duration).

ETIOLOGY AND PATHOPHYSIOLOGY

- Pulse pressure: difference between systolic and diastolic blood pressure (BP)
- Variations in left ventricular stroke volume are detected as variation in arterial pulse pressure.
- With premature beats, the weak ventricular contraction may not generate sufficient systolic pressure to open the aortic valve, and no S^2 or pulse is produced (S! is still normally heard).
- Variations in stroke volume will also occur with the phase of respiration with cardiac tamponade, where increased filling of the right heart during inspiration leads to decreased filling of the left heart and a reduced pulse pressure.
- Pulsus alternans is an uncommon finding characterized by alternate pulses that are very weak or even absent despite consistent electrical activation (due to abnormal intracellular calcium cycling in myocardial failure).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A pulse abnormality is inherently a physical exam finding, and its significance may vary from harmless (e.g., seemingly weak pulse in an obese patient) to indicative of systemic or primary cardiac disturbances. An intermittent pulse deficit should be investigated initially with an electrocardiogram; a weak pulse should be assessed with evaluation of the patient's intravascular volume status (hydration) and cardiac function (auscultation, thoracic radiographs, echocardiogram).

DIFFERENTIAL DIAGNOSIS

- Hypokinetic pulse: obesity, arterial disease/disorder. The combination of hypokinetic pulse and a palpably strong or hyperdynamic heartbeat (apex beat) is strongly suggestive of outflow obstruction (e.g., moderate to marked aortic stenosis or, less commonly, pulmonic stenosis).
- Hyperkinetic pulse: thin body condition
- Variation in pulse amplitude: normal variation as occurs with respiratory sinus arrhythmia (pulse is stronger after pause)

INITIAL DATABASE

- The presence of pulse deficit should prompt recording of an electrocardiogram.
- The presence of alternate pulse deficits with normal sinus rhythm (pulsus alternans) should prompt a thoracic radiographic exam and an echocardiographic exam.

TREATMENT

TREATMENT OVERVIEW

Management of underlying cause

PROGNOSIS AND OUTCOME

Highly variable and dependent on underlying cause

PEARLS & CONSIDERATIONS

COMMENTS

- Palpation of the peripheral arterial pulse can give useful information about stroke volume and cardiac output.
- Palpation of the arterial pulse is not a useful way of detecting systemic hypertension.
- Presence of a hyperkinetic pulse may be more obvious than a diastolic murmur with severe aortic insufficiency (as with infective endocarditis of the aortic valve).
- Pulsus paradoxus is a very helpful finding when cardiac tamponade is suspected, but it may be difficult to detect if the dog is

panting.

SUGGESTED READING

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AUTHOR: VIRGINIA LUIS FUENTES

EDITOR: ETIENNE CÔTÉ

Pulmonic Stenosis

BASIC INFORMATION

DEFINITION

A fixed or dynamic impediment to the ejection of blood from the right ventricle (RV) due to abnormal narrowing of the right ventricular outflow tract, pulmonic valve orifice, or main pulmonary artery

SYNONYM

Pulmonic valve dysplasia

EPIDEMIOLOGY

SPECIES, AGE, SEX

Pulmonic stenosis (PS) is the third most common congenital heart defect in dogs. It is an uncommon congenital defect in cats, which are more likely to develop acquired, benign dynamic infundibular RV outflow tract obstructions as adults, most often in association with other systemic or cardiac diseases.

GENETICS & BREED PREDISPOSITION

Inherited as a polygenic trait or single gene defect with variable penetrance. English bulldogs, miniature Schnauzers, Chihuahuas, Samoyeds, miniature pinschers, boxers, Labrador retrievers, mastiffs, beagles, fox terriers, Scottish terriers, West Highland white terriers, other terrier breeds are overrepresented.

ASSOCIATED CONDITIONS & DISORDERS

Pulmonic stenosis occurs most often as an isolated defect but may be combined with other defects of the conotruncal septum (e.g., tetralogy of Fallot). The tricuspid valve apparatus is concurrently malformed in about one-third of dogs with pulmonic stenosis.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Four anatomic types of obstruction can occur: supravalvular, valvular, subvalvular, and infundibular. While the functional consequences of these different types of obstruction are similar, their distinction is important if repair is contemplated.

HISTORY, CHIEF COMPLAINT

Affected animals may show no overt clinical manifestations or may exhibit exercise intolerance or syncope. Signs of right heart failure (venous engorgement, hepatomegaly, ascites) or sudden death occur in severely affected animals.

PHYSICAL EXAM FINDINGS

A systolic ejection murmur is typically best heard at the left heart base, specifically over the pulmonic area. It may also radiate loudly cranially along the sternal border. Arterial pulses are unremarkable unless severe heart failure is present. Jugular distension, jugular pulses, hepatosplenomegaly, and ascites develop with the onset of right heart failure. Cyanosis may be observed when PS is complicated by right-to-left shunting across a patent foramen ovale or coexisting atrial or ventricular septal defect.

ETIOLOGY AND PATHOPHYSIOLOGY

- Increased resistance to ejection results in concentric RV hypertrophy (RVH), which develops in proportion to the severity of obstruction.
- The resulting decline in right ventricular diastolic compliance impairs ventricular filling, resulting in elevated right atrial pressure.
- Tricuspid regurgitation from progressive ventricular dilation or concurrent valvular dysplasia further increases right atrial pressure.

- Hypertrophy of the infundibular region of the right ventricular outflow tract may also contribute to outflow tract obstruction, particularly during exercise. This additional mechanism of obstruction can be particularly problematic following surgical valvotomy or balloon valvuloplasty.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected in a patient with a systolic heart murmur with point of maximal intensity over the left cardiac base. Signalment, pattern of murmur radiation on the chest and neck, and thoracic radiographic findings can help raise or lower suspicion of pulmonic stenosis (versus subvalvular aortic stenosis or other lesions); confirmation requires echocardiography.

DIFFERENTIAL DIAGNOSIS

Other congenital heart defects causing a systolic murmur, such as subvalvular aortic stenosis, ventricular septal defect, and tetralogy of Fallot

INITIAL DATABASE

- Electrocardiography: RVH is usually evident; right axis deviation, S1; S2, S3 deep S waves in CV6LU (or V4), CV6LL (or V2).
- Thoracic radiography: characteristic findings include right ventricular enlargement and dilation of the main pulmonary artery segment. These changes are usually most evident on the dorsoventral view. Pulmonary vasculature is usually normal, but in severe cases, the lungs may appear hypoperfused.
- Echocardiography: site of obstruction, severity of RVH, and poststenotic dilation of the main pulmonary artery are best demonstrated by a two-dimensional echocardiogram. The pulmonic valve area is best visualized from right parasternal short-axis views, from the left cranial parasternal position, or by transesophageal echocardiography. Color flow and spectral Doppler studies are useful to confirm the diagnosis and determine the severity of obstruction. Estimation of peak blood flow velocity through the stenotic area by Doppler interrogation permits calculation of the pressure gradient using the modified Bernoulli equation, pressure gradient = $4 \times V^2$.

ADVANCED OR CONFIRMATORY TESTING

Angiocardiography is performed as a prelude to balloon valvuloplasty or surgical repair. Such studies are useful for clarifying the anatomic location of the obstruction, identifying leaflet fusion and thickening, identifying the severity of RV hypertrophy, and verifying the presence of other abnormalities such as hypoplasia of the pulmonic annulus, tricuspid regurgitation, or a patent foramen ovale. Left ventricular angiography or coronary arteriography should be performed when abnormalities of the left heart are suspected or when concurrent developmental abnormalities of the coronary arteries are suspected in boxer dogs and English bulldogs. The hemodynamic severity of outflow tract obstructions is determined by measuring the systolic pressure gradient across the lesion and estimating the effective valve orifice area.

TREATMENT

TREATMENT OVERVIEW

Definitive treatment eliminates severe obstructing lesions prior to the development of heart failure

ACUTE GENERAL TREATMENT

- Dogs with mild pulmonic stenosis that is not causing overt manifestations do not require treatment.
- Dogs with such overt manifestations as exercise intolerance, syncope, or signs of right heart failure and dogs with severe fixed anatomic obstructions should be referred for surgical repair or balloon valvuloplasty, depending on the precise anatomy of the defect and/or presence of concurrent defects.
- Balloon valvuloplasty is the preferred method of treatment when the main abnormality is fusion of the pulmonic leaflets. Surgery is often required to effectively remedy complex lesions with annular hypoplasia and fixed or persistent subvalvular obstruction.
- Dynamic obstructions during stress or exercise can often be effectively palliated by beta-receptor blockade (e.g., atenolol 0.25-0.5 mg/kg PO q 12 h). Such therapy is sometimes required following balloon valvuloplasty or surgical repair.
- When balloon valvuloplasty or surgical correction are not possible, treatment with beta-receptor blocking drugs and exercise restriction are thought to minimize the chance of sudden death.

POSSIBLE COMPLICATIONS

Dogs with severe untreated disease frequently develop progressive right heart enlargement, tricuspid regurgitation, right heart failure, and atrial fibrillation. Recurrent syncope is common and sudden death has been reported.

RECOMMENDED MONITORING

Color-flow Doppler echocardiography is the most useful tool for assessing dogs with pulmonic stenosis over time. Some lesions that are modest in severity in juvenile animals can become progressively more severe over time. The short-and long-term success of surgery or balloon valvuloplasty is best determined by periodic echocardiographic evaluation. Chest radiographs and electrocardiography are useful for evaluating overall heart size and cardiac arrhythmias, respectively.

PROGNOSIS AND OUTCOME

- Dogs with mild obstructions have a very good prognosis and often reach old age.
- Dogs with severe obstructions (systolic pressure gradient >100 mm Hg) have a guarded prognosis, as they often develop heart failure or die suddenly.
- Balloon valvuloplasty improves outcome, particularly when the pressure gradients are substantially reduced.
- Restenosis occurs in about 10% of dogs treated by balloon valvuloplasty.

PEARLS & CONSIDERATIONS

PREVENTION

- Conscientiously performed physical examinations with careful cardiac auscultation are key to early recognition.
- Dogs with confirmed pulmonic stenosis should not be bred.

CLIENT EDUCATION

Owners should be advised of the high likelihood of heart failure or sudden death in animals with severe untreated pulmonic stenosis. Balloon valvuloplasty and surgical repair are recommended for patients with severe obstructions.

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Pulmonary Thromboembolism

BASIC INFORMATION

DEFINITION

The occlusion of a pulmonary artery or arteriole by a thrombus that forms in the systemic venous system/right heart (i.e., embolism) or in the pulmonary arterial system (i.e., in-situ thrombus). Pulmonary thromboembolism (PTE) is infrequently confirmed by direct visualization; therefore diagnosis can be difficult and incidence may be underestimated.

EPIDEMIOLOGY

SPECIES, SEX, AGE

- Dogs: 10 months to 18 years, median age 11 years
- Cats: 2-14 years, median age 7 years

RISK FACTORS

Numerous predisposing conditions are identified as risk factors for PTE, and treatment of these underlying causes is a cornerstone of case management.

- Neoplasia
- Heartworm disease
- Sepsis
- Hyperadrenocorticism
- Disseminated intravascular coagulation
- Immune-mediated hemolytic anemia
- Protein-losing nephropathy/enteropathy
- Central catheters
- Vasculitis
- Pancreatitis
- Cardiac disease
- Surgical procedures especially total hip replacement
- Trauma

ASSOCIATED CONDITIONS & DISORDERS

Hypoxemia, right-sided congestive heart failure, pulmonary hypertension

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Acute onset dyspnea/tachypnea; may be mild or progressive when PTE is small or gradual
- Signs of the underlying disorder may predominate.
- Occasionally signs of right-sided heart failure (abdominal distension, exercise intolerance)
- Uncommonly, cough or hemoptysis
- Nonspecific signs (lethargy, anorexia/inappetence, weight loss, collapse)

PHYSICAL EXAM FINDINGS

- Dyspnea/tachypnea
- Cyanosis
- Pulmonary crackles/increased bronchovesicular sounds; however, pulmonary auscultation often is normal.
- Tachycardia and weak pulses
- Findings reflecting the predisposing condition
- Occasionally, findings consistent with right-sided congestive heart failure are present (jugular venous distension/pulsation, ascites)

- Right apical murmur or split second heart sound possible with pulmonary hypertension

ETIOLOGY AND PATHOPHYSIOLOGY

- Generally, PTE should be thought of as secondary to an underlying condition which causes venous stasis, endothelial damage, and/or hyperco-agulability (Virchow's triad).
- PTE leads to mechanical obstruction of a pulmonary artery or arteriole and reactive pulmonary vasoconstriction. This results in reduced blood flow to the affected region of lung. Other forms of emboli including parasites, neoplastic cells, fat, or gas may also cause pulmonary vascular obstruction.
- While small PTE are often clinically silent and rapidly lysed endogenously, large or numerous PTE cause ventilation/perfusion mismatch and hypoxemia.
- Since the lung has a dual blood supply with bronchial arteries from the aorta perfusing the lung parenchyma with oxygenated blood, even massive PTE generally does not cause lung infarction.
- Increased pulmonary vascular resistance due to pulmonary vascular obstruction and pulmonary vasoconstriction may cause pulmonary hypertension. This leads to a pressure overload of the right ventricle and if severe, right-sided heart failure.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Clinical diagnosis is challenging, and definitive diagnosis may require advanced imaging. Often a presumptive diagnosis is made based on high clinical suspicion from identifying a predisposing disorder, plus thoracic diagnostic imaging results.

DIFFERENTIAL DIAGNOSIS

- Pulmonary parenchymal disease (bron-chopneumonia, pulmonary edema, neoplasia, parasitism, contusion, hemorrhage)
- Upper or lower airway disease (bronchitis/asthma, acquired or congenital structural abnormalities, neoplasia, obstruction)
- Pleural space disease (pleural effusion, restrictive pleuritis, neoplasia)
- Other causes of pulmonary hypertension (see p. 1422)

INITIAL DATABASE

- Thoracic radiographs; initial test of choice, though minimally specific and sensitive: central pulmonary artery dilation, abrupt distal pulmonary artery attenuation, regional oligemia, interstitial or alveolar pulmonary parenchymal pattern (often with lobar distribution), right heart enlargement, pleural effusion. Radiographs may be normal.
- Coagulation profile: not useful because rapid (abnormally low) coagulation values do not indicate a hypercoagulable state.
- CBC, serum biochemistry panel, and urinalysis: not useful in the diagnosis of PTE but important for diagnosis of predisposing diseases
- Echocardiography: evidence of pulmonary hypertension, right atrial and ventricular enlargement, occasionally visible thrombus

ADVANCED OR CONFIRMATORY TESTING

- Blood gas analysis: hypoxemia/hypocapnia (hypercapnia if severe); metabolic acidosis; elevated alveolar-arterial (A-a) gradient
  - A-a gradient = Fio2 (Pb-Ph2o) -(Paco2/R) − Pao2, where Fio2 is the fraction of inhaled oxygen (e.g., 0.21 for room air; 0.4 for 40% oxygen; etc.), Pb = barometric pressure (627-643 mm Hg; www.weather.com), Ph2o = 47 mm Hg, R = 0.8, and Pao2 and Pco2 are obtained from the arterial blood gas result.
  - Normal: <15 mm Hg
  - 15/15 dogs with necropsy-confirmed PTE had elevated A-a gradient.
- Plasma D-dimer concentration: some problems with specificity, but high concentrations (i.e., >2000 ng/mL) consistent with thromboembolic disease in the dog. Normal D-dimer levels should reduce the suspicion of PTE.
- Nuclear ventilation/perfusion scanning: safe and noninvasive but very limited availability
- Pulmonary angiography: gold standard for definitive diagnosis. Invasive and unstable patient condition may preclude sedation/anesthesia.
- CT and magnetic resonance angiography: noninvasive, but require anesthesia

TREATMENT

TREATMENT OVERVIEW

PTE is often a life-threatening emergency, and initial treatment is focused on respiratory support. If clinical suspicion is high or a definitive diagnosis can be made, specific therapy should be provided.

ACUTE GENERAL TREATMENT

- Oxygen therapy (see p. 1318)
- Ventilation with positive end expiratory pressure if severe (see p. 1362)
- Judicious parenteral fluid therapy to maintain tissue perfusion without exacerbating right heart failure
- Anticoagulant therapy to prevent additional thrombus formation:
  - Unfractionated heparin: 100-300 U/kg IV or SQ q 6-8 h to prolong PTT to 1.5-2 times baseline; *or*
  - Low-molecular-weight heparin (LMWH): dalteparin, 100-150 U/kg SQ q 8-12 h; or enoxaparin, 1 mg/kg SQ q 12 h. Doses not well defined.
- Antiplatelet therapy may be considered:
  - Aspirin, 0.5 mg/kg PO q 12-24 h (dogs); 5-20 mg PO q 3 d (cats); *or*
  - Clopidogrel, 1-2 mg/kg PO q 24 h (dogs); 18.75 mg PO q 24 h (cats)
- Thrombolytic therapy (streptokinase, tissue plasminogen activator) may be useful in acute stage, but experience is limited in veterinary medicine, and proposed dosing regimens vary widely.
- Surgical embolectomy is feasible with central thrombi but associated with significant morbidity/mortality. Percutaneous catheter thrombectomy/thrombolysis may be possible with reduced mortality/morbidity but requires specialized equipment.

CHRONIC TREATMENT

- Treatment of underlying condition
- Anticoagulant therapy:
  - LMWH: dalteparin or enoxaparin as above; *or*
  - Warfarin, 0.05-0.2 mg/kg PO q 24 h, to attain an international normalization ratio of 2-3. Must be overlapped with heparin therapy for 3-5 days owing to initial hypercoagulable phase.
- Antiplatelet therapy:
  - Aspirin or clopidogrel as above

POSSIBLE COMPLICATIONS

- Pulmonary hypertension and right-sided heart failure
- Potentially severe hemorrhage is possible with any anticoagulant or thrombolytic therapy. This limits the use of warfarin and thrombolytics but risk appears low with LMWH.

RECOMMENDED MONITORING

- Respiratory rate, arterial blood gas analysis, and thoracic radiography provide relative indications of response to therapy or deterioration of patient condition.
- Careful monitoring of coagulation times with unfractionated heparin or warfarin therapy. This may not be necessary with LMWH.

PROGNOSIS AND OUTCOME

Variable depending upon size of thrombus and degree of pulmonary vascular occlusion. Large thrombi resulting in occlusion of large portions of the pulmonary vascular bed are associated with a poor prognosis.

PEARLS & CONSIDERATIONS

COMMENTS

- PTE should be suspected in any patient with severe dyspnea and/or hypoxemia and normal thoracic radiographs.
- Even with management of an underlying disease, recurrence is possible, and long-term anticoagulant therapy may be necessary.

PREVENTION

Elimination of predisposing conditions is imperative. Prophylactic anticoagulant therapy may be considered when this is not possible.

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AUTHOR: HERBERT W. MAISENBACHER, III

EDITOR: ETIENNE CÔTÉ

1ST EDITION AUTHOR: BRUCE KORNREICH

Pulmonary Nodules

BASIC INFORMATION

DEFINITION

Single or multiple masses of varying sizes occurring in the lung parenchyma; usually detected radiographically

SYNONYM

Lung nodules

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs: 9-11 years
- Cats: 11-12 years
- Females may be at increased risk.
- The prevalence of pulmonary nodules in dogs and cats is not known. Pulmonary neoplasms have an average reported incidence rate of 5.6/100,000 in dogs and 2.2/100,000 in cats.

RISK FACTORS

Exposure to secondhand smoke may be a risk factor.

ASSOCIATED CONDITIONS & DISORDERS

Paraneoplastic syndromes reported to occur secondary to primary or metastatic lung neoplasms:

- Hypertrophic osteopathy
- Hypercalcemia
- Fever
- Elevated ACTH with associated signs of hyperadrenocorticism

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Most primary lung neoplasms are adenocarcinomas (75%) or carcinomas (20%).

HISTORY, CHIEF COMPLAINT

- Pulmonary nodules or masses may be found incidentally in patients undergoing radiography for other reasons.
- When lung neoplasms cause clinical signs, the most frequent complaints from the owner are cough and dyspnea.
- Sputum with or without blood or hemoptysis is possible.
- Other possible signs: fever, weight loss, dysphagia, vomiting, regurgitation, wheezing
- Cats often manifest signs related to metastatic disease to their digits as opposed to respiratory signs.

PHYSICAL EXAM FINDINGS

- Physical exam: usually normal
- Pulmonary nodules due to metastatic disease: physical abnormalities from the primary tumor may be found in other parts of the body.
- In patients with pulmonary nodules, careful evaluation of the more common sites of origin of tumors that metastasize to the lungs is indicated, including the oral cavity, the area of the thyroid, mammary glands, and toenails (especially in cats).
- A rectal exam is essential in every dog with pulmonary nodules (assess prostate, anal sacs, bladder/urethra, sub-lumbar lymph nodes).
- A fundic exam (seep. 1313) and careful dermatologic evaluation (see) may be helpful in identifying disseminated fungal

disease.

ETIOLOGY AND PATHOPHYSIOLOGY

- The main concern with pulmonary nodules is malignancy; neoplasms from virtually any part of the body, including primary lung tumors, may metastasize to the lungs.
- Metastatic neoplasia may reach the lungs via lymphatics or via the bloodstream; both can produce a nodular pulmonary pattern.
- The development of metastasis is a complex, multistep process, and failure to complete any of the steps will prevent the development of a metastatic focus. It is estimated that less than 1 in 100 neoplastic cells that leaves the primary tumor survives the metastatic cascade. This multistep process includes the induction of neovascularization detachment of the tumor cell from the primary tumor, dissolution of the basement membrane and invasion into the bloodstream, evasion of the host immunity and survival in the bloodstream, margination in a new capillary and attachment to the endothelium, dissolution of the basement membrane and extravasation into the extracellular matrix, survival in the new tissue by evading the host immunity, and finally the induction of neovascularization to support continued growth of the new metastatic focus. This neovascularization begins the process again.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis of pulmonary nodules is usually made with a radiographic evaluation. A systematic approach to rule out infectious or granulomatous causes (as warranted by geography) or other foci of neoplasia (i.e., primary lesions elsewhere that have resulted in the identified pulmonary nodules) is paramount.

DIFFERENTIAL DIAGNOSIS

- Solitary lung mass: primary neoplasia, metastatic neoplasia, granuloma, cyst, infarct, localized hemorrhage, focal pneumonia, abscess
- Multiple pulmonary masses: primary or metastatic neoplasia, fungal disease (blastomycosis, histoplasmosis), pulmonary osteomas (rarely more than 3-4 mm in diameter and more radiopaque than soft-tissue nodules because of mineral composition). Bacterial abscesses and granulomas uncommonly cause multiple pulmonary masses.
- One or more cutaneous or subcutaneous nodules, one or more nipples, and intrahepatic mineralizations can be mistaken for focal pulmonary lesions, especially if only one radiographic projection is made.

INITIAL DATABASE

- Thoracic radiographs: the source of initial identification of pulmonary nodules in most cases (less commonly at surgery or necropsy)
- CBC, serum biochemistry profile, urinalysis: typically unremarkable in patients with incidentally discovered pulmonary nodules. Hypercalcemia may occur with neoplasia, fungal, and other granulomatous diseases.
- Pleural effusion, if present, should be sampled and evaluated with fluid and cytologic analysis, and if evidence of infection exists, bacterial culture (aerobic and anaerobic).
- Repeated meticulous physical exam (with particular attention paid to the mammary chains, anal sacs, oral cavity, skin, and digits)

ADVANCED OR CONFIRMATORY TESTING

- Thoracic radiographs: three views if the lesion was found incidentally
- Ultrasonographic studies (of the abdomen and of the heart to screen for primary sites of disease; of the lesion with aspiration for diagnosis if possible)
- CT to assess for lesions too small to be identified with plain-film radiography and/or to be used for CT-guided aspirates or biopsies. See p. 1233.
- The minimum database should be supplemented with fungal serologic examination and microbial (fungal and bacterial) culture based on clinical suspicion and history.
- Thoracotomy with histopathologic evaluation of biopsy specimens. The hilar lymph nodes and lung lobes should be carefully evaluated and sampled as necessary at the time of thoracotomy.

TREATMENT

TREATMENT OVERVIEW

- Resolution of clinical signs (for instance, cough or dyspnea) if present
- Control or elimination of primary disease process (exception: clinically unimportant pulmonary nodules, i.e., pulmonary osteomas)
- Single pulmonary masses are more commonly addressed surgically (focal process).
- Multiple pulmonary masses are usually not addressed surgically, because they typically are part of a generalized process (e.g., neoplastic, fungal). Rather, identifying the underlying cause and systemic (medical) treatment are usually most important.

ACUTE GENERAL TREATMENT

- Once a lesion has been identified, surgical excision should be considered.
  - Treatment of choice for primary pulmonary neoplasia (single pulmonary nodule in which the diagnosis was established with ultrasound- or CT-guided aspiration or biopsy).
- Surgical excision may be considered for solitary pulmonary nodules/masses of unknown tissue type. The slow-growing nature of some single pulmonary nodules means that other concerns (concurrent illnesses, patient age, etc.) may supersede the need for thoracotomy.
- In specific cases, metastasectomy (excision of metastases) can be performed. Consultation with an oncologist is recommended beforehand.

CHRONIC TREATMENT

- Chemotherapy may be attempted for primary pulmonary neoplasia deemed unresectable or with evidence of lymphatic metastasis at the time of diagnosis. Options may include doxorubicin, platinum compounds (cisplatin, carbo-platin), gemcitabine, or vinorelbine.
- Chemotherapy is largely unproven in the management of pulmonary tumors in veterinary medicine.

POSSIBLE COMPLICATIONS

- Hypertrophic osteopathy; typically resolves with removal of pulmonary disease
- Digital or ocular metastasis (cats), particularly with angioinvasive neoplasms

RECOMMENDED MONITORING

- Monthly to quarterly radiographs to assess for recurrence, progression, or changes (cavitation is not uncommon but is often misinterpreted as abscess/infection)
- As required per protocol for chemotherapy patients (i.e., CBC), quality-of-life assessments

PROGNOSIS AND OUTCOME

- Guarded and extremely variable (median survivals in parentheses)
- Dogs with primary lung tumors:
  - 50% of dogs without clinical signs and having peripheral, solitary, small (<5 cm), well-differentiated, low-grade pulmonary adenocarcinomas without lymph node metastasis or pleural effusion have median survival >1 year (12-20 months).
  - In contrast, median survival is shorter (8 months) for patients with clinical signs referable to the pulmonary nodule/mass, or with a large solitary (>5 cm or 100 cm^3) neoplasm, one that involves an entire lobe, squamous cell carcinoma histologically, or nodal metastasis (1-2 months)
- Cats with primary lung tumors: median survival 4 months after lobectomy. Cats with poorly differentiated tumors or enlarged tracheobronchial lymph nodes: median 2 months.

PEARLS & CONSIDERATIONS

COMMENTS

- Metastatic neoplasia is much more common than primary pulmonary neoplasia.
- Half of patients with newly diagnosed pulmonary neoplasia are deemed inoperable because regional or systemic extension is identified at presentation.
- Pulmonary osteomas are benign mineralizations often identified incidentally on the radiographs of older dogs. The diagnosis

of osteoma versus metastasis can be made empirically based on size and relative opacity. The limit of detection for soft-tissue lesions in the pulmonary parenchyma is considered to range from 5-10 mm. Because osteomas are of mineral or bone density, they can be identified in the 2-5 mm range.

- In this author's experience, cats with pulmonary metastases tend to show overt signs, have more advanced disease at the time of presentation, and have markedly shorter survival times than dogs.

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Pulmonary Lymphoid Granulomatosis

BASIC INFORMATION

DEFINITION

Rare lymphoproliferative neoplasm in which infiltrates of atypical lymphoid cells develop around and destroy pulmonary blood vessels

SYNONYMS

PLG, lymphomatoid granulomatosis

EPIDEMIOLOGY

SPECIES, AGE, SEX: Rare in dogs and reported in a single cat. Young to middle-aged adults of either gender are typically affected.

ASSOCIATED CONDITIONS & DISORDERS: Lymphomatoid granulomatosis may be observed in sites other than the lungs, including lymph nodes, liver, heart, spleen, kidneys, pancreas, adrenal gland, or skin.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Nonproductive cough that is unresponsive to treatment with antimicrobials
- Increased respiratory effort
- Lethargy
- Anorexia and weight loss
- Rarely: fever, lameness, peripheral lymphadenopathy, ascites, or vomiting

PHYSICAL EXAM FINDINGS

- Nonproductive cough
- Tachypnea
- Areas of decreased bronchovesicular lung sounds
- Areas of increased bronchovesicular lung sounds
- Peripheral lymphadenomegaly (occasionally)
- Other sites of infiltration may be identified, including the skin

ETIOLOGY AND PATHOPHYSIOLOGY

- In humans, pulmonary lymphoid granulomatosis (PLG) is considered a precursor to low-grade T-cell lymphoma.
- The disease also seems to be T-cell mediated in the few animals studied to date, although T-and B-cell infiltrates have been documented in a single dog.
- Infiltrates of atypical lymphocytes are centered on the vasculature. While pulmonary vasculature is most commonly targeted, other lymphatic tissues or solid organs may be affected as well.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Metastatic pulmonary neoplasia
- Pulmonary lymphoma
- Other primary lung tumors
- Granulomatous fungal pneumonia
- Eosinophilic bronchopneumopathy/pulmonary infiltrates with eosinophils/eosinophilic granulomatosis
- Severe bacterial pneumonia

INITIAL DATABASE

- CBC: leukocytosis, eosinophilia, and basophilia are common.
- Serum biochemistry profile and urinalysis: usually unremarkable
- Heartworm serology: negative
- Thoracic radiographs:
  - Large pulmonary masses or lobar consolidation are typical.
  - An interstitial lung pattern is commonly observed.
  - Tracheobronchial and/or sternal lymph nodes are often enlarged.
  - Pleural effusion is sometimes present.

ADVANCED OR CONFIRMATORY TESTING

- Pulmonary biopsy is the only means of definitive diagnosis. Samples may be obtained via sternal or intercostal thoracotomy, keyhole biopsy, or thoracoscopy.
- Tracheal wash, bronchoalveolar lavage, and fine-needle aspirates may reveal cells suggestive of either inflammation or lymphoma, but cytologic examination cannot confirm a diagnosis of PLG. These tests are, however, useful in ruling out other potential causes of lung disease.

TREATMENT

TREATMENT OVERVIEW

Goals of treatment are to achieve remission via chemotherapy, and provide short-term support for hypoxemia if required.

ACUTE GENERAL TREATMENT

- If required, oxygen supplementation for hypoxemic animals (seep. 1318)
- Chemotherapy protocols (see pp. 675 and 674) similar to those used for treatment of lymphoma, including the use of cytotoxic agents
- Glucocorticosteroids alone will seldom produce remission.

CHRONIC TREATMENT

Chemotherapy should proceed as for lymphoma (see pp. 671 and 675).

POSSIBLE COMPLICATIONS

Extensive and serious adverse reactions, including leukopenia and immune suppression, are possible in response to many chemotherapeutic agents; drug-specific reactions are also possible (e.g., cyclophosphamide-induced sterile hemorrhagic cystitis).

RECOMMENDED MONITORING

- Repeat thoracic radiographs 2-3 weeks after initial chemotherapy and periodically thereafter. The interval between radiographs can be prolonged as the duration of remission endures.
- Periodically assess CBC for dogs receiving chemotherapy for lymphoma; other specific tests may be needed, depending on the chemotherapeutic agent employed (e.g., cardiac ultrasound for dogs receiving doxorubicin).

PROGNOSIS AND OUTCOME

- Guarded
- Many dogs attain durable remission.
- Lymphoma may follow PLG by months to years.

PEARLS & CONSIDERATIONS

COMMENTS

In humans, PLG is regarded as a slowly progressive precursor to lymphoma.

PREVENTION

There is no means to prevent development of PLG.

TECHNICIAN TIPS

Needle aspiration of lung lesions is commonly performed with 23-G needles and a 6- or 12-mL syringe (seep. 1277).

CLIENT EDUCATION

Owners should understand that even if durable remission is achieved, the disease may progress to lymphoma years later.

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Pulmonary Hypertension (Arterial)

BASIC INFORMATION

DEFINITIONS

- Pulmonary hypertension (PH) is defined as elevated pulmonary arterial pressure (PAP) secondary to various disease mechanisms causing cor pulmonale (right ventricular hypertrophy secondary to PH) and eventually right sided heart failure. The World Health Organization (WHO) classification of PH is based on similarities in pathophysiologic mechanisms (see box).
- Pulmonary arterial hypertension (PAH) is a progressive vasoproliferative condition characterized by increased PAP. Patients with PAH by definition do not have significant left heart disease, lung disease, or chronic thromboembolic disease. Idiopathic PAH (formerly primary PH or PPH) is diagnosed when no underlying cause for PH is found, and characteristic histologic abnormalities in small pulmonary arteries can be identified. Histologic abnormalities include intimal, medial, and adventitial proliferation, plexogenic changes consisting of proliferating epithelial cells mixed with myofibroblasts, and necrotizing arteritis. Specific hemodynamic criteria include systolic PAP > 30 mm Hg, diastolic PAP > 20 mm Hg, mean PAP > 25 mm Hg, pulmonary capillary wedge pressure < 15 mm Hg.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs: dependent on underlying cause
- Cats: data on any cause of PH are scant, but PAH associated with congenital cardiovascular shunt is probably underrecognized.

GENETICS & BREED PREDISPOSITION

Depending on underlying cause:

- Myxomatous mitral valve disease in poodles, dachshunds, terriers, and other small breeds
- Chronic obstructive upper airway disease in brachycephalic breeds
- Pulmonary fibrosis in West Highland white terriers

Classification of Pulmonary Hypertension

From WHO classification in Chin KM, Rubin U: Pulmonary arterial hypertension, J Am Coll Cardiol 51:1527-1538, 2008, modified and adapted for the dog

WHOGroup 1:Pulmonary Arterial Hypertension (PAH)

- Idiopathic (formerly primary PH, PPH)
- Associated with congenital systemic-to-pulmonic shunts
- Persistent pulmonary hypertension of the newborn
- Associated with drugs, toxins, inflammatory conditions

Group 2:Pulmonary Hypertension Associated With Left Heart Disease

- Left ventricular or atrial disease
- Left-sided valvular disease

Group 3:Pulmonary Hypertension Associated With Respiratory Disease and/or Hypoxemia

- Interstitial lung disease (e.g., pulmonary fibrosis)
- Chronic upper airway obstruction
- Chronic exposure to high altitude

Group 4:Pulmonary Hypertension Due to Thromboembolic Disease

- Primary pulmonary arterial lesion (e.g., *Dirofilaria immitis, Angiostrongylus vasorum)*

- Medical conditions predisposing to pulmonary thromboembolism

Group 5:Miscellaneous

RISK FACTORS

- Protein-losing nephropathies and enteropathies, hyperadrenocorticism, immune-mediated hemolytic anemia, pancreatitis, neoplasia, heartworm disease are risk factors for pulmonary thromboembolism (PTE).
- Ingestion of snails for infection with *Angiostrongylus vasorum* (French heartworm) in Europe and Newfoundland, Canada
- Septic shock, pancreatitis, other systemic inflammatory states for adult respiratory distress syndrome (ARDS)

GEOGRAPHY AND SEASONALITY

- *Dirofilaria immitis* in endemic areas
- *A. vasorum* in endemic areas, Europe, and Newfoundland, Canada
- High altitude (hypobaric hypoxia) causes or contributes to pulmonary hypertension. Dogs living at 2300 m and 3500 m altitude (7500 ft and 11,500 ft) have a mean arterial Po2 of around 62 mm Hg and 52 mm Hg, respectively, and a mean systolic pulmonary artery pressure of around 30 mm Hg and 40 mm Hg, respectively, as determined by Doppler evaluation of tricuspid regurgitation.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

From an intensive care and therapeutic point of view, PH may be further subdivided into acute and chronic categories. Acute PH may reflect a sudden worsening of a chronic condition causing PH (e.g., left-sided congestive heart failure), or it may be precipitated by an acute condition (e.g., acute respiratory distress syndrome, massive PTE).

HISTORY, CHIEF COMPLAINT

- Depends on underlying cause
- Signs of PH itself or of the underlying cause may predominate.
- Signs associated with PH include:
    - Exercise intolerance
    - Collapse, syncope (reflex bradycardia caused by high resistance to forward flow from the right ventricle)
    - Dyspnea, coughing
    - Abdominal distension
    - Rear limb weakness in reverse patent ductus arteriosus (PDA)
    - Right ventricular hypertrophy as incidental finding during echocardiography or electrocardiography

PHYSICAL EXAM FINDINGS

- PAH: exam may be unremarkable. Possible findings include:
    - Pale mucous membranes
    - Respiratory distress
        - May be precipitated or exacerbated by exercise
    - Tachycardia
    - Weak pulse
    - Signs of right-sided congestive heart failure (distended jugular veins or jugular venous pulse, abdominal distension) o Split second heart sound (pulmonic valve closing after aortic valve)
    - Murmur of tricuspid regurgitation (systolic, right-sided)
    - Murmur of pulmonic regurgitation (rare; diastolic and loudest over left heart base)
    - Cyanosis
    - Red oral and conjunctival mucous membranes due to polycythemia in reverse PDA
    - Differential cyanosis in reverse PDA
- PH with left-sided heart disease: depends on underlying disease; possible findings include:
    - Same as PAH (except polycythemia signs and differential cyanosis)
    - Loud murmur of mitral regurgitation
    - Arrhythmia associated with dilated cardiomyopathy
    - Increased lung sounds

- Crackles
- PH with respiratory disease/hypoxia:
  - Same as PAH (except differential cyanosis)
  - Stertorous breathing in brachycephalic syndrome
  - Cough
  - Increased lung sounds, wheezes, crackles
- PH due to PTE:
  - Same as PAH (except polycythemia signs and differential cyanosis)
  - Cough
  - Hemoptysis
  - Increased lung sounds

ETIOLOGY AND PATHOPHYSIOLOGY

- In PAH, the underlying vascular injury is thought to be a final common response to various inciting factors coupled with genetic susceptibility. Eliciting factors may be mechanical (overperfusion), drugs (experimentally inducible with appetite suppressants), toxins, infections, and genetically determined susceptibility to such injuries.
  - Thrombosis elicited by diseased vessel walls may complicate PAH.
- PH is a common complication of different cardiac and extracardiac diseases and results from two main mechanisms: increased left atrial pressure and increased pulmonary vascular resistance. Important causes are:
  - Cardiac:
    - Pulmonary venous hypertension due to increased left atrial pressure in left myocardial failure, most common in advanced chronic mitral regurgitation, also in dilated cardiomyopathy; cor triatriatum sinister, mitral stenosis
  - Hypoxic vasoconstriction:
    - Chronic obstructive lower airway disease (bronchitis, emphysema)
    - Chronic obstructive upper airway disease
    - High-altitude hypoxia
  - Occlusion of the pulmonary vascular bed:
    - PTE
    - Parasites *(D. immitis, A. vasorum)*
  - Pulmonary parenchymal disease:
    - Pulmonary fibrosis (see p. 615)
    - ARDS
  - Combination of mechanisms (e.g., heartworm infection; *D. immitis, A. vasorum):* obstruction by intravascular parasites, vasculitis, thrombosis, and hypoxic vasoconstriction.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A practical clinical diagnosis of PH is made when high-velocity valvular regurgitation (tricuspid, pulmonic, or both) is documented by Doppler echocardiography in the absence of pulmonic stenosis.

DIFFERENTIAL DIAGNOSIS

- For right-sided heart failure:
  - Congenital cardiac disease: pulmonic stenosis, tricuspid dysplasia, tetralogy of Fallot, tricuspid stenosis, cor triatriatum dexter
  - Acquired cardiovascular disease: severe tricuspid myxomatous valve disease/endocardiosis, right ventricular dilated cardiomyopathy, peri-cardial effusion
- For right ventricular hypertrophy:
  - Pulmonic stenosis, tetralogy of Fallot

INITIAL DATABASE

- Thoracic radiographs; dorsoventral view is particularly important.
  - Document right ventricular and main pulmonary artery enlargement; somewhat nonspecific, as findings of “reversed D” and “increased sternal contact” on the lateral view are often overinterpreted in normal dogs and cats (expiratory films, rotation of patient, thoracic conformation).
  - Peripheral pulmonary vasculature may be tortuous and enlarged.
  - Peripheral pulmonary arterial markings may abruptly stop with PTE.
  - Left atrium is enlarged and pulmonary veins are congested with underlying left atrial, ventricular, or mitral valve

disease.
    - Signs of underlying bronchial, interstitial, or alveolar pulmonary disease may be evident.
- Echocardiogram, dual role:
    - Rule in or out causes of PH, including acquired left ventricular heart disease (myxomatous mitral valve disease, dilated cardiomyopathy) and congenital cardiovascular shunt.
    - Confirmation of PH qualitatively and quantitatively:
        - Qualitatively: characteristic two-dimensional and M-mode findings in moderate to severe PH are dilation of right ventricle and atrium, thickening of right ventricular wall and papillary muscles, paradoxical septal motion, and decreased left ventricular chamber size.
        - Quantitatively: Doppler examination is the most useful noninvasive clinical tool to confirm and quantitate severity of PH.
            - Systolic: velocity of tricuspid regurgitation (TR) correlates to right ventricular systolic pressure, and therefore, barring pulmonic stenosis, to pulmonary arterial systolic pressure. The modified Bernoulli equation allows Doppler-derived blood flow velocities to be used for estimating intracardiac pressures: $PG = 4 \times (Vmax)^2$, where PG is the peak pressure gradient between right ventricle and right atrium, in mm Hg, and Vmax is the peak velocity of tricuspid regurgitation (TR), in m/sec. It is assumed that right atrial pressure approximates 0 mm Hg during ventricular systole, such that the right atrial/right ventricular systolic PG equals systolic right ventricular pressure. A TR-PG > 30mmHg (Vmax > 2.8 m/s) suggests/indicates systolic PH.
            - Diastolic pulmonary artery pressure is calculated with Doppler quantification of pulmonary valve insufficiency (PI) instead of tricuspid regurgitation; by this method, PH is considered to be present when PI-PG is >20 mm Hg (Vmax > 2.2 m/s).
- ECG: document right ventricular hypertrophy (RVH; deep S waves in leads I, II, III, aVF), right axis deviation, and possible arrhythmias; in acute PH, ECG abnormalities may not be present; in chronic PH, marked PH must be present to cause ECG abnormalities. Less sensitive and specific than echocardiography.
- Serology for *D. immitis* and Baermann fecal examination for *A. vasorum*
- Platelet count, coagulation profile, and parameters associated with hypercoagulability (e.g., antithrombin levels, D-dimer levels) may be abnormal with vasculitis and thrombosis.
- Arterial blood gas analysis: may show hypoxemia in primary respiratory disease or right-to-left cardiovascular shunt.
- CBC, biochemistry panel, urinalysis: may show abnormalities suggestive of parasitic disease (eosinophilia, baso-philia), chronic inflammation (throm-bocytosis, hyperglobulinemia), and systemic disease predisposing to PTE (e.g., proteinuria, hypoproteinemia, hypoalbuminemia, increased liver enzyme activities consistent with steroid hepatopathy, increased amylase and lipase activity, and increased pancreatic lipase activity consistent with pancreatitis).

ADVANCED OR CONFIRMATORY TESTING

- Contrast ultrasound (microbubbles) of the heart and descending aorta to rule out cardiovascular right-to-left shunt. Shunt is also possible due to pulmonary arteriovenous fistula secondary to pulmonary hypertension; in this case, bubbles will take at least three cardiac cycles from their appearance in the right atrium until their appearance in the left atrium.
- Right-sided cardiac catheterization for invasive measurement of pulmonary wedge pressure as an estimate of left atrial pressure, systolic and diastolic pulmonary artery pressure; evaluation of therapeutic intervention
- Pulmonary angiography; tortuous pulmonary arteries indicate PH; perfusion deficits are present in PTE.
- Pulmonary CT to identify/rule out parenchymal disease and CT-angiography for PTE
- Pulmonary ventilation/perfusion scintigraphy to rule out PTE
- Pulmonary histopathologic evaluation to confirm PAH

TREATMENT

TREATMENT OVERVIEW

- PH of any genesis with signs referable to right ventricular forward or backward failure: lower pulmonary artery pressure.
- PH of any genesis with signs referable to hypoxia: improve oxygenation.
- PH with known pathogenesis and treatable cause: focus should be to correct/improve underlying disease.

ACUTE GENERAL TREATMENT

Oxygen therapy (cage or nasal). See p. 615.

CHRONIC TREATMENT

There is no randomized trial documenting efficacy of medical treatment in naturally occurring PH in dogs; thus the following are merely treatment considerations:

- Therapeutic trial with amlodipine (Norvasc) in moderate PH, starting at 0.05 mg/kg PO q 24 h and titrating dose based on response and systemic blood pressure (avoid hypotension)
- Anticoagulant therapy with low-dose aspirin, 0.5 mg/kg PO q 12 h (dog)
- Sildenafil (Viagra) in severe PH, 2-3 mg/kg PO q 8-12 h. Improves clinical condition in the absence of significant effects on PAP as estimated by TR-PG.
- Oral L-arginine, a precursor of nitric oxide, may be a simple and useful oral medical treatment; however, there are no studies documenting a positive effect.
- Dedicated owner may consider intermittent oxygen therapy at home.
- Pimobendan may lower PAP.
- Furosemide, ACE inhibitor, spironolactone in cases of overt right-sided congestive heart failure (seep. 470)
- Specific treatment of underlying mechanism or disease in secondary PH (see Heart Failure, Chronic, p. 470; Pulmonary Thromboembolism, p. 940; Heartworm Disease, Dog, p. 477; Heartworm Disease, Cat, p. 474; Acute Respiratory Distress Syndrome, p. 34)

POSSIBLE COMPLICATIONS

- PH: right ventricular failure
- Treatment: systemic arterial hypotension with syncope, prerenal azotemia

RECOMMENDED MONITORING

- Most important are simple clinical parameters: general attitude, exercise tolerance, respiration, severity of ascites
- Systemic blood pressure
- Vmax of TR and PR

PROGNOSIS AND OUTCOME

Depends on underlying disease and stage of disease:

- Good in parasitic pulmonary vasculature disease with acute PH
- Fair in right-to-left cardiovascular shunts, myxomatous mitral valve disease, PH secondary to chronic parasitic pulmonary vasculature disease
- Poor in advanced PAH, advanced pulmonary fibrosis, ARDS, nonparasitic PTE, presence of right-sided heart failure

PEARLS & CONSIDERATIONS

COMMENTS

- Most causes of secondary PH are readily detectable.
- Pulmonary thromboembolism and right-to-left PDA in particular may be missed if not considered.
- Idiopathic PAH is a clinical diagnosis of exclusion and definitive confirmation is available only histologically.
- Newer human drugs to decrease pulmonary artery pressure are very expensive: iloprost = prostaglandin analog for inhalation, and bosentan = endo-thelin antagonist for oral administration.

TECHNICIAN TIPS

Oxygen can be administered to patients with respiratory distress secondary to PH by nasal oxygen catheters, flow-by techniques, or by placing the animal in an oxygen cage. Changes in Pao2 following a change in inspired oxygen concentration require time to be appreciated by an arterial blood gas measurement.

CLIENT EDUCATION

In dogs with cardiac disease, travel to higher altitude (above 7000 feet) may aggravate PH to a clinically relevant degree, owing to hypobaric hypoxia.

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Pulmonary Edema, Noncardiogenic

BASIC INFORMATION

DEFINITION

The well-recognized phenomenon of pulmonary interstitial/alveolar fluid accumulation caused by a disorder other than cardiac congestion

SYNONYMS

Acute respiratory distress syndrome (ARDS), neurogenic pulmonary edema

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs and cats of any age or sex may be affected.

RISK FACTORS

- Acute upper airway obstruction (laryngeal paralysis, brachycephalic upper airway syndrome, critical tracheal collapse, foreign body, mass or infiltration, strangulation, others)
- Electrocution
- Protracted seizures or head trauma
- Major trauma or surgery
- Sepsis or nonseptic systemic inflammatory disease (e.g., pancreatitis, hepatitis)
- Any cause of vasculitis
- Acid aspiration or pneumonia
- Smoke inhalation or other inhaled irritants
- Near-drowning experience
- Drug reaction or overdose

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Cough, tachypnea, and respiratory distress are the most common:
  - Severe edema may cause coughing with expectoration of blood-tinged fluid.
- Other complaints could reflect primary diseases, as already mentioned.

PHYSICAL EXAM FINDINGS

- Acute severe respiratory distress and tachypnea
  - Increased effort noted during inspiration and expiration from increased lung stiffness
- Cyanosis may be present if there is severe alveolar involvement.
- Fine crackles, often at end inspiration and early expiration, in the dorsocau-dal lung fields:
  - Coarse crackles throughout inspiration more often indicate airway disease or progression of an interstitial disease into airways.
  - Crackles may be absent in early or mild edema.
- Lung sounds may be exceptionally quiet in very severe edema, particularly in cats.
- Cardiac murmurs and arrhythmias do not always indicate that edema is of cardiogenic origin.
- Other clinical signs associated with the primary underlying disease process may be present.

ETIOLOGY AND PATHOPHYSIOLOGY

- Pulmonary edema results in arterial hypoxemia and respiratory distress:
  - Hypoxemia is caused by ventilation/perfusión mismatches and, to a lesser extent, diffusion barriers to oxygenation of pulmonary capillary blood.

- Noncardiogenic pulmonary edema arises from three mechanisms:
  - Increased vascular permeability is the most common and is seen with a wide variety of pulmonary and systemic disorders as akeady described.
  - Decreased plasma oncotic pressure, most often from hypoalbuminemia. Pleural effusions (transudative) are more common than pulmonary edema in animals with reduced oncotic pressure as a single driving mechanism.
  - Impaired lymphatic drainage is an uncommon etiology that is usually secondary to neoplasia or lymphangitis.
- Regardless of the mechanism, the edema fluid that infiltrates the interstitial and alveolar spaces is rich in protein (same concentration as plasma), in contrast to cardiogenic pulmonary edema that is characterized by protein-poor fluid.
- Cardiogenic pulmonary edema arises most commonly from increased pulmonary venous hydrostatic pressure secondary to left-sided congestive heart failure (seepp. 468 and 470).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Noncardiogenic edema is typically a secondary phenomenon; recognizing its existence is not analogous to diagnosing the patient's underlying condition. Early differentiation from cardiogenic edema is helpful to discern prognosis and delineate the next diagnostic steps.

DIFFERENTIAL DIAGNOSIS

Any cause of tachypnea, cough, or pulmonary parenchymal infiltration, such as:

- Pneumonia
- Neoplasia
- Fungal disease
- Protozoal infection (e.g., toxoplasmosis in cats)
- Thromboembolic disease
- Complicated bronchial disease
- Inflammatory respiratory disease (i.e., pulmonary infiltrates with eosinophils/eosinophilic bronchopneumopathy)
- Pulmonary contusions
- Cardiogenic pulmonary edema

INITIAL DATABASE

- Thoracic radiographs: “fluffy” interstitial opacities that may progress to an alveolar pattern.
  - Opacities are most often in the caudodorsal lung fields with edema caused by increased vascular permeability (similar to cardiogenic edema).
  - Absence of cardiac and pulmonary venous abnormalities can help distinguish cardiogenic from noncardiogenic edema.
- CBC, biochemical profile, urinalysis, and other tests deemed clinically appropriate may be helpful in determining underlying causes (e.g., pancreatitis, sepsis).
- Historic information may help confirm underlying causes, such as electrocution, major trauma, or near-drowning experience.

ADVANCED OR CONFIRMATORY TESTING

- Respiratory washes or lung aspiration do not often yield abnormalities; occasionally, a primary pulmonary disorder is detected.
- Arterial blood gas (ABG) analysis:
  - Hypoxemia
  - Hypocapnia
  - Widened alveolar-arterial (A-a) gradient
- The ratio of protein content of expectorated edema fluid (E) to circulating plasma protein content (P) in noncardiogenic edema is 79%-90%, whereas E:P ratio in cardiogenic edema is typically <50%. Protein may be measured by refractometer or with biochemical methods.

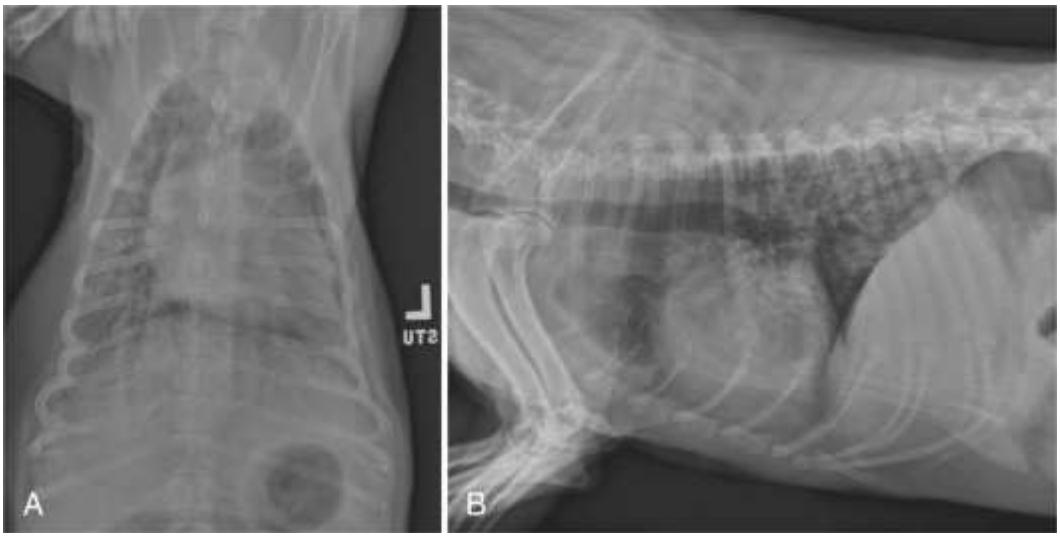
TREATMENT

TREATMENT OVERVIEW

- Improve oxygenation and support respiratory function.
- Minimize stress in severely distressed animals that could experience cardio-pulmonary arrest from simple manipulations.
- Provide other supportive care while primary causes are identified and treated.

ACUTE GENERAL TREATMENT

- Administer oxygen:
  - Face mask, nasal catheter, or oxygen cage (seep. 1318)
- Relieve anxiety and minimize unnecessary oxygen consumption:
  - Light sedation if needed:
    - Dogs: morphine, 0.1-1 mg/kg IV
    - Cats and dogs: acepromazine, 0.03-0.05 mg/kg IV, IM, or SQ
- Diuretics may be overall less beneficial for animals with noncardiogenic (versus cardiogenic) pulmonary edema; the greatest response if noted is usually seen in the initial 24-48 h
  - Furosemide: 2-4 mg/kg IV q 4-12 h
- Bronchodilators may combat bronchospasm, enhance mucociliary function, and diminish diaphragmatic fatigue:
  - Aminophylline, theophylline: dogs, 5-10 mg/kg PO, IV, IM q 8-12 h cats, 5 mg/kg PO, IV, IM q 8-12 h



PULMONARY EDEMA, NONCARDIOGENIC A-B, Dorsoventral and lateral radiographic projection in a Lhasa apso, depicting noncardiogenic pulmonary edema, primarily of caudal lung fields. Note normal cardiac and pulmonary venous structures. Pulmonary edema was thought to be the result of an inhaled irritant (repeat exposure to the substance at a later date produced the same response).

CHRONIC TREATMENT

- Specific therapies that address underlying cause
- Intubation and positive-pressure ventilation (IPPV; see p. 1362) may be necessary in severe cases:
  - IPPV constitutes the treatment of choice for critically dyspneic animals with noncardiogenic pulmonary edema caused by a reversible event (e.g., airway obstruction).

POSSIBLE COMPLICATIONS

- Secondary pneumonia
- Pulmonary thromboembolism
- Fluid therapy may exacerbate fluid exudation into the pulmonary interstitium and should be administered cautiously if at all in animals with pulmonary edema from any cause.
  - Intravenous infusions of vasoactive agents such as dopamine (2.5-10 mcg/kg/min) and/or dobutamine (2.5-20 mcg/kg/min) may help support euvolemic animals with severe systemic hypotension.

RECOMMENDED MONITORING

- Respiratory rate and effort
- Thoracic radiographs
- Blood gas analysis or pulse oximetry
- Monitor hydration status by evaluating volume-related changes

  - Cardiac output, arterial blood pressure
  - Pulmonary capillary wedge pressure
  - Serial packed cell volume (PCV), total protein (TP), electrolyte assays
  - Renal function tests, urine output
  - Body weight
- Underlying disease state

PROGNOSIS AND OUTCOME

- Prognosis guarded to poor
- Depends upon severity of the respiratory dysfunction and underlying disorder
- Early intervention, aggressive treatment, and intensive monitoring can improve outcomes.

PEARLS & CONSIDERATIONS

TECHNICIAN TIPS

- Providing supplemental oxygenation and minimizing unnecessary handling is prudent to avoid acute respiratory compromise during diagnostic evaluation.
- Patients with marked respiratory distress are likely to be more tolerant of thoracic radiographs obtained in ventral recumbency.
- Search online for constant-rate infusion (CRI) calculators to facilitate dose and administration calculations.

PREVENTION

- Avoid leaving unsupervised puppies and kittens in environments where electrical cords could be easily reached.
- Early evaluation in cases of suspected inhalant injury or drug reaction

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Pulmonary Edema, Cardiogenic

BASIC INFORMATION

DEFINITION

Extravasation of fluid from the pulmonary vasculature into the interstitial and alveolar spaces as a result of elevated pulmonary venous hydrostatic pressure. Hallmark abnormality of left-sided congestive heart failure (CHF).

SYNONYM

Pulmonary congestion

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dependent on underlying cause

GENETICS & BREED PREDISPOSITION

Predisposition reflects breed predilection for underlying heart diseases (e.g., cardiomyopathies, myxomatous mitral valve disease).

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Varies with severity of fluid accumulation
- Tachypnea or exertional dyspnea
- Dry cough (uncommon in cats)
- Open-mouth breathing (cats)
- Difficulty breathing in lateral recumbency; trouble sleeping

PHYSICAL EXAM FINDINGS

- Auscultation can vary (absence of auscultable abnormalities or presence of cardiac murmurs, gallop sounds, and arrhythmias).
- Lung sounds: crackles and wheezes possible during both inspiration and expiration.
- Femoral pulse strength might vary based on cardiac output and arrhythmias.
- Severe cardiogenic pulmonary edema may produce pink-tinged secretions from mouth and nares.
- Cyanosis

ETIOLOGY AND PATHOPHYSIOLOGY

- In cardiogenic pulmonary edema, fluid moves from the pulmonary vasculature to the interstitial space as a result of elevated hydrostatic pressure in the pulmonary capillaries.
- This is in contrast to noncardiogenic pulmonary edema, in which fluid extravasates as a result of increased pulmonary vascular permeability.
- Elevated pulmonary capillary pressures secondary to left-sided heart failure:
    - Left ventricular volume overload caused by:
        - Primary valve disease (mitral or aortic insufficiency). Causes include myxomatous valve disease/endocardiosis, endocarditis, valve dysplasia, and mitral valve stenosis.
        - Primary heart muscle disease (dilated cardiomyopathy in dogs, various cardiomyopathies in cats)
        - Congenital left-to-right cardiac shunts (patent ductus arteriosus, aorticopulmonary window, atrial septal defect, ventricular septal defect, arteriovenous fistula)
        - Iatrogenic (overzealous fluid therapy)
        - Severe anemia
    - Left ventricular dysfunction:
        - Arrhythmias
        - Ischemic disease (rare)
        - Myocarditis

- Thyrotoxic cardiac disease
- Sepsis
- Myocardial toxins (i.e., chemotherapeutic agents such as doxorubicin)
- Constrictive pericarditis.
- Obstructive disease of the left atrium (rare): neoplasia, thrombus, cor triatriatum sinister.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Pulmonary edema is suspected when a patient is presented for evaluation of cough, dyspnea, or orthopnea/discomfort/restlessness. Suspicion is heightened if a cardiovascular abnormality such as a heart murmur is present. Still, many patients have such signs from coexisting disorders (without pulmonary edema), and thoracic radiographs are required for confirmation.

DIFFERENTIAL DIAGNOSIS

- Other causes of pulmonary edema (e.g., head trauma, seizures, electrocution) versus other cause for coughing and dyspnea:
  - Primary lower respiratory disease (pneumonia, bronchitis, heartworm disease, neoplasia)
  - Upper airway disease (collapsing trachea, tracheitis)
- Expiratory-phase radiographs
- Obesity

INITIAL DATABASE

- Thoracic radiographs: interstitial and/or alveolar infiltrates are present, primarily in the caudal dorsal region (perihilar region in dogs). With severe disease, the pulmonary opacities can occur throughout the lung fields. A large cardiac silhouette, particularly with left atrial enlargement, is common.
- CBC: usually normal. Abnormalities may suggest a noncardiogenic cause (severe anemia, increased white blood cell count may suggest sepsis).
- Serum biochemistry panel: electrolyte abnormalities/azotemia from concurrent renal failure or previous diuretic usage, increased liver enzymes from passive congestion
- Urinalysis: usually unremarkable except with systemic disorders
- Electrocardiogram (ECG): sinus tachycardia may be present with ectopic premature contractions (depends on severity of cardiac disease and underlying etiology). The presence of atrial enlargement (wide and/or tall P waves) and left ventricular enlargement (tall R waves) are sensitive (although nonspecific) for chronic chamber enlargements.

ADVANCED OR CONFIRMATORY TESTING

- Echocardiography: cannot identify pulmonary edema but can pinpoint underlying cardiac disorder
- Right heart catheterization: pulmonary capillary wedge pressure can be measured using a Swan-Ganz catheter: this is a surrogate for left atrial pressure (pressures > 20 mm Hg are indicative of cardiogenic pulmonary edema). Rarely performed clinically.
- Measurement of plasma BNP and ANP levels: may help distinguish between cardiac and noncardiogenic causes of congestive heart failure.
- Response to treatment: administration of appropriate doses of diuretics should be followed by improvement/resolution of radiographic markings in 24-48 hours.

TREATMENT

TREATMENT OVERVIEW

Three main goals: (1) reduction of excessive pulmonary venous return (preload); (2) reduction of systemic vascular resistance (afterload); and (3) inotropic support in a subset of patients (see pp. 468 and 470)

ACUTE GENERAL TREATMENT

- Avoid/reduce stress.
- Oxygenation
- Intravenous furosemide (2-5 mg/kg in dogs, 2-4 mg/kg in cats) q 1-2 h until labored respirations and respiratory rate decrease to normal, then decrease the dose of furosemide and frequency of administration based on clinical response.

- Furosemide constant rate infusion IV CRI for refractory cases (0.7-1 mg/kg/h, cats and dogs). The authors have used up to 2 mg/kg/h. If starting a CRI, initially give a 2 mg/kg IV bolus, then start the CRI. Judicious monitoring of blood pressure and renal function is necessary.
- ± Nitroprusside (see p. 468)
- ± Dobutamine (see p. 468)

CHRONIC TREATMENT

See Heart Failure, Chronic (p. 470)

POSSIBLE COMPLICATIONS

Pulmonary edema eventually returns despite medical therapy (lesion progression).

RECOMMENDED MONITORING

- Thoracic radiographs to assess response to therapy. A 12- to 24-hour lag period between clinical improvement and radiographic improvement is common, however.
- Serum electrolytes and renal status
- Respiratory status

PROGNOSIS AND OUTCOME

Long-term prognosis is guarded because underlying disease is rarely cured. Exceptions can include correctable congenital defects (patent ductus arteriosus, pulmonic stenosis, others) and taurine-responsive dilated cardiomyopathy.

PEARLS & CONSIDERATIONS

COMMENTS

Owners should monitor resting respiratory rate at home. If it increases by more than 25% for 2 days in a row, a call to the veterinarian is warranted.

CLIENT EDUCATION

- Monitor for recurrence of presenting signs (see History, Chief Complaint above).
- Rapid deterioration is possible; rechecks necessary.

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EDITOR: ETIENNE CÔTÉ

Pulmonary Contusions

BASIC INFORMATION

DEFINITION

A pulmonary contusion is a lesion consisting of intrapulmonary hemorrhage and inflammation secondary to blunt trauma.

SYNONYM

Traumatic lung injury

EPIDEMIOLOGY

SPECIES, AGE, SEX

Young male dogs are at increased risk of trauma.

GENETICS & BREED PREDISPOSITION

None; larger dogs are more likely to roam unsupervised.

RISK FACTORS

Free-roaming behavior

GEOGRAPHY AND SEASONALITY

More common in warmer months

ASSOCIATED CONDITIONS & DISORDERS

- Pneumothorax
- Diaphragmatic hernia
- Flail chest
- Hit by car (HBC) injury
- Fracture

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

Traumatic event; increased respiratory rate and effort

PHYSICAL EXAM FINDINGS

- External evidence of trauma: cutaneous abrasions or lacerations, fractures
- Increased respiratory rate and effort
- Increased bronchovesicular sounds
- Pale mucous membranes
- Tachycardia

ETIOLOGY AND PATHOPHYSIOLOGY

- Trauma results in intraparenchymal pulmonary hemorrhage. Extracapillary hemorrhage results in the recruitment of inflammatory cells and protein into the alveolar and interstitial spaces.
- Pulmonary hemorrhage results in ventilation/perfusion mismatch and subsequent hypoxemia.
- Sequelae of pulmonary contusion may vary from very mild to rapidly fatal.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Suspected clinically because of association with blunt trauma; clinical confirmation is generally radiographic.

DIFFERENTIAL DIAGNOSIS

- Nontraumatic pulmonary hemorrhage (anticoagulant rodenticide, neoplasia)
- Congestive heart failure (pulmonary edema)
- Pneumonia
- Pain (tachypnea)

INITIAL DATABASE

- Thoracic radiographs: document a patchy to diffuse interstitial alveolar pattern.
  - Radiographic changes may lag behind clinical signs.
  - May be indistinguishable from other patchy interstitial infiltrates, especially pulmonary edema in cats
- CBC, serum biochemistry profile: generally unremarkable

ADVANCED OR CONFIRMATORY TESTING

- Arterial blood gas (ABG) analysis (seep. 1196) or pulse oximetry may be useful to characterize the degree of hypoxemia. These are especially useful for determining whether tachypnea is due to pain (results are normal) or pulmonary lesions (hypoxemia commonly observed).
- Central venous pressure monitoring (seep. 1227), pulmonary wedge pressure measurement: Assess right- and left-sided vascular pressures, respectively (helps rule out cardiogenic causes). Pulmonary wedge pressure specifically assesses the propensity for pulmonary edema but is a somewhat cumbersome procedure and is especially challenging in cats and small dogs.

TREATMENT

TREATMENT OVERVIEW

Treatment goals are to maintain adequate intravascular volume but avoid overhy-dration, which may worsen pulmonary contusions, and to provide supplemental oxygen and rest.

ACUTE GENERAL TREATMENT

- Judicious administration of IV fluids as needed to maintain perfusion
  - Administration of boluses of 5-10 mL/kg of crystalloid fluids (e.g., lactated Ringer's solution) until adequate blood pressure (BP) and pulse quality are obtained
- Administration of supplemental oxygen
- Evaluation for other associated injuries
- Note that glucocorticoids, antibiotics, and diuretics are not indicated for treatment of pulmonary contusions.

POSSIBLE COMPLICATIONS

- Infection (rare)
- Respiratory failure
- Severe pulmonary contusion may require intermittent positive-pressure ventilation (see p. 1362) with positive end-expiratory pressure (PEEP) and/or may progress to acute respiratory distress syndrome (ARDS).

RECOMMENDED MONITORING

- Hourly respiratory rate and effort
- Pulse oximetry

PROGNOSIS AND OUTCOME

Guarded to good prognosis. Most animals surviving a trip to the hospital will also survive pulmonary contusions with appropriate supportive care. Concurrent injuries (e.g., vertebral body fractures) are more likely to compromise the prognosis; other than very severe cases, pulmonary contusions are generally incidental findings that resolve with supportive care.

PEARLS & CONSIDERATIONS

COMMENTS

Avoid excessive volume resuscitation; administer IV fluids judiciously, and adjust the rate frequently based on the animal's response and evolution of the case.

PREVENTION

Prevent roaming.

CLIENT EDUCATION

Pulmonary contusions are “lung bruises;” the injured animal will often get worse over the first 24 hours, and then the lesions regress in the following 48 hours.

SUGGESTED READING

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AUTHOR & EDITOR: ELIZABETH ROZANSKI

Ptyalism

BASIC INFORMATION

DEFINITION

Production of excessive amounts of saliva, commonly manifested as drooling

SYNONYMS

Hypersalivation, polysialia, sialonhea

EPIDEMIOLOGY

SPECIES, AGE, SEX

- No species, age, or sex predilection except as dependent on underlying etiology
- Young animals: portosysternie shunts, seizure disorders
- Older animals: oral neoplasia, such as malignant melanomas (dogs), and squamous cell carcinoma (cats)

GENETICS & BREED PREDISPOSITION

Predisposition dependent on underlying cause

RISK FACTORS

- Trauma of oral/pharyngeal region or nerves
- Exposure to toxins
- Esophageal disorders (esophagitis, esophageal obstruction)
- Oral foreign bodies
- Severe dental disease and/or dental abscesses
- Metabolic or physical disorders causing nausea or abdominal pain
- Primary or secondary neurologic disorders affecting saliva production
- Nausea
- Unvaccinated pets exposed to contagious diseases that may cause oral lesions or metabolic disorders

CONTAGION & ZOONOSIS

- Zoonotic: rabies
- Contagion: viral infections causing oral lesions, such as calicivirus in cats

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

All or some may be present:

- Dysphagia
- Pawing at mouth
- Halitosis
- Oral discomfort with oral or pharyn-geal causes
- Anorexia or weight loss
- Coughing and/or dyspnea (from aspiration pneumonia)
- Gagging or retching with esophageal or gastric causes
- Seizures, facial twitching, behavioral changes possible with intoxications or portosystemic shunts

PHYSICAL EXAM FINDINGS

- Saliva around mouth, salivary staining of fur

- Oral lesions, including masses, foreign bodies, abscesses, stomatitis, gingivitis, or other dental diseases
- Swelling of salivary glands, facial paralysis, atrophy of temporal or facial muscles
- Loss of gag reflex, inability to use tongue, dysphagia
- Mentation changes, seizures, tremors, or anxiety
- Painful abdomen
- Nausea

ETIOLOGY AND PATHOPHYSIOLOGY

Etiology:

- Oral lesions: stomatitis, gingivitis, dental disease, neoplasia, foreign bodies
- Neurologic: peripheral nerve injury affecting swallowing, movement of tongue, pharynx; central nervous system (CNS) lesions, including neoplasia and infectious disorders such as rabies and feline infectious peritonitis (cats)
- Neuromuscular disorders (myasthenia gravis causing megaesophagus; masticatory myositis, muscular dystrophies)
- Metabolic: hepatic disease (portosystemic shunts), renal disease, nausea
- Toxins: caustic or noxious substances, pesticides (organophosphates), drugs (marijuana)
- Immune disease: polymyositis, pemphigus
- Pain, anxiety, excitement, fear

Pathophysiology:

- Oral secretions are produced by sub-mandibular, parotid, and sublingual salivary glands. Innervation to salivary glands is controlled by the autonomic nervous system, with primary control by the parasympathetic nervous system. Many environmental, physical, or metabolic events may stimulate increased saliva production.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A complete medical history and thorough oral examination, possibly under sedation, will often lead the clinician in the right direction for diagnosis. For instance, an outdoor cat with acute onset of drooling may have oral ulcers, evidence of intoxication, or a foreign body.

DIFFERENTIAL DIAGNOSIS

Ptyalism must be differentiated from drooling caused by certain conformations of the lips (but in which the amount of saliva produced by the salivary glands is normal). History (ptyalism is usually recent in onset, whereas conformation-associated drooling is chronic) and physical examination of the lips are generally sufficient for correct identification.

INITIAL DATABASE

- CBC to evaluate for anemia and evidence of infectious/inflammatory disease
- Serum biochemistry profile and urinalysis to evaluate for metabolic disorders
- Neurologic exam (seep. 1311)
- Thoracic, abdominal, and neck/head radiographs

ADVANCED OR CONFIRMATORY TESTING

- Oral examination with sedation or anesthesia
- Serum bile acids if history, exam, and minimum database consistent with liver disorder
- Abdominal ultrasound
- Electroencephalogram/CT scan, and MRI to evaluate CNS lesions
- Endoscopy to evaluate esophageal or gastric lesions
- Toxin screens
- Specific tests, such as acetylcholine (ACh) receptor antibody testing for myasthenia gravis

TREATMENT

TREATMENT OVERVIEW

Ptyalism is a sign of a predisposing disorder; therefore treatment is aimed at resolution of underlying cause

ACUTE GENERAL TREATMENT

Supportive and nonspecific; possible use of anticholinergics and antinausea or antianxiety medications; identification of underlying etiology and prevention of aspiration

CHRONIC TREATMENT

Treatment as appropriate for underlying etiology. Although surgical ligation or transposition of salivary ducts is sometimes performed in people with ptyalism, this surgery is usually not indicated in animals.

BEHAVIOR/EXERCISE

Behavioral modification and anti-anxiety medication for stress-related hypersalivation

POSSIBLE COMPLICATIONS

- Anticholinergics often cause tachycardia, constipation, and behavioral changes; these require frequent dosing. Antiemetics such as chlorpromazine may cause sedation.
- Antisialagogues may reduce salivary output but do not correct the underlying problem.
- Antianxiety medications may cause sedation, anorexia, gastrointestinal upset.

RECOMMENDED MONITORING

Monitor signs, including coughing, breathing difficulty, and fever, which may suggest aspiration of excessive saliva.

PROGNOSIS AND OUTCOME

Fair to guarded prognosis depending on response to treatment of underlying etiology of disorder. Removal of foreign bodies, resolution of dental disease, repair of traumatic injury, and response to decontamination may have very favorable outcomes. Prognosis may be guarded with more serious disease processes such as immune diseases and neoplasia.

PEARLS & CONSIDERATIONS

COMMENTS

Ptyalism is usually a sign of a more serious disorder and deserves attention aimed at identifying the underlying cause. In addition, many owners find that their pets' hypersalivation is unacceptable even if caused by minor problems and may cause them to choose euthanasia for the animals.

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Pseudorabies

BASIC INFORMATION

DEFINITION

Disease caused by infection with pseudorabies virus (PRV), an alphaherpesvirus in the family Herpesviridae. An economically important disease of swine, pseudorabies is capable of causing subclinical, neurologic, or respiratory disease in pigs and causing a rare but severe and almost inevitably fatal central nervous system (CNS) disease in dogs and cats.

SYNONYMS

Aujeszky's disease, mad itch, bulbar paralysis

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs and cats are sporadically affected with pseudorabies (uncommon). Pigs are the primary reservoir of the virus because they have become well adapted to the virus and are often only subclinically affected.

RISK FACTORS

- Pets living in areas where pseudorabies virus is enzootic in the swine population
- Feeding raw pork from endemic areas to dogs and cats

CONTAGION & ZOONOSIS

- Pseudorabies virus may be found in porcine respiratory secretions, saliva, blood, and in the CNS and tonsillar tissues. Dogs and cats are commonly infected via the oral route after ingesting contaminated porcine tissue. Pseudorabies has also reportedly been transmitted to a dog by either biting or being bitten by an infected pig.
- Pseudorabies is not considered a zoonotic disease.

GEOGRAPHY AND SEASONALITY: Pseudorabies can be found in most countries of the world except Australia.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

Acute onset and rapid progression of neurologic signs until death occurs (usually within 48 hours of disease onset). Initial signs may include lethargy, depression, restlessness, or aggression and occasionally vomiting and diarrhea. Hypersalivation is commonly noted. Intense pruritus, usually of the head region, is probably the most clinically striking and consistent sign of pseudorabies. Animals will frequently excoriate the skin of the face and ears secondary to violent scratching.

PHYSICAL EXAM FINDINGS

- Pruritus with swelling, erythema, excoriation, or ulceration of the skin secondary to self-mutilation, especially of the face and head. Intense scratching may include rubbing the head against floors or walls.
- Altered mentation
- Ptyalism
- Cranial nerve deficits indicative of a brainstem lesion(s)
- Dyspnea secondary to severe pulmonary edema
- Seizures
- Anisocoria and a hoarse voice (see p. 1172) are highly consistent signs in cats.

ETIOLOGY AND PATHOPHYSIOLOGY

- Once infection with pseudorabies virus has occurred, the virus travels retrograde along peripheral nerves from the site of inoculation to the CNS.
- Damage to brain parenchyma results from inflammation and interference of normal neuronal function by the virus.
- Microscopic lesions are located almost exclusively in the brainstem. The incubation period for pseudorabies in dogs and cats

is 3-6 days.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is suspected in dogs with a history of exposure to pigs or raw pork products. Dogs present with severe, acute pruritus of the head and neck. Confirmation requires histopathologic evaluation of the brainstem.

DIFFERENTIAL DIAGNOSIS

- Rabies
- Canine distemper
- Neurotoxicoses

INITIAL DATABASE

- A provisional diagnosis of pseudorabies is usually made on clinical suspicion of the disease. Confirmatory testing is required for definitive diagnosis.
- There are no characteristic hematologic or biochemical abnormalities associated with pseudorabies.

ADVANCED OR CONFIRMATORY TESTING

- Cerebrospinal fluid analysis may show increased protein and mononuclear pleocytosis.
- Definitive diagnosis of pseudorabies has classically been made postmortem. Histopathologic abnormalities are generally limited to the brainstem and include perivascular cuffing, multifocal gliosis, neuronal degeneration, and weak eosinophilic inclusions within the nuclei of glial cells and neurons.
- Immunohistochemical techniques can be used for identifying viral antigen in fixed tissue sections (brain, tonsils).
- Alternatively, inoculation of cell cultures with brain homogenate for virus isolation can be performed. Cultures are observed for cytologic changes characteristic of herpesvirus infection, and immunofluorescent techniques can be applied to the cultures to identify pseudorabies virus.

TREATMENT

TREATMENT OVERVIEW

With very few exceptions, the treatment of pseudorabies in dogs and cats is futile, owing to a generally unavoidable fatal outcome. If treatment is initiated, it is aimed at controlling the major clinical signs and providing supportive care until the animal recovers (rare) or dies.

ACUTE GENERAL TREATMENT

- Heavy sedation or anesthesia as required for control of self-mutilation and/or seizures
- IV fluids if needed and patient not showing dyspnea
- Furosemide (1-3 mg/kg IV, IM, or PO q 6-12 h) for pulmonary edema if causing dyspnea

PROGNOSIS AND OUTCOME

Grave prognosis; despite treatment, death usually occurs within 2-3 days of the onset of clinical signs.

PEARLS & CONSIDERATIONS

COMMENTS

Vaccination of dogs and cats against pseudorabies virus (usually in endemic areas) is possible but of questionable efficacy in the prevention of disease.

PREVENTION

Preventing contact with infected pigs or contaminated pork products is paramount to the prevention of pseudorabies in dogs and cats.

SUGGESTED READING

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1ST EDITION AUTHOR: JODI SMITH

Pseudocyesis

BASIC INFORMATION

DEFINITION

A common syndrome observed in nonpregnant diestrous or early anestrous bitches. It is characterized by different degrees of maternal behavior, mammary gland enlargement, and lactation.

SYNONYMS

Nervous anorexia, pseudopregnancy, overt false pregnancy

EPIDEMIOLOGY

SPECIES, AGE, SEX

Postpubertal female dogs of any age; has not been described in cats

GENETICS & BREED PREDISPOSITION

Any breed; incidence is higher in dalmatian, basset hound, and pointer-breed dogs. German shepherds are rarely affected.

RISK FACTORS

Exogenous administration of progestins, diestrous ovariectomy, and hypothyroidism may trigger its occurrence.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Depending on intensity of clinical signs:

- Covert (physiologic although recognizable from the rest of the estrous cycle)
- Overt, where manifestations can become a clinical problem (clinical pseudocyesis)

HISTORY, CHIEF COMPLAINT

- Estrus 6-12 weeks earlier without an ensuing pregnancy
- Chief complaints: mammary problems (engorgement, lactation, licking of the glands) and abnormalities associated with aberrant maternal behavior (nesting, digging, adoption of animals or objects)
- Depression or anxiety, anorexia, and excessive vocalization (whining) are possible.

PHYSICAL EXAM FINDINGS

- Mammary enlargement, ranging from turgid nipples to painful engorgement and galactostasis:
  - Most evident in the caudal pair of glands
- Intramammary dermatitis is occasionally present if excessive licking occurs.
- Mastitis may also be present.

ETIOLOGY AND PATHOPHYSIOLOGY

- The high plasma concentration of prolactin at the end of the luteal phase, when progesterone concentrations decrease abruptly, is associated with the development and maintenance of pseudocyesis.
- Individual and breed sensitivity to these hormonal changes and environmental factors have been hypothesized to influence its occurrence.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected in any diestrous, nonpregnant bitch with mammary enlargement (and milk secretion) in which other mammary disease has been ruled out. Diagnostic imaging confirms absence of pregnancy if necessary.

DIFFERENTIAL DIAGNOSIS

- Pregnancy
- Pyometra
- Mastitis
- Mammary tumors
- Any other cause of anorexia, depression, or anxiety should be ruled out.
- Pseudocyesis can coexist with pyometra, mastitis, and mammary tumors.

INITIAL DATABASE

CBC results are unremarkable.

ADVANCED OR CONFIRMATORY TESTING

Ultrasonographic or radiographic confirmation of the absence of pregnancy or pyometra

TREATMENT

TREATMENT OVERVIEW

Treatment mainly consists of the administration of prolactin-decreasing drugs (dopamine agonists or antiserotonergic compounds).

ACUTE GENERAL TREATMENT

- Administer dopamine agonists with food to reduce digestive side effects: Cabergoline, 5 mcg/kg PO q 24 h for 5-7 days, is a safer choice compared to other prolactin-decreasing compounds.
- Avoid steroid hormones (progestins/androgens); they usually postpone the problem.
- Treat mastitis (see p. 688), acute moist dermatitis (see p. 30).

CHRONIC TREATMENT

Clinical chronic, unresponsive, or recurring pseudocyesis cases should be treated surgically (ovariectomy) after the acute phase of the syndrome has been controlled or during anestrus.

NUTRITION/DIET

No benefit from short-term partial food restriction

BEHAVIOR/EXERCISE

- Discourage maternal behavior, using aversion methods.
- Avoid stimulation of the mammary glands (e.g., padding [either hot or cold], touching, or milking).
- If necessary, Elizabethan collars can be used for preventing licking and self-milking.

DRUG INTERACTIONS

- Avoid administering phenothiazine drugs during pseudocyesis; they increase plasma prolactin concentrations.
- Do not administer antiserotonergic drugs (e.g., metergoline) for anxious and restless bitches because this could potentiate pseudocyesis behavior.

POSSIBLE COMPLICATIONS

- Mammary dermatitis and mastitis (seep. 688) are the most frequent complications and may have an influence in perpetuating the problem.
- Repeated episodes of pseudocyesis have been hypothetically associated with the future development of mammary tumors.

RECOMMENDED MONITORING

Follow up cases until complete resolution. If pseudocyesis does not resolve spontaneously, look for predisposing

PROGNOSIS AND OUTCOME

Pseudocyesis typically resolves spontaneously within a few weeks (2 or 3 weeks) from its onset but can occasionally persist until the next estrous cycle.

PEARLS & CONSIDERATIONS

COMMENTS

- Pseudocyesis is a good indicator of ovulatory estrous cycles.
- Predisposed bitches usually suffer the syndrome after each estrous cycle, with the disorder becoming more severe throughout life.

PREVENTION

- Ovariectomy in predisposed bitches
- Pregnancy does not prevent future episodes.

CLIENT EDUCATION

Teach clients to recognize pseudocyesis and to ask for treatment if it becomes clinically relevant.

SUGGESTED READING

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AUTHOR: CRISTINA GOBELLO

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Pruritus

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

The unpleasant sensation that triggers the desire to scratch, chew, rub, lick, or bite at the skin

SYNONYM

Itch

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Common in dogs and cats
- Sex and age of onset depend on the underlying etiology.
- Contagious acarioses (mite infestations) are more common in young animals.
- Canine atopic dermatitis is first seen in young adults (6 months to 3 years of age).
- Food allergy, although seen most commonly in young adults, may develop at any age.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

Animals scratch, chew, rub, lick, or bite at the skin. In addition, cats can be secretive lickers and present only for extensive self-induced alopecia.

PHYSICAL EXAM FINDINGS

- Skin lesions vary according to etiology.
- Self-induced alopecia, excoriation, and erythema are common findings.
- Typically, no primary skin lesions are noted in canine atopic dermatitis.
- Papules and/or pustules are noted in infectious or parasitic conditions.
- In cats: miliary dermatitis, eosinophilic granuloma complex, self-induced symmetric alopecia, or self-induced ulcerative facial dermatitis.

ETIOLOGY AND PATHOPHYSIOLOGY

- Etiologies of pruritus are numerous.
- For most parasitic infestations, a hyper-sensitivity reaction develops and is responsible for most if not all of the pruritus (often disproportionate to the number of parasites found).
- Pyoderma and yeast dermatitis are frequent causes of pruritus in dogs but are uncommon in cats.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Causes of pruritus are numerous, and the history (notably environment) and physical exam (e.g., lesion distribution) help focus the differential diagnosis. Diagnostic procedures aimed at identifying infections or infestations should be selected first, as these disorders are common, and treatment is generally straightforward. A precise diagnosis is necessary to administer a specific treatment.

DIFFERENTIAL DIAGNOSIS

- Parasitic: fleas, contagious acarioses (*Sarcoptes, Notoedres, Cheyletiella, Otodectes* spp.), lice, *Trombicula* (chiggers), and *Pelodera* spp.

- Bacterial: staphylococcal pyoderma
- Fungal: *Malassezia* sp. dermatitis and otitis
- Allergic: flea bite hypersensitivity, atopic dermatitis, food hypersensitivity, contact hypersensitivity, drug reaction
- Miscellaneous: calcinosis cutis, cutaneous lymphoma

INITIAL DATABASE

- Complete history and dermatologic examination (see p. 1248)
  - Skin scrapings
  - Skin cytologic examination
  - Wood's lamp and dermatophyte culture (in cats)

ADVANCED OR CONFIRMATORY TESTING

- Therapeutic trial with broad-spectrum antiparasitic agents (this is an integral part of the case work-up) is always indicated whenever there is a possibility of a parasitic problem, even if it is low, and in spite of negative skin scrapings.
- Clinicians occasionally use therapeutic trials with antibiotics or antifungal agents in dogs to document the contribution of bacteria and yeast in the degree of pruritus seen.
- Elimination diet: a hypoallergenic dietary trial ideally using home-cooked novel protein and carbohydrate sources; should be initiated after infections and infestations have been excluded/controlled.
- Intradermal skin test: preferred test for identifying atopic dermatitis. Serologic testing is also available, but false-positive reactions are more common.
- Skin biopsies are useful in unusual cases (e.g., calcinosis cutis, cutaneous lymphoma) and may be considered if the diagnosis remains elusive despite approaches described above, or if the clinician suspects these unusual disorders from other aspects of the case. A biopsy may corroborate the diagnosis of allergic skin disease but rarely confirms the specific cause.

TREATMENT

TREATMENT OVERVIEW

The goal is to find the cause to find as specific a treatment as possible. When possible, treatment is limited to one medication at a time to facilitate interpretation of response. When doing therapeutic trials, the most effective treatment regimen that is available and safe should be used to eradicate parasites or infections so interpretation of response is clear.

ACUTE GENERAL TREATMENT

An acute intense pruritic episode can be treated with IM or IV short-acting glucocorticoids (dexamethasone sodium phosphate, 0.1-0.2 mg/kg) followed by a few days of prednisone or prednisolone (1 mg/kg PO q 24 h). Short-term use of glucocorticoids seldom causes serious problems.

CHRONIC TREATMENT

- In long-term management of pruritus, such as in cases of canine atopic dermatitis (seep. 106), clinicians rely on immunotherapy (hyposensitization), glucocorticoids, oral cyclosporine, anti-histamines and/or essential fatty acid supplementation.
- Long-term administration of glucocorticoids should be avoided if possible, unless the maintenance dose is low and/or if the treatment is intermittent. For example, a maintenance dose of 0.2-0.3 mg/kg q 48 h of prednisone and/or a total annual dose of 30-50 mg/ kg or less are rarely responsible for significant side effects.
- Induction and maintenance doses of prednisolone are typically 30% lower than prednisone doses, at least when administered concomitantly with trime-prazine (Temaril-P, Vanectyl-P). Along term treatment goal with these combination products is also to try to administer the minimal effective dose q 48 h.
- In food hypersensitivity, clinicians must find a commercial hypoallergenic diet that maintains the animal free of clinical signs.
- In flea bite hypersensitivity, maintain an effective flea elimination treatment.

RECOMMENDED MONITORING

Animals receiving chronic glucocorticoid therapy should be monitored every 6 months for signs of iatrogenic hyperadrenocorticism or other complications (e.g., urinary tract infection, pyoderma).

PROGNOSIS AND OUTCOME

- Varies according to the etiology
- Excellent for most parasitic and infectious skin problems and food hypersensitivity
- Atopic dermatitis is an incurable disease that requires long-term management of pruritus.

PEARLS & CONSIDERATIONS

COMMENTS

- Treatment of pruritic dermatoses does not always imply use of antipruritic drugs specifically. In fact, antiparasitic drugs, antibiotics, and antifungal drugs (for yeast dermatitis), which are not inherently antipruritic, are among the most useful "antipruritic" drugs. They have a key role in pruritus management because they control or eliminate the underlying cause. Superficial pyoderma is a frequent cause of pruritus in dogs.
- Always rule out parasitic and infectious causes of pruritus before administering long-term steroidal or nonsteroidal antipruritic drugs or before initiating an elimination diet (food trial).
- If pruritus is refractory to a usual maintenance dose of glucocorticoid (i.e., >0.5 mg/kg q 48 h of prednisone in dogs), consider the following diagnoses: sarcoptic mange/scabies, *Malassezia* dermatitis, pyoderma, food hypersensitivity, calcinosis cutis, contact allergic dermatitis, epitheliotropic lymphoma.
- More than one disease may be contributing to pruritus; for example, dogs with atopic dermatitis often have secondary bacterial and/or yeast infections.
- In cats, prednisone is generally not as effective as other glucocorticoids at equivalent doses. Instead, use oral prednisolone, methylprednisolone, dexamethasone, or triamcinolone.

CLIENT EDUCATION

- Owners of dogs with canine atopic dermatitis must be well informed of the chronic and multifaceted aspect of the disease.
- In order to evaluate response to treatment or disease progression, a pruritus score (e.g., on a scale of 0 to 10, 0 = normal and 10 = worst level of pruritus observed so far) can be very useful. It is worth explaining it to the animal's owner. Doing so can add a measure of objectivity and may reduce the owner's perception that treatment is ineffective, or conversely, may support the severity of pruritus perceived by the owner.

SUGGESTED READING

Scott DW, Miller WH, Griffin CE, eds: Muller and Kirk's small animal dermatology, ed 6, Philadelphia, 2001, WB Saunders.

AUTHOR & EDITOR: MANON PARADIS

Protozoal Enteritides

BASIC INFORMATION

DEFINITION

Infection of the small or large intestine with protozoal organisms

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Giardiasis, trichomoniasis, and amebiasis occur in dogs, cats, humans, and many other domestic species.
- Balantidiasis is common in pigs but can also occur in dogs and humans.
- *Tritrichomonas foetus* infection principally causes reproductive problems in cattle but may also cause enteric signs in cats.
- *Cystoisospora* enteritis may affect dogs, cats, pigs, fowl, and other domestic animals.
- Young animals are at higher risk of developing overt, and potentially more severe, clinical signs.

RISK FACTORS: Overcrowding, kennel boarding, unsanitary conditions, and immunosuppression increase the risk of protozoal enteritis.

CONTAGION & ZOONOSIS

- *Cystoisospora:* each species of the organism is host specific and cannot be transmitted between other domestic animal species.
- *Giardia lamblia, Balantidium coli*, and *Pentatrichomonas hominis* enteritides pose a known or suspected zoonotic risk.
- *Entamoeba histolytica* can be transmitted from humans to dogs or cats but generally not from dogs or cats to humans. Dogs and cats do not shed the infective cyst form of *E. histolytica*.

GEOGRAPHY AND SEASONALITY: Protozoal enteritides are distributed worldwide, with increased infection rates in areas of poverty, overcrowding, and poor sanitation-characteristics often associated with puppy mills, animal shelters, and pounds.

ASSOCIATED CONDITIONS & DISORDERS

Many protozoal enteritides are detected as secondary infections due to underlying primary gastrointestinal (GI) diseases.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

B. coli (balantidiasis), *Cystoisospora* or related organisms (coccidiosis; protozoan parasites formerly known as *Isospora*), *E. histolytica* (amebiasis), *G. duodenalis* (giardiasis; see p. 447), *P. hominis* or *T. foetus* (trichomoniasis; see), *Cryptosporidium parvum* (see)

HISTORY, CHIEF COMPLAINT

Most infections with protozoa are subclinical. However, severe infections or infections in young or immunosuppressed animals may be serious, with overt, potentially debilitating clinical signs. The most common clinical sign is acute to chronic diarrhea. Some animals may be depressed or occasionally vomit. *G. duodenalis* and *Cystoisospora* spp. may cause small- or large-bowel diarrhea, while other protozoa generally cause only large-bowel diarrhea.

PHYSICAL EXAM FINDINGS

Physical examination findings may be nonspecific and include depression, mild to severe dehydration, and discomfort on abdominal palpation, with gas or fluid-filled intestinal loops. In milder cases, no physical abnormalities may be present.

ETIOLOGY AND PATHOPHYSIOLOGY

- Transmission of protozoal enteritides is fecal-oral.
- Infective cysts are ingested from the environment and commonly from water contaminated with feces.
- Upon exposure to intestinal enzymes, cysts open and release motile trophozoites that mature and attach to the intestinal epithelium.
- *G. duodenalis* and *Cystoisospora* spp. remain on the surface of the epithelium, causing damage to the microvilli.
- *Entamoeba* and *Balantidium* spp. may invade the colonic wall, causing ulceration.
- *P. hominis* is considered rarely pathogenic.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Standard fecal examinations are simple and provide a definitive diagnosis for these disorders; they are indicated in all cases of acute or chronic diarrhea.

DIFFERENTIAL DIAGNOSIS

- Young dogs: parvoviral, distemper viral, and bacterial enteritides; enteritis caused by helminths (*Toxocara, Ancylostoma, Trichuris* spp.)
- Young cats: feline panleukopenia, feline leukemia virus (FeLV)
- *Sarcocystis* oocysts may be observed on fecal examination; however, this coccidian is not pathogenic in dogs or cats. Herbivores are the intermediate host and develop parasitic cysts in muscle and nervous tissues after consuming the infected feces of dogs.
- *Hammondia* and *Besnoitia* oocysts may be seen on fecal examination; these coccidians are also nonpathogenic.
- Older animals with acute to chronic diarrhea may have a primary underlying intestinal disorder such as inflammatory bowel disease or neoplasia (dogs and cats), ulcerative colitis (dogs), or feline immunodeficiency virus-associated enteritis (cats).
- *Cryptosporidium parvum* (see p. 269) may also produce a primary gastroenterocolitis in both dogs and cats.

INITIAL DATABASE

- Direct fecal smear may reveal motile trophozoites.
- Zinc sulfate fecal flotation may reveal protozoal cysts.
- CBC and chemistry panel are nonspecific but may help rule out other diseases.

ADVANCED OR CONFIRMATORY TESTING

- Multiple fecal examinations may be necessary to find trophozoites or cysts, which may be shed intermittently. Three fecal examinations performed over a period of 3-5 days are recommended in challenging cases.
- A therapeutic trial with fenbendazole and metronidazole may be helpful in animals with chronic diarrhea but multiple negative fecal samples.

TREATMENT

TREATMENT OVERVIEW

Treatment consists of antiprotozoal medication in most cases. Supportive care may be indicated in severe cases.

ACUTE GENERAL TREATMENT

- Initial treatment consists of parenteral fluid therapy to correct hypovolemia and electrolyte and acid base disturbances.
- Fenbendazole, 50 mg/kg PO q 24 h for 3-5 days is the current treatment of choice for giardiasis.
- Metronidazole, 10-20 mg/kg PO q 12-24 h for 5-7 days is an effective treatment for enteritis caused by *Pentatrichomonas, Entamoeba*, and *Balantidium* spp.
- *Cystoisospora* enteritis may be treated with amprolium, 110-200 mg/kg PO q 24 h (dogs), or 50-60 mg/kg PO q 24 h (cats); or sulfadimethoxine for 14 days. Combination therapy may be more effective and allow use of lower doses with fewer side effects.
- There are no effective treatments known at this time for eradication of *T. foetus* in cats. Paromomycin, 125-160 mg/kg PO q 12 h for 5 days may be effective, but some cases of renal toxicity have been reported with the use of this drug in cats.

NUTRITION/DIET

High-quality, easily digestible diets. High-fiber diets may help formation of a firm stool.

PROGNOSIS AND OUTCOME

- Prognosis for most protozoal enteritides is good. Recurrent infection is possible, and complete elimination of the organism may be challenging because some protozoa are commensalistic organisms and/or opportunistic pathogens.
- The prognosis for elimination of *T. foetus* from cats is guarded, although treatment may reduce clinical signs.

PEARLS & CONSIDERATIONS

COMMENTS

- Protozoal enteritides are often secondary infections in adult animals. If appropriate antiprotozoal therapy is not effective, further testing is warranted to seek an underlying disease.
- Protozoal enteritis should not be eliminated as a possible cause of diarrhea in a young animal based on a single negative fecal result.

PREVENTION

Prevention of overcrowding and maintaining a clean environment for young animals will help prevent protozoal infections. Prompt removal of feces should be encouraged.

TECHNICIAN TIPS

Technicians should be able to recognize all forms (both cysts and trophozoites) of the organisms producing protozoal enteritides.

CLIENT EDUCATION

Clients should be advised to seek medical attention if their pet has been diagnosed with protozoal enteritis; *G. duodenalis*, *B. coli*, and *P. hominis* enteritides carry a zoonotic risk.

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Washabau RJ: Gastrointestinal infectious diseases of dogs and cats. Western Veterinary Conference, Las Vegas, NV, Feb. 15-19, 2004. Available from: www.vin.com/ Members/Proceedings/Proceedings.plx?CID =WVC2004&O=VIN. Accessed July 31, 2006.

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Protothecosis

BASIC INFORMATION

DEFINITION

A multisystemic disease caused by infection with *Prototheca* algal species

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Cats: cutaneous infection
- Dogs: disseminated infections are more common. Female dogs are overrepresented.

GENETICS & BREED PREDISPOSITION

Collies and German shepherds appear to be predisposed to infection.

RISK FACTORS

Successful infection requires some degree of immunodeficiency in the host.

CONTAGION & ZOONOSIS

Prototheca is an opportunistic pathogen found in soil, sewage, and tree slime flux. Clinical disease has been reported in multiple animal species including humans. Zoonotic transmission is not recorded, but immunocompromised persons should observe hygienic precautions around affected animals (and the environmental source).

GEOGRAPHY AND SEASONALITY

In North America, most cases are reported in the southeastern United States.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Colitis-type diarrhea: mucoid, bloody, and foul-smelling; intermittent or protracted. Weight loss possible in chronic cases.
- Many dogs with diarrhea have ocular lesions (owners may note red or cloudy eyes).
- Central nervous system (CNS) signs include depression, stumbling, falling, or head tilt.

PHYSICAL EXAM FINDINGS

- Palpable fluid-filled bowel loops and blood on thermometer can be noted. Rectal palpation may reveal thickened rectal tissues in some dogs.
- Cachexia with muscle atrophy possible
- Ocular manifestations include signs of conjunctivitis, uveitis, vitreous clouding, and acute blindness due to retinal detachment.
- Neurologic examination findings are consistent with disseminated CNS disease; asymmetric signs of ataxia, head tilt, circling, and paresis are reported in fewer cases.
- Mucocutaneous ulceration, ulcerative, and/or nodular cutaneous lesions: less common

ETIOLOGY AND PATHOPHYSIOLOGY

- *Prototheca zopfii* and *Prototheca wick-erhamii* are the two algae species responsible for clinical disease. Immu-nosuppression due to concurrent disease, administration of immunosup pressive agents, or genetic predisposition at time of exposure are considered key to development and persistence of infection.
- *Prototheca* organisms can be found in the kidney (where they may cause renal failure), liver, heart, intestine, brain, and eyes of infected animals.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected in a patient with signs of chronic colitis, with or without ocular or neurologic signs, who lives in a geographic area where *Prototheca* spp. are endemic. Clinical confirmation requires demonstration of the organism cytologically (usually via rectal scrape) or histologically (intestinal biopsy).

DIFFERENTIAL DIAGNOSIS

- Bloody diarrhea: parvovirus infection, clostridial infection, salmon poisoning, giardiasis, *Salmonella* enteritis, inflammatory bowel disease/ulcerative colitis, rectal adenocarcinoma, pythiosis, whipworm infection, coagulopathies caused by tickborne diseases or rodenticide poisoning, and gastrointestinal (GI) lymphoma
- In dogs with protothecal colitis, ocular lesions, and/or neurologic signs, systemic infectious diseases (e.g., mycoses) and lymphoma are important differential diagnoses.

INITIAL DATABASE

- CBC is usually unremarkable. Serum chemistry analysis usually shows mild increases in liver enzymes (alkaline phosphatase [ALP] and alanine amino-transferase [ALT]).
- Urinalysis usually is unremarkable, but inflammatory urine sediment may be seen, indicating possible renal involvement. *Prototheca* organisms have been isolated from the urine of dogs with renal failure secondary to renal invasion.
- Fecal analysis consisting of Sheather's flotation and ZnSO4 flotation is indicated in all suspected cases; *Prototheca* is occasionally found this way (many false-negative results).

ADVANCED OR CONFIRMATORY TESTING

- Organisms can be demonstrated in the cytologic examination of a rectal scrape (see p. 1334) stained with Diff-Quik or Wright's stain. Many falsenegative results.
- Intestinal biopsy (surgical or endoscopic) may yield a diagnosis when lesser invasive means are unsuccessful.
- A complete ophthalmic examination (seep. 1313) is indicated in suspected or confirmed cases, since ocular lesions may be missed initially. Organisms can be recovered from vitreous centesis.
- Neurologic examination (seep. 1311) should be performed on dogs showing CNS signs. Spinal radiographs or CT may be needed in dogs showing paresis. Organisms can be recovered from cerebrospinal fluid, which indicates severe clinical disease and dissemination.
- Culture can be performed on rectal scrape or any biopsy samples.
- Fluorescent antibody testing can differentiate *P. zopfii* from *P. wicker-hamii*

TREATMENT

TREATMENT OVERVIEW

- Abort infection.
- Reduce or prevent further dissemination of infection, particularly to CNS.
- Decrease frequency and volume of diarrhea.

ACUTE GENERAL TREATMENT

- Initial treatment consists of parenteral fluid therapy.
- Antifungal treatment (amphotericin B with/without one of the following: itraconazole, ketoconazole, tetracycline, doxycycline) is beneficial to prevent immediate dissemination.
- Amphotericin B (patient must be hydrated): 0.25-0.5 mg/kg diluted in 5% dextrose and given IV q 48 h to total cumulative dose of 8-10 mg/kg or first signs of nephrotoxicity (monitor BUN, creatinine daily).
- Liposomal amphotericin B: as above, but SQ and for a shorter time period. Less nephrotoxic but still requires monitoring.

CHRONIC TREATMENT

Tetracycline, 25 mg/kg PO q 8 h for 30 days; or doxycycline, 5-10 mg/kg PO q 24 h for 30 days; or ketoconazole or itraconazole, 5-10 mg/kg PO q 24 h with food for 30 days. Limited or no success in most cases.

DRUG INTERACTIONS

Ketoconazole, itraconazole: vomiting, inappetence, and elevated liver enzymes possible. If such signs occur, the drug therapy should be stopped and liver enzymes evaluated.

POSSIBLE COMPLICATIONS

- Treatment of concurrent infections and secondary *Escherichia coli* and *Clostridium* infections can reduce frequency and volume of diarrhea.
- Metronidazole, 7.5-15 mg/kg PO q 12 h can be used for *Clostridium* overgrowth.

RECOMMENDED MONITORING

- Monthly monitoring of the success of therapy is recommended.
- Rectal scrapes with cytologic analysis and culture, ophthalmologic examinations, CBC, serum chemistry, and urinalysis are recommended.

PROGNOSIS AND OUTCOME

- Prognosis is poor, especially with CNS signs, multiple organ involvement, and/or renal failure.
- Survival for >1 year has been reported in some animals with only GI and ocular lesions.

PEARLS & CONSIDERATIONS

COMMENTS

Prototheca is a ubiquitous organism and only an opportunistic pathogen in the irnmunocompromised dog. Further immunosuppressive therapy with glucocorticoids or other agents is contraindicated and counterproductive.

PREVENTION

If a potential area of patient exposure can be identified, the patient and possibly humans should be prevented from further contact with this environment.

CLIENT EDUCATION

The disease is not transmissible. However, owners who are irnmunocompromised should be cautious in handling the feces of infected animals.

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Protein-Losing Nephropathy

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

A common cause of kidney disease and kidney failure in dogs but less common in cats. Protein-losing nephropathy (PLN) is any condition in which glomerular damage leads to biologically significant loss of plasma proteins. Subsequent nephron loss may lead to chronic or acute kidney failure.

SYNONYMS

PLN, proteinuric renal failure

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Familial nephropathy:
  - Dogs > cats
  - Age at onset of illness varies with breed.
  - Sex predilection present for some (see Genetics & Breed Predisposition)
- Glomerulosclerosis:
  - Either sex
  - Incidence increases with age; average 8 years
- Membranous nephropathy:
  - Either sex
  - Most common PLN in the cat
  - Mean age: cats 3-4 years; dogs 7 years
- Minimal change nephropathy:
  - Uncommonly described in dogs and cats
- See Glomerulonephritis, p. 450
- See Amyloidosis, p. 61

GENETICS & BREED PREDISPOSITION

Familial nephropathy: inheritance not always defined; typical age of onset of signs is in parentheses.

- Glomerular disease:
  - Bernese mountain dog (2-5 years), suspected autosomal recessive inheritance
  - Brittany spaniel (4-9 years), autosomal recessive inheritance
  - Rottweiler (<1 year)
  - Soft-coated wheaten terrier (2-11 years)
  - Beagle (2-8 years)
- Amyloidosis:
  - Beagle (5-11 years)
  - English foxhound (5-8 years)
  - Shar-pei (1-6 years)
  - Abyssinian cat (1-5 years), autosomal dominant with incomplete penetrance
  - Oriental shorthair (<5 years)
  - Siamese (<5 years)
- Basement membrane abnormality:
  - Bull terrier (1-10 years), autosomal dominant inheritance
  - Doberman pinscher (<1-6 years)
  - English cocker spaniel (<2 years), autosomal recessive inheritance
  - Samoyed (<1 year), X-linked dominant (males affected)
- Tubular dysfunction:
  - Basenji (1-5 years)
- Membranous nephropathy:
  - Doberman pinscher, possibly (3-4 years)

RISK FACTORS

- Corticosteroid excess (iatrogenic, hyperadrenocorticism)
- Systemic hypertension
- Diabetes mellitus
- Chronic infections (bacterial, rickettsial, protozoal, fungal, viral, parasitic)
- Chronic inflammatory disease, including immune-mediated disease
- Neoplasia

CONTAGION & ZOONOSIS

Some infectious causes of glomerulonephritis (GN) are zoonotic (see p. 450).

GEOGRAPHY AND SEASONALITY

Some infectious causes of GN are geographically and/or seasonally limited (see p. 450).

ASSOCIATED CONDITIONS & DISORDERS

- Nephrotic syndrome
- Chronic kidney disease (chronic renal failure)
- Hypertension
- Hyperlipidemia
- Thromboembolic disease, including pulmonary thromboembolism

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- GN
- Amyloidosis
- Familial nephropathy
- Glomerulosclerosis
- Membranous nephropathy
- Minimal change disease

HISTORY, CHIEF COMPLAINT

Clinical signs are often absent prior to development of azotemia or severe hypoalbuminemia. Shar-pei dogs may present for lameness and/or fever (see online chapter: Shar-Pei Fever). When signs are present, they may be due to kidney failure, nephrotic syndrome, or to an underlying disease process:

- Lethargy
- Anorexia
- Weight loss
- Polyuria and polydipsia (PU/PD)
- Vomiting (if uremic)
- Halitosis (if uremic)
- Pendulous abdomen (ascites; if hypoalbuminemic)
- Edema (if hypoalbuminemic)
- Dyspnea (if severely uremic, after thromboembolic event, or effusion present)
- Blindness (if hypertensive)

PHYSICAL EXAM FINDINGS

Often unremarkable. Shar-pei dogs may have fever, tibiotarsal joint pain, and joint effusion. Other findings may suggest an underlying disease process. In addition to findings mentioned under clinical signs, other abnormalities may include:

- Dehydration
- Poor haircoat
- Pallor
- Oral ulceration
- Lipid corneal deposits

- Retinal hemorrhage/detachment
- Kidneys may be normal-sized, small, or rarely large

ETIOLOGY AND PATHOPHYSIOLOGY

- Familial nephropathy:
  - Diverse group of hereditary renal diseases
  - Defects vary with individual diseases but include familial amyloidosis, failure of tubular protein resorption, and defects in type IV collagen in the glomerular basement membrane.
  - In some cases, nephropathy is associated with other conditions (e.g., food sensitivity [soft-coated wheaten terrier], complement deficiency [Brittany spaniel]).
- Glomerulosclerosis:
  - Results from hyperfiltration in dogs with “typical” chronic kidney disease, often as an end-stage lesion.
  - Reported in dogs with familial nephropathy, systemic hypertension, diabetes mellitus, hyperadrenocorticism, and postradiation therapy. Multiple other causes described in people.
  - Sclerosis ultimately leads to altered intraglomerular hemodynamics and progressive renal failure.
- Membranous nephropathy:
  - Immune complex deposition in the glomerular basement membrane, without evidence of inflammation
  - Primary (most common) and secondary forms can be distinguished by the location of the immune complex deposition.
- Minimal change nephropathy:
  - Loss of anionic charge in glomerulus leads to selective albumin loss.
  - Because electron microscopy is required for diagnosis, may be underreported in veterinary medicine.
- See Glomerulonephritis, p. 450.
- See Amyloidosis, p. 61.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A diagnosis of PLN is suspected based on proteinuria and an elevated protein/creatinine ratio obtained from a sterile urine sample with inactive sediment. Diagnosis is confirmed after ruling out preglomerular or postglomerular causes of proteinuria.

DIFFERENTIAL DIAGNOSIS

Proteinuria:

- Preglomerular:
  - Bence Jones proteinuria
  - Exercise
  - Hemolysis
  - Fever
  - Seizure
- Glomerular (i.e., the disorders that can cause protein-losing nephropathy):
  - GN
  - Amyloidosis
  - Glomerulosclerosis
  - Familial nephropathy
  - Minimal change disease
- Postglomerular:
  - Urinary tract infection
  - Acute renal failure
  - Neoplasia (e.g., transitional cell carcinoma, prostatic carcinoma)
  - Urolithiasis
  - Urinary hemorrhage
  - Fanconi syndrome
  - Trauma
  - Endocrine disease (e.g., hyperadrenocorticism)

INITIAL DATABASE

- Retinal exam: hemorrhages (acute or chronic) or retinal detachments are possible (both a result of severe systemic hypertension).

- Blood pressure (BP): systemic hypertension is possible (systolic BP > 180 mm Hg repeatably in a calm environment).
- CBC: often unremarkable; nonregenerative anemia may occur with advanced kidney disease, leukocytosis may occur if inflammatory disease is present.
- Serum biochemical profile:
  - Hypoalbuminemia with normal globulin level is common.
  - Hypercholesterolemia accompanies hypoalbuminemia.
  - Hypocalcemia (due to hypoalbuminemia)
  - Azotemia (in advanced disease)
  - Hyperphosphatemia (in advanced disease)
  - Metabolic acidosis (with azotemia)
- Urinalysis: proteinuria is a consistent finding. Urine concentration is variable but often minimally concentrated. Hematuria sometimes present.
  - Proteinuria must be interpreted in light of urine concentration and urine sediment examination.
  - Dipstick measure of proteinuria should be confirmed by sulfosalicylic acid (SSA) method or quantitative measures (e.g., urine protein/creatinine ratio).
  - Proteinuria may be mild in subset of shar-pei dogs and Abyssinians with renal medullary amyloidosis.
  - Significant proteinuria may precede loss of urine concentration or azotemia.
- Urine culture: indicated in all cases.
- Thoracic radiographs: unremarkable. Evidence of underlying disease (neoplasia, chronic infectious or inflammatory disease) or pulmonary thromboembolism occasionally identified.
- Abdominal radiographs: often unremarkable. Kidneys may be large (amyloidosis) or small (chronic GN, sclerosis); may identify evidence of underlying disease (neoplasia, chronic infectious or inflammatory disease).
- Abdominal ultrasound: hyperechoic kidneys (though this is a normal finding in some cats), decreased corticomedullary junction, medullary rim sign, cortical cysts.

ADVANCED OR CONFIRMATORY TESTING

- Microalbuminuria test (early renal disease [ERD] screen) can detect small amounts of urine albumin before dipstick protein is positive:
  - Significance of this test in apparently healthy dogs is not known.
  - May identify animals with familial nephropathy before overt renal damage apparent
  - Used in humans with diabetes mellitus and hypertension as early indicator of glomerulosclerosis
- Urine protein/creatinine ratio:
  - Normal ratio < 0.5 in dogs and <0.4 in cats
  - Only useful when urine sediment is inactive
  - Protein loss tends to be higher in amyloidosis than in GN.
- Urine protein excretion, 24 hours: largely replaced by single-sample protein/creatinine ratio
- Biopsy of the renal cortex for light microscopy, electron microscopy (EM), or immunofluorescence:
  - Amyloidosis: Congo red stain for amyloid
  - GN: morphologic description and immunologic classification
  - Glomerulosclerosis: immunofluorescent microscopy is negative; immunoglobulin and C3 trapping may be present. A segmental increase in mesangial matrix and basement membrane is typically seen.
  - Membranous nephropathy: thickened glomerular basement membrane due to immune complex deposition. Location of immune complexes determined by EM.
  - Minimal change disease: lack of light microscopic glomerular changes; foot process effacement seen on EM
- Antithrombin levels to determine risk of thromboembolic disease
- Blood gas analysis: increased alveolar-arterial (A-a) gradient may support ventilation/perfusion mismatch due to pulmonary thromboembolism.
- Search for underlying disease; in addition to causes of GN (see p. 450), causes of glomerulosclerosis should be considered as well (e.g., systemic hypertension, hyperadrenocorticism, diabetes mellitus).
- Possible C3 levels or perinuclear antineutrophilic cytoplasmic autoantibodies in soft-coated wheaten terriers

TREATMENT

TREATMENT OVERVIEW

Whenever possible, the cause for PLN should be addressed directly. Regardless, treatment of PLN includes measure to reduce proteinuria, reduce thromboembolic risk, address uremic signs and complications, and control systemic hypertension.

ACUTE GENERAL TREATMENT

- Underlying causes should be identified and addressed directly whenever possible.
- Immediate care for PLN includes measures to address uremia (see p. 207), hypertension (see p. 1068), thromboembolic risks

(see pp. 450and88), edema formation (see pp. 131,270 , and 61), and acid/base or electrolyte disorders (see p. 450).
- Occasionally, manual drainage of abdominal or thoracic fluid accumulation will be needed to relieve respiratory effort (see pp. 1338 and 1192).

CHRONIC TREATMENT

- Identification and treatment of causative disease provide the best prognosis for affected animals. PLN is often idiopathic, or causation cannot be treated (e.g., familial disease). In these cases, supportive, nonspecific measures are employed (seepp. 762 ,450 , and 11).
- Specific treatment for amyloidosis may be attempted (see p. 61).
- Immunosuppression (glucocorticoids 2 mg/kg PO q 24 h) may be useful for membranous nephropathy, but only if infectious causes have been ruled out.

DRUG INTERACTIONS

ACE inhibitors may cause hypotension when combined with diuretics or other vasodilators. Nonsteroidal antiinflammatory drugs (NSAIDs) may reduce efficacy of angiotensin-converting enzyme (ACE) inhibitors.

POSSIBLE COMPLICATIONS

- Third-space retention of fluids/nephrotic syndrome
- Worsening renal azotemia as a result of ACE inhibitor use
- Hypotension secondary to ACE inhibitor and Ca channel blocker
- Worsening of renal azotemia with dextran use
- Thromboembolic disease as a result of abnormal antithrombin and protein C
- Bleeding tendency from aspirin, warfarin use
- Gastrointestinal (GI) ulceration as a result of azotemia or aspirin therapy

RECOMMENDED MONITORING

Stable animals may be monitored every 3-4 months. Rechecks should be more frequent when changes are made in therapy or when indicated by changes in clinical signs.

- Physical examination
- Urine protein/creatinine ratio
- Serum blood urea nitrogen (BUN), serum creatinine, and serum phosphorus levels
- Serum albumin
- BP
- Urinalysis and culture

PROGNOSIS AND OUTCOME

- The prognosis of PLN is extremely variable, depending on cause and severity of renal compromise.
- If an underlying disease can be identified and treated, the prognosis may be good.
- If it is not possible to identify or correct an underlying disease process, PLN is usually progressive.
- Animals with PLN may be medically managed for variable periods of time, even when uremic signs develop.
- In general, the prognosis for animals with renal amyloidosis is worse than that of GN.
- Familial renal diseases often begin at a young age and are rapidly progressive with a poor prognosis.
- When glomerulosclerosis is associated with end-stage renal disease, the prognosis is poor.
- Animals with membranous nephropathy may have a better prognosis with appropriate treatment. It is often slowly progressive, and the animal can occasionally go into remission.

PEARLS & CONSIDERATIONS

COMMENTS

- Renal cortical biopsy is the only method to distinguish amyloidosis and GN. While treatment is impacted occasionally, it provides useful prognostic information.
- Shar-pei dogs and Abyssinian cats occasionally have a normal cortical biopsy, since the amyloid may be deposited in the renal medulla.

PREVENTION

- Heartworm prophylaxis
- Tick prophylaxis
- Breeder education for dogs and cats with familial disease

CLIENT EDUCATION

Renal biopsy can help definitively identify the disease process. This may be important for animals with familial renal disease.

SUGGESTED READING

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Prostatic Neoplasia

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Prostatic neoplasia is uncommon in dogs and rare in cats. The most common tumor types include adenocarcinoma, urothelial carcinoma, and undifferentiated carcinoma. Prostate tumors are locally invasive and highly metastatic.

EPIDEMIOLOGY

SPECIES, AGE, SEX

Prostate tumors occur almost exclusively in dogs. Sporadic cases have been reported in cats. Median age at diagnosis in dogs is 10 years.

GENETICS & BREED PREDISPOSITION

No breed predilection has been reported; medium- to large-breed dogs are more commonly affected.

RISK FACTORS

The effects of reproductive status on the development of prostate tumors are not fully understood. Exposure to endogenous androgens has been associated with development of prostatic adenocarcinoma in dogs. Castration at a young age appears to increase the risk of other types of prostate tumors.

ASSOCIATED CONDITIONS & DISORDERS

Many patients with prostate tumors may develop secondary lower urinary tract infections.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Forms of disease include the various histologic types including adenocarcinoma, urothelial carcinoma, and undifferentiated carcinoma. The natural behavior of and diagnostic approach to each subtype is identical.

HISTORY, CHIEF COMPLAINT

Clinical signs are often chronic, linked to the urinary tract, and most commonly include hematuria, incontinence, and stranguria. Rarely, patients may present with complete urinary obstruction. Animals with large masses may present with tenesmus caused by compression of the colon by the tumor. Lameness may occur in animals with bone metastasis.

PHYSICAL EXAM FINDINGS

External physical examination is often unremarkable. A large, irregular mass that may be firmly adhered to surrounding pelvic structures is typically found on rectal palpation. Animals with bone metastasis may display evidence of pain during orthopedic examination of the spine, pelvis, and/or hind limbs.

ETIOLOGY AND PATHOPHYSIOLOGY

- Castrated dogs are more likely to develop prostatic neoplasia than intact dogs:
  - Intact or recently castrated dogs are more likely develop adenocarcinoma, while castrated dogs likely develop other tumor types.
- Tumor location often precludes early diagnosis; most tumors are consequently locally advanced and have metastasized (70%-80%) at the time of diagnosis:
  - The ultimate metastatic rate for prostate tumors is 85%-100%.
  - The most common sites for metastasis include lungs (50%), lymph node (>30%), and bone (15%-45%). The pelvis and lumbosacral spine are the most common sites of bony metastasis.

- Cyclooxygenase 2 (COX-2) expression may play a role in tumor development and progression, as 75% of prostatic carcinomas have been shown to express COX-2 protein, whereas such expression is not evident in normal prostatic tissue.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

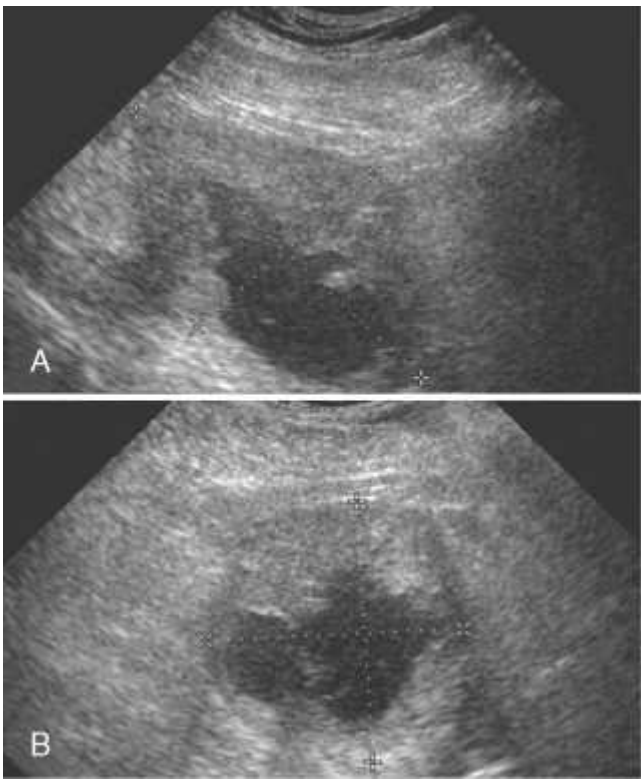
The diagnosis is suspected based on the presence of lower urinary tract signs in a patient with a large, irregular prostate on rectal examination; confirmation requires cytologic or histopathologic evaluation.

DIFFERENTIAL DIAGNOSIS

- Benign prostatic hyperplasia (BPH)
- Prostatic abscess
- Paraprostatic cyst
- Locally invasive transitional cell tumor of the urinary bladder

INITIAL DATABASE

- CBC
- Serum biochemistry profile
- Urinalysis and urine culture if indicated
- Thoracic and abdominal radiographs (including evaluation of bony structures for metastasis)
- Abdominal ultrasound
- Aspirate of regional lymph nodes if indicated to identify the presence of metastatic disease

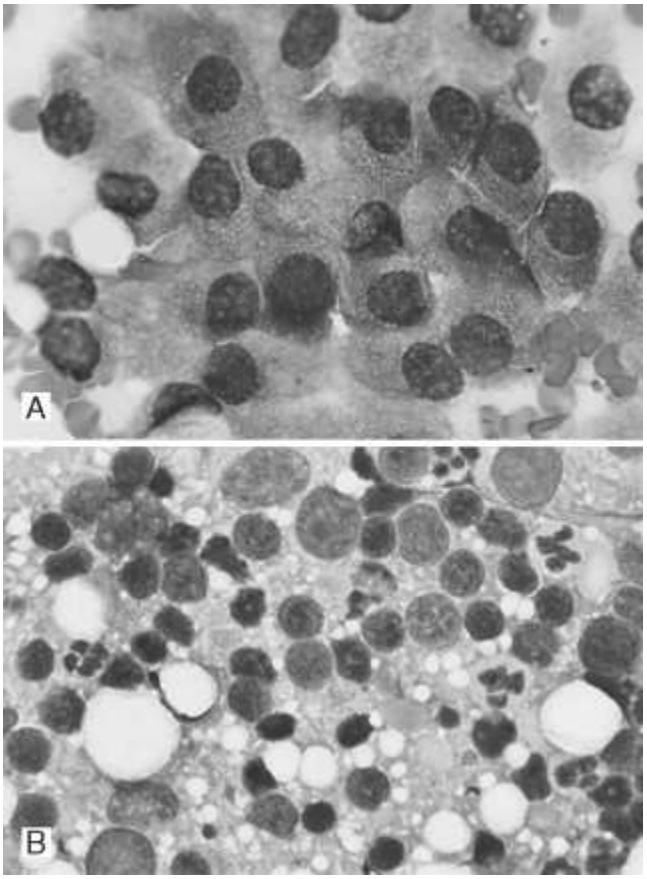


PROSTATIC NEOPLASIA Sagittal **(A)** and transverse **(B)** ultrasonographic images of prostatic adenocarcinoma. Note enlarged size of prostate for a castrated male dog, and increased echogenicity and presence of large, coalescing cysts with hypoechoic luminal contents. Ultrasonographic appearance of a prostatic cyst or abscess may be similar to prostatic carcinoma. Diagnosis should be confirmed by prostatic fluid analysis and/or biopsy.

(From Ettinger SJ, Feldman EC, editors: Textbook of veterinary internal medicine, ed 6, St Louis, 2004, Saunders.)

ADVANCED OR CONFIRMATORY TESTING

- Biopsy for histopathologic evaluation of tumor tissue
- Cytologic evaluation and culture of prostatic aspirate or wash may aid in establishing a diagnosis and rule out concomitant prostatitis.
- Histopathologic evaluation of biopsied tissue for confirmation is essential prior to having patients undergo definitive therapy. Percutaneous aspiration or biopsy of the prostate may be associated with a risk of tumor seeding; however, the need to establish a definitive diagnosis usually supersedes the risk of iatrogenic tumor dissemination with the biopsy instrument.
- CT scan for surgical or radiation treatment planning



PROSTATIC NEOPLASIA Prostatic wash samples made from a normal dog **(A)** and a dog with adenocarcinoma **(B)** (×100).

(From Ettinger SJ, Feldman EC, editors: Textbook of veterinary internal medicine, ed 6, St Louis, 2004, Saunders, pp 1809-1819.)

TREATMENT

TREATMENT OVERVIEW

Long-term disease control is the ultimate goal in any animal but is often not possible owing to extensive local or metastatic disease. In patients with lesions not amenable to definitive therapy, palliation of clinical signs is the primary goal.

ACUTE GENERAL TREATMENT

- Definitive therapy:
  - Curative therapy should only be considered in dogs with no evidence of metastases.
  - Reports describing definitive therapy for dogs with localized prostate tumors are limited. The following treatments could be considered:
    - External beam radiotherapy to prostate ± regional lymph nodes
    - Partial prostatectomy with preservation of the urethra (animals with focal prostatic lesions)
    - Complete prostatectomy with urethral resection/permanent cystostomy tube placement
    - Given the high metastatic rate, chemotherapy (e.g., doxorubicin, mitoxantrone, carboplatin) is indicated in definitively treated animals. The efficacy of chemotherapy has not been established conclusively.
    - COX-2 inhibition with piroxicam, 0.3 mg/kg PO q 24-48 h (caution: gastric ulcerogenic potential) is beneficial in animals with prostatic carcinoma of urothelial origin.

CHRONIC TREATMENT

Palliative therapy:

- Palliative care should be considered in animals with metastatic disease and those with advanced localized disease not amenable to definitive therapy. The efficacy of palliative treatments has not been established conclusively.
- Palliative radiotherapy may provide short-term relief from urinary obstruction or other clinical signs resulting from local disease.
- Permanent cystostomy tube placement/urinary bladder marsupialization may provide relief from urinary obstruction.
- Electrosurgical transurethral resection may result in significant palliation of clinical signs.
- Castration may provide alleviation of signs in intact dogs with concurrent prostatic hyperplasia.
- Systemic treatment with chemotherapy and/or piroxicam

DRUG INTERACTIONS

Patients receiving piroxicam therapy should be given corticosteroids or other nonsteroidal antiinflammatory medications.

POSSIBLE COMPLICATIONS

Potential complications of chemotherapy and radiation treatment are similar to those observed for other tumors. Such complications include gastrointestinal toxicity, bone marrow suppression, and local tissue irritation. Piroxicam therapy may be associated with gastrointestinal ulceration as well as renal failure.

RECOMMENDED MONITORING

Following treatment, recommended monitoring includes routine examination, abdominal ultrasound, and thoracic radiographs. For chemotherapy, routine monitoring should be undertaken based on protocol.

PROGNOSIS AND OUTCOME 

- Due to the severity of clinical disease (advanced local and distant metastasis), most dogs with clinical signs caused by prostate tumors are euthanized within 1 month of diagnosis.
- The prognosis for definitive therapy is largely unknown, with the exception of radiotherapy. Animals treated with a single 30-Gy dose of intraoperative radiation have shown a median survival of 4 months; animals treated with conventional external beam radiotherapy (57 Gy) have shown a median survival of 7 months.
- Dogs receiving COX-2 inhibition therapy have a median survival of 7 months, compared to a median survival of <1 month in those not receiving such therapy.

PEARLS & CONSIDERATIONS 

COMMENTS

- With rare exception, the prognosis for animals with prostatic tumors is poor; advanced disease at the time of diagnosis is the major causative factor for poor prognosis.
- Advances in the treatment of dogs with prostate tumors will more likely come from earlier detection rather than improved treatment.

SUGGESTED READING

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Prostatic Infections (Prostatitis, Prostatic Abscessation)

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

- Prostatitis: inflammation of the prostate, almost always as a consequence of infection. There are acute and chronic forms that can differ in clinical presentation.
- Prostatic abscess: severe disorder involving infection of the prostate gland, resulting in the production of pocket(s) of suppurative material and destruction of glandular tissue.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Any age; more likely in dogs >5 years of age
- Male cats have prostate glands, but prostatitis is extremely rare in this species.

GENETICS & BREED PREDISPOSITION

- Doberman pinschers have been reported to have a higher incidence of all prostatic diseases.
- Prostatitis: increased risk reported in the Bouvier des Flandres, Scottish terrier, Bernese Mountain dog, German pointer, and Doberman pinscher.

RISK FACTORS

Sexually intact males are at greatest risk.

CONTAGION & ZOONOSIS

Prostatitis can occasionally be caused by *Brucella canis,* a potential zoonotic pathogen, via a hematogenous route.

ASSOCIATED CONDITIONS & DISORDERS

- Chronic form of prostatitis is almost always associated with benign prostatic hypertrophy/hyperplasia (BPH; see p. 919).
- Squamous metaplasia of the parenchymal ducts and prostatic neoplasia can also predispose to infection and therefore may also increase the likelihood of prostatitis and abscess formation.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Acute prostatitis: often associated with systemic illness
- Chronic prostatitis: not associated with systemic illness:
    - Prostatic abscess

HISTORY, CHIEF COMPLAINT

- Signs arise from compression or displacement of adjacent structures, prostatic pain, or systemic illness (sepsis).
- Acute prostatitis: tenesmus, dysuria, lethargy, anorexia, weakness, stiff gait, hematuria:
    - >70% of dogs with acute prostatitis have signs of systemic illness.
    - Primarily in younger male (usually intact) dogs
- Chronic prostatitis: clinical signs reported by owner may be minimal:
    - Primarily occurs in older intact male dogs with concurrent BPH
    - Initially, clinical signs include a recurrent urinary tract infection, preputial discharge, and hemospermia/pyospermia.
    - Depending on duration of illness: tenesmus and/or dysuria
    - Infertility is weakly correlated with chronic prostatitis.
    - Signs of systemic illness are unlikely in dogs with chronic prostatitis.
- Prostatic abscess: may be incidental finding or produce signs similar to prostatitis

PHYSICAL EXAM FINDINGS

- Acute prostatitis:
  - Fever
  - Tense, painful abdomen
  - Prostatic pain on rectal exam
  - Abdominal pain
  - Systemic signs of illness such as anorexia and lethargy
- Chronic prostatitis:
  - Urethral/preputial discharge possible (may be hemorrhagic or purulent)
  - Variable rectal examination findings: possibilities include:
    - Prostatomegaly
    - Normal prostatic palpation; minimal prostatic pain on palpation
- Prostatic abscess:
  - Urethral/preputial discharge (may be hemorrhagic or purulent)
  - Asymmetric prostatomegaly on rectal exam
  - Abdominal mass palpated if prostate severely enlarged
  - Prostatic and/or abdominal pain
  - Systemic signs (e.g., fever, depression, systemic shock)

ETIOLOGY AND PATHOPHYSIOLOGY

- Disturbances in normal defense mechanisms (urine flow during micturition, urethral high-pressure zone, bactericidal effects of prostatic fluid, and local IgA production) may predispose to prostatitis.
- Bacterial infection may spread to the prostate from elsewhere in the urinary tract, can be hematogenous, or occur secondary to a cyst that has become infected:
  - The most common organism reported in canine prostatitis is *Escherichia coli,* which gains access to the prostate via an ascending urinary tract infection.
  - Other bacterial causes of prostatitis and abscessation: *Staphylococcus* spp., *Streptococcus* spp., *Proteus* spp., *Pseudomonas* spp., and *B. cants.*
  - Hypersecretory and cystic degenerative changes that occur with BPH create ideal conditions for bacterial overgrowth. In rare cases, prostatitis can result from nonbacterial organisms (e.g., *Blastomyces, Pythium)* that cause systemic disease.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

These disorders may be encountered incidentally (e.g., on routine physical/rectal examination) or when a patient shows overt signs of illness. Rectal palpation of the prostate is essential, and any palpable abnormality or other clue of prostatic disease (e.g., radiographic changes) warrants ultrasound examination +/− diagnostic sampling.

DIFFERENTIAL DIAGNOSIS

- Other prostatic disease: prostatic abscess, prostatic/paraprostatic cyst, benign prostatic hyperplasia, prostatic neoplasia
- Other lower urinary tract disease: neoplasia, urethral calculi, cystitis
- Colonic disease: colitis, neoplasia
- Mass of other tissue origin (e.g., transitional cell carcinoma, fibrosarcoma)
- Other causes of hemospermia/urospermia

INITIAL DATABASE

- CBC: may have an inflammatory leu-kogram (more common in acute prostatitis)
- Serum biochemistry profile: generally unremarkable
- Urinalysis: inflammatory sediment present (regardless of method of collection)
  - Caution if obtaining urine by cystocentesis: do not lacerate a prostatic abscess.
- Urine culture: may be positive for bacterial growth and is essential for accurate antibiotic selection
- Abdominal radiographs:
  - Acute: prostate commonly of normal size, but mild to moderate prostatomegaly may be present.
  - Chronic: often mildly to moderately enlarged; occasionally normal size
  - Prostatic mineralization has been shown to be highly predictive of neoplasia in neutered male dogs but less reliable in intact male dogs.

- Abdominal ultrasound: focal or diffuse heterogenous echogenicity, prostatomegaly, cystic changes

ADVANCED OR CONFIRMATORY TESTING

- Prostatic fluid cytologic analysis (from ejaculate or prostatic massage): increased erythrocytes and leukocytes; bacteria may be seen within neutrophils (see p. 1332).
- Prostatic fluid culture: usually large numbers of a single bacterial species isolated.
- Prostatic fine-needle aspiration is also an effective method of obtaining cells for cytologic examination and culture (should not be performed in dogs with systemic illness):
  - Septic suppurative inflammation
  - Caution with suspected prostatic abscess; risk of spreading infection or causing septic peritonitis.
- *B. canis* testing (see p. 162)

TREATMENT

TREATMENT OVERVIEW

Treatment of prostatic bacterial infections requires prolonged antibiotic therapy with appropriate antibiotics that can penetrate the tissue. Abscessation requires drainage of the abscess.

ACUTE GENERAL TREATMENT

- Initiate antibiotic therapy:
  - Lipid solubility, acid dissociation constant (p*K*a, and degree of protein binding affect penetration into the prostate.
  - Antibiotic penetration into abscess may be inadequate, therefore is combined with surgery or percutaneous drainage.
  - Antibiotics known to readily penetrate the prostatic capsule include:
    - Chloramphenicol, 30-50 mg/kg PO q 8 h (bacteriostatic)
    - Trimethoprim-sulfadiazine, 15 mg/kg PO q 12 h (bactericidal)
    - Fluoroquinolones:
      - Enrofloxacin, 5 mg/kg PO q 12-24 h (bactericidal)
      - Ciprofloxacin has poorer penetration of prostatic tissue.
- Acute prostatitis:
  - Blood-prostate barrier is disrupted.
  - Most antibiotics will penetrate.
  - Initial choice based on likely organism, then adjusted based on culture and sensitivity (C&S) results
- Chronic prostatitis:
  - Antibiotics that can penetrate the intact prostatic capsule (above) must be used, and choice is ideally based on C&S.
  - Reduction of prostatic size allows infection to be cleared more readily (castration or treatment with drugs that reduce prostate size [e.g., finasteride, 5 mg/dog PO q 24 h, assuming 10-40 kg body weight]).
  - Castration may be mandatory if *Brucella* is identified. In some states, *Brucella canis* is a reportable disease. Check local regulatory guidelines for this zoonotic infection.
- Prostatic abscess:
  - Drainage of cavities greater than 1 cm on ultrasound is the standard of care, either by ultrasound guidance or surgery.
  - Current surgical recommendations involve débridement and intracapsular omentalization followed by postdrainage antibiotic therapy.

CHRONIC TREATMENT

- Adjust antibiotic therapy based on culture results.
- Antibiotic therapy should be continued at least 4-6 weeks.
- Finasteride therapy should be continued until the dog is castrated.

BEHAVIOR/EXERCISE

It may be advisable to discontinue breeding of stud dogs during therapy.

DRUG INTERACTIONS

- Chloramphenicol decreases clearance of other drugs that are cleared by cytochrome P450 enzymes (e.g., phenobarbital, phenytoin).
- Trimethoprim-sulfadiazine may prolong coagulation times when used concurrently with warfarin. It displaces highly bound drugs such as thiazide diuretics, among others. Some antacids will increase bioavailability of this antibiotic. It also decreases

the efficacy of cyclosporine when used concurrently.
- Fluoroquinolones may increase theophylline blood levels when used concurrently. Some antacids may prevent absorption of fluoroquinolones. Synergism may occur with other antibiotics (e.g., aminoglycosides, third-generation cephalosporins, and some penicillins).

POSSIBLE COMPLICATIONS

- Antimicrobial side effects
- Trimethoprim-sulfamethoxazole may cause anemia, polyarthritis, and keratoconjunctivitis sicca if given long term.
- Chloramphenicol has been associated with bone marrow toxicity.
- Prostatic abscess formation is a possible sequela of acute prostatitis.
- Prostatic abscess:
  - Morbidity can be high with surgical intervention, but incidence of complications is decreased with prostatic omentalization technique compared to older techniques (e.g., placement of Penrose drains and marsupialization).
  - Possible complications include urinary incontinence; chronic draining tracts; and with uncontrolled abscesses that rupture and/or produce sepsis, peritonitis, septic shock, and death are possible.

RECOMMENDED MONITORING

- Repeat examination including rectal palpation approximately every 2 weeks during therapy.
- Repeat ultrasound of the prostate 2-3 weeks after initial therapy and as needed thereafter to ensure resolution of abscess.
- Prostatic fluid and urine should be collected for culture and cytologic analysis 2 weeks after completion of antibiotics, and again 4 weeks later.
- Infection generally will not recur if finasteride is continued or castration is performed.

PROGNOSIS AND OUTCOME

- Prognosis is fair for prostatitis in general:
  - Acute prostatitis is generally more amenable to cure than chronic prostatitis, but systemic illness makes it a more urgent and potentially life-threatening disease than chronic prostatitis.
- Prognosis is guarded to poor for prostatic abscess:
  - Historically, reported mortality rates of 24%-51% within the first year following therapy for prostatic abscess, but prognosis appears to be better if prostatic omentalization or percutaneous ultrasound guided drainage technique is used.

PEARLS & CONSIDERATIONS

COMMENTS

- Radiographic evidence of prostatic mineralization can occur with bacterial prostatitis or prostatic neoplasia but is more common with the latter.
- Castrated dogs are much less likely to develop prostatitis, compared to the incidence of prostatic neoplasia, which is not reduced by castration.
- Semen cryopreservation may be considered following resolution of the bacterial infection in a valuable breeding animal, so that castration can be performed.
- Owners need to be aware that percutaneous drainage may have to be performed more than one time.

PREVENTION

Castration

CLIENT EDUCATION

- Warn clients of necessity of treating chronic cases with both an antibiotic and finasteride when castration is not an option.
- Warn clients of the guarded prognosis, long-term problems of urinary incontinence, and possible need for subsequent surgery following initial therapy for prostatic abscess.

SUGGESTED READING

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50:167, 2009.

Kutzler MA, Yeager AE: Prostatic diseases. In Ettinger SJ, Feldman EC, editors: Textbook of veterinary internal medicine. St Louis, 2005, Elsevier, pp 1809–1818.

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Prostatic Enlargement (Noninfectious, Non-Neoplastic)

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

- Enlargement of the prostate gland due to noninfectious, non-neoplastic cause. In dogs, these are benign prostatic hyperplasia (BPH), prostatic cysts and squamous metaplasia. Prostatomegaly is extremely rare in cats.
- Prostatic abscess, prostatitis (see p. 922), and prostatic neoplasia (see p. 924) are discussed separately.

EPIDEMIOLOGY

SPECIES, AGE, SEX

Adult male dogs, almost exclusively sexually intact (exception: prostatic neoplasia, which occurs in castrated or intact dogs)

RISK FACTORS

- Endogenous (e.g., gonadal) or exogenous source of androgens or estrogens
- Increasing age. BPH: 50% prevalence at age 5 years, 95% prevalence by age 9 years.

CONTAGION & ZOONOSIS

Antiandrogen drugs are teratogenic and must not be handled by pregnant women.

ASSOCIATED CONDITIONS & DISORDERS

Prostatic cysts may be at risk for infection. Feminization and bone marrow suppression or other signs of hyperestrogenism in dogs with prostatic squamous metaplasia.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- BPH: most common cause of prostatomegaly in sexually intact, adult dogs
- Prostatic cysts: observed within the prostatic parenchyma, often associated with BPH
    - Large (several centimeters) intraprostatic cysts referred to as retention cysts.
- Paraprostatic cysts: located outside the prostatic parenchyma but are attached to it by a stalk; often extremely large; not necessarily associated with other prostatic pathology.
- Squamous metaplasia of the prostatic epithelium: occurs in response to estrogen

HISTORY, CHIEF COMPLAINT

- Prostatomegaly due to any cause may be an incidental finding, or it may cause tenesmus.
- BPH often causes no clinical signs. When it does, tenesmus and sanguineous urethral discharge not associated with urination are the two most common signs.
    - Unlike the situation in men, BPH rarely causes stranguria or urine retention in dogs.
- Paraprostatic cysts often cause no clinical signs (incidental findings).
    - When present, clinical signs are associated with mechanical interference with abdominal viscera.
- Squamous metaplasia of the prostate may be asymptomatic or cause signs similar to BPH +/− signs of hyperestrogenism.

PHYSICAL EXAM FINDINGS

Careful rectal (see online chapter: Rectal Palpation) and abdominal palpation of the prostate:

- Prostatomegaly in a castrated dog should immediately prompt a search for prostatic neoplasia or the possibility of a remaining crypt orchid testicle(s).
- BPH:

- Symmetric, nonpainful enlargement of the prostate
- ± Sanguineous urethral (preputial) discharge
- Otherwise healthy, sexually intact adult

- Prostatic cysts:
  - Paraprostatic cyst: large mid- or caudal-abdominal mass; otherwise healthy
  - Intraprostatic cyst: as for BPH +/− asymmetry if large
- Squamous metaplasia of the prostate:
  - Symmetric, nonpainful prostate
  - Testicular mass with atrophy of the contralateral testis
  - ± Alopecia, pigmentation, gyneco-mastia, pendulous prepuce and scrotum, or other findings (e.g., bone marrow suppression) caused by hyperestrogenism

ETIOLOGY AND PATHOPHYSIOLOGY

- Prostatomegaly may cause tenesmus due to mechanical interference with defecation.
- BPH and prostatic cysts are androgen dependent:
  - Normal reflux of prostatic fluid into the urinary tract results in sanguineous urethral (preputial) discharge in some dogs with BPH.
- Estrogen causes squamous metaplasia of the prostatic epithelium:
  - The most common source is an estrogen-secreting testicular tumor (e.g., Sertoli cell tumor).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

- Prostatomegaly is identified during routine physical examination by careful abdominal and rectal palpation.
- BPH, the most common cause of prostatomegaly in an intact male dog, should be on the differential diagnosis list for tenesmus and for sanguineous urethral (preputial) discharge.
- Ultrasound of the prostate is the single most helpful method for narrowing the list of causes of prostatomegaly; it shows the internal architecture of the prostate, which radiographs do not.

DIFFERENTIAL DIAGNOSIS

- Prostatomegaly from infectious causes (e.g., bacterial prostatitis or abscess; see p. 922)
- Prostatomegaly from neoplastic causes. Prostatic neoplasia (see p. 924) is the most common cause of prostatomegaly in castrated dogs.

INITIAL DATABASE

- Physical examination findings of prostatomegaly and the presence of testicles:
  - Rectal palpation: when symmetric, nonpainful, prostatomegaly is an incidental physical exam finding in an otherwise normal, healthy, older intact male, a tentative diagnosis of BPH is justified. Ultrasound would be confirmatory, but there is usually no urgency. Watchful waiting would also be reasonable
  - The next diagnostic step is to palpate the scrotum for the presence of testicles ± a testicular tumor (see p. 1081).
- Ultrasound:
  - BPH causes symmetric prostatomegaly with a smooth capsule and homogeneous mixed echotexture of the parenchyma ± a few small (<10 mm) cysts. The urethra is normal.
  - Anechoic fluid within intra- and paraprostatic cysts ± concomitant BPH are common. Paraprostatic cysts are often very large (e.g., >15 cm diameter) and may mimic the urinary bladder in ultrasonographic appearance.
  - No lymphadenopathy, which might be present with prostatic infection or neoplasia.
  - Ultrasound testicles if estrogen-secreting tumor is suspected but not palpable.
- Abdominal radiographs indicated if tenesmus is present:
  - BPH, intraprostatic cyst, and squamous metaplasia cause prostatomegaly ± dorsal displacement of colon.
  - Paraprostatic cyst appears as a mid- or caudal-abdominal, soft-tissue mass, sometimes with calcification. Displacement of colon and/or urinary bladder. On survey radiographs alone, may be difficult to differentiate from urinary bladder.
  - No evidence of bone metastasis in pelvis or lumbar vertebra, which might be present with prostatic neoplasia.
- Urinalysis and urine culture indicated if urinary signs are present:
  - Macroscopic or microscopic hematuria may be found.
  - Culture results negative. Positive culture results indicate concomitant urinary tract infection and/or bacterial prostatitis.

ADVANCED OR CONFIRMATORY TESTING

- Not immediately necessary when symmetric, nonpainful prostatomegaly typical of BPH is found in an otherwise normal, healthy, older intact male dog.
- CBC:
  - Indicated if suspected squamous metaplasia (bone marrow suppression from hyperestrogenism)
  - Otherwise should be unremarkable
- Cytologic analysis and culture of prostatic tissue and/or fluid (see p. 1332):
  - Samples are easily obtained by fine needle aspiration using ultrasound guidance.
  - If the lesion does not communicate with the urethra, samples obtained by prostatic wash or third fraction of the ejaculate may produce a false-negative result.
  - Culture results should be negative. Positive culture results indicate concomitant bacterial prostatitis or abscess, and/or urinary tract infection, and/or contamination of the ejaculate with preputial organisms.
  - Hemospermia is often present with BPH, ± the occasional macrophage and nondegenerative neutrophil.
  - Increased numbers of squamous epithelial cells typically are found in prostatic wash and ejaculate samples from dogs with prostatic squamous metaplasia.
- Retrograde cystourethrogram (see p. 1237):
  - Urethra is normal with BPH. o Will clearly differentiate urinary bladder from paraprostatic cyst
- Biopsy, histopathologic evaluation:
  - Rarely necessary or indicated when all the testing described above is consistent with BPH, prostatic cyst, or squamous metaplasia and nothing else.

TREATMENT

TREATMENT OVERVIEW

- Healthy intact dogs with BPH or intraprostatic cysts, showing no clinical signs, do not necessarily require treatment, only watchful waiting. However, dogs with prostatic cysts and BPH may be at greater risk for ascending infection by urethral flora.
- Dogs with squamous metaplasia should be treated promptly by removing the source of estrogen (e.g., via castration if Sertoli cell tumor) before additional sequelae of estrogen toxicity develop.

ACUTE GENERAL TREATMENT

Surgical—castration:

- Castration is the treatment of choice (curative) for dogs with clinical signs due to BPH, prostatic cysts, or estrogen-secreting testicular tumors.
  - Prostatic involution is detectable within days of castration.
  - Prostatic size is expected to decrease by 50% within 3 weeks and 70% within 9 weeks.
  - Clinical signs of BPH typically are completely resolved within 4 weeks after castration.
  - Unilateral castration possible if estrogen-secreting testicular tumor in a valuable stud dog.

Surgical/medical:

- For paraprostatic cysts, complete surgical excision with castration is recommended. When the cyst is not amenable to complete surgical excision, omentalization is recommended. For a valuable stud dog, pharmacologic management, fine-needle drainage, or both may be an alternative, albeit temporary, solution.

CHRONIC TREATMENT

Pharmacologic:

- Less effective alternative to castration
- Treatment is typically given on an asneeded basis when clinical signs recur, until or unless castration is performed.
- Response to pharmacologic therapy is temporary. Semen quality and libido may be altered.
- 5α-Reductase inhibitors suppress conversion of testosterone to dihydrotestosterone, the androgen most active on the prostate:
  - Contraindicated in dogs with hepatic impairment
  - Finasteride (Proscar and Propecia [Merck]), 0.1-0.2 mg/kg PO q 24 h, or 5 mg/dog/d PO; off-label use
  - Clinical improvement of BPH in 1 week. Substantial reduction in prostate size by 8 weeks.
  - Optimal duration of therapy has not been determined, but beneficial effects on BPH appear to persist for 6 months or more after discontinuation.
- Progestins have multiple antiandro-genic mechanisms of action:
  - Contraindicated in dogs with diabetes mellitus

- Medroxyprogesterone, 3 mg/kg SQ once. Clinical signs of BPH relieved for 10-24 months in ≈84% of dogs.
- Delmadinone (Tardak [Pfizer]), 1.5 mg/kg IM or SQ on days 0 and 8. Remission of clinical signs of BPH for 6 months in ≈83% of dogs.
- Osaterone (Ypozane, Virbac), 2.5 mg/kg PO q 24 h for 7 days. Remission of clinical signs of BPH for 6 months in ≈83% of dogs.

NUTRITION/DIET

An herbal remedy from the saw palmetto plant *(Serenoa repens)* was suggested for use in men with BPH. It has no significant effect on the canine prostate.

DRUG INTERACTIONS

- Anticholinergic drugs may precipitate urine retention in BPH.
- Aminoglutethimide, felbamate and rifampin may interfere with progestins.

POSSIBLE COMPLICATIONS

- Adrenal axis suppression, insulin resistance and diabetes mellitus, increased appetite with progestins
- Alopecia and change in coat color may occur at injection site of medroxyprogesterone.
- Decreased fertility (semen quality, libido, and testicular size) with any antiandrogen
- Antiandrogens must not be used in sexually immature animals.

RECOMMENDED MONITORING

If castration is not performed, watchful waiting is recommended. Following castration for testicular tumor, submit for histopathologic analysis to confirm Sertoli cell tumor. Monitor CBC if bone marrow suppression, and treat accordingly.

PROGNOSIS AND OUTCOME

- Excellent for BPH and intraprostatic cysts:
  - Dogs not showing clinical signs may remain so for months to years.
  - Castration is curative of clinical signs of BPH, and cysts decrease in size.
- Pharmacologic therapy will temporarily improve clinical signs, but signs eventually (usually many months later) recur after treatment ends.

PEARLS & CONSIDERATIONS

COMMENTS

- Unlike the situation in men, BPH in dogs rarely causes stranguria or urine retention. When canine prostatic disease causes those signs or urethral involvement, it is more likely due to neoplasia than to BPH.
- Prostatomegaly in a castrated dog should prompt a search for neoplasia, not BPH.
- Dogs with BPH are usually otherwise healthy. If the dog is ill, a diagnosis other than or in addition to BPH should be pursued.

PREVENTION

Castration of juvenile dogs prevents BPH, intraprostatic cysts, and testicular tumors.

TECHNICIAN TIPS

- Care should be taken to avoid the enlarged prostate during urine collection by cystocentesis.
- Adequate restraint and analgesia (usually sedation or anesthesia) are needed to safely perform fine-needle aspiration or percutaneous biopsy of the prostate.

CLIENT EDUCATION

- Treatment may be delayed until clinical signs develop in otherwise healthy, normal, intact dogs with asymptomatic BPH or intraprostatic cysts.
- Castration is the treatment of choice because it is curative for BPH.

- Medical management can be done, but clinical signs will recur sometime (often many months later) after treatment is discontinued.
- The medications used for treating BPH are teratogenic, FDA category X. Women who might be pregnant must not handle the drugs.

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Proptosis of the Globe

BASIC INFORMATION

DEFINITION

Forward displacement of the globe (exophthalmos), with posterior entrapment of eyelids

EPIDEMIOLOGY

GENETICS & BREED PREDISPOSITION

Brachycephalic breeds of dogs and cats are at higher risk; however, if traumatic forces are sufficient, proptosis can occur in any breed of either species.

RISK FACTORS

Traumatic forces to the head (mild for brachycephalic; moderate to severe for mesaticephalic and dolichocephalic breeds)

ASSOCIATED CONDITIONS & DISORDERS

Retrobulbar mass or severe orbital abscess or cellulitis (see p. 790) may predispose the eye to proptosis.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

Caused by peracute event, usually blunt head trauma (e.g., hit by car, fighting)

PHYSICAL EXAM FINDINGS

Exophthalmos with eyelids entrapped caudal to globe. Any or all of the following may also be present:

- Conjunctival hyperemia or hemorrhage
- Corneal ulceration (see p. 250)
- Abnormal pupil size: constricted or dilated
- Intraocular inflammation and/or hemorrhage (seepp. 1151 and 571)
- Ruptured globe
- Avulsion of extraocular muscle(s), mainly medial and/or ventral oblique recti muscles
- Optic nerve rupture/transection
- Orbital fractures
- Other fractures: facial or appendicular skeleton
- Neurologic deficits from brain trauma
- Hypovolemic shock
- Intrathoracic abnormalities: diaphragmatic hernia, pulmonary contusions, hemothorax, pneumothorax

ETIOLOGY AND PATHOPHYSIOLOGY

- Force(s) applied to the head (i.e., trauma), leading to rostral displacement of the globe and posterior entrapment of eyelids.
- The orbit encircles a lesser proportion of the globe (i.e., is shallower) in brachycephalic individuals, allowing proptosis to occur despite a comparatively milder force of trauma.
- The medial rectus is the first extraocular muscle to avulse during trauma, leading to lateral strabismus. Multiple extraocular muscle avulsions produce a greater degree of proptosis, which indicates a worse prognosis.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

History and physical exam provide the diagnosis. Additional evaluation is directed at assessing vision and identification of trauma to the rest of the body.

DIFFERENTIAL DIAGNOSIS

- Exophthalmos secondary to orbital abscess (opening mouth may cause pain), benign or malignant orbital mass (opening mouth is rarely painful), congenital vascular anomalies (opening mouth is rarely painful; forward displacement of globe, but eyelids are in a normal position; rarely peracute; see p. 790).
- Buphthalmos secondary to congenital, primary, or secondary glaucoma (enlarged globe; eyelids in normal position; rarely acute). Unlike proptosis, is not associated with a blunt traumatic event (see p. 778).

INITIAL DATABASE

- Complete physical examination
- Ophthalmic examination (see p. 1313), including:
  - Pupillary light reflexes; a dilated, unresponsive pupil (both direct and consensual) carries a poor prognosis for the eye because optic nerve avulsion or transection is likely.
  - Fluorescein dye application
  - Intraocular pressure (IOP: >30 mm Hg with glaucoma; low [<10-15 mm Hg] with uveitis). IOP measurement should only be performed after the globe has been replaced in the orbit, thus releasing the pressure of the eyelids on the globe.
- Chest radiographs if hit by car, signs of trauma beyond the face, and/or dyspneic
- Skull radiographs if suspect orbital and/or skull fractures (e.g., extensive facial/cranial trauma, bony crepitus, and neurologic compromise such as obtundation).

TREATMENT

THEATMENT OVERVIEW

Although the primary goal is to return the globe to its proper anatomic location, enucleation may be preferable if grave prognostic indicators for vision are present.

ACUTE GENERAL TREATMENT

- Hemodynamic, respiratory, and neurologic stabilization if severe trauma (see pp. 1565,1592 , and1561)
- Keep cornea lubricated. If surgical correction is not immediately possible (e.g., grave anesthetic risk), hourly topical ointment application (alternating between bacitracin-neomycin-polymyxin antibiotic q 2 h and sterile lubricant q 2 h) is recommended.
- Placement of an Elizabethan collar to prevent self-inflicted trauma
- Repositioning of the globe, with patient under general anesthesia:
  - Lateral canthotomy: 1-2 cm incision at the lateral canthus to relieve pressure on the eyelids
  - Eyelids replaced over globe
  - Two to three horizontal mattress sutures exiting meibomian gland openings (4-0 to 6-0 suture material)
  - Segments of Penrose drain or IV tubing stents to distribute tension evenly on upper and lower eyelids
  - Simple interrupted sutures to close lateral canthotomy
  - Removal of medial-most sutures in 1-2 weeks and lateral-most sutures in 2-3 weeks, depending on resolution of exophthalmos
  - Vision, tear production, cornea, and intraocular structures (i.e., lens, retina) assessment within 1-2 weeks following surgery
- Enucleation if globe is ruptured, optic nerve is transected, and/or three or more extraocular muscles are avulsed

CHRONIC TREATMENT

- Topical atropine in medial canthus q 12 h for 3 to 5 days
- Topical triple antibiotic ointment q 6 h for 2 weeks
- Nonsteroidal antiinflammatory drugs (NSAIDs) systemically for 5-7 days. Dogs: carprofen, 2.2 mg/kg PO q 12 h or meloxicam, 0.1 mg/kg PO q 24 h. Cats: tolfenamic acid, 4 mg/kg SQ, IM, or PO q 24 h for 3-5 days.
- Broad-spectrum systemic antibiotics for 5-7 days (e.g., cephalexin, 10-20 mg/kg PO q 8 h)
- Placement of an Elizabethan collar until suture removal
- After repositioning and healing of the globe (days/weeks later), enucleation is sometimes still necessary if:
  - Eye is blind and painful (e.g., chronic uveitis, glaucoma)
  - Glaucoma occurs, especially in cats, owing to risk of posttraumatic ocular sarcoma (see p. 620)

POSSIBLE COMPLICATIONS

- Glaucoma
- Uveitis
- Strabismus (frequently lateral or dorso-lateral due to avulsion of medial rectus or medial and ventral oblique recti muscles, respectively; see p. 790)
- Blindness with mydriasis
- Keratoconjunctivitis sicca (KCS)
- Neurotrophic keratitis (damage to ophthalmic branch of trigeminal nerve supplying cornea, such as in corneal denervation) with chronic corneal ulceration

RECOMMENDED MONITORING

Recheck suture placement 24-48 hours postoperatively, since eyelid swelling could have dramatically improved, thereby causing loosening of sutures.

PROGNOSIS AND OUTCOME

- Varies depending on the extent of trauma (e.g., diffuse hyphema is a poor prognosticator).
- Most proptosed eyes with mild trauma can be salvaged.
- Overall prognosis for vision varies:
  - Poor to grave (dolichocephalic breeds and cats; dilated unresponsive pupil; marked proptosis [globe displaced several centimeters rostral to the l orbit])
  - Guarded to good (brachycephalic l breeds)

PEARLS & CONSIDERATIONS

COMMENTS

- True ocular emergency
- Avoid using topical corticosteroids (corneal ulceration is common).
- A blind comfortable eye can remain and have an excellent cosmetic appearance for the pet.

TECHNICIAN TIP

In the postoperative stage, avoid excessive pressure around the neck to avoid reproptosis (e.g., use harness instead of collar).

PREVENTION

Permanent partial tarsonhaphy (surgery to shorten palpebrai fissure [length of eyelid opening]) in brachycephalic breeds of dogs

CLIENT EDUCATION

- If globe is replaced but remains blind and painful in the postoperative stage, enucleation or evisceration with intraocular prosthesis is warranted.
- Early enucleation of blind and painful eyes in cats to prevent posttraumatic ocular sarcoma

SUGGESTED READING

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Prolonged Estrus

BASIC INFORMATION

DEFINITION

- In the dog, a combined proestrus and estrus of >6 weeks or a Cytologie estrus that lasts for >21 days
- In the queen, estrus lasting longer than 10 days is considered prolonged.
- *Ovarian remnant syndrome* (ORS) refers to clinical signs indicating presence of functional ovarian tissue in a previously ovariohysterectomized bitch or queen.

SYNONYMS

Persistent estrus (heat), nymphomania

EPIDEMIOLOGY

SPECIES, AGE, SEX: Female dogs and cats >4 months of age.

GENETICS & BREED PREDISPOSITION: Oriental cat breeds (e.g., Siamese) are predisposed to overlapping follicular waves that may present as prolonged or persistent estrus.

RISK FACTORS: Young and very old bitches; previous history of follicular cysts; abnormal karyotype

ASSOCIATED CONDITIONS & DISORDERS: Secondary to chronic estrogen exposure, bone marrow suppression, uterine disease, and mammary disease may occur.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- More than 21 days (dog) or 10 days (cat) of behavioral estrus
- Estrous behaviors in the bitch include receptivity to males, vulvar edema, and serosanguineous vaginal discharge; and in the queen, lordosis and vocalization.
- Recent use of estradiol cypionate as an abortifacient for unintended breedings is sometimes reported although not recommended.
- Use of estradiol supplements to treat urinary incontinence may be reported in the history.

PHYSICAL EXAM FINDINGS

- Bitch or queen may be in good health.
- Chronic exposure to estrogen can result in disease states manifesting as cystic endometrial hyperplasiapyometra complex, bone marrow suppression (anemia, agranulocytosis, thrombocytopenia), mammary and uterine neoplasia, and endocrinologic alopecia.
- Palpable unilateral abdominal mass (ovarian tumor)
- The most common presentation of ORS is recurrent estrus (e.g., vulvar swelling, flagging, standing to be mounted) after ovariohysterectomy.

ETIOLOGY AND PATHOPHYSIOLOGY

Prolonged estrus:

- Etiology depends on source of persistently circulating estradiol (exogenous or endogenous).
- Estrogen-secreting follicular cysts or granulosa cell tumors can result in persistent estrus.
    - Follicular cysts have been reported to occur in 3%-62% of dogs with ovarian cystic disorders. These cysts occur as either single or multiple thin-walled structures that contain a clear, serous fluid.
- In the queen, persistent estrus may result from the overlapping waves of maturing ovarian follicles, resulting in prolonged high concentrations of estradiol.

Recurrent estrus after ovariohysterectomy:

- Failure to remove all ovarian tissue at the time of ovariohysterectomy can result in recurring estrous cycles.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on the presence of estrous behaviors in an ovariohysterectomized animal or prolonged in an intact bitch or queen. Confirmation requires identification of the source of estradiol (exogenous or endogenous) and functional ovarian tissue.

DIFFERENTIAL DIAGNOSIS

- Persistent proestrus
- Split estrus (proestrus without subsequent estrus followed by a normal cycle in about 4 weeks)
- Recurrent estrus (low progesterone or premature luteal failure)
- Pyometra
- Vaginitis
- Coagulopathy
- Ovarian remnant syndrome

INITIAL DATABASE

- CBC (anemia, thrombocytopenia), serum biochemistry profile, urinalysis
- Exfoliative vaginal cytologic examination indicative of estrus: >90% cornification of epithelial cells
- Abdominal ultrasonography to look for endogenous sources of estradiol:
    - Identification of abnormal ovarian structures: anechoic spherical regions in the ovary (follicles) or mixed echogenicity of a tumor
    - Identification of ovarian remnant in an ovariohysterectomized animal

ADVANCED OR CONFIRMATORY TESTING

- Vaginoscopy to rule out foreign body and vaginitis
- Exclusion of abnormal karyotype
- Coagulation panel to rule out coagulopathy
- LH testing (using an in-house kit) is 99% reliable at diagnosing ORS in both cats and dogs.

TREATMENT

TREATMENT OVERVIEW

Treatment of abnormal estrus consists of removing the source of estradiol. For persistent estrus, induction of follicular luteinization, with subsequent monitoring of progesterone concentrations and vaginal cytology for signs of diestrus, or alternatively performing an ovariohysterectomy. For ORS, surgically remove any remaining ovarian tissue.

ACUTE GENERAL TREATMENT

Medical:

- Follicular cysts in dogs and cats may be treated with gonadotropin-releasing hormone (GnRH, 25 mcg IM; use 2.2 mcg/kg if >11 kg) or human chorionic gonadotropin (hCG, 500-1000 IU IM), which results in luteinization of the follicles.
- Monitor serum progesterone, and perform a vaginal cytologic examination weekly following GnRH or hCG administration; monitor for signs of diestrus or anestrus.
- Canine GnRH vaccine can be used in the treatment of ORS where surgical removal of the remnant is not an option.

Surgical:

- When genetic qualities of the dam are not superior, ovariohysterectomy is the treatment of choice following reduction of current hyperestrogenic state.
- Removal of remaining ovarian tissue is the recommended treatment for ORS.

CHRONIC TREATMENT

If acute medical treatment is not effective, surgical treatment is required.

POSSIBLE COMPLICATIONS

- Pyometra sequelae:
  - Progesterone promotes endometrial growth and glandular secretion while decreasing myometrial activity. Cystic endometrial hyperplasia and accumulation of uterine secretions ultimately develop and provide an excellent environment for bacterial growth.
  - Chronic estradiol production by the cystic follicles upregulates progesterone receptors in the uterus. This enhances the effect of the progestins produced following treatment to luteinize the cystic follicles.
- Complication rate for surgical removal of an ovarian remnant in dogs is unknown.

RECOMMENDED MONITORING

Monitor signs of estrus that should subside within 5-7 days of treatment.

PROGNOSIS AND OUTCOME

- Recurrence is possible, but prognosis is good if signs of diestrus follow treatment.
- If estrus persists, increased suspicion of neoplasia or abnormal karyotype yields a poorer prognosis for subsequent fertility, and an ovariohysterectomy is indicated.
- Surgical removal of ovarian remnants results in a good prognosis if signs of cycling cease.

PEARLS & CONSIDERATIONS

COMMENTS

- Although ovarian cancer is rare in the bitch or queen, failure of medical treatment to end signs of behavioral estrus or decrease circulating estradiol concentrations greatly increases the possibility of this diagnosis.
- Timing of exploratory surgery to remove ovarian remnants is important: surgery should be performed when the animal is under an estrogenic influence so ovarian tissue is enlarged and easier to identify.

PREVENTION

In animals of nonbreeding stock, complete ovariohysterectomy will prevent reproductive abnormalities and their sequelae.

CLIENT EDUCATION

- Train owners to recognize signs of estrus, or discuss outward signs of behavioral estrus for the bitch and queen.
- Clinicians and owners should discuss multiple benefits of spaying nonbreeding stock while young.
- Recurrence is more likely in animals with previous follicular cysts.

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Prolonged Anestrus

BASIC INFORMATION

DEFINITION

Duration of interestrous interval >40 weeks. Overall, a rare disorder.

SYNONYMS

Primary or secondary anestrus; prolonged interestrous interval

EPIDEMIOLOGY

SPECIES, AGE, SEX

Female dogs and cats

- Bitches > 12 months old (more common in older bitches)
- Queens > 6 months old

GENETICS & BREED PREDISPOSITION: Longhaired queens have a tendency to experience delayed puberty.

RISK FACTORS: Previous ovariectomy, exogenous hormonal treatment (including glucocorticoids), hyperthyroidism, ovarian disease (cysts or neoplasia), or abnormal karyotype

GEOGRAPHY AND SEASONALITY

- Bitches are nonseasonally monoestrous (exception: basenji dog that only comes into estrus in the fall). The normal interestrous interval in dogs is 26-36 weeks.
- The queen is a seasonally polyestrous long-day breeder (see p. 909). The normal interestrous interval in queens is 12-22 days.

ASSOCIATED CONDITIONS & DISORDERS

Ambiguous or infantile external genitalia may be associated with an intersex condition or abnormal karyotype.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Primary anestrus: delayed puberty
- Secondary anestrus: increased interestrous interval

HISTORY, CHIEF COMPLAINT

Failure to show external signs of proestrus or estrus (failure to cycle)

PHYSICAL EXAM FINDINGS

Abnormal physical findings may include poor or excessive general body condition, overall immature appearance, and ambiguous or infantile external genitalia. The physical examination may be unremarkable.

ETIOLOGY AND PATHOPHYSIOLOGY

- Variable, depending on the cause
- Disruption in the normal cyclical hormonal milieu

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on the absence of estrous behaviors in an intact animal, followed by excluding anatomic abnormalities and endocrine-related illnesses. Confirmation requires histopathologic identification of oophoritis or diagnostic imaging (CT scan) demonstrating pituitary abnormalities.

DIFFERENTIAL DIAGNOSIS

Dogs:

- Silent heat
- Abnormalities in sexual differentiation
- Hyperadrenocorticism
- Hypothyroidism
- Pituitary insufficiency
- Lymphocytic oophoritis
- Luteal ovarian cyst
- Ovarian aplasia
- Ovariohysterectomy

Cats:

- Seasonal or lighting changes
- Pseudopregnancy
- Diabetes mellitus
- Silent heat (social stress in cattery)
- Ovariohysterectomy

INITIAL DATABASE

- CBC and serum biochemistry profile for systemic health status
- Assessment of endocrine-related illnesses via thyroid hormone analysis and dexamethasone suppression tests
- Exclusion of silent heats, using exfoliative vaginal cytologic examination and serum progesterone determination
- Exclusion of abnormal reproductive tract, using abdominal ultrasonography
- Exclusion of abnormal karyotype

ADVANCED OR CONFIRMATORY TESTING

- Confirmation of oophoritis with ovarian histologic examination
- CT scan of pituitary to identify cystic dilation or absence of the gland

TREATMENT

TREATMENT OVERVIEW

Treatment mainly consists of correcting insufficiencies or excesses in endocrine hormones (e.g., hyperadrenocorticism), as well as observation and monitoring for reproductive cyclicity.

ACUTE GENERAL TREATMENT

- Observe bitch or queen closely while housing her near an intact male dog or tom.
- Monitor serum progesterone concentrations monthly to assess cyclicity (serum progesterone >2 ng/mL for 2 months after each estrus in the normal bitch).
- Cohouse anestrous bitch with cycling bitches to stimulate a “dormitory” effect.
- Increase lighting in cattery to 14 hours of light per day.

CHRONIC TREATMENT

Estrus induction: no approved methods of estrus induction in the dog or cat, but many protocols have been described. Possible methods:

- Dogs: after confirming a progesterone concentration <1 ng/mL, administer 1 Ovuplant (deslorelin implant) under the subvestibular mucosa. Proestrus will be initiated in <10 days.
- Cats: after one subcutaneous injection of human chorionic gonadotropin (hCG, 1000 IU), naloxone (0.04 mg/kg) in 20% calcium gluconate solution is administered intramuscularly once a day beginning the day of the hCG injection. A compounded solution can be made by adding naloxone powder to 20% calcium gluconate solution to achieve a final concentration of 0.4 mg/mL naloxone for a dose of 0.1 mL/kg. Proestrus will be initiated in <8 days.

POSSIBLE COMPLICATIONS

Continued release of deslorelin from the Ovuplant implant may result in pituitary downregulation and premature luteal failure. To prevent premature luteal failure, remove the implant once serum progesterone concentration is >2 ng/mL.

RECOMMENDED MONITORING

- Initially, progesterone concentrations should be measured to determine time for implant removal.
- Monitor the bitch and queen for signs of behavioral or physical estrus.

PROGNOSIS AND OUTCOME

- With correction of endocrine abnormalities, future reproductive success is not compromised.
- If chromosomal abnormality, ovarian aplasia, or autoimmune disease exists, the prognosis for successful return to cyclicity is poor.

PEARLS & CONSIDERATIONS

COMMENTS

Evaluation of the entire clinical picture is important:

- Review estrus identification techniques with owner.
- Identify all medications and supplements the animal is receiving.
- Assess the animal's overall metabolic health status.
- Evaluate thyroid and adrenal gland function in bitches.

PREVENTION

In cats, ensure 14 hours of light exposure daily to induce seasonal cycles.

CLIENT EDUCATION

- Provide training for the client so he or she can recognize estrus in the animal, or discuss outward signs of estrus for the bitch and queen.
- Discuss age as a factor for the absence of cyclicity (prepubertal, photoperiod, and older animals).

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Johnston S: Infertility in the bitch. In Kirk RW, Bonagura JD, editors: Current veterinary therapy VIII: small animal practice. Philadelphia, 1992, WB Saunders, pp 954–960.

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Primary Ciliary Dyskinesia

BASIC INFORMATION

DEFINITION

A rare congenital disorder in which defective ciliary motility leads to impaired mucociliary transport and recurrent respiratory infection

SYNONYMS

Immotile cilia syndrome, Kartagener's syndrome, PCD

EPIDEMIOLOGY

SPECIES, AGE, SEX: Young dogs of either sex

GENETICS & BREED PREDISPOSITION: Numerous breeds of dogs are affected with primary ciliary dyskinesia (PCD); a monogenic autosomal recessive pattern of inheritance has been demonstrated in Newfoundland dogs and is likely to be present in other breeds as well.

ASSOCIATED CONDITIONS & DISORDERS

- Rhinitis, sinusitis, and pneumonia occur as a result of PCD.
- Bronchiectasis results from repeated airway infections.
- Defective ciliary function in other organs may lead to male infertility, hydrocephalus, or otitis media.
- Situs inversus (mirror-image reversal of the position of organs in the body), bronchiectasis, and PCD define Kartagener's syndrome, seen in a subset of animals.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

Young dogs present with signs of recurrent upper and/or lower respiratory tract infection. Nasal discharge, sneeze, and cough are common features, while dyspnea occurs less frequently. Infections often improve dramatically with antibiotic treatment but recur after cessation of antibiotics.

PHYSICAL EXAM FINDINGS

- Bilateral mucopurulent nasal discharge
- Sneezing
- Coughing
- Dyspnea with crackles when pneumonia is present
- Fever possible when pneumonia is present

ETIOLOGY AND PATHOPHYSIOLOGY

- The mucociliary escalator is a major contributor to physical defense of the airways.
- Pathogens and particulates are normally trapped in a layer of mucus overlying the ciliated epithelium.
- Synchronized movement of the cilia propels entrapped pathogens and particles orad for removal from the airways.
- In animals with PCD, structural and/or functional defects in the cilia themselves lead to uncoordinated, asynchronous ciliary motion and ineffective clearance of pathogens and particles trapped in the mucus layer.
- Failure of the mucociliary escalator results in recurrent bacterial infection of the airways.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Secondary (acquired) ciliary dyskinesia

- Primary respiratory infections/inflammatory airway disease
- Inhalation of toxic substances (e.g., smoke)

- Noninfectious respiratory inflammatory disease (e.g. lymphoplasmacytic rhinitis, eosinophilic bronchopneumopathy)
- Congenital immunodeficiency syndromes
- Chronic bacterial or fungal respiratory infections, either treated inappropriately or from infection with atypical pathogens

INITIAL DATABASE

- CBC:
  - Neutrophilic leukocytosis possible if pneumonia is present
- Serum biochemistry: nonspecific
- Thoracic radiographs:
  - Alveolar, bronchiolar, and/or interstitial lung patterns may be observed.
  - Bronchiectasis
  - Situs inversus is detected in some dogs (apex of the heart points to the right; lung anatomy is reversed on the median plane) and is strongly suggestive of PCD.

ADVANCED OR CONFIRMATORY TESTING

- Semen evaluation: abnormal motility of spermatozoa
- Tracheal wash or bronchoalveolar lavage: neutrophilic inflammation, often with intracellular bacteria; samples should be cultured.
- Nuclear scintigraphy: technetium-99 macroaggregated albumin is deposited at the carina, and movement is followed with a gamma camera for 30 minutes. Isotope fails to move orad in dogs with congenital or acquired ciliary dysfunction.
- Electron microscopy: ultrastructural defects can be detected on glutaraldehyde-fixed biopsies of nasal or tracheal mucosa, but detection is technically demanding. Thus, samples should be sent to a pathologist with experience in interpreting these biopsies. Alternatively, ciliated epithelium may be cultured in vitro and resultant tissues examined by electron microscopy.
- Ciliary beat frequency and synchronization: technically demanding process requiring special equipment; allows functional observation of cilia from freshly obtained biopsies; impractical in most instances.

TREATMENT

TREATMENT OVERVIEW

Affected animals typically require repeated courses of antimicrobials throughout life to control infection, as there is no treatment for the primary disease.

ACUTE GENERAL TREATMENT

- Appropriate antimicrobial therapy, based ideally on culture and sensitivity (C&S) results from tracheal or bronchial lavage samples
- For dogs with pneumonia:
  - Consider oxygen supplementation if respiratory distress is present in the face of hypoxemia (Pao2 < 80 mm Hg or SpO2 < 94%). See p. 1318.
  - Maintain hydration with parenteral fluids as needed.
  - Encourage expectoration of mucus from airways via saline nebulization and coupage (see p. 1310).

CHRONIC TREATMENT

- Repeated courses of antimicrobial drugs are required for recurrent infections.
- Avoid treatment with cough suppressants.
- Avoid exposure to respiratory irritants, such as cigarette smoke.

POSSIBLE COMPLICATIONS

- Bronchiectasis
- Pneumonia
- Sepsis
- Cor pulmonale
- Reactive systemic amyloidosis

RECOMMENDED MONITORING

- Evaluate thoracic radiographs at least every 6-9 months in animals with prior episodes of pneumonia.
- Exacerbations of clinical signs due to lower respiratory disease should prompt tracheal or bronchial lavage for cytologic examination and culture.
- Culture and sensitivity testing of respiratory washes becomes increasingly important the more often an affected animal has been treated with antimicrobials.

PROGNOSIS AND OUTCOME

Dependent on severity of ciliary dysfunction. Illness can range from occasional episodes of upper respiratory infection to severe and frequent bronchopneumonia. Lifespan is usually negatively impacted by the condition.

PEARLS & CONSIDERATIONS

COMMENTS

Even when episodes of pneumonia are rapidly addressed, affected dogs are often euthanized because of the inconvenience and expense of treating recurrent respiratory disease and chronic nasal discharge despite appropriate antimicrobial therapy; these treatments may be a nuisance for owners of affected dogs.

PREVENTION

Affected dogs should not be bred.

TECHNICIAN TIPS

Label thoracic radiographs, especially the ventrodorsal or dorsoventral projections, with right or left markers to help confirm the radiographic diagnosis of situs inversus.

CLIENT EDUCATION

Clients should understand that this is an inherited condition that cannot be cured.

SUGGESTED READING

Edwards DF, et al: Primary ciliary dyskinesia in the dog. Prob Vet Med 4:291, 1992.

Watson PJ, et al: Primary ciliary dyskinesia in Newfoundland dogs. Vet Rec 144:718, 1999.

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Priapism

BASIC INFORMATION

DEFINITION

Persistent penile erection (uncommon disorder)

SYNONYM

Persistent erection

EPIDEMIOLOGY

SPECIES, AGE, SEX: Male dog or cat

GENETICS & BREED PREDISPOSITION: None reported

RISK FACTORS: Reproductive status: intact males are more likely than neutered males to develop priapism secondary to trauma.

ASSOCIATED CONDITIONS & DISORDERS

- Neurologic disorder (e.g. spinal cord injury, distemper encephalomyelitis)
- Circulatory disturbance (e.g. hemoglobinopathy)
- Penile neoplasia
- Achalasia

CLINICAL PRESENTATION

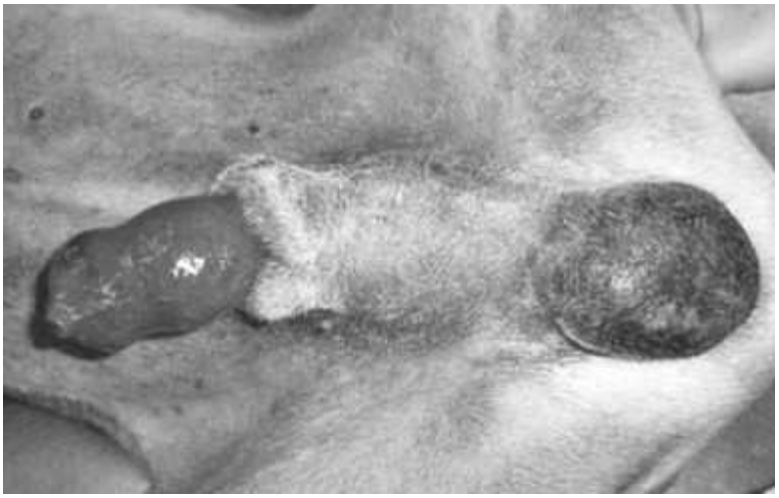
DISEASE FORMS/SUBTYPES

- Traumatic: during mating or castration
- Nontraumatic: priapism results from disturbances in the normal mechanisms of penile flaccidity (not sexual stimuli).
    - Neurologic: spinal cord injuries (trauma), inflammation (genitourinary, spinal cord [distemper]), mechanical compression (constipation) or pharmacologic (acepromazine-induced priapism [dogs, cats]), leading to the stimulation of the erection center or the pelvic nerve
    - Circulatory: occlusive penile thromboembolism that decreases venous outflow; occlusive pelvic mass (tumor, abscess) impairing glans penis venous drainage; secondary to systemic disease (e.g. hemoglobinopathy)

HISTORY, CHIEF COMPLAINT: Persistent erection or inability to withdraw erect penis into prepuce

PHYSICAL EXAM FINDINGS

- Persistent, usually painful, erection lasting >1 hour
- Bulbus glandis may be within or outside the prepuce.
- Penile mucosa may be dry, inflamed, excoriated and is often purple (blood stasis). Eventually, the penis will become necrotic. The male frequently licks the penis and self-mutilation may occur.
- An enlarged (or ruptured) bladder is possible if urethral obstruction is present.



PRIAPISM Priapism in a 7-year-old male boxer; ventral aspect of inguinal region, cranial is to the left. This penis had been persistently erect for 7 days. Penile mucosal erosion and congestion were evident as well as periscrotal edema.

(Used with permission from Martins-Bessa A, Santos T, Machado J, et al: Priapism secondary to perineal abscess in a dog: a case report. Reprod Domest Anim 45:558-563, 2010. Published online Dec 2008, DOI: 10.1111/j/1438-0531.2008.01257.x.)

ETIOLOGY AND PATHOPHYSIOLOGY

- Alteration of penile blood, causing vascular stasis in the corpus cavernosum and spongiosum
- Sluggish, damaged erythrocytes occlude venous outflow.
- Erythrocyte stagnation triggers carbon dioxide release, trabecular edema.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is made entirely on physical examination. Diagnostic tests aim to identify the cause; test selection is based on other features of the history and general physical exam.

DIFFERENTIAL DIAGNOSIS

- Normal erection
- Paraphimosis (see p. 835) without priapism
- Penile paralysis

INITIAL DATABASE

- Examination and palpation will confirm whether the penis is firm (persistently erect) or flaccid (as in the case of paraphimosis without priapism).
- Observation of urination or urethral catheterization to confirm that the urethra is not obstructed
- Neurologic examination to determine if any other neurologic deficits are present
- CBC if suspicious of hemoglobinopathy

ADVANCED OR CONFIRMATORY TESTING

- Serum chemistry panel and urinalysis if patency of the urethra and integrity of the bladder is questioned
- A penile cavernogram can be used for identifying thromboemboli or masses and the extent of venous outflow impairment
    - Dynamic cavernosography consists of infusing heparinized saline at increasing rates (3-25 mL/min) until the intracavernous pressure plateaus at full erection pressure, followed by infusing 60% Hypaque meglumine contrast medium to opacity abnormally draining veins.
    - Butterfly needles (21-G) can be inserted into the corpora cavernosa and connected to a pressure transducer.
- Angiography can also be used for identifying abnormal circulatory patterns.

TREATMENT

TREATMENT OVERVIEW

The goal of priapism therapy is to achieve detumescence and restore normal circulation in the penile erectile tissues. Treatment aims to preserve the penis from severe exposure and constrictive injury, and prevent urethral obstruction. A prompt diagnosis of the underlying cause is essential for optimal treatment, though the underlying cause may not be identifiable in many cases.

ACUTE GENERAL TREATMENT

- Conservative treatment: cool hypertonic compresses several times daily; topical lubrication; systemic corticosteroids at antiinflammatory doses (e.g., prednisone, 1 mg/kg PO q 12 h × 5 days), antibiotics, and diuretics. Generally unsuccessful.
- Manual reduction of the penis into the prepuce (with or without incisional preputioplasty) is unrewarding or impossible.
- Medical treatment with intravenous benztropine mesylate (0.015 mg/kg), an anticholinergic and antihistaminergic drug, has been used successfully in horses but must be administered within 6 hours after the onset of priapism.
- Increasing venous outflow via drainage and flushing of the erectile tissues to remove the clotted blood with heparinized saline (0.9% NaCl) solution in combination with infusion of phenylephrine, norepinephrine, or epinephrine (successful in humans and horses; must be applied soon after onset)
- Surgery: tunica albuginea incision (includes incision of the bulbus glandis and pars long glandis) is usually successful without permanent damage; must be performed within 12 hours of onset.

CHRONIC TREATMENT

If the penis is irreparably damaged or urethral patency cannot be maintained, penile amputation with a prescrotal urethrostomy (and castration if still intact) are necessary.

RECOMMENDED MONITORING

- Urination should be closely monitored and a catheter placed if stranguria develops.
- If severe penile necrosis develops, the penis should be amputated.

PROGNOSIS AND OUTCOME

If priapism is treated aggressively, the prognosis is guarded, but aggressive acute treatment may prevent the necessity for penile amputation.

PEARLS & CONSIDERATIONS

COMMENTS

Priapism is an emergency condition requiring aggressive acute treatment to induce detumescence.

PREVENTION

Care should be taken during surgical castration to avoid the stimulating pelvic nerves, which could result in priapism.

CLIENT EDUCATION

Breeders should confirm that detumescence occurs after each breeding and contact their veterinarian if an erection persists for more than 1 hour.

SUGGESTED READING

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AUTHOR AND EDITOR: MICHELLE KUTZLER

Preputial Discharge

BASIC INFORMATION

DEFINITION

Common disorder consisting of the presence of normal or abnormal secretions emerging from the penile sheath (prepuce). Discharge can be physiologic or pathologic and either primary or secondary to other reproductive or systemic diseases.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Canine; prepubertal or adult
- Normal males, males with preputial abnormalities or with preputial tumors, male pseudohermaphrodites

GENETICS & BREED PREDISPOSITION: Prevalence is higher in inbred lines or certain breeds (i.e., brachycephalic).

RISK FACTORS

- Acquired or congenital penile anatomic abnormalities
- Acquired or iatrogenic hormonal imbalances
- Poor hygiene/kennel management
- Transmissible venereal tumor (sticker sarcoma)
- Canine herpesvirus type 1 or *Brucella canis* infection
- Prostatic disease
- Anticoagulant rodenticide exposure
- Foreign body (e.g., grass awn)

CONTAGION & ZOONOSIS

Preputial discharge may be contagious if caused by canine herpesvirus type 1 (seep. 525), *B. canis* (seep. 162), or transmissible venereal tumor (see p. 162p. 1114).

ASSOCIATED CONDITIONS & DISORDERS

Balanitis (inflammation of the penis), balanoposthitis (inflammation of penis and prepuce), urinary tract infection, prostatic disease

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Preputial discharge of any type (observed by owner)
- Preputial licking
- Preputial discomfort/pain if touched
- Preputial enlargement or lesions observed
- Additional signs depend on underlying disease (e.g., lethargy, pollakiuria, dysuria)

PHYSICAL EXAM FINDINGS

Depending upon cause:

- Preputial anatomic abnormalities
- Preputial or penile lesions
- Pain resulting from inflammation exacerbated during manipulation
- Preputial opening atrophy
- Preputial mucosal vesicles (canine herpesvirus type 1)
- Prominent preputial lymphoid follicles (nonspecific)
- Masses (e.g., cauliflower-like friable lesions in transmissible venereal tumor [TVT])

- Systemic signs (e.g., lethargy, sluggishness, possibly other sites of bleeding) with anticoagulant rodenticide toxicosis

ETIOLOGY AND PATHOPHYSIOLOGY

- Normal preputial discharge: small amount of yellow-white smegma
- Abnormal preputial discharge:
  - Mucoid: hormonal imbalance in prepubertal dogs
  - Purulent: infection, foreign body
  - Hemorrhagic: coagulopathy, trauma, neoplasia, prostatic disease, testicular disease
    - In juvenile dogs, most common causes include:
      - Congenital abnormality
      - Coagulopathy
      - Hormonal imbalance preceding puberty (diagnosis of exclusion for mucoid discharge in juvenile animal)
    - In mature dogs, potential causes include:
      - Chronic congenital abnormality
      - Infectious disease of the external genitalia (canine herpesvirus type 1 or *B. canis*) or urinary tract or iatrogenic origin (improper antibiotic treatment)
      - Systemic or reproductive tract diseases including prostatic disease, trauma, or tumor

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Age allows for discrimination between juvenile or adult forms of preputial discharge. Juvenile forms are generally benign, most often involving hormonal imbalance rather than infection or congenital abnormalities. Adult forms generally are more serious, more often are chronic, and require a diagnostic workup that is more extensive (typically including microbiologic and serologic testing).

DIFFERENTIAL DIAGNOSIS

- Primary: preputial or penile problem:
  - Anatomic abnormality (phimosis or paraphimosis, penile frenulum, adhesion, hypospadias)
  - Trauma (fighting, biting, mating, os penis fracture)
  - Foreign body (e.g., grass awn)
  - Infection (canine herpesvirus type 1, *B. canis,* or abnormal microbiological flora)
  - Neoplasia
- Secondary: other general or reproductive diseases:
  - Prostatic disease
  - Hormonal imbalance (particularly around puberty or associated with Sertoli-cell tumor or hormonal treatments)
  - Urinary tract infection
  - Urethral neoplasm
  - Bladder disease
  - Coagulopathy

INITIAL DATABASE

- Complete preputial examination, including retraction of the prepuce to caudal to the bulbus glandis; may require sedation or anesthesia if painful
- Coagulation profile and platelet count if hemorrhagic preputial discharge
- Preputial swab for culture and cytologic examination:
  - Normal flora: mixed, including *Escherichia coli, Pseudomonas* spp., *Streptococcus* spp., *Pasteurella* spp., *Staphylococcus* spp., *Klebsiella* spp., *Mycoplasma* spp., *Ureaplasma* spp.
  - Antibiotics are not indicated and should not be administered to treat a normal mixed population of preputial bacteria.
  - A heavy growth of a single type of bacteria associated with clinical signs suggests infection.

ADVANCED OR CONFIRMATORY TESTING

- Physical examination of the penis at rest and during erection
- Complete systemic and urogenital exam, including urinalysis, prostatic ultrasonography, semen and prostate fluid analysis, and possibly urethrography if stranguria/pollakiuria
- *Ureaplasma* spp. and *Mycoplasma* spp. culture
  - Both isolated from the prepuce of 60%-85% of normal dogs

- *Mycoplasma* spp. more prevalent (92%-95%) when balanoposthitis is present
- *Ureaplasma* spp. infection associated with infertility

- CBC and serum biochemistry profile if systemic signs of illness are manifested
- Endoscopic examination of prepuce: if foreign body or mass is suspected but not seen otherwise
- Biopsy or cytologic examination of preputial masses

TREATMENT

TREATMENT OVERVIEW

Treatment depends on the cause and may vary from local cleansing and disinfection to surgical removal of any masses or systemic antibiotics.

ACUTE GENERAL TREATMENT

- Varies depending on the origin and the causal agents
- In all cases, excessive discharge should be cleansed by flushing with warm (98°F/38°C) saline.
- Selected examples:
  - Anatomic defects: surgical correction of the abnormality
  - Hormonal imbalance: benign neglect; antibiotic treatment is contraindicated
  - Preputial foreign body: removal

CHRONIC TREATMENT

Chronic cases refractory to basic treatment should be referred to a theriogenologist, particularly if the future reproductive potential is a concern.

BEHAVIOR/EXERCISE

Owners should prevent the dog from licking the prepuce and/or penis.

POSSIBLE COMPLICATIONS

- Primary recurrent and/or chronic infections: urinary tract infections, prostatic disease, and possibly orchitis
- Canine herpesvirus type 1 and *B. canis:* associated with infertility and transmissible to other dogs
- If transmissible venereal tumor is diagnosed, check for the presence of oral and/or respiratory mucosal lesions (licking) and prevent transmission to other dogs.

RECOMMENDED MONITORING

In adult animals, long-term systemic antibiotic treatment is indicated to reduce the risk of complications (e.g., prostatitis, urinary tract infection).

PROGNOSIS AND OUTCOME

Generally good in young animals. Fair to guarded in older animals, depending upon the origin.

PEARLS & CONSIDERATIONS

COMMENTS

- A small amount of yellow-white smegma is normal at the preputial opening of male dogs of any age or neuter status.
- More of an annoyance than a real disease in juvenile animals, except if it is of anatomic origin (defect) or systemic (e.g., coagulopathy).
- Preputial discharges generally resolve spontaneously without treatment in juvenile (prepubertal) dogs.
- Secondary infection is rare except when systemic antibiotics are administered, leading to selection of resistant bacteria.
- Preputial discharges are often of secondary origin in older animals, and identifying the primary cause of the discharge should always be the initial objective after a systematic physical exam of the external genitalia.

PREVENTION

- Often related to prepubertal hormonal imbalance, prevention is impossible.
- As potentially related to canine herpesvirus type 1, *B. canis,* or transmissible venereal tumor, avoiding contact with affected or potentially affected animals is advised.

TECHNICIAN TIPS

- Preputial discharge can be considered normal and of no clinical significance in most dogs except if abundant or associated with clinical signs. Pain can then be a component of the disease and should be considered at the time of examination as well as during the period of treatment.
- Normal preputial discharge in dogs used for reproduction may need to be cleaned away before semen collection, using physiologic saline to avoid possible contamination of the ejaculate.

CLIENT EDUCATION

- The benign nature of normal preputial discharge should be explained to clients. Antimicrobial therapy should never be used without bacterial culture demonstration of pathogens.
- Clients should be informed to call their veterinarian if the discharge is unusual, abundant, or associated with clinical signs including licking or pain.

SUGGESTED READING

Johnston S, et al: Disorders of the canine penis and prepuce. In Johnston S, Root Kustritz MV, Olson P, editors: Canine and feline theriogenology. Philadelphia, 2001, WB Saunders, pp 356–367.

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Pregnancy

BASIC INFORMATION

DEFINITION

- The period of gestational development within the uterus, beginning at conception and continuing through parturition
- Bitch: gestation length is 65 days from the luteinizing hormone (LH) surge (54-60 days from the first day of diestras and 57-72 days from breeding)
- Queen: gestational length is 64 days from LH surge. Cats are induced ovulators, and the LH surge corresponds to 24 hours following the first breeding date.

SYNONYM

Gestation

EPIDEMIOLOGY

SPECIES, AGE, SEX

Canine and feline: postpubertal intact female (usually >6 months old)

GENETICS & BREED PREDISPOSITION

Fertility and fecundity are heritable traits. Mixed breeds and outcross matings generally result in higher pregnancy rates and larger litter sizes. Litter size is also dependent on maternal size; smaller breeds have fewer offspring/litter.

RISK FACTORS

Intact females exposed to intact males

GEOGRAPHY AND SEASONALITY

- Canine: most domestic breeds cycle twice yearly irrespective of season, with the potential to become pregnant during each estrous cycle. Wolf hybrids cycle annually during the spring (long-day breeders), and basenjis cycle annually during autumn (short-day breeders).
- Feline: domesticated cats are polyestrous, long-day breeders (queening during spring and summer) with seasonal anestrus during the winter months. It is possible for a queen to have multiple litters each year.

ASSOCIATED CONDITIONS & DISORDERS

- Insulin resistance (pregnancy-associated diabetes)
- Pregnancy anemia
- Pyometra
- Hydrops (amnion or allantois)
- Overt false pregnancy/pseudocyesis
- Abortion or early embryonic loss

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Intentional breeding
- Unintentional breeding
- Unexplained weight gain
- Unexplained mammary development and lactation
- Nesting behavior

PHYSICAL EXAM FINDINGS

- Embryonic vesicles or fetuses palpable abdominally:
  - Embryonic vesicles are palpable approximately 25-35 days post LH surge.
  - Fetuses are palpable after approximately 45 days post LH surge.
- Mammary development and lactation usually emerge in the last 2 weeks of pregnancy.

ETIOLOGY AND PATHOPHYSIOLOGY

- Ovulation occurs 48 hours post-LH surge in dogs and 48 hours post breeding in cats.
  - Bitches are most fertile 2-4 days post ovulation (4-6 days post LH surge); however, pregnancy can result from breedings preceding ovulation by as much as 7 days if the sperm survive within the uterine tubes until the ova mature.
- Fertilization occurs in the uterine tube (ampulla-isthmus junction), and the embryos enter the uterus approximately 10-11 days post-LH surge in the bitch (5-6 days post-LH surge in the queen).
- Embryos migrate within the uterus and may implant in the horn ipsilateral or contralateral to ovulation.
- Implantation occurs 15-17 days post-LH surge in the bitch (14-15 days post-LH surge in the queen).
- Pregnancy is progesterone-dependent throughout gestation. Corpora luteal production of progesterone is required for pregnancy maintenance. Prolactin is luteotropic and maintains the corpus luteum during the second half of pregnancy in both dogs and cats.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

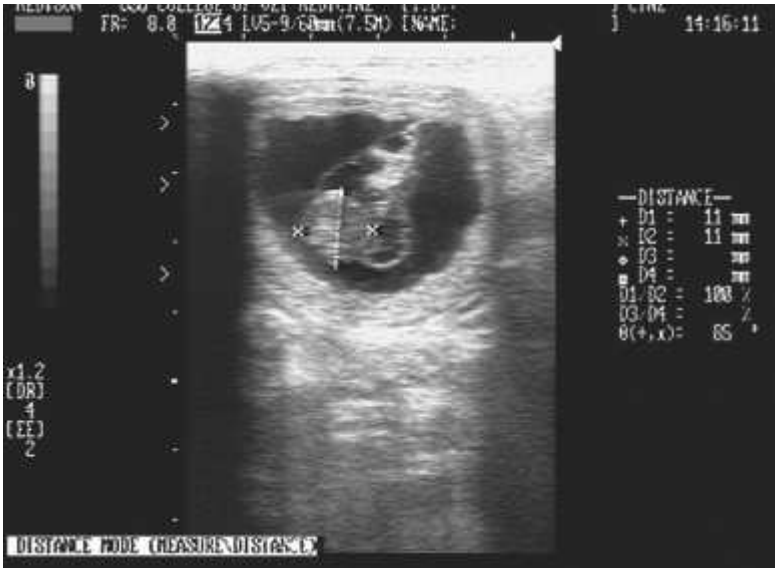
Transabdominal ultrasound (>20 days post-LH surge) is the most informative method to confirm pregnancy, but it also requires the greatest experience. All methods of diagnosis may result in misdiagnosis if performed too early in gestation and warrant repeat evaluation 1-2 weeks later if a definitive diagnosis cannot be made.

DIFFERENTIAL DIAGNOSIS

- Pyometra
- Mucometra
- Overt false pregnancy/pseudocyesis

INITIAL DATABASE

- Abdominal ultrasound (see figure): Embryonic vesicles can be detected as early as 20 days post-LH surge (16 days post-LH surge in cats). The embryo can be detected after 25 days post-LH surge.
  - False positives (diagnosis of pregnancy in a nonpregnant animal) may result from misinterpretation of early pyometra or mucometra.
  - False negatives (diagnosis of no pregnancy in a pregnant animal) may occur in early pregnancy if the ultrasonographer is inexperienced or if the embryonic vesicle is too small to visualize or obscured by viscera.
  - Fetal viability can be readily assessed by evaluating fetal heart rates after 25 days post-LH surge.
  - Gestational age can be estimated by fetal measurements and presence of fetal structures.
  - Litter size can only be approximated. Accurate counts are especially difficult in late gestation or with large litters.
- Serum relaxin: relaxin is a hormone produced by the placenta and is a confirmatory test of pregnancy after 30 days post-LH surge. A commercially available test is labeled for dogs and has been validated for use in cats.
  - False positives may result when relaxin levels remain elevated after fetal death (up to 2 days) or in cases of large ovarian cysts (queens).
  - False negatives can occur in early pregnancy or in singleton litters that do not generate sufficiently elevated relaxin for detection.
  - Litter size and fetal viability do not correlate well with relaxin concentrations.
- Abdominal radiographs: pregnancy can be diagnosed by visualization of ossified fetal skeletons >45 days post-LH surge.
  - False negatives may occur with small litters if a full colon obscures fetuses.
  - False negatives may occur prior to 45 days post-LH surge.
  - Fetal loss of viability can be evaluated by fetal posture (appearance of disarticulation), bone juxtaposition (especially skull), and intrafetal presence of gas.
  - Litter size is most reliably estimated by radiographs.



PREGNANCY Transabdominal ultrasonogram from a pregnant bitch that illustrates a gestational sac containing a fetus. The body diameter measurement made between the cursors indicates that this fetus is 34 days past the LH surge (31 days before whelping).

(Courtesy Dr. Michelle A. Kutzler.)

ADVANCED OR CONFIRMATORY TESTING

- Serum progesterone levels can be monitored to ascertain if endogenous levels are high enough to maintain pregnancy (>2 ng/mL).
  - May be assessed on bitches diagnosed nonpregnant to rule out luteal insufficiency as the cause (see p. 7)
  - May be run on bitches with high-risk pregnancy to monitor progesterone supplementation therapy
- Uterine monitoring (www.WhelpWise.com) may be required for high-risk pregnancies.

TREATMENT

TREATMENT OVERVIEW

- Intentional, normal pregnancies require no treatment.
- Unintentional, unwanted pregnancies may be terminated (see p. 912).
- High-risk, threatened pregnancies require advanced and continuous monitoring. Many of the therapeutic options are inferred from human medicine, may have no proven efficacy, and may be detrimental to the welfare of the dam or the fetuses.

ACUTE GENERAL TREATMENT

- To halt premature uterine contractions: terbutaline, 0.01-0.03 mg/kg PO or SQ q 8 h. Dosage should be titrated to effect based on uterine monitoring.
  - If terbutaline treatment is required throughout the remainder of pregnancy, it should be discontinued 24 hours prior to due date.
  - Efficacy of oral treatment is disputed in human literature.
  - Safety and efficacy in dogs has not been properly researched.
  - Tachycardia is a common and potentially life-threatening side effect of terbutaline. The effect on fetuses is uncertain.

CHRONIC TREATMENT

- For maintenance of pregnancy when endogenous progesterone levels prematurely fall below 2 ng/mL:
  - Progesterone in oil: 2 mg/kg IM q 72 h. Discontinue 3 days prior to due date.
  - Altrenogest (Regumate): 0.088 mg/kg PO q 24 h. Discontinue 24 hours prior to due date.
- Serum progesterone levels can be used for monitoring endogenous progesterone if altrenogest is used but not if progesterone in oil is used. Altrenogest is a synthetic progestogen that is not reliably measured with standard progesterone assays.

NUTRITION/DIET

- No supplemental nutrition is required during pregnancy if the bitch or queen is receiving high-quality feed. Supplementing calcium during pregnancy may be detrimental to whelping or result in postpartum complications (see pp. 1552 and 332).
- Caloric intake should be increased 1.5-to 3-fold following whelping/queening to sustain the dam's energy requirements during lactation.

BEHAVIOR/EXERCISE

No alteration to normal physical activity is required during pregnancy. Active and athletic dogs may continue normal activity throughout gestation. Obese dogs may be encouraged to increase exercise during pregnancy to improve muscle tone and reduce fat stores (decreasing feed is not recommended for weight loss during pregnancy).

DRUG INTERACTIONS

- Certain drugs may be detrimental to the developing fetuses and should be avoided unless the health of the dam outweighs the risk to the fetus. Consult package inserts for all drugs prior to use.
  - Antifungals (e.g., ketoconazole, griseofulvin)—teratogenic
  - Antibiotics (penicillins and cephalosporins are the antibiotics of choice):
    - Fluoroquinolones (e.g., enrofloxacin)—inhibit cartilage formation
    - Tetracyclines—inhibit dental enamel production
    - Chloramphenicol—suppresses bone marrow
    - Aminoglycosides—may be neurotoxic (gentamicin appears to be safe but should be used with caution and owner consent).
  - Chemotherapeutics—teratogenic or abortifacient
  - Cimetidine—may decrease androgen production, resulting in increased risk of cryptorchidism
  - Glucocorticoids—may cause anasarca or induce abortion
  - Hormone supplementation (e.g., altrenogest, diethylstilbestrol, estradiol benzoate, testosterone)—may affect sexual development
  - NSAIDs (e.g., ketoprofen, aspirin, carprofen)—teratogenesis
  - Opioids (e.g., buprenorphine)—are the analgesics of choice during pregnancy and lactation. However, chronic use has been associated with adverse fetal effects; overdosage may result in the dam's inattention to neonates and accidental smothering.

POSSIBLE COMPLICATIONS

- Dystocia (see p. 329)
- Abortion (see p. 7)
- Early embryonic loss (fetal resorption)

RECOMMENDED MONITORING

- In high risk, threatened pregnancies, serum progesterone levels should be monitored every other day or as needed to confirm that levels are above 2 ng/mL.
- Uterine monitoring (www.WhelpWise.com) may be required for high-risk pregnancies in bitches with a history of premature labor or uterine inertia.

PROGNOSIS AND OUTCOME

Parturition usually occurs without complications.

PEARLS & CONSIDERATIONS

COMMENTS

- Superfecundation: a bitch bred to multiple males can have pups within the same litter that are from different sires. Paternity can be determined for registration by DNA testing.
- Elevated serum progesterone levels do not automatically indicate pregnancy. Progesterone concentrations remain elevated throughout diestrus whether or not pregnancy is established. Progesterone concentrations remain elevated for ≥65 days post-LH surge in the nonpregnant bitch and for 40 days post-LH surge in the nonpregnant queen.

PREVENTION

Preventing unwanted pregnancies: castration of nonbreeding animals and proper supervision of intact animals.

TECHNICIAN TIPS

Pregnant dogs and cats brought to the veterinary clinic for pregnancy diagnosis are generally healthy. Because other patients visiting the veterinary clinic may have contagious diseases detrimental to pregnancy (e.g., herpesvirus, parvovirus, *Leptospira* spp.), it is recommended that bitches or queens presenting for pregnancy diagnosis be escorted out of the public waiting room as soon as possible to await examination in a clean and disinfected exam room.

CLIENT EDUCATION

- Over 4 million unwanted dogs and cats are euthanized annually in humane societies; up to 30% of these are purebred.
- Breeding is recommended to improve the breed standard and is not encouraged “to witness the miracle of birth.”
- “Designer breeds” (e.g., cockapoo, labradoodle) are first-generation crosses of purebred dogs. They do not breed true to their own phenotype and should not be purchased as breeding animals.

SUGGESTED READING

Concannon PW, et al: Recent advances in small animal reproduction. International Veterinary Information Service (IVIS): http://www.ivis.org/advances/Concannon/ wanke/chapter_frm.asp, 2001.

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AUTHOR: RICHARD WHEELER

EDITOR: MICHELLE A. KUTZLER

Pregnancy Termination

BASIC INFORMATION

DEFINITION

Elective nonsurgical abortion of a litter prior to 55 days of gestation, where gestation is based upon days from the LH surge (term = 65 ± 1 days).

SYNONYMS

Elective abortion, mismating/misalliance options

EPIDEMIOLOGY

SPECIES, AGE, SEX: Postpubertal intact bitches and queens

RISK FACTORS: Intact cycling females

ASSOCIATED CONDITIONS & DISORDERS: Depending upon the method of pregnancy termination used and the timing, pyometra, pseudocyesis, or delivery of premature viable offspring may occur.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Stages when pregnancy termination may be performed:

- Prior to pregnancy diagnosis (<20 days past the onset of the LH surge)
- Prior to fetal ossification (20-44 days past the onset of the LH surge)
- After fetal ossification (>44 days past the onset of the LH surge)

HISTORY, CHIEF COMPLAINT

Female bred to an unintended male and/or at an unintended time

PHYSICAL EXAM FINDINGS

- Typically healthy female
- Abdominal palpation of focal, discrete uterine enlargements during the fourth week of gestation. Accuracy will depend on the expertise of the examiner and the stage of pregnancy.

ETIOLOGY AND PATHOPHYSIOLOGY

- Luteal support (via progesterone production) is required for the entire length of a successful canine or feline pregnancy.
- Pregnancy in the bitch and queen can be terminated by administration of drugs that prematurely lyse the corpora lutea (CL) on the ovary.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Pregnancy diagnosis (see p. 909)

DIFFERENTIAL DIAGNOSIS

For pregnancy:

- Pseudopregnancy
- Pyometra
- Mucometra/hydrometra

INITIAL DATABASE

The diagnosis of pregnancy can be made with abdominal ultrasound, serum progesterone assay, abdominal radiographs, or serum relaxin assay. The advantages, drawbacks, and expected results of each are described in Pregnancy, p. 909.

TREATMENT

TREATMENT OVERVIEW

- Reduce serum progesterone concentrations to <2 ng/mL via lysis of the corpus luteum (CL).
- Perform a complete evacuation of the uterus.
- The owner and clinician should discuss the advantages and drawbacks of medical versus surgical (ovariohysterectomy) pregnancy termination to develop an appropriate treatment plan.

ACUTE GENERAL TREATMENT

Depending on the protocol, premature lysis of the CL (luteolysis) can be induced before or after a pregnancy diagnosis has been made.

- Prostaglandin F2a(PGF2α): q 8-12 h SQ to effect; usually 3-9 days of therapy is needed. PGF2α therapy can be initiated as soon as day 5 of diestrus, as determined by vaginal cytologic examination, and as late as day 45.
  - Canine: dinoprost, 0.1-0.25 mg/kg; or cloprostenol, 1-2.5 mcg/kg
  - Feline: dinoprost, 0.25-0.5 mg/kg
- Combination of PGF2α with a prolactin inhibitor
  - PGF2α: SQ q 8 h (see dose previously listed). PGF2α may be needed for an additional 1-2 days following the last treatment with a prolactin inhibitor for complete uterine evacuation.
  - Prolactin inhibitor: bromocriptine, 10 mcg/kg (0.01 mg/kg); or cabergoline, 5 mcg/kg (0.005 mg/kg) PO q 8 h. Usually 3-4 days of therapy needed. Protocols using prolactin inhibitors are initiated during the middle third of pregnancy (from 20-44 days from the onset of the LH surge), when the clinician is able to verify the diagnosis of pregnancy by palpation or ultrasonography.
- Prolactin inhibitor in queens: cabergoline, 25-50 mcg/cat PO q 24 h for 3-5 days
- Dexamethasone: 0.1-0.2 mg/kg PO q 8-12 hr at decreasing dose for 5-10 days or 5 mg IM q 12 h for 10 days (large dog). Fetal death occurs 5-13 days post treatment and fetal expulsion starts at 7-15 days. Treatment efficacy is highest when treated up to 10 days after day 35 of gestation. Treatment failure has been reported in bitches treated between 30-35 days of gestation. Concurrent treatment with PGF2α does not improve efficacy.
- Aglepristone in bitches and queens: 10 mg/kg SQ, two doses 24 hours apart. Aglepristone is a progesterone receptor antagonist and has few side effects. Not manufactured in the United States. May be administered during mid-pregnancy and has been successful at terminating pregnancies between 23-42 days post breeding. Side effects include localized swelling at the injection site.

CHRONIC TREATMENT

If pregnancy termination does not occur following an initial treatment, and pregnancy termination is still desired, the protocol should be repeated or a different treatment regimen should be used.

BEHAVIOR/EXERCISE

Depending upon the pregnancy-termination method utilized, pseudocyesis (inappropriate lactation) may develop. If this occurs, dams should not be allowed to lick the mammary glands, as this may stimulate further lactation.

POSSIBLE COMPLICATIONS

- Side effects secondary to pregnancy termination include anorexia, vaginal discharge, discomfort, depression, and shortened interestrus interval at first estrus post treatment.
- Side effects of PGF2α (occur 30-40 minutes after injection; decrease with subsequent injections) include salivation, panting, vomiting, defecation/diarrhea, and vocalization in queens.

RECOMMENDED MONITORING

Ultrasonography and serum progesterone concentrations to verify completion of abortion and uterine evacuation.

PROGNOSIS AND OUTCOME

Good prognosis for future fertility

PEARLS & CONSIDERATIONS

COMMENTS

- Since >50% of bitches will not be pregnant after a misalliance situation, waiting until the pregnancy is positively diagnosed to begin a protocol to terminate a pregnancy is recommended.
- Administration of estrogen during estrus has been reported to be a safe and effective method for pregnancy termination. Estrogen treatment should not be repeated even if the bitch or queen gets bred again during the same estrus.
  - Estradiolcypionate:canine, 0.044 mg/kg IM once; feline, 0.25 mg/cat IM once
  - Possible side effects of estrogen treatment include pyometra and severe, irreversible bone marrow suppression (canine). Due to the potential severe side effects of estrogen therapy, client education and specific written permission should be obtained prior to its use.
- The combination protocols using PGF2α and prolactin inhibitors achieve success more quickly and with fewer side effects than using either individually.
- If pregnancy termination protocols are initiated after 50 days of gestation, birth of viable puppies or kittens may occur.

PREVENTION

- Effective physical control of cycling bitch or queen during estrus.
- Ovariectomy or ovariohysterectomy will eliminate the problem of mismating permanently.

CLIENT EDUCATION

- In the bitch or queen not intended for breeding, ovariectomy or ovariohysterectomy should be performed as early in gestation as possible.
- Shortening the luteal phase will shorten the interestrus interval. Clients should be advised to expect the next cycle to occur sooner than normally expected.

SUGGESTED READING

Eilts BE: Pregnancy termination in the bitch and queen. Clin Tech Small Anim Pract 17:116–123, 2002.

AUTHOR: BEVERLY PURSWELL

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Potpourri Toxicosis

BASIC INFORMATION

DEFINITION

Liquid potpourri: combination of essential oils and cationic detergents. Acute toxicosis occurs (mostly in cats) from accidental dermal and oral exposure and is characterized by hypersalivation, vomiting, protrusion of the tongue, dysphagia, corrosive burns on the skin and oral cavity, hyperthermia, muscle weakness, and ataxia.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- All pets of all ages and both sexes are susceptible.
- Cats are more sensitive to essential oils, and grooming behavior can increase toxicosis from dermal exposures.

RISK FACTORS: Preexisting liver disease can increase risk and severity of toxic effects.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Dermal and/or oral contact with liquid potpourri
- Clinical signs begin within minutes to up to 8 hours post exposure.
- Lethargy, drooling, vomiting, vocalizing, anorexia, and tongue protrusion

PHYSICAL EXAM FINDINGS

- Liquid potpourri may be felt (oily texture on haircoat) or smelled on the coat and/or breath.
- Hypersalivation, dysphagia, vomiting (± hematemesis), diarrhea, corrosive burns of the oral, pharyngeal, and/or esophageal mucosa (ulceration could take several hours to appear).
- Hyperthermia
- Dyspnea, wheezing, abnormal respiratory sounds (caused by aspiration pneumonia or pulmonary edema), hypotension
- Muscular weakness, ataxia
- Hair loss (focal), skin erythema, dermatitis, edema, pain, and ulceration (dermal exposure)
- Ocular exposure: mild irritation to severe corneal injury (ulcer)

ETIOLOGY AND PATHOPHYSIOLOGY

- Liquid potpourri is a mixture of essential oils and cationic detergents.
- Essential oils are volatile oils or a mixture of terpenes (complex hydrocarbons) obtained from plants through a distillation process.
- Cationic detergents include quaternary ammonium compounds (benzalkonium and benzethonium chlorides), pyridinium compounds (cetylpyridinium, cetrimonium), and quinolinium compounds (dequalinium chloride).
- Cationic detergents (depending on concentration) can be irritating or corrosive to mucous membranes. They can cause local as well as systemic effects. Usually <1% concentration causes irritation to mucous membranes and >7.5% can cause corrosive injury.
- The exact mechanism responsible for the systemic effects of cationic detergents is not known. Current belief is that these compounds have a ganglionic blocking effect and a curare-like action, with paralysis of the neuromuscular junction of striated muscle.
- Essential oils can cause mucous membrane irritation and have central nervous system (CNS) depressant effects. Metabolism of terpenes occurs in the liver. The terpenes and their metabolites are mainly conjugated through glucuronidation before excretion through the kidneys. Cats are deficient in their glucuronidation ability and therefore more sensitive to essential oil toxicosis.
- Toxicosis is acute, with signs occurring within minutes to a few hours after exposure.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis rests on history and physical exam: observed or suspected exposure may be described, but evidence of exposure (smell, oily skin) is highly specific. Compatible clinical signs are supportive (hypersalivation, oral ulcers, anorexia, lethargy, protrusion of tongue) when seen within minutes to hours after the exposure. Specific confirmation is possible but not clinically practical.

DIFFERENTIAL DIAGNOSIS

- Corrosives (acids, alkali) toxicoses
- Household products (detergents, bleaches, pine oils) toxicoses
- Acetylcholinesterase (AChE) inhibitor pesticides (organophosphates, carbamates) toxicoses
- Upper respiratory tract infection
- Uremic ulcers (renal failure)
- Food indiscretion, garbage toxicosis
- Foreign body

INITIAL DATABASE

- CBC: inflammatory leukogram
- Serum chemistry profile ± blood gas analysis: essential oils causing hepatic damage may produce increased serum levels of liver enzymes (uncommon) and acid-base or electrolyte abnormalities.

ADVANCED OR CONFIRMATORY TESTING

- Gas chromatography and mass spectrometry (GC/MS) on urine can identify both essential oils and metabolites (this can confirm exposure if history of exposure not available).
- Necropsy: no characteristic lesions
- If indicated by clinical findings, endoscopic examination of esophagus and stomach may be considered within 12-24 hours to rule out perforation of gastrointestinal (GI) tract.

TREATMENT

TREATMENT OVERVIEW

Immediate treatment is topical (oral exposure: rinse mouth and dilute by giving milk or water; topical exposure: bathing using mild dishwashing liquid solution; ocular exposure: ocular rinse with tepid water or saline for several minutes). Subsequent treatment is supportive in response to specific lesions if any.

ACUTE GENERAL TREATMENT

- Oral: dilution with oral administration of milk or water (dogs: ½ cup [125 mL] per 15 kg; cats: 1-2 tbsp [15-30 mL] per cat; most effective if performed early)
- Dermal exposure: immediate bathing of the pet, using a mild liquid dishwashing detergent solution; monitoring for erythema, swelling, pain, or pruritus. Adjunctive treatment may include administering analgesics, anti-inflammatories, and antibiotics, because lesions may be painful and portals of entry for bacterial infection.
- Ocular: ocular flushing for 20-30 minutes with tepid tap water or physiologic saline; fluorescein stain of the cornea to assess for corneal ulceration (see p. 250).
- Induction of vomiting, gastric lavage, and activated charcoal administration are contraindicated (liquid potpourri is a caustic agent).
- Protecting GI mucosa:
  - Sucralfate slurries (dog: 0.5-1 g PO q 8-12 h; cat: 0.25-0.5 g PO q 8-12 h)
  - Gastric acid reduction:
    - H2 antagonist: famotidine (dogs/cats): 0.5 mg/kg PO, SQ, IM, IV q 12-24 h; *or*
    - Proton pump inhibitor: omeprazole, 0.5-1 mg/kg PO q 24 h
- Pain control: buprenorphine (dogs/cats), 0.005-0.03 mg/kg IV, IM, SQ q 6-12 h; *or*
- Tramadol: dogs 1-4 mg/kg PO q 8-12 h; cats: 12.5 mg/cat or 4 mg/kg PO q 12 h
- Fentanyl patch: see formulary (Section VI) for various sizes.
- Broad-spectrum antibiotics (for caustic burns)
- Antiinflammatory medications:
  - Corticosteroids (dexamethasone, 0.1-0.2 mg/kg IV or IM q 24 h for 3-5 days; *or* prednisolone, 0.25-1 mg/kg PO q 24 h). Use is controversial; may use for several days if esophageal damage has occurred; appear to help reduce risk of esophageal stricture but concurrently increase risk of GI ulcers and opportunistic infection (e.g., pneumonia);

concurrent use of broad-spectrum antibiotics unproven to reduce risk.

- IV fluids: most commonly indicated in cases involving anorexia, dehydration, electrolyte imbalances, or hyperthermia

CHRONIC TREATMENT

If aspiration pneumonia develops (due to dysphagia), oxygen supplementation and a broad-spectrum antibiotic may be necessary (see p. 885).

NUTRITION/DIET

Nutritional support: with severe oral lesions, food prepared as a liquid slurry or soft, mashed foods are appropriate. In 2/6 cases, placement of an esophagostomy tube was necessary for nutritional support (see p. 1267). With severe oral lesions and/or concurrent anorexigenic disorders (e.g., hepatic lipidosis) such treatment should be considered.

DRUG INTERACTIONS

Nonsteroidal antiinflammatory drugs (NSAIDs) can worsen GI ulcers by reducing protective prostaglandins. Corticosteroids use can also worsen GI ulcers (weigh benefits and risks before using).

POSSIBLE COMPLICATIONS

- Esophageal stricture/perforation, infection
- Aspiration pneumonia

RECOMMENDED MONITORING

- Body temperature (elevation may indicate inflammation, pneumonia or other secondary infection)
- White blood cell count
- Endoscopic examination of esophagus and stomach if clinical concern of severe mucosal erosion, perforation, or subsequent stricture

PROGNOSIS AND OUTCOME

With supportive care, signs resolve in a few hours to several days, depending on the degree of exposure and severity of damage.

PEARLS & CONSIDERATIONS

COMMENTS

- Essential oils in liquid potpourri are rapidly absorbed both orally and dermally.
- Hepatic damage from essential oils in potpourri is possible but very uncommon.
- Dry potpourri contains small amounts of essential oils and is essentially a foreign-body risk if ingested.
- Liquid potpourri can cause burns even if the liquid is not hot (chemical burns).

TECHNICIAN TIP

Patients with lesions that are not so severe as to require feeding tube placement may benefit greatly from gentle coaxing (see p. 1377), slurry-like food preparation, and a variety of diets to encourage them to eat despite the oral lesions.

PREVENTION

Owners should keep simmer pots out of the reach of pets.

SUGGESTED READING

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1ST EDITION AUTHOR: TINA WISMER

Postpartum Management of the Bitch

BASIC INFORMATION

DEFINITION

Care of the female dog and offspring following parturition

SYNONYMS

Postparturient care, postwhelping management

EPIDEMIOLOGY

SPECIES, AGE, SEX: Canine postpubertal female

GENETICS & BREED PREDISPOSITION: Toy breeds are at a greater risk of developing postparturient hypocalcemia.

RISK FACTORS

- Maiden bitches: some do not have good mothering ability; some are susceptible to subinvolution of placental sites (SIPS; see p. 1060).
- Older bitches are more predisposed to postpartum disorders (e.g., metritis, mastitis; see p. 688).
- Excessively large litters (more than 6 pups for small breeds [<9 kg], more than 9 pups for medium breeds [9-20 kg], more than 10 pups for large breeds [20-40 kg], and more than 12 pups for giant breeds [>40 kg])

CONTAGION & ZOONOSIS: Canine herpesvirus (see p. 525), *Brucella canis* (see p. 162), and *Leptospira* spp. organisms may be shed in high concentrations in lochia following late-term abortions.

ASSOCIATED CONDITIONS & DISORDERS

SIPS, metritis, mastitis, caesarean section

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Healthy dam and pups versus unhealthy dam and/or pups

HISTORY, CHIEF COMPLAINT

- Recent whelping
- No complaints unless a postpartum disorder exists

PHYSICAL EXAM FINDINGS

- Healthy dam and pups
- If postpartum problems exist: exam findings in the dam may reveal depression, inappetence, poor mothering, inadequate lactation (evident by anxious or distressed puppies), prolonged or abnormal vaginal discharge, and engorged or inflamed mammary glands.
    - Rectal temperatures may normally be elevated for 24-48 hours postpartum but should not be >103°F (>39.4°C).
    - Lochia (vaginal discharge; normal endometrial drainage) can be evident for 4-6 weeks postpartum and may last as long as 12 weeks.
    - Typically green-black to brick red and has no significant odor
    - Abnormal if creamy color or if associated with a foul odor
- Mammary glands should be evaluated daily for heat, pain, or changes in consistency.
    - Milk should be white or slightly yellow.
    - Discoloration or purulent discharge is abnormal and suggests mastitis.

ETIOLOGY AND PATHOPHYSIOLOGY

Variable, depending on associated conditions

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Most problems can be clarified and some fully diagnosed from thorough history (environmental, medical) and physical exam of the dam and offspring.

DIFFERENTIAL DIAGNOSIS

- Normal postpartum female
- Prolonged or abnormal-appearing vaginal discharge: SIPS, metritis, retained placenta
- Swollen mammary glands: mastitis, galactostasis

INITIAL DATABASE

None necessary unless abnormalities present in history or physical

ADVANCED OR CONFIRMATORY TESTING

- CBC, serum chemistry panel, fibrinogen: healthy postpartum dams may be slightly anemic with an elevated fibrinogen.
- Vaginal cytologic examination: healthy dams typically have erythrocytes and hemosiderophages present in vaginal discharge for 4-6 weeks postpartum.
- Vaginal culture: healthy postpartum dams have positive vaginal bacterial cultures, similar to all healthy bitches.
- Milk cytologic examination, pH, and culture
- Abdominal ultrasonography

TREATMENT

TREATMENT OVERVIEW

To wean as many pups as possible

ACUTE GENERAL TREATMENT

- Oxytocin injections are often requested postpartum by breeders.
    - These are no longer considered necessary postpartum; suckling puppies have the same effect.
    - May give 2-10 units (up to a maximum of 20 units) IM to aid in uterine involution if retained placentas are suspected or pups are born dead and obstructive dystocia is ruled out

CHRONIC TREATMENT

Treatment of an associated disorder depends upon the specific condition; dam may need to be separated from pups (weaning).

NUTRITION/DIET

Cooked pumpkin is a useful food additive to help correct diarrhea following placental ingestion.

BEHAVIOR/EXERCISE

Dog Appeasing Pheromone diffuser may help to calm nervous or agitated bitches.

POSSIBLE COMPLICATIONS

Many therapeutics are excreted into the milk, which can then be ingested at high (even toxic) levels by the nursing offspring. Verification of the potential for milk excretion and the effects of the drug on the neonatal pups is essential prior to prescribing a drug to a lactating bitch.

RECOMMENDED MONITORING

- Physical exam, then diagnostic testing based on findings.
- Exam allows for early detection of periparturient disorders should they arise.

PROGNOSIS AND OUTCOME

- Good prognosis for bitches without associated disorders
- Specific prognosis depends on accompanying disorder

PEARLS & CONSIDERATIONS

COMMENTS

- A clean, warm environment affording the bitch privacy should be provided postpartum.
- Attention to hygiene reduces the risk of infection both to the dam and pups.

PREVENTION

Ambient temperature in the puppy area should be maintained at 75°F-85°F (24-29°C), with space away from the puppies available for the bitch.

TECHNICIAN TIPS

Behavior:

- Owners should not leave first-time mothers and nervous bitches alone with puppies until they are sure the mother will not cannibalize the pups.
- Typically it takes 2-3 days, especially after a caesarean section, before a bitch can be left alone.
- It may be necessary initially to hold the bitch down to allow the puppies to suckle.
- If the bitch continues to refuse to accept the puppies, she needs to be evaluated for causes such as mastitis (causing mammary pain).

CLIENT EDUCATION

Nutrition:

- It is important during lactation to provide enough energy to the bitch so she will produce enough milk for the puppies and maintain her own body weight:
  - Small breeds have a higher energy requirement per pound of body weight than larger breeds.
  - First week, 1½ times maintenance; second week, two times maintenance; and third week to weaning, three times maintenance.
  - Good quality, high-energy, easily digested food is recommended.
- The bitch may express reluctance to leave the whelping box and her puppies, so food and water may need to be provided in the whelping/nursing box.
- The bitch should be encouraged to get fresh air and exercise while the whelping box is being cleaned.

SUGGESTED READING

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1ST EDITION AUTHOR: VIVIEN SURMAN

Portosystemic Shunt

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

- Macroscopic vascular communication allowing blood flow between the portal and systemic circulation without first passing through the liver
- The shunt can be congenital or acquired

SYNONYM

Portocaval shunt, portosystemic vascular anomaly, PSS

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs and cats
- Congenital shunts typically produce clinical signs by 6 months of age; with rare exceptions, most animals are diagnosed by 2 years of age.
- Acquired shunts can occur at any age but typically are noted in middle-aged to older dogs.
- Congenital PSS: 2:1 male to female ratio in the cat; in the bichon frise, the relative risk is 12 times greater in females than males.

GENETICS & BREED PREDISPOSITION

- Congenital PSS:
  - Inherited in the Maltese terrier and Irish wolfhound and thought to be inherited in the Yorkshire terrier (relative risk: 20 times greater than general dog population)
  - Dogs: golden and Labrador retrievers, Old English sheepdog, Irish wolfhound, Samoyed, bichon frise, Australian shepherd, and Australian cattle dog (intrahepatic); Yorkshire terrier, poodle, Maltese, shih tzu, dachshund (extrahepatic)
  - Cat: Persian and Himalayan
  - Prevalence: in cats, 2.5 per 10,000; in dogs, variable reports ranging from 2.5 to 60 per 10,000
- Acquired PSS: greater prevalence in breeds with breed-associated chronic hepatopathies (cocker spaniels, Doberman pinschers)

RISK FACTORS

Acquired: chronic hepatic diseases causing portal hypertension

ASSOCIATED CONDITIONS & DISORDERS

Hepatic microvascular dysplasia and cryptorchidism

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Congenital versus acquired:
  - Congenital shunts are typically single, are present from birth, and are usually treated surgically. They are intrahepatic or extrahepatic.
  - Acquired shunts are multiple, occur in the context of chronic liver disease (they are portosystemic anastomoses resulting from chronic portal hypertension), and are not treated surgically because new shunts would arise to replace them. They are always extrahepatic.
- Congenital intrahepatic versus congenital extrahepatic:
  - Intrahepatic: more common in larger breed dogs and more difficult to correct surgically
  - Extrahepatic: more common in smaller breed dogs and more easily corrected surgically

- Cats: either (extrahepatic > intrahepatic)

HISTORY, CHIEF COMPLAINT

- Congenital or acquired:
  - Waxing/waning course of clinical signs is typical.
  - Animals often have only one or a few signs.
- Congenital:
  - Central nervous system (CNS) signs are all secondary to hepatic encephalopathy: lethargy, ataxia, weakness, abnormal behavior, abnormal vocalization, hypersalivation/ptyalism (especially cats), head pressing, bumping into objects due to central blindness, incessant pacing or circling, stupor, seizures, or coma.
  - Gastrointestinal (GI): intermittent anorexia, vomiting, diarrhea or constipation, polyphagia, pica
  - Urinary tract: hematuria, pollakiuria, or dysuria from ammonium urate urolithiasis
  - Miscellaneous: stunted growth, polyuria and polydipsia (PU/PD), intense pruritus
  - High-protein meal, GI bleeding, constipation, azotemia, hypokalemia, metabolic alkalosis, tranquilization, and methionine-containing supplements or medications can exacerbate clinical signs.
  - Intolerance to or slow recovery from anesthetic agents or tranquilizers
  - Incidental findings of microhepatica, ammonium biurate crystalluria, shunt visualization on abdominal ultrasound
- Acquired: signs of chronic hepatopathy/liver failure usually predominate.

PHYSICAL EXAM FINDINGS

- Signs: see History, Chief Complaint above.
- Plump kidneys
- Small body stature
- Small liver (inability to palpate liver margins)
- Poor haircoat, excoriations if intensely pruritic
- Copper-colored irises without green or yellow pigment in some cats with congenital shunts
- Ascites:
  - Since congenital PSSs represent a path of lesser resistance than the normal hepatic vasculature, ascites does not typically occur. Congenital shunts presenting with ascites usually have severe hypoalbuminemia, or a disorder other than congenital PSS (e.g., hepatic arteriovenous malformation) is present.
  - Acquired PSSs, since they occur due to portal hypertension, often exist concurrently with ascites.
- Icterus:
  - Does not typically occur with congenital PSS; if icterus is present, consider another diagnosis (primary hepatobiliary disorder, hemolysis).
  - Commonly observed with chronic liver diseases causing acquired PSS
- Physical exam can be unremarkable.

ETIOLOGY AND PATHOPHYSIOLOGY

- Congenital intrahepatic shunts are most often embryonic vessels that failed to regress postnatally. In dogs, persistent ductus venosus is the most common form. Congenital extrahepatic shunts are usually anomalous vessels that are not present in a normal dog or cat.
- Acquired shunts arise from rudimentary nonfunctional collateral vessels when portal hypertension occurs due to end-stage parenchymal disorders, such as cirrhosis, or severe vascular disorders (noncirrhotic portal hypertension).
- Hepatic encephalopathy and resultant CNS signs (see p. 501) occur with either type of PSS from toxins and nutrients absorbed from the intestines that are allowed to bypass metabolism by the liver and circulate in much higher concentrations than normal. Many of these substances (ammonia, methyl mercaptans, short-chain fatty acids, benzodiazepine-like substances) are directly toxic to the CNS or alter its normal metabolism.
- Reduced hepatic blood flow and lower concentrations of hepatotrophic factors, such as glucagon, insulin, and nutrients, result in microhepatica.
- High levels of urinary excretion from elevated blood levels of ammonia and uric acid can result in development of urate urolithiasis (renal, ureteral, bladder) in up to 50% of cases.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Congenital PSSs are identified for the purpose of treatment: surgical ligation or occlusion, or transvenous coil occlusion. Acquired PSSs may be identified incidentally in animals with chronic hepatopathies, but their presence does not typically affect the diagnostic and treatment approach used for managing animals with chronic liver disease.

DIFFERENTIAL DIAGNOSIS

- CNS signs: infectious diseases, toxins, other metabolic encephalopathy (hypoglycemia), idiopathic epilepsy, and congenital malformations (e.g., hydrocephalus)
- GI signs: parasitism, foreign body, dietary indiscretion, dietary allergy, inflammatory/infiltrative intestinal diseases
- Urinary tract signs: urinary tract infections, other calculi

INITIAL DATABASE

Tests for acquired shunts are those for underlying chronic hepatopathy. For congenital PSS:

- CBC: microcytic normochromic red blood cells (RBCs), mild nonregenerative anemia, and target cells are possible. In vitro changes in blood stored in EDTA may mask microcytosis, especially if there is a delay in processing.
- Serum biochemistry panel: mild elevations in hepatic enzyme activities, low blood urea nitrogen (BUN) concentration, hypoglycemia, hypoalbuminemia, hypocholesterolemia may be seen.
- Coagulation profile: mild activated partial thromboplastin time elevation and low fibrinogen concentration can be present. Will normalize after shunt ligation.
- Urinalysis: isosthenuria or hyposthenuria, ammonium biurate crystalluria, hematuria, or pyuria possible
- Abdominal radiographs: microhepatica, mild to moderate renomegaly; urate calculi often undetectable unless complexed with magnesium and phosphate
- Initial testing can be normal in affected animals.

ADVANCED OR CONFIRMATORY TESTING

Tests for acquired shunts are those for underlying chronic hepatopathy. For congenital PSS:

- Serum bile acids (preprandial and postprandial): Preprandial sample (drawn after a 12-hour fast) may be normal in 20% of cases. Postprandial sample (drawn 2 hours after a meal) is typically markedly elevated, often over 100 µM/L. False-positive and false-negative results are uncommon; if clinical suspicion persists despite normal postprandial bile acid values, additional testing is warranted.
- Urinary bile acids: though urinary bile acids are highly specific in detecting hepatobiliary disease, they are less sensitive than serum bile acids for detecting portosystemic shunting. Therefore they should not be used as a screening test
- Fasting serum ammonia levels: may be more sensitive and specific than serum bile acids testing, but inappropriate sample handling when samples are not assessed on site may dramatically increase false-positive results.
- Plasma protein C levels may increase suspicion for clinically significant liver disease and may aid in differentiating between PSS and hepatic microvascular dysplasia (HMD). In one study, a protein C activity of <70% was much more likely to indicate PSS and >70% more indicative of HMD, although some overlap between groups existed.
- Abdominal ultrasound: skilled clinicians may be able to image a shunting vessel. Intrahepatic shunts are easier to identify than extrahepatic shunts. A portal vein/aortic ratio of <0.75 is strongly suggestive of PSS.
- Other common findings are a small liver and a subjective decreased visualization of hepatic vascular structures.
- Transcolonic portal scintigraphy (see p. 1259): identifies excessive shunting of portal blood bypassing the liver; confirms the presence of a shunt but cannot identify its location or differentiate between congenital or acquired shunts. False-negative results can rarely occur, and the test is only available at referral institutions.
- Transsplenic portal scintigraphy: requires less radionuclide than transcolonic administration and may result in a more detailed image, allowing for more accurate identification of shunt location and number.
- Radiographic mesenteric portography:
  - Performed either intraoperatively or with percutaneous splenic catheterization guided with ultrasound
  - Intrahepatic most likely if the most caudal loop of the shunt or the point where the shunt diverges from the portal vein is cranial to vertebra T13
- Helical CT angiography:
  - Noninvasive and very accurate for both the presence of a shunt and in identifying its anatomic location
  - CT or portography is the test of choice to confirm the presence of a shunt and identify its location.
- Liver biopsy: indicated in all suspected and confirmed PSS cases; typically reveals hepatic arteriolar hyperplasia, small portal triads, increased smooth muscle thickness of hepatic venules, and an increase in small vascular structures in the periportal area in dogs with congenital PSS. If a PSS is absent, these histologic findings are diagnostic for micro vascular dysplasia. Many pathologists believe the histologic findings in dogs with hepatic microvascular dysplasia are indistinguishable from those of dogs with PSS. Histologic changes are not prognostic for outcome after shunt ligation.

TREATMENT

TREATMENT OVERVIEW

- Aimed at reversal of hepatic encephalopathy
- Congenital: complete or partial attenuation of congenital shunts, which halts or limits the bypass of blood around the liver and reverses some or all of the signs of hepatic encephalopathy and other clinical signs
- Acquired: management of the underlying liver disease. Acquired PSSs are not treated surgically (other shunts would form to replace them).

ACUTE GENERAL TREATMENT

- See Hepatic Encephalopathy,p. 501.
- Congenital: supportive care prior to general anesthesia for portography or shunt attenuation/ligation

CHRONIC TREATMENT

Treatment for congenital PSS:

- Primary therapy for congenital PSS is complete or partial shunt attenuation.
    - Preoperative patient preparation is essential and typically involves:
        - Prophylactic medical treatment and nutritional modification for prevention of hepatic encephalopathy for several days or more prior to general anesthesia if the animal's neurologic status is stable
        - More aggressive or intensive management in cases of severe hepatic encephalopathy (seizures, coma)
        - Identification and treatment of associated abnormalities that could create complications if not addressed (e.g., hypoglycemia, hypoalbuminemia, gastric ulceration)
- With complete shunt ligation or obliteration (e.g., complete occlusion or with ameroid constrictor/cellophane band placement), most animals are able to live normal lives without dietary therapy and medications. Complete ligation may not be possible, owing to the development of intraoperative portal hypertension, requiring partial ligation only.
- Without surgery or with only partial attenuation, animals may need to be managed chronically with restricted protein diets, lactulose, and/or antibiotic therapy.

NUTRITION/DIET

Restricted protein diets or those formulated for use in hepatic disease should be considered to reduce the overall production of ammonia. Avoid methioninecontaining supplements.

DRUG INTERACTIONS

- Be careful with drugs requiring hepatic metabolism.
- Congenital portosystemic shunts increase glomerular filtration rate, which may raise the rate of excretion of some medications.

POSSIBLE COMPLICATIONS

- Intraoperative and postoperative complications include portal hypertension, hypoglycemia, hemorrhage, and intractable seizures.
- Sedative and anesthetic agents should be used with caution.

RECOMMENDED MONITORING

Monitoring for congenital PSS:

- Post ligation: monitor for reversal of clinical signs while discontinuing medications and changing to a normal protein diet after 6-8 weeks. If clinical signs recur, then repeat transcolonic scintigraphy to ensure complete shunt attenuation. If scintigraphy indicates continued shunting, repeat portography and consider surgery.
- Partial ligation: complete closure facilitated by scar tissue formation may occur after 2-3 months. If clinical signs recur after termination of medications and low-protein diet, consider repeat transcolonic scintigraphy after 3 months. If shunting is still present, a second surgery can be considered to attempt complete ligation.
- Repeat bile acids measurement 6-8 weeks postoperatively; bile acids concentrations may decrease dramatically but often continue to be abnormally elevated even with complete attenuation, owing to the presence of concomitant hepatic microvascular dysplasia.
- Obtain a serum biochemical profile 6-8 weeks postoperatively. With complete ligation, serum liver enzyme activities, albumin, and glucose levels will typically normalize.

PROGNOSIS AND OUTCOME 

- Excellent long-term prognosis with complete ligation
- Fair to poor prognosis for cure with partial ligation. Many partially ligated shunts will completely close over time, but up to 50% of animals with partial ligation will have recurrence of clinical signs.
- Poor prognosis with medical therapy alone. In some animals, clinical signs can be controlled for a few years, but most develop refractory neurologic signs.
- Animals that present later in life with clinical signs (often due to urinary tract calculi) have a good prognosis with surgery.

PEARLS & CONSIDERATIONS 

COMMENTS

- Always obtain postprandial bile acid concentrations to increase the sensitivity of the test.
- Consider a congenital portosystemic shunt as a differential diagnosis in any young cat or dog with clinical signs of neurologic disease or with unexplained poor or stunted growth, delayed or difficult anesthetic recovery, waxing and waning appetite or GI signs, or in any animal presenting with urate urolithiasis.
- In unexplained polyuria and polydipsia (PU/PD) in young animals, consider bile acids measurement to assess for a portosystemic shunt.
- Intrahepatic shunts are much more difficult to ligate, either partially or completely, and have a much higher perioperative mortality rate than extrahepatic shunts. Percutaneous transvenous coil embolization has been performed successfully in dogs with this type of shunt and has a much lower mortality rate.

SUGGESTED READING

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Polyuria/Polydipsia

BASIC INFORMATION

DEFINITION

- Polydipsia (PD): excessive consumption of water (>60-80 mL/kg/d)
- Polyuria (PU): production of excessive volumes of urine (>30-40 mL/kg/d)

EPIDEMIOLOGY

SPECIES, AGE, SEX

Cats and dogs, any age, either sex

ASSOCIATED CONDITIONS & DISORDERS

Diet (e.g., formulation [dry kibble versus moist/canned], salt content) will affect water consumption in both normal and ill dogs and cats.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- PU with secondary PD
- PD with secondary PU

HISTORY, CHIEF COMPLAINT

- Common chief complaints:
  - Increased frequency and amount of drinking
    - "Water-starved" behavior (pets actively seeking to drink water from abnormal or typically inaccessible locations) is possible in extreme cases or if owner is restricting water intake.
  - Urination in inappropriate indoor locations
  - Prolonged duration of individual urinations
  - Need to change litter with increased frequency (cats)
- Clinicians should initially ask owners what the water consumption is like as compared with 6-12 months earlier. The clinician can also ask whether there has been any change in water consumption, not whether water consumption has increased (to avoid leading the owner's answer).
- It is usually not possible to determine whether PU is primary, with secondary PD, or vice versa from the history alone.
- History should aim to differentiate PU from pollakiuria, stranguria, inappropriate elimination/urinary incontinence, and urinary marking/spraying.
- Basic environmental questions include duration of time indoors between walks (most normal dogs need to urinate at least every 8-12 hours), introduction of new pets or family members (suggesting behavioral changes/marking), new environment (behavior/marking or exposure to toxins), and change in litter type, location, or hygiene (cats).
- Some owners may not be aware of water consumption or urination because the pet mainly lives outdoors. Clinicians should view PD in dogs in a hospital setting with initial skepticism because occasionally, dogs drink voluminous amounts of water because of anxiety or excitement. More commonly, dogs with a history of PD drink less in the hospital as a result of excitement or anxiety.
- Medication history: glucocorticoids, phenobarbital, diuretics, thyroid supplementation can cause PU/PD
- Intoxication history should cover recent and distant potential exposures (ethylene glycol, grapes, raisins, lilies [cats]) and nephrotoxic medications (see p. 1411).

PHYSICAL EXAM FINDINGS

- Dehydration: consistent with any cause of PU/PD other than psychogenic PD
- Thin body condition
  - Some dogs with diabetes insipidus drink excessively and choose water over food, leading to weight loss.
  - With a poor haircoat: consistent with chronic kidney disease, chronic liver disease, diabetes mellitus, hyperthyroidism,

chronic gastrointestinal (GI) disease
- Dyspnea, tachypnea: may occur concurrently with metabolic acidosis, severe hypovolemia/shock (many possible causes)
- Panting (excessive): may be noted in dogs whose PU/PD is due to:
  - Hyperadrenocorticism
  - Hyperthyroidism
  - Also common in anxious or obese animals (i.e., nonspecific finding)
- Bilaterally symmetric truncal alopecia: endocrine disease (e.g., hyperadrenocorticism)
- Rectal examination: assess for primary disorders (e.g., adenocarcinoma of the anal sac causing PU/PD via hypercalcemia) and for causes of urinary incontinence other than PU (urethral or trigone thickening, suggesting inflammation or infiltration; prostatitis).
- Vaginal exam (seep. 1360):
  - Always attempt to identify a neoplastic process (mass) that might cause PU/PD via hypercalcemia of malignancy.
  - Purulent exudative discharge suggests pyometra.
- Abdominal palpation:
  - Kidneys: small (e.g., chronic kidney disease) or large (e.g., polycystic kidney disease, renal lymphoma, other renal neoplasia, pyelonephritis)
  - Hepatomegaly (e.g., primary hepatopathies, hyperadrenocorticism, diabetes mellitus, iatrogenic [glucocorticoids, barbiturates], lymphoma causing malignancy-associated hypercalcemia)
  - Splenomegaly (e.g., lymphoma causing malignancy-associated hypercalcemia)
  - Duodenal/jejunal thickening may be palpable with diffuse intestinal infiltrative diseases.
  - Uterine enlargement may be palpable (abdominal palpation must be performed gently because the uterus is potentially friable) with pyometra.
- Cardiac auscultation: tachycardia, heart murmur, third heart sound/gallop, and/or arrhythmia possible with hyperthyroidism

ETIOLOGY AND PATHOPHYSIOLOGY

- Normal daily water consumption:
  - Dogs: up to 60-80 mL/kg/d (higher in dogs <4 kg; up to 132 mL/d in dogs that weigh 1 kg)
  - Cats: up to 250 mL/d
- Mechanisms of PU/PD:
  - Chronic kidney disease: overload of glomerular filtrate to remaining functional nephrons presents excessive amounts of urea and sodium to distal tubules, eliciting an osmotic diuresis (primary PU, secondary PD).
  - Pyelonephritis: inflammation of the renal pelvis can destroy the counter-current concentrating mechanism in the renal medulla (primary PU, secondary PD).
  - Hyperadrenocorticism: suspected secondary antidiuretic hormone (ADH) deficiency (i.e., reversible central diabetes insipidus; primary PD, secondary PU)
  - Liver disease: compromised renal medullary concentration gradient due to impaired urea synthesis (primary PU, secondary PD); possibly impaired cortisol metabolism (primary PD, secondary PU)
  - Hypokalemia: interferes with renal tubular action of ADH (i.e., reversible nephrogenic diabetes insipidus; primary PU, secondary PD)
  - Hypoadrenocorticism: chronic hyponatremia depletes the renal medullary concentration gradient (primary PU, secondary PD).
  - Diabetes mellitus: glucosuria creates an osmotic diuresis (primary PU, secondary PD).
  - Diabetes insipidus (DI): lack of adequate ADH formation or release at the hypothalamic level (central DI) or ineffective ADH action on the renal collecting tubules (nephrogenic DI). Both central and nephrogenic DI cause a primary PU with secondary PD.
  - Intoxication: osmotic diuresis initially, followed by renal failure (ethylene glycol; both mechanisms cause primary PU, secondary PD). Mechanisms for lily, raisin, grape toxicosis: unknown.
  - Psychogenic PD: neurobehavioral changes with secondary renal medullary washout (primary PD, secondary PU)
  - Hyperthyroidism: increased medullary blood flow causing secondary decreased renal medullary concentration gradient; also hypokalemia (both primary PU, secondary PD).
  - Renal medullary washout: usually a secondary effect of other disorders listed here. Decreased renal medullary concentration gradient causes osmotic diuresis (primary PU, secondary PD).
  - Pyometra: *Escherichia coli* endotoxin interferes with ADH action on renal tubules (reversible nephrogenic diabetes insipidus; primary PU, secondary PD).
  - Hypercalcemia: calcium in excess interferes with the action of ADH at renal tubular level (reversible nephrogenic diabetes insipidus; primary PU, secondary PD).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

When present, polyuria and/or polydipsia are generally noticed and reported by owners in the medical history. Physical exam and

basic laboratory tests identify the cause in a large proportion of cases.

DIFFERENTIAL DIAGNOSIS

- PD:
  - Normal water intake (e.g., overinterpretation of seasonal variation)
- PU:
  - Inappropriate elimination/urinary incontinence: poor control of voiding, but overall daily volume of urine is normal (post-spay incontinence, for example).
  - Pollakiuria: frequent voiding of small volumes of urine, but overall daily volume is normal (bladder stones, bladder mass, for example).
  - Spraying/marking: small amounts of urine are eliminated, usually onto vertical surfaces.

INITIAL DATABASE

- CBC:
  - Anemia of chronic disease occurs with a few causes of PU/PD.
  - Stress leukogram possible with many disorders that cause PU/PD (though not common with central or nephrogenic diabetes insipidus).
  - Neutrophilia with evidence of inflammation (band forms, toxic change in neutrophils): rule out pyometra; may not be present with pyelonephritis (counterintuitive).
  - Normal lymphocyte and eosinophil counts in a clinically severely ill dog (i.e., absence of stress leukogram): rule out hypoadrenocorticism.
- Serum chemistry profile:
  - Hyperglycemia: rule out diabetes mellitus (clinical signs, glucosuria, fructosamine).
  - Increased blood urea nitrogen (BUN), creatinine, and phosphorus with isosthenuria (urine specific gravity [USG] 1.008-1.012): most consistent with kidney disease; less commonly, may also occur in animals with normal kidneys that have hypoadrenocorticism or diabetes insipidus.
  - Hypoalbuminemia, low BUN, hypocholesterolemia, hypoglycemia, hyperbilirubinemia (all, or any combination): consider liver failure (remember, many causes of PU lead to decreases in BUN; diabetes insipidus or hyperadrenocorticism are examples).
  - Hypercalcemia: rule out malignancy, primary hyperparathyroidism (both usually have concurrent low-normal to hypophosphatemia), vitamin D toxicosis, chronic kidney disease (cats; phosphorus usually normal or elevated), and other conditions (seep. 553). Idiopathic hypercalcemia (cats) is not usually associated with PU/PD.
  - Hyperkalemia with hyponatremia suggests hypoadrenocorticism.
- Urinalysis:
  - Owners should collect a fresh sample prior to the appointment.
  - True PU is almost always associated with dilute urine (USG < 1.012), “relatively” dilute urine (USG > 1.012 but <1.022), or glucosuria.
  - Concentrated urine (USG > 1.025) without glucosuria is inconsistent with PU/PD; other causes to explain clinical signs, such as lower urinary tract disorders, should be sought.
  - Diabetes mellitus causes PU but relatively concentrated urine (USG 1.025-1.045), at least in part due to glucosuria.
  - Isosthenuria (USG = 1.008-1.012) can be caused by kidney disease (tubules fail to concentrate urine) or by normal free water excretion (e.g., after a normal animal has drunk a large volume of water).
  - Calcium oxalate dihydrate crystals suggest postacute ethylene glycol ingestion.
  - Ammonium biurate crystals suggest liver failure (shunt, cirrhosis, etc).
- Urine culture and sensitivity (C&S): routinely performed in all animals with PU/PD. Urinary tract infection may complicate virtually any cause of PU/PD, may not produce additional overt clinical signs, often escapes diagnosis on urinalysis alone due to dilute urine, and is treatable and curable.
- Serum thyroid hormone levels: rule out hyperthyroidism (cats >6 years old).

ADVANCED OR CONFIRMATORY TESTING

- Abdominal ultrasound: evaluate kidneys (chronic kidney disease, pyelonephritis, neoplasia); urinary bladder (signs of cystitis, urolithiasis, or mass [e.g., neoplasm] producing pollakiuria or stranguria rather than PU); GI tract (evidence of infiltration); liver (chronic hepatopathies, portosystemic shunt, nonspecific enlargement, and hyperechogenicity [diabetes mellitus, hyperadrenocorticism, others]); adrenal glands (mass; subtle changes related to pituitary-dependent hyperadrenocorticism, although 50% of dogs with pituitary-dependent hyperadrenocorticism have structurally normal adrenal glands on ultrasound exam); and uterus (pyometra)
- Radiographs (thoracic, abdominal)
- Others as dictated by specific etiologies suspected

TREATMENT

TREATMENT OVERVIEW

Successful treatment requires identification of cause. PU and PD are not diseases but clinical manifestations of primary underlying disorders. Therefore, nonspecific treatment such as withholding water is unlikely to succeed and may be dangerous.

GENERAL TREATMENT

Withholding water can be dangerous or life threatening in all cases of PU/PD for which the underlying disease produces primary PU with secondary PD (see Etiology and Pathophysiology above).

POSSIBLE COMPLICATIONS

- Dehydration
- Progression of the primary problem if not identified and addressed

RECOMMENDED MONITORING

Physical examination, including body weight; diagnostic testing as indicated by underlying disease process, results obtained to date, and evolution of case.

PROGNOSIS AND OUTCOME

Highly variable from excellent to poor, depending on underlying cause and response to treatment.

PEARLS & CONSIDERATIONS

COMMENTS

- Any time an owner is concerned about their pet exhibiting “inappropriate urination” (any problem with urine), they should be instructed to collect about a teaspoon (5 mL) of urine to bring in at the time of examination. This allows easy separation of a pet with lower urinary tract disease (bladder stones) from one with diabetes mellitus (glycosuria) from one with nondiabetic PU/PD. Urine specific gravity <1.012 (sometimes <1.020; see below) always indicates PU.
- Isosthenuria (USG = 1.008-1.012) implies that the USG is the same as the specific gravity of plasma. Since dehydrated animals may have hyperosmolar plasma, USG up to 1.020 may still be consistent with isosthenuria in some

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Polyradiculoneuritis

BASIC INFORMATION

DEFINITION

An idiopathic inflammatory disorder primarily involving both axons and myelin of ventral nerve roots; probably the most common polyneuropathy in dogs. An analogous polyneuropathy has been described in cats (much less common).

SYNONYMS

Acute idiopathic polyradiculoneuritis (PRN), Coonhound paralysis (CHP)

EPIDEMIOLOGY

SPECIES, AGE, SEX

Affects dogs of any breed and either sex; usually adult age

GENETICS & BREED PREDISPOSITION

Hunting dogs, specifically coonhounds of certain lineages may be predisposed

RISK FACTORS

Raccoon bites or scratches in a genetically susceptible animal

ASSOCIATED CONDITIONS & DISORDERS

- Aspiration pneumonia
- Urinary tract infections
- Muscle atrophy/contracture
- Pressure induced skin ulcerations
- Hypoventilation/respiratory paresis or paralysis

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Two subcategories appear identical in terms of onset, clinical signs, disease course, diagnostics, and pathology and are likely representative of the same disease syndrome:

- Coonhound paralysis (CHP)
  - History of being bitten or scratched by a raccoon 7-10 days before onset of signs
- Acute idiopathic polyradiculoneuritis (PRN)
  - Identical disorder but no possible exposure to raccoons

HISTORY, CHIEF COMPLAINT

- Acute-onset lower motor neuron (LMN) paresis/plegia, usually beginning in pelvic limbs and eventually progressing to thoracic limbs. Some dogs may initially develop a stilted gait.
- Progression to nonambulatory tetraparesis/tetraplegia typically within 10 days of onset (as little as 72 hours)
- Clinical signs occasionally begin in the thoracic limbs and progress to pelvic limbs or present as acute-onset tetraparesis/tetraplegia.
- Duration of paralysis varies from several weeks to 2-5 months.

PHYSICAL EXAM FINDINGS

- Nonambulatory LMN paraparesis/plegia or tetraparesis/plegia

- Recumbent, yet alert with normal mentation
- Afebrile
- Generalized hyporeflexia or areflexia; absent spinal reflexes (with exception of perineal reflex)
- Hypotonia/atonia
- Neurogenic muscle atrophy commonly develops within 7-10 days and can be severe.
- Sensory function is normal to heightened; some dogs are hyperesthetic.
- Hypoventilation and/or development of a life-threatening respiratory paralysis can occur, especially in acute-onset, rapidly progressive cases.
- Loss of voice (dysphonia, aphonia) is common.
- Cranial nerves are usually normal; occasionally slight facial weakness. Proprioceptive placing is normal in those animals with enough remaining motor ability.
- Patients retain the ability to urinate and defecate and will readily eat and drink if the head is supported.

ETIOLOGY AND PATHOPHYSIOLOGY

Presumptive Etiology:

- The antigenic stimulus in dogs is currently unknown, although raccoon saliva is thought to be one source.
- There may also be a genetic predisposition for this disease in breeds of coonhounds.

Pathophysiology:

- After exposure to the specific antigen, whether from raccoon saliva, vaccine, or some other source, alteration of the patient's immune system occurs. An autoimmune reaction against axons and myelin of the ventral nerve roots is theorized. In humans with polyradiculoneuritis (Landry-Guillain-Barré syndrome), molecular mimicry and concurrent infection with *Campylobacter jejuni* gastroenteritis are thought to be involved in the pathogenesis. The bacterium's capsular antigens mimic the components found on the patient's peripheral nerves. After the immune system is exposed to *Campylobacter jejuni,* the antibodies formed during the immune attack destroy not only the bacterium but also the peripheral nerve.
- Numerous exogenous antigens have components that mimic molecules found in canine axons; molecular mimicry may be involved in the pathogenesis.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Polyradiculoneuritis is a diagnosis of exclusion. A working clinical diagnosis is based on the typical clinical presentation of an acute-onset LMN paraparesis/plegia that rapidly progresses to tetraparesis/plegia. Although not confirmatory, ancillary testing is helpful in ruling out other differential diagnoses.

DIFFERENTIAL DIAGNOSIS

Botulism, tick paralysis (United States and Australia), myasthenia gravis, protozoan polyneuritis/polymyositis, paraneoplastic neuropathy

INITIAL DATABASE

- Three-view thoracic radiographs: unremarkable unless secondary aspiration pneumonia or metastasis; useful in ruling out paraneoplastic neuropathies and megaesophagus
- CBC, serum biochemistry profile, urinalysis: unremarkable unless secondary urinary tract infection present
- Antiacetylcholine receptor antibody test: should be negative; useful in ruling out myasthenia gravis
- Lumbar cerebrospinal fluid (CSF) tap (see p. 1228): can support diagnosis if an increase in protein with a normal cell count (albuminocytologic dissociation) is seen
- Serum muscle enzyme levels: should be normal or only mildly elevated due to recumbency (versus marked elevations in polymyositis)
- Electrodiagnostics (see online chapter: Electromyography and Nerve Conduction Velocity): majority of (if not all) affected dogs will exhibit abnormal electromyographic activity (fibrillation potentials and positive sharp waves consistent with denervation) with normal or slightly reduced motor nerve conduction velocities (NCV).

ADVANCED OR CONFIRMATORY TESTING

- Nerve biopsies: demyelination, leukocytic infiltration, axonal degeneration, and segmental demyelination are consistent with polyradiculoneuritis but nonspecific because the inflammatory process occurs primarily at the ventral nerve roots.

- Arterial blood gas analysis: to help determine if mechanical ventilation is warranted

TREATMENT

TREATMENT OVERVIEW

Therapy is nonspecific, supportive, and often very protracted (major determinant of prognosis). Cornerstones are persistent supportive care and rehabilitation to prevent secondary complications. Most patients will show signs of improvement within 3 weeks and completely recover by 3-5 months. Rarely, severe, rapidly progressive cases require mechanical ventilation.

ACUTE GENERAL TREATMENT

Monitor pulmonary function and ventilatory status with arterial blood gas analysis inrecumbent patients. If hypoventilation is evident, provide mechanical ventilatory support (seep. 1362).

CHRONIC TREATMENT

- Supportive care, physical rehabilitation, and proper nutrition are essential for recovery:
  - Animals should be turned at least 6-8 times daily to prevent complications secondary to prolonged recumbency (hypostatic lung congestion, decubital ulcers etc.).
  - Passive range-of-motion exercises and massage of limbs should be performed at least four to five times daily to keep joints flexible and muscle supple (see p. 1329).
  - Hydrotherapy provides exercise and helps preclude muscle atrophy.
  - Proper bedding is essential to prevent pressure-induced skin ulcerations; water beds are useful.
  - Assisted feedings help prevent aspiration pneumonia.
  - Ensure the patient's environment is clean and dry.
  - Monitor for bladder overdistension, and intervene as necessary.
- Glucocorticoid treatment has been suggested, but there is no evidence of efficacy.
- The role of plasmapheresis and intravenous immunoglobulin administration, an established treatment in humans with signs of PRN, has not been proven in dogs.

POSSIBLE COMPLICATIONS

- Aspiration pneumonia, pressure-induced skin ulcerations, urinary tract infections, and muscle contracture and severe atrophy occur secondary to prolonged recumbency.
- Respiratory paresis/paralysis can occur in severe cases.

RECOMMENDED MONITORING

If patient is not hospitalized, weekly recheck examinations to assess recovery progress

PROGNOSIS AND OUTCOME

- Prognosis for full recovery is usually favorable. Owing to the transient nature of the inflammatory phase, damaged axons remyelinate and to some degree regrow over a period of 3-6 weeks. If pulmonary function is unaffected, with adequate supportive care, most animals will show signs of improvement within 3 weeks and full recovery within 3-5 months.
- Large/heavy dogs, dogs living in dense urban environments, and dogs whose owners or families are unable to provide supportive care may have a worse prognosis because of the difficulties these factors impose on home care.
- If mechanical ventilation is needed or if severe disease complications such as aspiration pneumonia and significant muscle contracture are present; recovery may be significantly prolonged or incomplete.
- Animals with significant axonal degeneration may not show clinical improvement.

PEARLS & CONSIDERATIONS

COMMENTS

- Once an animal has been affected with polyradiculoneuritis, recurrence of clinical signs is possible if the patient is subsequently reexposed to the inciting antigen.
- Chronic forms of this disease do exist and are characterized by waxing and waning clinical signs. Tetraplegia is generally not

seen with such forms of disease.

PREVENTION

Reexposure to raccoons should be avoided in dogs having recovered from CHP, as it may trigger a disease relapse.

TECHNICIAN TIPS

Treatment success for this disease greatly relies upon intensive daily nursing care and physical rehabilitation. Patience and persistence over extended periods of time do tend to be rewarded with recovery of the patient. Sometimes it can take months for these patients to recover.

CLIENT EDUCATION

- Clients need to be aware of, and persistent with, at-home nursing care and physical rehabilitation. They must also be aware of secondary complications. Frequent rechecks are necessary.
- Veterinary physical rehabilitation centers are available to aid with physical therapy.

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Polyphagia

BASIC INFORMATION

DEFINITION

Increased appetite or frequency of eating. Caloric consumption exceeding expected metabolic requirement.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dependent on underlying cause. In any age group, behavioral polyphagia (gluttony) is possible.
- Cats:
  - Young: parasites, pregnancy, lactation
  - Adult and geriatric: diabetes mellitus (DM), acromegaly, hyperthyroidism, intestinal infiltration (e.g., inflammatory bowel disease [IBD], gastrointestinal [GI] lymphoma)
- Dogs:
  - Young: parasites, pregnancy, lactation, exocrine pancreatic insufficiency (EPI)
  - Adult: DM, sudden acquired retinal degeneration syndrome (SARDS), hyperadrenocorticism (HAC), IBD, GI lymphoma
  - Geriatric: DM, SARDS, HAC (Cushing's disease), IBD, GI lymphoma, hyperthyroidism (rarely)

GENETICS & BREED PREDISPOSITION

Dogs: EPI in German shepherd; HAC in poodle, dachshund, terriers

RISK FACTORS

Risk factors exist for certain diseases that commonly cause polyphagia:

- DM: obesity (cats), concurrent HAC, concurrent acromegaly
- EPI: severe pancreatitis (rarely)

ASSOCIATED CONDITIONS & DISORDERS

Certain polyphagia-inducing diseases are in turn associated with other disorders:

- Acromegaly: DM, myocardial hypertrophy
- Hyperthyroidism: myocardial hypertrophy, cardiac arrhythmias, systemic hypertension, retinal detachment, renal failure, cerebral vascular accident, vomiting, diarrhea, weight loss, thyroid carcinoma (rare)
- DM: hyperlipidemia, pancreatitis, cataracts (dog), urinary tract infection (UTI)
- HAC: hyperlipidemia, DM, pyoderma, calcinosis cutis, UTI, pulmonary thromboembolism, cranial cruciate ligament rupture

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Iatrogenic/drug-induced (anticonvulsants, benzodiazepines, glucocorticoids, insulin excess, cyproheptadine)
- Primary polyphagia: behavioral, psychogenic, ventromedial hypothalamic lesion
- Secondary polyphagia: increased metabolic rate/physiologic (growth, pregnancy, lactation), hyperthyroidism, acromegaly. Decreased nutrient availability: DM, EPI, parasitism, infiltrative bowel diseases. Hypoglycemia: insulinoma. Miscellaneous: SARDS, HAC

HISTORY, CHIEF COMPLAINT

- Increased food consumption with:
  - Weight loss: hyperthyroidism, EPI, DM, infiltrative bowel disease, parasitism
  - Weight gain: psychogenic, drug-induced, physiologic, acromegaly, HAC, SARDS, insulinoma
- Polyuria and polydipsia: DM, HAC, acromegaly, hyperthyroidism, SARDS

- Panting: HAC, SARDS
- Hair loss: HAC
- Vomiting, diarrhea: hyperthyroidism, EPI, infiltrative bowel disease
- Weakness, seizures: insulinoma, HAC (rare)

PHYSICAL EXAM FINDINGS

- Disorientation: insulinoma, HAC (rarely), SARDS, hypothalamic lesions
- Alopecia, comedones: HAC
- Cataracts: DM
- Dilated pupils: SARDS (initially normal fundic examination)
- Thin to emaciated: EPI, hyperthyroidism, DM, infiltrative bowel disease
- Tachycardia, murmur, arrhythmias: hyperthyroidism.
- Panting: HAC, SARDS, obesity
- Obesity: behavioral, DM (especially cats), SARDS, HAC, insulinoma
- Hepatomegaly: HAC, DM

ETIOLOGY AND PATHOPHYSIOLOGY

- Varies with disease
- Primary: damage to satiety center (trauma, infectious, inflammatory, neoplastic)
- Behavioral: may be related to boredom or interindividual variation
- Secondary:
  - Accelerated metabolism
  - Diminished nutrient availability

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

The first diagnostic step consists of establishing whether polyphagia exists as a clinical sign of a medical disorder or whether the animal is simply gluttonous. This should be extracted from the history by: (1) asking the client whether any changes have occurred in food consumption independent of dietary change and mirroring the course of other clinical signs if present; and (2) avoiding leading questions (“Does your pet consume a lot of food?”), which can lead to overdiagnosis of polyphagia as a medical sign, in favor of open-ended questions (“Have you noticed a change in food consumption? How so, and since when?”).

DIFFERENTIAL DIAGNOSIS

- Weight loss: poor nutrient quality, owner underfeeding
- Weight gain: physiologic (cold environment, growth, pregnancy)

INITIAL DATABASE

- CBC: anemia (parasites), leukocytosis (HAC, SARDS), eosinophilia (parasites)
- Serum biochemistry panel: liver enzymes (HAC, DM, SARDS), glucose (DM, insulinoma)
- Urinalysis: low specific gravity (HAC, SARDS, hyperthyroidism), glucose, (DM), ketones (DM), bacteriuria (HAC, DM)
- T4: hyperthyroidism

ADVANCED OR CONFIRMATORY TESTING

- Low-dose dexamethasone suppression or ACTH stimulation: HAC
- Ultrasound: pancreatic nodules, adrenal size, thickened bowel, pregnancy
- CT/MRI of brain: hypothalamic lesions, pituitary macrotumors
- High-dose dexamethasone suppression: discriminates between adrenal-dependent HAC and pituitary-dependent HAC; generally replaced by abdominal ultrasound
- Endogenous ACTH level: discriminates between adrenal-dependent HAC and pituitary-dependent HAC
- Free T4: may clarify thyroid status that is unclear with total T4
- Technetium-99 thyroid scan: to confirm hyperthyroidism, determine bilateral versus unilateral disease

TREATMENT 

TREATMENT OVERVIEW

Depends on underlying causes

DRUG INTERACTIONS

With HAC: concurrent phenobarbital and o,p'-DDD (mitotane [Lysodren]) lessens effectiveness of o,p'-DDD. Trilostane concurrently with ketoconazole can result in hypoadrenocorticism.

POSSIBLE COMPLICATIONS

- Iatrogenic hypoadrenocorticism (o,p'-DDD, or trilostane treatment)
- Renal insufficiency, hypothyroidism (hyperthyroidism treatment)
- Ketoacidosis (uncontrolled diabetes)
- Thromboembolism (untreated HAC)
- Urinary tract infection (secondary to DM or HAC)

RECOMMENDED MONITORING

- EPI: weight gain
- DM: clinical signs improving, glucose curves, fructosamine
- HAC: clinical signs improving; ACTH stimulation
- Hyperthyroidism: weight gain; lower or normal serum T4 levels

PROGNOSIS AND OUTCOME

Varies depending on underlying cause

PEARLS & CONSIDERATIONS

COMMENTS

- Start by distinguishing polyphagia with weight gain from polyphagia with weight loss. A shorter list of problems causes polyphagia with weight gain.
- Thorough history and physical examination will help eliminate many differential diagnoses.

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Polymyositis, Autoimmune

BASIC INFORMATION

DEFINITION

An autoimmune inflammatory disease of unknown pathogenesis that primarily affects appendicular musculature

EPIDEMIOLOGY

SPECIES, AGE, SEX: Although any breed or age of dog can be affected, the majority of reported cases are middle-aged, large breeds. There is no apparent sex predilection.

GENETICS & BREED PREDISPOSITION: Newfoundlands and boxers appear to be overrepresented. Newfoundlands tend to develop the disease at a younger age than other breeds. A substantial number of boxers with polymyositis may develop the disorder as a preneoplastic condition.

ASSOCIATED CONDITIONS & DISORDERS: Uncommonly, dogs with autoimmune polymyositis may have concurrent masticatory myositis. This combination is referred to as *overlap syndrome*. Another uncommon associated condition in dogs with autoimmune polymyositis is thymoma.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Clinical signs may be acute or chronic. The animal's medical history or clinical complaints include generalized weakness (often worsened by exercise), stiff gait, generalized muscle atrophy, dysphonia, myalgia, dysphagia, regurgitation (megaesophagus may be present), fever, and muscle swelling.

PHYSICAL EXAM FINDINGS: Physical examination findings typically concur with the animal's medical history and clinical complaints.

ETIOLOGY AND PATHOPHYSIOLOGY

This is an idiopathic autoimmune disorder.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected in a dog with signs of regional or diffuse muscle weakness and pain. Elevation of muscle enzymes on routine serum biochemistry panels is common. A definitive clinical diagnosis is achieved with muscle biopsy results in combination with normal (negative) serologic titers for potential infectious causes.

DIFFERENTIAL DIAGNOSIS

- Infectious polymyositis (e.g., toxoplasmosis, neosporosis)
- Overlap syndrome
- Preneoplastic myositis
- Myasthenia gravis

INITIAL DATABASE

- CBC, serum chemistry profile, urinalysis: elevated aspartate aminotransferase (AST) possible
- Serum creatine kinase: usually elevated, often markedly so
- Serologic titers for infectious diseases (e.g., toxoplasmosis, neosporosis)

ADVANCED OR CONFIRMATORY TESTING

- Electrodiagnostics: electromyogram (EMG) is usually abnormal

- Muscle biopsy (see p. 1305). A nonsuppurative inflammatory infiltrate is typically evident. Immunohistochemical staining of muscle tissue can verify immunoglobulin localization to the sarcolemma.

TREATMENT

TREATMENT OVERVIEW

The goal of therapy is to achieve clinical remission of myopathic signs.

ACUTE GENERAL TREATMENT

Immunosuppressive doses of prednisone (e.g., 1-2 mg/kg PO q 24 h) are generally used as initial therapy.

CHRONIC TREATMENT

- Once clinical remission of signs is achieved, the dosage of prednisone is slowly tapered over several months and is discontinued if possible.
- If prednisone cannot be effectively tapered or discontinued, alternative immunosuppressive drugs can be instituted (e.g., azathioprine, 2 mg/kg PO q 24 h for 5 days, then q 48 h; or mycophenolate mofetil, 5-10 mg/kg PO q 12 h).

POSSIBLE COMPLICATIONS

- Either inadequate or excessive immunosuppression
- Drug side effects or complications, including polyuria and polydipsia (PU/PD), polyphagia, weight gain, iatrogenic hyperadrenocorticism (glucocorticoids), bone marrow effects (azathioprine), and others

PROGNOSIS AND OUTCOME

The prognosis is favorable in approximately 80% of cases. Relapses may occur with tapering or discontinuation of immunosuppressive drugs.

PEARLS & CONSIDERATIONS

COMMENTS

When tapering prednisone in cases of autoimmune polymyositis, dose reductions should not be made more frequently than every 4 weeks.

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Polycythemia Vera

BASIC INFORMATION

DEFINITION

An inappropriate, absolute increase in red blood cell (RBC) mass as measured by RBC count, hematocrit (Hct), and hemoglobin (Hb) concentration

SYNONYMS

- Polycythemia rubra vera
- Primary erythrocytosis. Strictly speaking, this is the more accurate term for this disorder *(polycythemia* implies increases in all circulating blood cell lines), but *polycythemia vera* is used more commonly.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Usually middle-aged to older dogs or cats

ASSOCIATED CONDITIONS & DISORDERS: Hyperviscosity syndrome (see p. 570)

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Mainly caused by or associated with hyperviscosity

- Neurologic changes (e.g., behavior, motor, or sensory), mental dullness
- Seizures
- Lethargy, exercise, intolerance
- Hemorrhage (e.g., epistaxis, hyphema)

PHYSICAL EXAM FINDINGS: None, one, or many may be present:

- Hyperemic or cyanotic mucous membranes
- Erythema of the skin
- Polyuria and polydipsia (PU/PD)
- Splenomegaly

ETIOLOGY AND PATHOPHYSIOLOGY

- Absolute primary erythrocytosis
- Autonomous production of RBCs (erythropoietin independent)
- Myeloproliferative clonal disease
- Arises from a multipotent hematopoietic progenitor cell in the bone marrow, resulting in the accumulation of morphologically and functionally normal RBCs
- Polycythemia may lead to the hyperviscosity syndrome and resultant clinical signs.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The goals are to determine whether a true increase in red cell mass is present, and then rule out erythrocytosis secondary to increased erythropoietin. Since polycythemia vera is an autonomous increase in red cells, repeatable elevations in Hct, RBC count, and Hb are expected. Polycythemia vera is a diagnosis of exclusion: a complete diagnostic workup is indicated to rule out all other possibilities in the differential diagnosis.

DIFFERENTIAL DIAGNOSIS

- Relative polycythemia (pseudoerythrocytosis):

- Elevated Hct, with normal or decreased RBC mass
- Decrease in plasma volume associated with severe dehydration and increased serum total protein (TP) concentration
- Rarely causes clinical signs of hyperviscosity

- Absolute secondary polycythemia; erythropoietin dependent; appropriate or inappropriate response:
  - Appropriate (secondary to decreased tissue oxygenation):
    - High altitude
    - Chronic pulmonary disease
    - Right-to-left cardiovascular shunts (ventricular septal defect, reversed patent ductus arteriosus [PDA], tetralogy of Fallot, atrial septal defect)
    - Hemoglobinopathies (abnormal hemoglobins, methemoglobin reductase deficiency)
  - Inappropriate (normal tissue oxygenation):
    - Renal neoplasia (e.g., lymphoma, nephroblastoma, carcinomas, fibrosarcomas)
    - Other renal disease (e.g., polycystic kidney disease, rarely amyloidosis or glomerulonephritis)
    - Other neoplasms (e.g., cecal leiomyosarcoma, hepatic tumors)

INITIAL DATABASE

- CBC: persistently increased Hct, RBC count, and Hb concentrations with normal total protein concentration. The RBC morphology is normal.
- Serum biochemistry profile, urinalysis: generally unremarkable
- Arterial blood gas (ABG) analysis: to rule out hypoxemia as a cause of secondary polycythemia
- Abdominal ultrasound:
  - To identify renal masses or other potential erythropoietin-producing tumors
  - Nonspecific findings (hyperechoic kidneys, splenomegaly noted in 25% of cats and 10% of dogs with polycythemia vera).
- Thoracic radiographs:
  - Bronchial or interstitial changes are nonspecific. If thought to cause hypoxemia (and polycythemia secondarily), ABG measurement is indicated for confirmation.
- Echocardiography:
  - To identify myocardial hypertrophy (secondary to hyperviscosity [left ventricle; mild] or right ventricular outflow obstruction/pulmonary hypertension [right ventricle; marked]), right-to-left shunts, or other abnormalities that could cause secondary polycythemia.

ADVANCED OR CONFIRMATORY TESTING

- Measurement of plasma erythropoietin concentration:
  - Generally normal to low in polycythemia vera
  - Test has low diagnostic specificity; substantial overlap with the normal range; other types of polycythemia (e.g., relative polycythemia) are associated with similar results.
  - Measurement is indicated to help rule out secondary polycythemia (high plasma erythropoietin concentration).
- Bone marrow aspiration and cytologic examination or bone marrow core biopsy:
  - Not useful: cannot distinguish primary from secondary polycythemia

TREATMENT

TREATMENT OVERVIEW

Decrease blood viscosity and RBC mass to reduce or resolve clinical signs (palliation).

ACUTE GENERAL TREATMENT

Initial treatment is phlebotomy:

- 20 mL/kg of blood collected from external jugular or other central vein
- Avoid hypotension due to volume depletion by replacement with equivalent volume of IV 0.9% NaCl.
- Target Hct is <55% in dogs, <50% in cats.
- Replacement of coagulation factors and albumin if multiple phlebotomies in short period of time (rare). Clinicians can use autologous plasma (centrifuge phlebotomized blood, discard RBCs, and administer patient's own plasma) or use allogenic fresh frozen plasma.

CHRONIC TREATMENT

- Periodic phlebotomies if needed
- Alternatively, hydroxyurea (Hydrea), 30 mg/kg PO q 24 h for 7-10 days, then decrease the dose to 15 mg/kg daily, and titrate dose to maintain normal Hct; reduces RBC production. Monitor CBC for myelosuppression.
- Other chemotherapy agents such as chlorambucil have been used less often.
- Radioactive phosphorus (^{32}P) for myelosuppression: rarely used in animals. Only available in specialized centers.

POSSIBLE COMPLICATIONS

Hydroxyurea can cause myelosuppression. With chronic use, adverse effects including nail sloughing, macrocytosis (increased mean corpuscular volume [MCV]), methemoglobinemia (cats), and induction of secondary neoplasia, including leukemia, have been reported.

RECOMMENDED MONITORING

- CBC counts weekly at first until Hct stabilizes, then every 4-6 weeks
- Physical examination and diagnostic testing as needed; opportunistic infections, myelosuppression, and other complications of varying degrees of concern can occur during treatment with chemotherapeutic agents.

PROGNOSIS AND OUTCOME

Polycythemia vera can be successfully managed for years.

PEARLS & CONSIDERATIONS

COMMENTS

- The diagnosis is usually made by excluding other causes of polycythemia.
- Most pets tolerate treatment well.

CLIENT EDUCATION

Infections can occur secondary to myelosuppression. Routine follow-up evaluations are necessary during treatment, even when clinical signs are well controlled.

SUGGESTED READING

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Polycystic Kidney Disease

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Inherited renal disease characterized by the presence of at least one cyst in one kidney. The condition is common in certain cat breeds (especially Persians) and in bull terrier dogs.

SYNONYMS

PKD, autosomal dominant polycystic kidney disease (ADPKD)

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Cats of either gender affected. While diagnosis can be made in kittens, clinical signs become apparent from 3-10 years of age (average 7 years).
- Has been reported uncommonly in dogs with clinical signs in middle and late adulthood.

GENETICS & BREED PREDISPOSITION

- Persians, Himalayans, long-haired cats, and exotic short-haired cats are commonly affected; increasingly documented in short-haired cats.
- Inherited as an autosomal dominant trait that is not strictly associated with long haircoat or brachycephalic facial conformation. A mutation in PKD1 gene is responsible for most cases of feline PKD.
- About 40% of all Persians and Persian-related cats are affected.
- Bull terrier dogs also affected; very rare reports in other dog breeds.

ASSOCIATED CONDITIONS & DISORDERS

- Chronic kidney disease (CKD)
- Polycystic liver disease
- In bull terriers, may be inherited with hereditary nephritis; affected bull terriers have a higher incidence of cardiac disease.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Animals with overt manifestations of illness present for signs of chronic kidney disease (CKD): polyuria, polydipsia, anorexia, lethargy, nausea, vomiting, weight loss, poor body condition, and the like.
- Young animals presented for screening appear healthy.

PHYSICAL EXAM FINDINGS

- Early disease: normal
- Moderate disease: enlarged kidneys, but contour may be smooth
- Advanced disease: enlarged, irregular kidneys usually bilaterally, although may not be symmetric. Other findings of overt CKD (see p. 207)

ETIOLOGY AND PATHOPHYSIOLOGY

- Cysts (usually multiple) present at birth slowly enlarge compressing adjacent renal tissue. When sufficient renal parenchymal damage is present, CKD results. Rate of progression variable.
- Abnormal proteins, polycystin 1 and polycystin 2, are the result of mutations in the polycystic kidney gene. Cysts are abnormal dilations of renal tubules. Any section of the renal tubule may be affected by cyst formation.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Either genetic testing or ultrasound evaluation can be used to diagnose PKD in cats.

DIFFERENTIAL DIAGNOSIS

For enlarged kidneys: perinephric pseudocysts, renal lymphoma or other neoplasia, ureteral obstruction with hydronephrosis, feline infectious peritonitis, hematoma, perinephric abscess, and compensatory hypertrophy (unilateral)

INITIAL DATABASE

- Healthy-appearing young cats presenting for screening: renal ultrasound or genetic testing
- Clinically ill cats with enlarged kidneys: CBC, serum biochemistry profile, and urinalysis to assess renal function and identify uremia-associated complications (see p. 207)
- Abdominal ultrasound
- Blood pressure: especially important in azotemic animals

ADVANCED OR CONFIRMATORY TESTING

- Abdominal ultrasound can establish diagnosis (75% sensitivity for diagnosis in cats <16 weeks; 90% sensitivity in cats by 36 weeks). Cysts are anechoic, spherical structures with smooth, sharply marginated walls and far field enhancement. Cysts are easier to identify in cortex than medulla.
- Genetic testing is available for cats >8 weeks old (Veterinary Genetics Laboratory, University of California—Davis: www.vgl.ucdavis.edu). Buccal swab samples can be collected by owner.

TREATMENT

TREATMENT OVERVIEW

Affected animals should not be used for breeding. Animals with clinical signs related to PKD should be managed as are other animals with CKD.

ACUTE GENERAL TREATMENT

No treatment specific for polycystic kidney disease (PKD); treat for CKD and associated complications.

CHRONIC TREATMENT

Same as for CKD (see pp. 205 and 207)

POSSIBLE COMPLICATIONS

Cysts can become infected. Alkaline and lipid-soluble antibiotics including fluoroquinolones, clindamycin, chloramphenicol, and trimethoprim-sulfonamide penetrate cysts well.

RECOMMENDED MONITORING

- Cats with no clinical signs: blood urea nitrogen (BUN), creatinine, urine specific gravity every 6-12 months to help predict progression to renal failure
- Cats with azotemia: monitor as for CKD of any cause.

PROGNOSIS AND OUTCOME

- Not all cats with PKD will develop azotemia.
- Onset of clinical signs usually occurs after 7 years of age.
- PKD tends to progress more slowly than many other types of CKD. Once azotemia develops, long-term prognosis is poor.

PEARLS & CONSIDERATIONS

COMMENTS

Although hypertension is very common in people with ADPKD, hypertension is uncommon in overtly healthy cats with PKD.

PREVENTION

Eliminate affected animals from breeding population.

CLIENT EDUCATION

- Because PKD is an autosomal dominant trait, 50% of offspring from an affected animal will have PKD. Screening and subsequent removal of positive animals suggested in commonly affected breeds.
- Kittens can be screened by ultrasound at >16 weeks, but if negative, screening should be repeated at >10 months of age or genetic testing completed.
- Genetic screening can be completed at >8 weeks with samples that can be collected by owner.
- If an individual cat with PKD is important to a breeding program, breed only to PKD-negative cats and screen offspring. Half of the offspring will be affected and should be neutered; the unaffected individuals can be bred.

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Polyarthritis

BASIC INFORMATION

DEFINITION

Inflammation of two or more joints

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dependent on underlying cause.
- With immune-mediated polyarthritis (IMPA), the age of onset is variable.
- Infectious polyarthritis in dogs: male > female
- Cats: feline chronic progressive polyarthritis (male > female)

GENETICS & BREED PREDISPOSITION

- Certain histocompatibility alíeles are associated with rheumatoid arthritis in dogs.
- Breed-associated polyarthritis is seen in the Akita, weimaraner and boxer. Meningitis may also be present.
- Familial amyloidosis is a cause of polyarthritis in the shar-pei (see online chapter: Shar-Pei Fever).
- Adverse reaction to sulfonamide drugs, causing polyarthritis: Doberman pinscher

RISK FACTORS

- Dogs: recent vaccination, treatment with sulfonamides or other antibiotics, exposure to ticks, bacterial endocarditis, pyometra, diskospondylitis, urinary tract infection, neoplasia, inflammatory bowel disease, and bacterial enteritis
- Cats: calicivirus vaccination (especially kittens)

ASSOCIATED CONDITIONS & DISORDERS: IMPA is sometimes associated with systemic lupus erythematosus (SLE; see p. 1070) or drug eruption/hypersensitivity (seep. 323), secondary infections, and gastrointestinal (GI) disease or neoplasia.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Noninfectious, nonerosive IMPA
  - Idiopathic
  - Reactive disorder; an immune response to antigens outside the joint (see Risk Factors) can trigger polyarthritis.
  - Associated with SLE
  - Breed-associated
- Infectious, erosive and nonerosive arthritis
- Noninfectious erosive arthritis
  - Feline progressive polyarthritis: periosteal new bone formation and bony erosions; acute (more common, young cats) or chronic (less common, slower onset, adult/older cats)
  - Rheumatoid arthritis (see ',','');return false;">p. 989)

HISTORY, CHIEF COMPLAINT

- Difficulty walking
- Stiffness, lameness
- Weakness, inability to rise
- Inappetence
- Lethargy, weight loss, vomiting, diarrhea
- Animals that have idiopathic IMPA typically experience a sudden onset of signs with multiple symmetric joint involvement.

PHYSICAL EXAM FINDINGS

- Joint pain, swelling:
  - Characteristic physical finding in polyarthritis.
  - May be difficult to localize source of stiffness; sometimes articular pain may be absent on initial examination.
  - Firm, complete flexion of carpi should be performed whenever polyarthritis is possible; may reveal signs of pain that otherwise would escape notice.
  - Distal, symmetric joint involvement (commonly carpi and tarsi) in IMPA
  - Usually one but occasionally two or more proximal joints involved with septic bacterial polyarthritis
- Fever; in some cases of IMPA, pain and joint swelling may be absent and fever may be the only sign.
- Lymphadenopathy
- Neck pain if meningitis present

ETIOLOGY AND PATHOPHYSIOLOGY

- Noninfectious, nonerosive IMPA is the most common form.
  - Possible mechanisms include immune complex formation in response to a microbial infection, with subsequent deposition in joints; immune responses to microbial antigens in the joint; genetic predisposition in certain individuals; and molecular mimicry, in which antibodies to certain antigens (from bacteria, viruses, tumors, drugs, or diets) cross-react with joint antigens.
  - Once joint inflammation has occurred, autoantigens such as altered collagen are produced that stimulate an immune response, helping perpetuate the inflammation.
  - The majority of cases are idiopathic, indicating that the typical case of polyarthritis is “uncomplicated” by underlying disease.
- Infectious:
  - Recognized etiologies:
    - Bacterial: borreliosis, ehrlichiosis (especially *Ehrlichia ewingii), Streptococcus, Staphylococcus, Erysipelothrix, Corynebacterium, Escherichia coli,* and L-forms
    - Other: calicivirus, heartworm, *Mycoplasma, Leishmania, Babesia, Hepatozoon,* and systemic fungal infections
  - May occur following direct penetration of a joint (surgery, trauma, bite wound, arthrocentesis) or from hematogenous spread. Bite wounds are common in cats, whereas hematogenous spread from an unidentified source of infection is common in dogs. Preexisting damage to a joint may aid in the establishment of infection. Single joint involvement is more common, but infection may spread to a second joint; multiple joint involvement is more common with systemic bacterial infections (e.g., bacterial endocarditis [which may also cause IMPA], omphalophlebitis [umbilical vein inflammation/infection], deep pyoderma, pyelonephritis, diskospondylitis, pyometra, periodontal disease, and prostatitis).
- Vaccines (calicivirus, canine distemper, others): may trigger a nonerosive IMPA
- Drugs (especially sulfonamide antibiotics but also lincomycin, cephalosporins, penicillins, and others): may act as antigens or combine with haptens to form antigens and trigger a systemic vasculitis, which may manifest as polyarthritis, fever, thrombocytopenia, and other such conditions
- Autoantibodies to nuclear material (e.g., SLE; see ',','p1070');return false;">p. 1070):
  - Antibodies to nuclear material, immune complex formation, and subsequent deposition in tissues cause multisystemic disease that commonly manifests with nonerosive polyarthritis, dermatitis, and/or glomerulonephritis (GN).
- Erosive IMP As include rheumatoid arthritis (rare in the cat) and periosteal proliferative polyarthritis (common in the cat).
  - Rheumatoid arthritis (see',','');return false;">p. 989) is usually associated with autoantibodies to immunoglobulin G (rheumatoid factor).
  - Periosteal proliferative polyarthritis is characterized by periosteal new bone formation and bony erosions. It affects young adult cats, often castrated males, and is usually acute in onset. Chronic progressive polyarthritis is a milder form, is insidious in onset, and affects older cats.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Polyarthritis can be suspected and occasionally diagnosed with history and physical examination alone. Fever, lethargy, lameness, and the presence of painful or swollen joints, especially distal joints, should arouse the clinician's suspicion. Confirmation rests on arthrocentesis with fluid analysis of multiple joints. Radiography may be done to evaluate for erosive changes. Further testing —including tick titers, cultures, screening for cancer—is required to determine an underlying cause and guide management. Successful management of polyarthritis requires that any underlying cause be identified and treated.

DIFFERENTIAL DIAGNOSIS

Many conditions should be ruled out for a patient that is unable to rise and ambulate normally:

- Neurologic disease (e.g., spinal cord or brain disorders, neuromuscular diseases)

- Muscular disease (e.g., polymyositis)
- Orthopedic disease (e.g., bilateral cranial cruciate ligament rupture, degenerative joint disease)
- Cardiac disease (e.g., pericardial effusion)
- Metabolic disease (e.g., hypoglycemia, hypocalcemia)
- Hematologic disease (e.g., acute blood loss)

INITIAL DATABASE

- Orthopedic and neurologic examinations to help rule out other disorders
- CBC, serum biochemistry profile, urinalysis:
  - Anemia and leukocytosis are common in idiopathic polyarthritis but are nonspecific.
  - Serum chemistry profile to assess dysfunction in other organs
  - Proteinuria may be indicative of GN (immune-mediated) or amyloidosis
- Radiographs to distinguish erosive from nonerosive polyarthritis:
  - Erosive polyarthritis is characterized by subchondral bone destruction, which is seen as an irregular joint surface or "punched-out" erosion of bone at the joint space. In advanced cases of joint deformity, loss of mineralization of the epiphysis and calcification of soft tissues of the joint may be seen.
  - Nonerosive polyarthritis presents no bony radiographic abnormalities; signs of joint effusion and soft-tissue swelling may be apparent.

ADVANCED OR CONFIRMATORY TESTING

- Arthrocentesis (see ',",'cesec49');return false;">p. 1199); two or more joints should be sampled.
  - The tarsi and carpi are especially useful because of frequency of involvement and ease of access to the synovial space.
  - Gross appearance: normal synovial fluid is viscous (tenacious), scant in volume, and clear, whereas synovial fluid of animals with polyarthritis is generally thin/watery and may be copious (several milliliters) and potentially turbid (more so with infectious/septic polyarthritis).
- Synovial fluid analysis; neutrophils are the predominant cell in inflammatory polyarthritis (distinguishing them from the more common degenerative arthropathies), and total cell counts are always >3000/µL and often 40,000/µL or higher. Cytologic examination is seldom helpful in distinguishing septic from nonseptic arthritis (only occasionally are intracellular, phagocytized organisms seen), although the presence of degenerate or toxic neutrophils is suggestive of septic arthritis.
- Culture: synovial fluid cultures are usually negative. When clinicians suspect septic arthritis, they should consider a culture of synovial membrane, blood, and/or urine. Special media are needed to culture L-form bacteria and *Mycoplasma.*
- Titers: Lyme disease *(Borrelia burgdorferi), Ehrlichia* (especially *canis, ewingii),* and *Anaplasma phagocytophila* (formerly *Ehrlichia equi).*
- Echocardiogram if suspicious of bacterial endocarditis (e.g., heart murmur, especially if new in onset, and/or diastolic; see ',",'para693');return false;">p. 346)
- Serum antinuclear antibody and rheumatoid factor if the clinician suspects SLE or rheumatoid arthritis, respectively; the tests are of limited accuracy
- Cerebrospinal fluid tap if the clinician suspects meningitis
- Thoracic radiographs and abdominal ultrasound examination to evaluate for remote infection, GI disease, or neoplasia if suspected

TREATMENT

TREATMENT OVERVIEW

Treatment depends on the etiology. Sometimes despite treating the underlying cause, however, a course of prednisone is required to resolve the polyarthritis. For cases of IMPA, immunosuppressive doses of prednisone/prednisolone are the treatment of choice and following resolution of clinical signs, usually within 2 weeks, corticosteroids should be slowly tapered over 4-6 months. Insufficient dosages and/or administration for insufficient periods of time are important causes of treatment failure.

ACUTE GENERAL TREATMENT

- Doxycycline, 10 mg/kg PO q 24 h for 28 days for tickborne infections, *Mycoplasma,* and L-form bacteria
- Prednisone/prednisolone, 1.1 mg/kg PO q 12 h initially for nonerosive and erosive noninfectious IMPA
- Broad-spectrum antibiotics (e.g., amoxicillin-clavulanate, 22 mg/kg PO q 12 h) or cephalosporins (e.g., cephalexin, 22 mg/kg PO q 8 h) pending cultures in suspected or confirmed cases of septic arthritis
- Surgical joint lavage and drainage sometimes are required for septic arthritis.

CHRONIC TREATMENT

- For IMPA: prednisone/prednisolone, 1.1 mg/kg PO q 12 h (20 mg/m^2 PO q 12 h for dogs >25 kg; seep. 675) until resolution of signs (usually 2-4 weeks), then slowly reduce the dose and administer q 48 h. Average of 3-6 months and rarely lifelong treatment is required.
- If glucocorticoid side effects are marked or high doses are necessary, to suppress signs, consider other immunosuppressive drugs such as azathioprine, cyclophosphamide, gold salts, methotrexate, or leflunomide to keep clinical signs suppressed while using lower doses of glucocorticoids.
- Septic arthritis: antibiotics required until 2 weeks after infection has resolved; often a minimum of 6 weeks.

NUTRITION/DIET

Caloric control is necessary to avoid weight gain in patients on corticosteroids. Treatment of obesity when present is an important adjunctive therapy for chronic polyarthritis cases.

DRUG INTERACTIONS

Many drugs can potentially interact negatively with the drug in question; clinicians should consult a formulary for possible interactions.

POSSIBLE COMPLICATIONS

- Secondary infections from immuno-suppressive drugs
- Prednisone has many potential adverse effects including polyuria and polydipsia (PU/PD), polyphagia, panting, weight gain, muscle wasting, and elevated liver enzymes.
- Azathioprine: myelosuppression, hepatotoxicity, acute pancreatitis; avoid in cats
- Cyclophosphamide: myelosuppression, hemorrhagic cystitis

RECOMMENDED MONITORING

- Primarily resolution of clinical signs; if uncertainty exists, repeat arthrocentesis to see if cell counts have returned to normal.
- Monthly CBCs are required for animals receiving cyclophosphamide or azathioprine.
- Monitor liver enzymes in animals receiving glucocorticoids.

PROGNOSIS AND OUTCOME

- Nonerosive IMPA: good to guarded. About 30% of cases relapse and may be difficult to control or may require lifelong treatment.
- Juvenile hereditary arthritis of Akitas: very poor. Does not respond to immunosuppressive therapy.
- Calicivirus infection of cats: excellent. Generally resolves in 3 days with supportive care.
- Noninfectious erosive arthritis: guarded. Arthrodesis may improve quality of life.
- Infectious arthritis: provided the condition is nonerosive and the infection can be treated, the prognosis is good.

PEARLS & CONSIDERATIONS

COMMENTS

- Polyarthritis should be suspected in any animal that is reluctant to walk or in any case of fever of unknown origin. Even in the absence of joint pain or swelling, arthrocentesis of multiple joints is indicated in such animals to confirm or refute a diagnosis of IMPA.
- Cats with polyarthritis may be described only as lethargic by owners; polyarthritis might be missed unless cats are observed walking in the exam room.
- Empirical treatment with doxycycline may be considered while completing a workup.
- The majority of cases of polyarthritis are idiopathic, immune mediated, and nonerosive.

TECHNICIAN TIPS

- Dogs receiving immunosuppressive doses of prednisone/prednisolone should be monitored closely for adverse effects (see above). The goal is to start at a high dose, resolve clinical signs, then taper gradually to lowest possible dose so as to minimize unacceptable side effects including polyuria and muscle wasting.
- Pain associated with polyarthritis should not be mistaken for reluctance or other behavioral traits; these patients may be too painful to walk, may be more prone to aggression if handled, or both.

PREVENTION

Tick prevention if relevant (dogs in endemic regions)

CLIENT EDUCATION

- Close monitoring is required while patients are receiving immunosuppressive therapy.
- Relapses are possible.
- Genetic counseling for hereditary forms

SUGGESTED READING

Clements DN, et al: Type 1 immune-mediated polyarthritis in dogs: 39 cases (1997-2002). J Am Vet Med Assoc 224:1323–1327, 2004.

Stull JW, et al: Canine immune-mediated polyarthritis: clinical and laboratory findings in 83 cases in western Canada (1991-2001). Can Vet J 49:1195–1203, 2008

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Pollakiuria, Stranguria

BASIC INFORMATION

DEFINITION

- Pollakiuria: increased frequency of attempts to urinate
- Stranguria: straining to urinate
- Both are clinical signs of lower urinary tract inflammation, infection, and/or obstruction.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Owners may confuse these clinical signs with inappropriate elimination, polyuria, or tenesmus.
- Other clinical signs can include dysuria and malodorous urine.
- Often pollakiuria/stranguria is the only presenting clinical sign.

PHYSICAL EXAM FINDINGS

- Important to determine if urethral obstruction is the cause:
  - Obstruction: bladder enlarged/firm, nonexpressible, often painful
  - Nonobstruction: bladder small/soft, expressible; bladder wall may be thickened, often painful as well.
- Bladder should be palpated before and after the patient voids:
  - Uroliths, masses, and bladder wall thickness/irregularities may be assessed more easily in the flaccid bladder.
- Rectal exam may reveal urethral, prostatic, or bladder trigone abnormalities.

ETIOLOGY AND PATHOPHYSIOLOGY

- Any disease that causes lower urinary tract infection (LUTI), inflammation, or obstruction can cause pollakiuria or stranguria.
- Localizes the lesion to the lower urinary tract (bladder, urethra)

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Beyond a complete history and physical exam, a sterile urine sample for urinalysis (and bacterial culture and sensitivity [C&S] in the canine patient) should be the first diagnostic test in the pollakiuric or stranguric patient. Diagnostic imaging should be considered in a patient with a negative culture in the face of pollakiuria/stranguria.

DIFFERENTIAL DIAGNOSIS

Feline:

- Most common cause is idiopathic feline lower urinary tract signs (FLUTS; see p. 387):
  - Also called *feline idiopathic cystitis* (FIC), *feline lower urinary tract disorder* (FLUTD), and *feline urologic syndrome* (FUS)
  - Primary bacterial infection in cats is rare; infection is present in <2% of cats <10 years of age with lower urinary tract signs

Canine:

- Most common cause is bacterial cystitis
- Nonbacterial causes of cystitis:
  - Polypoid: chronic irritation
  - Emphysematous: bacterial fermentation of glucose in devitalized bladder wall
  - Drug induced: usually associated with cyclophosphamide

    - Idiopathic
    - Fungal, algal: uncommon
- Other bladder diseases:
    - Cystic calculi (uroliths)
    - Neoplasia
- Prostatic:
    - Neoplasia (transitional cell carcinoma [TCC], adenocarcinoma)
    - Trauma
- Urethral disease:
    - Urethrorectal fistula
    - Urethral prolapse
    - Urethritis
    - Urethrolithiasis
    - Neoplasia (TCC, squamous cell carcinoma)
    - Trauma

INITIAL DATABASE

- CBC and serum biochemistry panel
    - Metabolic or systemic disease (diabetes mellitus, pyelonephritis, many others)
- Urinalysis
    - Cystocentesis preferred
    - Comparison with free-catch sample may assist in anatomic localization of lesion
- Urine C&S
    - Cystocentesis preferred
- Abdominal radiographs
    - Mass effect
    - Prostatomegaly
    - Radiopaque calculi
- Abdominal ultrasound
    - Bladder wall thickness
    - Presence of bladder mass (inflammatory, neoplastic, or blood clot)
    - Architecture of prostate
    - Proximal urethra

ADVANCED OR CONFIRMATORY TESTING

- Advanced imaging
    - Double contrast cystogram
    - Voiding urethrogram
    - Excretory urethrogram
- Cystoscopy
- Voiding urohydropulsion
    - Appropriate if small calculi are present
    - Noninvasive method to collect calculi for chemical analysis
- Cystotomy
    - Biopsy of mass
    - Removal of calculi
    - Culture of bladder wall

TREATMENT

TREATMENT OVERVIEW

Goals of treatment are to relieve discomfort associated with LUTI and treat underlying cause.

ACUTE GENERAL TREATMENT

Of greatest immediate concern is urethral obstruction (see p. 1131). No matter the cause, establish urine flow to prevent life-threatening hyperkalemia if complete obstruction is present (urinary bladder moderately to markedly enlarged): see and

- Assess azotemia and potassium level.

- Gently try to pass a urinary catheter using retrograde hydropulsion if obstruction is met.
- If catheterization is unsuccessful:
  - Cystocentesis:
    - Relieving pressure may allow urethral catheter to pass.
    - Insert needle relatively caudally (near trigone) and direct it caudodorsally to minimize risk of contacting devitalized bladder wall.
  - Urethrotomy
  - Cystostomy tube
- Provide fluid and electrolyte support while diagnostic tests are pursued.
  - Consider IV fluid without potassium as first choice until serum potassium level is known (e.g., choose 0.9% NaCl).
- If a bacterial infection is suspected, a C&S is vital for directed antibiotic therapy.

CHRONIC TREATMENT

Dependent on accurate diagnosis of underlying cause

PEARLS & CONSIDERATIONS

- Pollakiuria and stranguria localize the problem to the lower urinary tract.
- Further diagnostic evaluation is necessary to determine the exact cause of these signs.
- While bacterial infection is the most common cause in dogs, this is rare in cats.
- FLUTS (FLUTD/FUS/FIC) is the most common cause of pollakiuria and stranguria in cats.
- With any episode of pollakiuria or stranguria, urinary obstruction must be ruled out as soon as possible.

TECHNICIAN TIPS

- Any client who calls with concerns of pollakiuria/stranguria should be advised of risk of urinary obstruction and urged to bring the pet in for examination without delay. Owners often misidentify stranguria as constipation (both involve “straining”), so a telephone question regarding constipation likewise warrants an immediate evaluation to rule out urethral obstruction.
- Concurrent analysis of cystocentesis and free-catch urine samples can help localize the lesion.

SUGGESTED READING

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Poisoning, General Management

BASIC INFORMATION

DEFINITION

A poison is a substance that causes death or injury when introduced into or absorbed by a living organism.

SYNONYM

Intoxication, toxicosis

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Young animals are more likely to accidentally ingest poisonous materials.
- A cat's unique metabolism may cause it to be predisposed to certain toxicoses (e.g., acetaminophen).

RISK FACTORS

- Lack of supervision
- Access to poisonous materials
- Individual behavior (some animals routinely ingest materials while others seldom do).
- Poisoning of companion animals is rarely malicious.

CONTAGION & ZOONOSIS: Several animals may be affected simultaneously from the same source.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Key components of the history may include witnessed exposure, evidence of exposure (e.g., chewed medication container), and characteristic behavior or clinical signs. It is common for some owners to believe their animal has been poisoned when it becomes ill for any reason. A thorough history will help establish the likelihood of poisoning.
- Additional important information may include the exact nature of the poison (if known), maximum possible dose ingested, time elapsed since ingestion, and time elapsed since clinical signs were first observed.

PHYSICAL EXAM FINDINGS: Highly dependent on the poison involved; common categories of signs include:

- Central nervous system (CNS) alterations and seizures (lead, metaldehyde, organophosphates, carbamates, tremorgenic mycotoxins, alcohol, blue-green algae, marijuana, chocolate, ivermectin)
- Muscle weakness, paresis, and paralysis (coral snakes, black widow spiders, phenoxy herbicides [including 2,4-D], macadamia nuts)
- Acute blindness (horse dewormer medication, salt)
- Oral mucosal lesions (corrosive acids, alkalis, cationic detergents, liquid potpourri, formaldehyde)
- Acute renal failure (ethylene glycol, lily plants [cats])
- Acute hepatic damage or failure (mushrooms, blue-green algae, iron, sago, or cycad palm plants/trees)
- Severe anemia (onions, garlic, naphthalene mothballs, anticoagulant rodenticides, acetaminophen [cats])
- Cardiac arrhythmias (foxglove, lily of the valley, oleander, azalea/rhododendron, and yew plants; bufo toads)
- Gastrointestinal (GI) signs (many, including several already listed; arsenic, castor beans, nitrogen-phosphate-potassium (NPK) fertilizers, zinc oxide, oxalate-containing plants)

ETIOLOGY AND PATHOPHYSIOLOGY

The possibility of poisoning should be considered when a young and otherwise healthy animal exhibits an acute onset of neurologic signs, organ failure, or other systemic signs and after all other common diseases have been ruled out.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

When an inciting cause is unknown, owners may express concern that their pet has been poisoned. The clinician should remember that unless clinical signs are consistent with poisoning and there is a reasonable chance of exposure to the poison, the illness is likely caused by something other than malicious poisoning.

DIFFERENTIAL DIAGNOSIS

Other systemic or metabolic diseases

INITIAL DATABASE

- Packed cell volume/serum total protein
- Azo stick (blood urea nitrogen)
- Blood glucose
- Urine specific gravity and dipstick
- Samples of urine, blood, and gastric contents should be saved for possible toxicologic analysis.

ADVANCED OR CONFIRMATORY TESTING

Serum levels or tissue analysis for specific toxin

TREATMENT

TREATMENT OVERVIEW

Treatment of poisoning should focus on maintaining cardiovascular, respiratory, and neurologic stability and preventing further absorption of toxin. ASPCA Animal Poison Control (888-426-4435; www.aspca.org/pet-care/poison-control/) may be a useful resource to determine the best method of treatment. Goals of treatment are to:

- Achieve cardiovascular stability.
- Prevent further absorption of the toxin.
- Administer antidote if available.

ACUTE GENERAL TREATMENT

- Triage principle: life-threatening complications must be addressed first if present. “Start with the animal, not the toxin.”
  - Airway support or intubation if respiratory arrest
  - IV catheter placement if animal is showing systemic signs
  - Electrocardiogram (ECG), blood pressure (BP), and pulse oximetry monitoring as dictated by physical examination findings
  - IV fluid and oxygen support as indicated by cardiovascular and respiratory status
- Decontamination of the patient:
  - Skin: dermal exposure (i.e., topical pyrethrin exposure) warrants bathing with warm water and a mild dishwashing detergent. Care should be taken to prevent hypothermia.
  - Emesis: (see p. 1364) consider if ingestion has occurred within 2 hours of visit. Contraindicated in animals that ingested potentially caustic substances (acids, alkalis, petroleum distillates) or are unable to protect the airway because of depression, seizures, or other neurologic dysfunction.
  - Gastric lavage (see p. 1281): used when emesis is contraindicated because of the animal's inability to protect its airway; requires induction of general anesthesia in conscious animals and intubation of the airway. This procedure involves passage of the distal end of a large-bore tube into the stomach and administration of 5-10 mL/kg of tepid water. The water is then withdrawn through the tube with gravity flow. Lavage is repeated until gastric contents are clear.
  - Activated charcoal: the most commonly used general treatment for intoxications; dose is 1-4 g/kg PO (suspension: 5-10 mL/kg PO). It is ineffective in removing heavy metals. Some animals will eat the activated charcoal willingly, but most require orogastric administration. Clinicians must be careful to prevent aspiration pneumonia. Elimination of toxins that undergo enterohepatic circulation may be hastened by additional doses of activated charcoal every 4-6 hours for up to 24 hours. Owners must be made aware the animal will have black stool for several days.
  - Cathartics: accelerate fecal elimination of toxin. Sorbitol is most commonly used in combination with activated

charcoal. Other available cathartics include sodium sulfate, magnesium sulfate, or citrate. Contraindications include GI obstruction, recent bowel surgery, volume depletion, electrolyte imbalance, and ingestion of a corrosive substance.
- Fluid diuresis: may be used for accelerating elimination of toxins that are renally extracted.

PROGNOSIS AND OUTCOME

Prognosis depends on the toxin, total dose of exposure, and severity of clinical signs.

PEARLS & CONSIDERATIONS

COMMENTS

- Most of the specific intoxications seen in small animal practice are discussed individually and in detail elsewhere in this book.
- Many poisons cause signs similar to those caused by other common diseases. The diagnosis of toxicity should not be reached without strong historical or physical evidence of exposure.

PREVENTION

Owners should prevent their pets from accessing toxins.

CLIENT EDUCATION

Discussions on common poisoning should be made available to clients.

SUGGESTED READING

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Pododermatitis

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

An inflammatory skin disease affecting the paw. Disorders of the footpads are discussed on .

SYNONYMS

Interdigital dermatitis, interdigital pyoderma, pedal dermatitis

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Pododermatitis is more common in dogs than cats. Foot lesions in cats more commonly involve the footpads, claws, and periungual areas, whereas dogs often present with interdigital lesions.
- Dogs and cats of any age or sex can be affected.

GENETICS & BREED PREDISPOSITION

- Short-haired dog breeds (e.g., English bulldog, Great Dane, basset hound, mastiff, bull terrier, boxer, dachshund, dalmatian, German short-haired pointer, weimaraner) are more commonly affected.
- Long-haired breeds that are more often affected include German shepherds, golden retrievers, Irish setters, and Pekingese dogs.

RISK FACTORS: In cats, immunosuppression caused by feline leukemia virus (FeLV), feline immunodeficiency virus (FIV), or diabetes mellitus can predispose to infectious pododermatitis.

CONTAGION & ZOONOSIS: Dermatophytosis is contagious and zoonotic. Sporotrichosis (especially feline: zoonotic hazard) and blastomycosis (common-point source of infection or accidental inoculation) also may affect humans.

GEOGRAPHY AND SEASONALITY: Atopic dermatitis and allergic or irritant contact dermatitis can be seasonal.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Owners can observe lesions on a single foot or multiple feet. Licking or chewing of the affected areas and lameness may also be apparent. In addition, pododermatitis may be part of a more generalized skin condition.

PHYSICAL EXAM FINDINGS: Lesions can be present on the dorsal and/or the ventral aspects of the feet. One or several interdigital spaces can be affected. Possible lesions include:

- Erythema
- Nodules
- Swelling of the feet
- Interdigital serosanguineous or seropurulent exudates
- Interdigital bullae or draining tracts
- Ulcers and erosions
- Scales and crusts
- Alopecia
- Paronychia (inflammation/infection of the claw folds)
- Eosinophilic plaques (cat)
- Salivary staining
- Occasional pitting edema of associated metatarsus or metacarpus
- Regional lymphadenopathy may be present

PODODERMATITIS Interdigital deep pyoderma on ventral aspect of a foot in a 5-year-old female weimaraner. Skin near the footpad of the second digit is mildly swollen, erythematous, and eroded.

(Courtesy Dr. Nadia Pagé.)

ETIOLOGY AND PATHOPHYSIOLOGY

Pododermatitis can arise following various pathologic mechanisms, including:

- Contact with irritant substances or physical trauma that can induce skin injury and inflammation
- Infectious agents that can induce an immune response from the host, resulting in tissue inflammatory cell infiltrates
- Hormonal imbalances (hypothyroidism, hyperadrenocorticism) that can predispose to infectious pododermatitis
- Allergic disease, where self-trauma can result in skin lesions, alopecia, and salivary staining
- Immune-mediated disorders: the development of antibodies or activated lymphocytes against normal body constituents or inciting antigens (drugs, bacteria, viruses) can cause tissue damage.
- Neoplastic cell infiltrates can disturb the normal structure of the skin.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Pododermatitis is apparent on physical examination; etiology is determined based on number of feet affected, appearance of lesions, possible environmental causes, and results of tests selected based on lesion distribution and extradermatologic physical exam findings.

DIFFERENTIAL DIAGNOSIS

- If lesions are restricted to one foot:
  - Foreign bodies, trauma
  - Neoplasia
  - Localized bacterial or fungal infection
  - Osteomyelitis
- If multiple feet are involved:
  - Environmental/traumatic: contact chemical dermatitis, clipper burn
  - Infectious: bacterial, fungal (dermatophytosis, *Malassezia* dermatitis, sporotrichosis, mycetoma, blastomycosis, cryptococcosis), parasitic (demodicosis, hookworm, and *Pelodera* dermatitis, trombiculiasis), rick-ettsial (canine Rocky Mountain spotted fever), viral (papillomatosis)
  - Allergic: food hypersensitivity, atopic dermatitis, contact allergic dermatitis
  - Immune-mediated: pemphigus (foliaceous, erythematosus, vulgaris), bullous pemphigoid, systemic lupus erythematosus (SLE), and immunomodulatory-responsive lymphocytic plasmacytic pododermatitis (dog) and plasma cell pododermatitis (cat)
  - Metabolic/endocrine: superficial necrolytic dermatitis (hepatocutaneous syndrome); hypothyroidism and hyperadrenocorticism can predispose an animal to bacterial or dermatophyte-induced pododermatitis and to

adult-onset demodicosis.
- Miscellaneous: behavioral (self-induced lesions), zinc-responsive dermatosis, foreign-body reaction (occasionally affects multiple feet), sterile pyogranulomas, nodular dermatofibrosis (German shepherds)

INITIAL DATABASE

Selection of diagnostic tests is based on evidence provided by the history and physical examination:

- Skin scrapings: *Demodex* spp.
- Wood's lamp examination: dermatophytosis (fluorescent strains of *Microsporum cants*)
- Cytologic examination: fungal organisms, bacteria and inflammatory cells (bacterial pododermatitis), acantholytic keratinocytes (pemphigus), neoplastic cells
- Elimination diet: food allergy
- Intradermal skin testing (serologic allergy testing could also be considered): atopic dermatitis
- Fecal flotation: hookworm ova
- Radiographs: osteomyelitis, radiopaque foreign bodies
- CBC, biochemistry panel, urinalysis: results depend on the underlying cause; often normal or nonspecific unless systemic disease.

ADVANCED OR CONFIRMATORY TESTING

- Culture: bacterial, fungal
- Skin biopsy: foreign bodies, demodicosis or other parasites, bacterial or fungal infections, neoplasia, immune-mediated diseases, superficial necrolytic dermatitis, zinc-responsive dermatosis
- Antinuclear antibody (ANA): positive in virtually all animals with SLE
- Endocrine tests and serologic titers if relevant

TREATMENT

TREATMENT OVERVIEW

The goal of treatment is to achieve permanent cure or control of the disease. Sometimes palliative treatment is the only option (nonresectable tumors).

ACUTE GENERAL TREATMENT

Specifics depend on the underlying cause:

- Minimizing foot trauma (e.g., owner education; use of booties)
- Draining lesions can benefit from soaks in a magnesium sulfate solution (Epsom salt, 30 mg/L of warm water), q 12-24 h until drainage stops (5-7 days).
- Surgery: neoplastic lesions, surgical exploration (foreign bodies), or débridement
- Laser surgery can be useful in removing cystic lesions and sinuses (dogs).
- Bacterial pododermatitis can necessitate several weeks (8-12 weeks) of appropriate systemic antibiotics. The causative organism is often *Staphylococcus pseudintermedius.* If cytologic examination suggests infection with this bacterium, an acceptable initial choice is cephalexin, 22-30 mg/kg PO q 12 h; or amoxicillin/clavulanate, 12.5-22 mg/kg PO q 12 h.
- If other bacteria are involved or the empirical choice of antibiotic does not resolve the infection, the clinician should correct the antibiotic selection based on culture and sensitivity (C&S) results.
- Manage parasitic or fungal infections with appropriate antiparasitic or anti-fungal medications.
- Atopic dermatitis often requires management with combination therapy: antiinflammatory agents, allergen-specific immunotherapy, and antimicrobial drugs to control secondary bacterial or yeast infections.
- Immunosuppressive treatments are usually required for treating immune-mediated diseases.

PROGNOSIS AND OUTCOME

Variable, depending on the cause of pododermatitis

PEARLS & CONSIDERATIONS

COMMENTS

- Interdigital pyoderma can often be a frustrating disease to treat. Even after the resolution of the infection, the remaining fibrosis and scarring may predispose the animal to relapse.
- In severe refractory cases, clinicians may have to consider drastic measures such as surgery (fusion podoplasty).
- Cases of canine pododermatitis with substantial footpad involvement are more commonly seen with autoimmune diseases, drug reactions, zinc-responsive dermatosis, superficial necrolytic dermatitis, and distemper.

TECHNICIAN TIP

Patients with pododermatitis may have painful feet. Their reluctance to walk should not be misinterpreted as stubbornness, and they may need support to walk comfortably.

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Pneumothorax

BASIC INFORMATION

DEFINITION

Accumulation of air within the pleural space

SYNONYM

Collapsed lung

EPIDEMIOLOGY

SPECIES, AGE, SEX: Young, large-breed male dogs are predisposed to trauma and subsequent pneumothorax.

GENETICS & BREED PREDISPOSITION: Northern breeds (Siberian husky or Alaskan malamute) are predisposed to spontaneous pneumothorax.

RISK FACTORS

- Trauma (hit by car, bite wounds, falls from elevated heights)
- Surgical intervention (cranial abdominal, intervertebral disk, and other surgeries)
- Pleural effusion (centesis may lead to iatrogenic pneumothorax)

GEOGRAPHY AND SEASONALITY: Trauma is more common in warmer months.

ASSOCIATED CONDITIONS & DISORDERS

- Pulmonary contusions
- Diaphragmatic hernia
- Flail chest
- Fracture
- Asthma
- Pleural effusion

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Traumatic: due to damage to the pulmonary parenchyma or chest wall
- Spontaneous: due to abnormal pulmonary parenchyma without trauma
- Iatrogenic: due to damage to the lung parenchyma following thoracocentesis for removal of pleural effusion, following aspiration of a pulmonary mass, or during surgery

HISTORY, CHIEF COMPLAINT

- Trauma
- Acute-onset coughing or tachypnea
- Worsening tachypnea following an intervention

PHYSICAL EXAM FINDINGS

- Dyspnea/increased respiratory effort is the hallmark finding:
  - Expiratory or both expiratory and inspiratory but not inspiratory alone (which would more commonly suggest upper airway disease, not pneumothorax)
  - May be absent in mild cases
- Other evidence of trauma, either blunt (e.g., hit by car) or penetrating (e.g., bite, gunshot, stabbing)
- Dull or muffled lung sounds (auscultation, percussion)

ETIOLOGY AND PATHOPHYSIOLOGY

- Air may enter the pleural space either from damage to the pulmonary parenchyma (e.g., rupture of a pulmonary bleb), which permits the leakage of air from the respiratory system into the pleural space, or via damage to the chest wall, which permits air to rush into the pleural space.
- When the lung parenchyma is normal, small injuries (e.g., needlestick during centesis) heal rapidly.
    - Intrapleural volumes of air of up to 45 mL/kg cause no clinical signs and take about 2 weeks to resorb spontaneously in healthy dogs.
    - Iatrogenic pneumothorax occurring during thoracocentesis is almost invariably associated with chronic effusions (especially chylothorax), diseased lung tissue, an uncooperative patient, or an inexperienced operator.
- A "tension" pneumothorax is a severe pneumothorax from any cause that results in cardiovascular collapse due to inadequate cardiac filling.
- Rarely, foreign bodies (grass awns, wooden toothpicks, porcupine quills, etc.) may migrate intrathoracically and cause pneumothorax.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on a history of thoracic trauma (field or surgical), dyspnea, or both. The confirmatory test of choice is thoracic radiography.

DIFFERENTIAL DIAGNOSIS

Dyspnea in an animal that has undergone trauma:

- Pleural effusion
- Pulmonary contusions
- Primary lung or airway disease
- Pain
- Hypovolemia

INITIAL DATABASE

- Thoracic radiographs are the test of choice; left-lateral recumbency is the most sensitive view for detecting small volumes of air in the pleural space.
- Routine laboratory testing (CBC, serum chemistry profile, urinalysis): generally unremarkable

ADVANCED OR CONFIRMATORY TESTING

- CT scan may be useful in spontaneous pneumothorax.
- Arterial blood gas (ABG) measurement or pulse oximetry: may help elucidate whether dyspnea in a trauma animal with pneumothorax may be in part due to the pneumothorax itself (e.g., Pao2 < 90 mm Hg on room air and/or O2 desaturation <96%) or to pain, hypovolemia, or other conditions associated with trauma. Pulmonary contusions may also cause hypoxemia and desaturation, however.
- Analysis of pleural effusion, if present

TREATMENT

TREATMENT OVERVIEW

The course and severity of the patient's clinical signs and suspected inciting cause help determine whether to pursue conservative management or thoracotomy. Treatment goals for conservative management include removal of air from the pleural space and measures that encourage formation of a seal to prevent further leakage; surgical treatment aims to eliminate the source of the leak.

ACUTE GENERAL TREATMENT

- Supplemental oxygen will result in more rapid resolution of a closed (not ongoing) pneumothorax, because the trapped air is higher in nitrogen, and if inhaled oxygen is administered, the trapped air will move more quickly down its concentration gradient.

- Traumatic pneumothorax:
  - No clinical signs, identified incidentally on radiographs: no treatment; monitoring is important.
  - Clinical signs: thoracocentesis warranted (see p. 1338). If large volumes (>200 mL/kg), no end point, or recurrent pneumothorax, then place thoracostomy tubes (see). Apply the "three-strike rule," meaning if three or more thoracocenteses are required within 24 hours following a trauma, a thoracostomy tube should be placed.
- Spontaneous pneumothorax (no trauma):
  - If the clinician suspects a bulla or bleb (no masses on radiographs), a thoracotomy is warranted.
  - If the clinician suspects a necrotic neoplasm, a thoracic CT scan followed by thoracotomy is warranted.
  - If the clinician suspects an underlying feline asthma or chronic bronchitis, conservative therapy may be adequate.
- Iatrogenic:
  - If there are no clinical signs (radiographic diagnosis only), monitoring of the patient is adequate.
  - If the patient is showing clinical signs, repeating the thoracocentesis and monitoring the animal closely are recommended. The animal may require a thoracostomy tube or exploratory thoracotomy if not responsive. Underlying disease may require specific treatment.

CHRONIC TREATMENT

Correction of the underlying cause if applicable

POSSIBLE COMPLICATIONS

Ongoing pleural effusion or pneumothorax

RECOMMENDED MONITORING

- Respiratory rate and effort
- Pulse oximetry

PROGNOSIS AND OUTCOME

- Fair to good; often with trauma, the associated injuries are more likely to predict outcome.
- Dyspnea and duration of intensive care are negative prognostic factors in dogs and cats with pneumothorax.

PEARLS & CONSIDERATIONS

COMMENTS

- Traumatic pneumothorax rarely requires surgical correction; most cases rapidly resolve (within 72 hours).
- Spontaneous pneumothorax commonly requires surgical treatment because most cases will not resolve without surgery.

TECHNICIAN TIP

Technicians involved in caring for patients with pneumothorax should be familiar with management of chest tubes.

PREVENTION

- Owners should prevent free roaming of pets.
- Clinicians should use caution when performing a thoracocentesis.

SUGGESTED READING

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Pneumonia, Bacterial

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Inflammation of the lower respiratory tract or interstitium from bacterial infection

EPIDEMIOLOGY

SPECIES, AGE, SEX: Puppies acquired from community situations (shelters, pet stores) are more likely to have pneumonia from *Bordetella bronchiseptica* than other pathogens. No other species, age, or gender predilections noted except in cases of bacterial pneumonia secondary to congenital defects (e.g., primary ciliary dyskinesia).

GENETICS & BREED PREDISPOSITION: No breed or genetic predispositions other than for those associated with underlying primary diseases or associated conditions

RISK FACTORS: Any disease that compromises respiratory defenses or increases the potential for aspiration:

- Laryngeal disease:
  - Laryngeal paralysis post tieback surgery
  - Laryngeal neoplasia
- Esophageal disease
  - Esophagitis
  - Megaesophagus
  - Esophageal diverticula
- Altered consciousness
- Chronic vomiting
- Bronchial masses or foreign bodies
- Bronchiectasis
- Viral respiratory infection (e.g., distemper)
- Congenital immune deficiencies
- Ciliary dyskinesia
- Risk factors for *B. bronchiseptica* pneumonia include dense housing (dogs and cats) and the presence of a dog with clinical signs of upper respiratory tract disease (cats).

ASSOCIATED CONDITIONS & DISORDERS

- Sepsis
- Systemic inflammatory response syndrome
- Multiple organ dysfunction syndrome
- Respiratory foreign body
- Bronchial obstruction (foreign body, mass)
- Hemothorax (uncommon)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Bronchopneumonia involves inflammation of both airways and alveolar/interstitial compartments.

HISTORY, CHIEF COMPLAINT: Chief complaint may be related to pneumonia or to the predisposing disease:

- Pneumonia:
  - Cough
  - Nasal discharge
  - Sneezing
  - Exercise intolerance
  - Anorexia, lethargy
  - Hemoptysis (uncommon)
  - Acute death (uncommon but reported)
- Predisposing disease:

    - Regurgitation
    - Recurrent/persistent infections (usually respiratory, but occasionally other)
- Some animals may exhibit no clinical signs.
- Mild, vague signs (e.g., delayed postoperative recovery, failure to thrive) may be the earliest manifestations of the onset of bacterial pneumonia as a complication of another disorder (e.g., sepsis, systemic inflammatory response syndrome, multiple organ dysfunction syndrome).
- The lack of signs referable to the respiratory system does not exclude the diagnosis.

PHYSICAL EXAM FINDINGS: Physical examination may be unremarkable or reflect only signs relating to the underlying predisposing disorder in the presence of mild or moderate bacterial pneumonia. Lack of signs referable to the respiratory system cannot exclude the diagnosis. Findings are variable:

- Cough
    - Hemoptysis possible
- Nasal discharge
- Crackles or wheezes, sometimes focally; focal absence of breath sounds also possible
- Fever
- Tachypnea
- Increased respiratory effort or overt respiratory distress

ETIOLOGY AND PATHOPHYSIOLOGY

- Bacterial pneumonia is most often a complication of another disease that disrupts mechanical or immunologic pulmonary clearance and defense mechanisms:
    - Impaired mucociliary clearance
    - Impaired reflex closure of the glottis
    - Absent or impaired cough reflex
    - Abnormal immune function:
        - Innate
        - Acquired
- *B. bronchiseptica* is capable of causing disease as a primary pathogen in dogs or cats without other apparent underlying risk factors or concurrent disease.
- Bacteria most often enter lungs via airways but can enter hematogenously. With impaired clearance and defense mechanisms, bacteria can proliferate and initiate local inflammatory responses:
    - Common isolates in dogs and cats include gram-negative aerobes such as *Escherichia coli, Klebsiella, Bordetella, Pasteurella,* and *Staphylococcus* spp.
        - Acutely fatal pneumonia associated with hemothorax and bleeding into airways, caused by *Streptococcus equi* subsp. *zooepidemicus,* has been described in dogs from dense housing situations.
    - Regionally endemic diseases, such as plague and tularemia, can be causes of primary pneumonia.
- Local inflammatory responses cause pulmonary lesions, impair lung function, and can contribute to respiratory and systemic disease manifestations.

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

Definitive diagnosis of bacterial pneumonia hinges on demonstration of bacteria either by culture and sensitivity testing (most sensitive) or by cytologic examination of respiratory wash samples. A second key for many patients is pursuit of underlying or concurrent disease that increases risk for bacterial pneumonia.

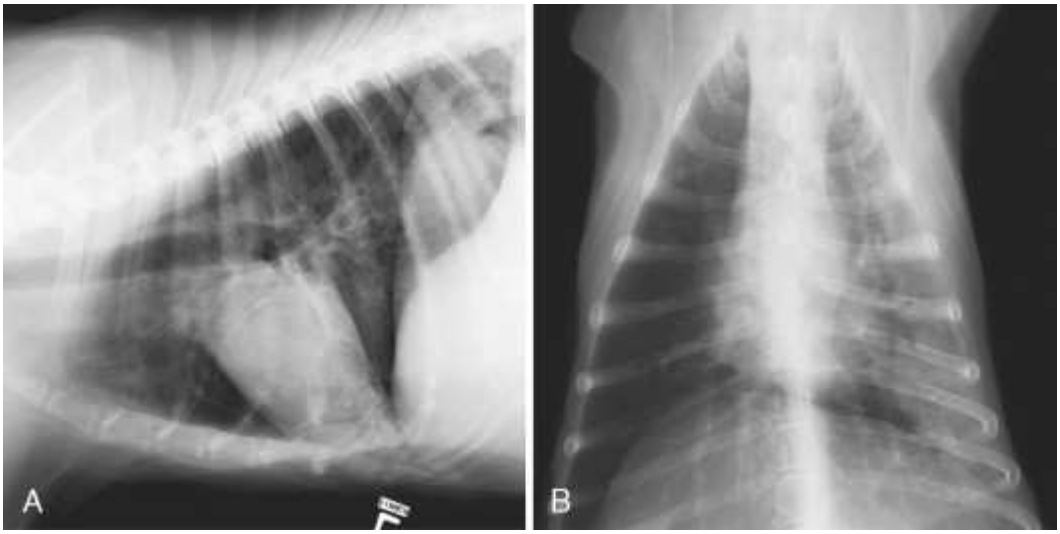
DIFFERENTIAL DIAGNOSIS

Many diseases share clinical and diagnostic similarities, including:

- Noninfectious inflammatory respiratory diseases
- Pulmonary neoplasia
- Respiratory parasites
- Pulmonary edema
- Fungal pneumonia, particularly blastomycosis and coccidioidomycosis in dogs

INITIAL DATABASE

- CBC: inflammatory leukogram (with or without left shift) expected although not seen in all cases
    - Neutropenia is also possible, especially with severe sepsis. Conversely, bacterial pneumonia can develop secondary to primary neutropenic disorders (e.g., myelosuppression from chemotherapy).
- Serum biochemical profile/urinalysis: often normal
- Thoracic radiographs:
    - Two or more views (at least one lateral and either a ventrodorsal [VD] or dorsoventral [DV]) are recommended in all cases.
        - Obtaining both right and left lateral recumbent views can be useful, since pneumonia infiltrates may only be apparent in nondependent lung.
    - Alveolar pattern in dependent regions of lung lobes expected in most cases.
        - Right middle lung lobe is commonly affected and may require careful examination on the lateral projection because it overlies the heart.
    - Interstitial patterns, with or without alveolar patterns, are also possible.
    - In some cases, lobar consolidation will be the prominent radiographic abnormality.
    - Other abnormalities that reflect underlying primary disease (as examples):
        - Megaesophagus
        - Bronchiectasis
        - Neoplasia



PNEUMONIA, BACTERIAL A, Left lateral thoracic radiograph in a 14-year-old mixed-breed dog with pneumonia. Alveolar infiltrates are visible over the cardiac silhouette (especially the apex) but are not striking. Microcardia is also present, suggesting hypovolemia. **B,** Dorsoventral thoracic radiograph of same dog. Left-sided alveolar infiltrates are more clearly apparent than in **A,** where they were obscured by being on the dependent side and overlying the cardiac silhouette.

ADVANCED OR CONFIRMATORY TESTING

- Confirmatory tests help rule out predisposing diseases/risk factors:
    - Respiratory washes (see p. 1350) and bronchoalveolar lavage (see p. 1220):
        - Primarily septic, suppurative inflammation:
            - Bacteria are not always evident in cytologic exams, so clinicians should submit wash specimens for culture and sensitivity testing irrespective of cytologic findings.
    - Fine-needle aspiration for cytologic analysis: may help exclude fungal pneumonia or neoplasms:
        - Limited sensitivity: absence of neoplastic cells or fungal organisms does not definitely exclude their presence
        - Theoretical risk of needle-tract seeding if aspiration of a solitary pulmonary tumor
    - Bronchoscopy (see p. 1220):
        - Endobronchial masses or foreign bodies may be evident in some cases.
        - Mucopurulent exudate in airways of affected regions may be seen.
        - Dilated/sacculated airways (bronchiectasis)
    - CT scan: superior delineation of the extent of pneumonia but often not needed when good-quality thoracic radiographs are consistent with the diagnosis.
    - Barium esophagram: if clinician suspects megaesophagus or esophageal motility dysfunction, and this condition is not clearly apparent on survey thoracic radiographs.
- Arterial blood gas (ABG) analysis:
    - Hypoxemia and hypocapnia are the most common abnormalities; when present, generally indicate severe pneumonia or presence of a complicating factor (e.g., acute respiratory distress syndrome [ARDS]) and therefore a more guarded prognosis.

- Other tests specific for underlying diseases (e.g., serum acetylcholine receptor antibody titers for myasthenia gravis-induced megaesophagus).

TREATMENT

TREATMENT OVERVIEW

Administration of antimicrobials is the cornerstone of treatment, but clinicians also need to treat/resolve predisposing factors to the extent possible.

ACUTE GENERAL TREATMENT

- Broad-spectrum antibiotics:
  - Clinically unstable animals should be treated with broad-spectrum IV antibiotics:
    - Ampicillin (22 mg/kg IV q 8 h) or cefazolin (22 mg/kg IV q 8 h) and either enrofloxacin (3-5 mg/kg IV q 24 h [dogs]) or an aminoglycoside such as amikacin (20 mg/kg SQ or IV q 24 h); aminoglycosides, however, should not be used in animals that are dehydrated or that have renal compromise.
    - The clinical condition of the animal, if severe, may warrant therapy before obtaining respiratory samples for culture.
  - Clinically stable animals may be treated with oral antibiotics, ideally selected based on culture and sensitivity (C&S) testing. Empirical choices while awaiting results include:
    - Ampicillin or amoxicillin/clavulanate 22 mg/kg q 8 h; *or*
    - Trimethoprim-sulfa 15 mg/kg q 12 h
  - Because of concerns about the pathogenic potential of *Mycoplasma* species in pneumonia, doxycycline (3-5 mg/kg PO q 12 h) may be considered, particularly for animals that show no response to therapy with other antibiotic choices.
- Saline nebulization several times daily
- Oxygen (nasal cannula, oxygen cage, face mask) for hypoxemic animals or those in respiratory distress (see p. 1318)
- IV fluids as needed
- Bronchodilators as needed
  - Theophylline: dosage varies with formulation.
  - Terbutaline: 1.25-5 mg/dog PO q 8 h; 0.625 mg/cat PO q 12 h, or 0.1-0.2 mg/kg PO q 12 h (cat)

CHRONIC TREATMENT

- Thoracic coupage and position changes in recumbent animals
- Identification and management of underlying causes when identified
- Antibiotic therapy continued at least 1 week beyond radiographic resolution of infection
- Lung lobectomy is occasionally needed to resolve infection when extensive single-lobe involvement has failed medical therapy or is associated with recurrent infection.
  - Prognosis associated with lobectomy is considered best if done for foreign-body pneumonia.

POSSIBLE COMPLICATIONS

- Lung lobe abscess
- Bronchiectasis
- Recurrence if underlying cause not identified and treated

RECOMMENDED MONITORING

- Clinical signs (respiratory rate, effort, etc.):
  - Carefully reevaluate animals that are not clinically better within 48-72 hours of starting empirical therapy or deteriorate substantially at any time; consider pursuing more diagnostic tests and/or changing therapy.
- Thoracic radiographs:
  - Radiographic changes can lag as much as 48 hours behind clinical changes.
  - Repeating thoracic radiographs approximately 1 week after cessation of antibiotics may demonstrate focal primary diseases (e.g., neoplasia) not evident on initial radiographs.
- ABG analysis
- CBC

PROGNOSIS AND OUTCOME

Varies with severity of disease and nature of predisposing factors:

- Prognosis for uncomplicated pneumonia is generally good.
- Prognosis for animals with risk factors depends on ability to treat/resolve the risk factor.
    - Recurrent infections are common in animals with unresolved primary diseases.

PEARLS & CONSIDERATIONS

COMMENTS

Bacterial pneumonia should be viewed as a complication of another underlying disease; *B. bronchiseptica* infections are an exception. Therefore, patients should be rigorously evaluated for risk factors if such factors are not immediately apparent.

TECHNICIAN TIPS

- Puppies with bacterial pneumonia, particularly those that came from pet stores or shelters, should ideally be isolated from other animals in the hospital, including cats, because *B. bronchiseptica* is common in those animals.
- For respiratory washes, make sure the wash solution does not contain bacteriostatic agents.

CLIENT EDUCATION

- Following recommended diagnostic and monitoring suggestions is important for most effective long-term resolution.
- Home treatment may include:
    - Respiratory humidification by inhalation of “cold steam” is best accomplished by having a pet in a closed, unventilated bathroom (but not in the bath/shower) for 10-15 minutes once to three times a day while a warm shower runs.
    - This is often followed by coupage, which is a series of brusque pats to both sides of the chest, performed for 10-30 seconds after each humidification session, with the intention of loosening pulmonary secretions and pus to facilitate expectoration.
    - Pet owners should only perform these treatments on the recommendation of a veterinarian; they can make a condition worse if used inappropriately.

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Pneumonia, Aspiration

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Infection associated with inhalation of oropharyngeal secretions. In veterinary medicine, the term is often used in reference to aspiration pneumonitis, which is chemical injury caused by inhalation of gastric contents (most commonly) or other materials (e.g., barium, mineral oil).

SYNONYMS

Aspiration pneumonitis, Mendelson syndrome

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs and cats of either sex and any age

RISK FACTORS

- Diseases of:
  - Pharynx or larynx (e.g., laryngeal paralysis)
  - Esophagus (e.g., megaesophagus)
  - Stomach or intestine (e.g., pyloric obstruction)
- Forced enteral administration of drugs or foods
- Impaired protective reflexes (e.g., coma, anesthesia, seizure)

ASSOCIATED CONDITIONS & DISORDERS

- Acute respiratory distress syndrome
- Bacterial pneumonia
- Hypoxemia
- Lung lobe abscessation
- Pneumothorax
- Shock
- Airway obstruction

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Acute or chronic
- Fulminant or insidious

HISTORY, CHIEF COMPLAINT: Clinical signs may be absent or severe; when present, they may include:

- Anorexia
- Collapse
- Cough
- Lethargy
- Respiratory distress
- Others that reflect predisposing cause (e.g., regurgitation, anesthetic episode)

PHYSICAL EXAM FINDINGS: Findings may be absent or severe; when present, they may include:

- Tachypnea
- Inspiratory and expiratory distress
- Auscultatory abnormalities (may be localized if present):
  - Crackles

    - Wheezes
    - Increased or decreased bronchovesicular sounds
- Cyanosis
- Fever (fewer than half of affected animals are febrile)
- Shock
- Others that reflect predisposing cause (e.g., exercise intolerance with myasthenia gravis)

ETIOLOGY AND PATHOPHYSIOLOGY

- Inhalation of particulates or fluid into the larynx and lower respiratory tract triggers injury.
    - Gastric contents are typically sterile, but acid and particulate matter can cause potentially severe damage:
        - Acid causes direct, caustic epithelial damage that is followed by inflammation.
        - Particulate material may obstruct airways.
    - Infection may follow aspiration of colonized oropharyngeal secretions or is a secondary (opportunistic) complication of respiratory damage.
- Severity of injury depends on volume, toxicity, pH, and particulate and pathogen content of aspirated material. Sequelae may include:
    - Airway obstruction
    - Bronchoconstriction
    - Pulmonary hemorrhage
    - Epithelial necrosis
    - Pulmonary inflammation

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Differentiation of aspiration pneumonia from bacterial pneumonia or pulmonary edema is often dependant on circumstantial evidence such as witnessed episodes of aspiration, history of vomiting or regurgitation, or involvement of the typical lung lobes.

DIFFERENTIAL DIAGNOSIS

- Infectious pneumonia
- Cardiogenic or noncardiogenic pulmonary edema
- Neoplastic infiltrates

INITIAL DATABASE

- Neurologic examination reflects underlying neurologic disease if present.
- CBC: neutrophilic leukocytosis common but not essential (absence does not exclude aspiration pneumonia)
- Serum biochemical profile and urinalysis: no specific changes
- Thoracic radiographs: abnormalities may lag aspiration by up to 24 hours:
    - Both right and left lateral views should be acquired.
    - Alveolar or interstitial pattern or consolidation in affected lung lobes:
        - Common in the lobes that were dependent at the time of aspiration
        - If the patient was conscious during aspiration, abnormalities usually occur in the right middle, right cranial, or caudal portion of the left cranial lung lobe.

ADVANCED OR CONFIRMATORY TESTING

- Pulse oximetry and/or arterial blood gas (ABG) analyses to assess oxygenation
- Tracheal lavage (submit samples for aerobic culture and sensitivity [C&S]):
    - Neutrophilic inflammation
    - Bacteria possible
    - Hemorrhage
    - Particulates/debris
    - Lipid-laden macrophage
- Bronchoscopy indicated only if clinician suspects large-airway obstruction
- Search for predisposing cause of aspiration (e.g., acetylcholine receptor antibody titer for myasthenia gravis-related megaesophagus)

TREATMENT

TREATMENT OVERVIEW

Severity of aspiration pneumonia varies, and therefore intensity of therapeutic intervention varies as well. Adequate oxygenation must be assured and further aspiration prevented when possible. Most animals are treated with antimicrobial drugs because of concerns related to secondary bacterial infection.

ACUTE GENERAL TREATMENT

- If aspiration is witnessed, immediately suction material from pharynx/airways and ensure airway patency.
- If respiratory distress or evidence of hypoxemia exists, administer supplemental oxygen using the lowest effective oxygen concentration (typically, Fio2 around 40%). See p. 1318.
    - If Pao2 < 50 mm Hg or if Pco2 > 50 mm Hg, intubate for positive-pressure ventilation.
- Bronchodilators may relieve bronchospasm (cats especially): aminophylline (dose varies with preparation of the medication) or terbutaline (0.01 mg/kg SQ).
- IV crystalloid fluids may be warranted:
    - Maintenance rate of 60 mL/kg per day after correction of dehydration; more if there are ongoing losses
    - Rarely, shock occurs, requiring aggressive fluid therapy.
        - Caution: excessive parenteral fluids may precipitate edema in the damaged lung.
- Antimicrobials are often suggested for these animals, since secondary infection is common.
    - Choice ideally based on C&S (tracheal or bronchial lavage)
    - Initial choice often parenteral broad-spectrum antibiotics (e.g., combination of ampicillin, 22 mg/kg IV q 8 h; and enrofloxacin, 5 mg/kg 12 h [dogs] or 5 mg/kg q 24 h [cats])
- Physiotherapy: coupage, movement (see p. 1310)
- Saline nebulization
- If aspiration is suspected but respiratory distress is absent, only careful observation may be warranted.

CHRONIC TREATMENT

- Prevent further aspiration or reduce severity of injury from aspiration (see Prevention below)
- Discontinue oxygen when Pao2 remains above 65 mm Hg and the animal can breathe comfortably without it.
- Continue antibiotics 1 week past radiographic resolution (typically 3-4 weeks).

NUTRITION/DIET

Animals with severe ongoing vomiting/regurgitation should not be fed by mouth.

BEHAVIOR/EXERCISE

- Recumbent animals with severe pneumonia should not be allowed to lie with the most functional lobes on the down side.
- Movement may facilitate beneficial cough and airway clearance.

POSSIBLE COMPLICATIONS

- Administration of high concentrations of oxygen for prolonged periods can contribute to respiratory epithelial injury.
- Parenteral fluids may worsen noncardiogenic pulmonary edema.

RECOMMENDED MONITORING

- Oxygenation (ABG or pulse oximetry): depending on severity of disease, q 4-24 h until normalized
- Thoracic radiographs: until abnormalities are resolved with frequency determined by severity of signs and baseline abnormalities; ideally repeated 1-2 weeks after discontinuation of antibiotics
- CBC: rechecked at least weekly until leukocytosis resolved

PROGNOSIS AND OUTCOME

Depends on volume and character of aspirated material. Prognosis cannot be predicted by severity of radiographic change.

PEARLS & CONSIDERATIONS

COMMENTS

Because aspiration pneumonia rarely occurs in the absence of an underlying cause, animals should be evaluated for risk factors.

TECHNICIAN TIPS

- Sudden respiratory signs in hospitalized animals should be brought to the attending veterinarian's attention immediately.
- For animals with regurgitation, maintaining an upright position with the head and chest elevated above the stomach for at least 30 minutes after oral feeding may minimize the risk of aspiration.

PREVENTION

- Address underlying diseases that predispose the animal to aspiration.
- Fast animals at least 6 hours before general anesthesia, and use properly inflated, cuffed endotracheal tubes during anesthesia.
- For animals at high risk, consider administration of antacids (H2 antagonists, proton pump inhibitors) to increase gastric pH, and administration of prokinetic agents (e.g., metoclopramide) to enhance gastric emptying and increase lower-esophageal sphincter tone. Unfortunately, these measures have not been shown to improve outcomes in humans at high risk for aspiration.
- Use caution in forced administration of drugs or foodstuffs.
- Feeding tubes should not cross the lower-esophageal sphincter.

CLIENT EDUCATION

When a predisposing cause is not reversible (e.g., idiopathic megaesophagus), repeated aspiration events are common.

SUGGESTED READING

Kogan DA, et al: Clinical, clinicopathologic, and radiographic findings in dogs with aspiration pneumonia: 88 cases (2004-2006). J Am Vet Med Assoc 233:1742, 2008.

Kogan DA, et al: Etiology and clinical outcome in dogs with aspiration pneumonia: 88 cases (2004-2006). J Am Vet Med Assoc 233:1748, 2008.

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Pneumocystosis

BASIC INFORMATION

DEFINITION

Infectious opportunistic disease of the lungs; associated with immune incompetence

SYNONYM

Pneumocystis carinii pneumonia

EPIDEMIOLOGY

SPECIES, AGE, SEX: Young animals, primarily dogs of either sex

GENETICS & BREED PREDISPOSITION: Miniature dachshunds, Shetland sheepdogs, and Cavalier King Charles spaniels

RISK FACTORS

- Congenital or acquired immune-suppressive diseases
- Syndrome of common variable immunodeficiency in the miniature dachshund

CONTAGION & ZOONOSIS: Transmission to an HIV-infected person is possible.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Some or all of the following may prompt an owner to seek veterinary consultation:

- Tachypnea/respiratory distress
- Exercise intolerance
- Weight loss

PHYSICAL EXAM FINDINGS

- Tachypnea
- Respiratory distress
- Poor body condition
- Marked increase in respiratory sounds on thoracic auscultation
- Cyanosis with severe infections

ETIOLOGY AND PATHOPHYSIOLOGY

- Pneumocystosis is caused by *P. carinii*, a saprophyte of the mammalian respiratory tract whose life cycle is completed within the alveolar spaces.

Only a single species name has been assigned to the genus *Pneumocystis*, but antigenic differences suggest that several strains may exist.

- Based on nucleic acid analysis, the organism is classified as an atypical fungal organism.
- *P. carinii* can be present in low numbers in the pulmonary alveoli of healthy animals and is only associated with pneumonia and respiratory distress when there is immune compromise.
- With immune compromise, *P. carinii* proliferates within the alveoli, resulting in alveolar capillary blockage and ventilation/perfusion mismatch. Thickening of alveolar septa occurs, but there is rarely extension of the infection into the pulmonary interstitium.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other infectious pneumonias:
  - Bacterial
  - Viral
  - Protozoal
  - Mycotic
- Pulmonary fibrosis
- Congestive heart failure

INITIAL DATABASE

- CBC:
  - Erythrocytosis
  - Thrombocytosis
  - Mild neutrophilic leukocytosis
  - Eosinophilia and monocytosis in some cases
- Serum biochemistry profile:
  - Normal serum protein levels or a low to low-normal globulin level
- Urinalysis: usually normal
- Serum protein electrophoresis: hypogammaglobulinemia
- Thoracic radiographs:
  - Mixed alveolar and interstitial pattern
  - Bronchial pattern
  - Cor pulmonale (right-sided cardiomegaly)

ADVANCED OR CONFIRMATORY TESTING

- Other laboratory tests:
  - Arterial blood gas (ABG) analysis:
    - Hypoxemia
    - Normocapnia to hypocapnia
    - Increased alveolar-arterial (A-a) oxygen gradient
- Serologic tests: available for humans but of uncertain value for dogs
- Other diagnostic procedures:
  - Definitive antemortem diagnosis of *P. carinii* is established by direct visualization of either the trophozoite or cyst in respiratory washes collected by transtracheal aspiration or bronchoalveolar lavage, lung needle aspirates, or lung biopsies obtained by thoracotomy or thoracoscopy.
  - Histochemical stains and diagnostic immunohistochemistry tests may facilitate observation of organisms.
  - PCR test on respiratory samples can also document presence of the organisms.

TREATMENT

TREATMENT OVERVIEW

Eradicate infection.

ACUTE GENERAL TREATMENT

- Oxygen administration (see p. 1318)
- Mucolytics:
  - Acetylcysteine (10% or 20% solution) 50 mL/hr for 30-60 minutes q 12 h by nebulization
  - Bromhexine, 1 mg/kg PO q 12 h
  - Administration of bronchodilators beforehand is recommended.
- Bronchodilators: aminophylline, 10 mg/kg PO q 8 h; or terbutaline, 0.625-2.5 mg PO total dose q 8 h
- Saline nebulization to liquefy hyperviscous mucus and thus promote the removal of secretions from the respiratory tree

CHRONIC TREATMENT

- Drug of choice: trimethoprim-sulfonamide, 15 mg/kg PO q 8 h for 3 weeks
- Pentamidine isethionate: 4 mg/kg IM q 24 h for 2 weeks
- Atovaquone: 15 mg/kg PO q 24 h for 3 weeks

- Clindamycin and primaquine: 3-13 mg/kg PO q 8 h for 3 weeks
- Carbutamide: 50 mg/kg IM q 12 h for 3 weeks
- Drug combinations: dapsone (1 mg/kg PO q 8 h) and pyrimethamine (1 mg/kg PO q 24 h)

POSSIBLE COMPLICATIONS

Respiratory failure, respiratory arrest

RECOMMENDED MONITORING

- Thoracic radiographs
- ABG analysis

PROGNOSIS AND OUTCOME

Dependent on severity of infection

PEARLS & CONSIDERATIONS

COMMENTS

Infection with *P. carinii* is associated with immunologic defects.

PREVENTION

Because of the probable genetic basis to immune compromise in most animals, owners should not breed affected animals.

TECHNICIAN TIPS

- When preparing for respiratory washes, be sure to use solutions that do not contain bacteriostatic additives. If available, prewarm solutions for respiratory lavage in a 37°C incubator (or suitable alternative).
- Needle aspiration of the lung is commonly performed with 23-G needles and a 6- or 12-mL syringe in the dorsal lung fields, defined by rib spaces 6-8.
- Educate the owners to the importance of ensuring good nutrition and warmth, short leash-controlled walks, and avoiding close contact with animal's face.

CLIENT EDUCATION

- Affected animals have an underlying immunologic defect.
- May be a zoonosis in persons who are immunocompromised.

SUGGESTED READING

Greene CE, Chandler F, Lobetti RG: Pneumocystosis. In Greene CE, editor: Infectious diseases of the dog and cat, ed 3, St Louis, 2005, Saunders, Elsevier, p 651.

Lobetti RG: Common variable immunodeficiency in miniature dachshunds affected with *Pneumocystis carinii* pneumonia. J Vet Diagn Invest 12:39, 2000.

Lobetti RG: Review of *Pneumocystis carinii* infection in miniature dachshunds. Compend Contin Educ Pract Vet 23:320, 2001.

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Pleural Effusion

BASIC INFORMATION

DEFINITION

Accumulation of fluid within the pleural space

SYNONYMS

Pleural fluid, thoracic effusion, hydrothorax (pure transudate or modified transudate), hemothorax (hemorrhage; see p. 493), chylothorax (chyle; see), pyothorax (exudate; see p. 956)

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs and cats
- Pyothorax may be more common in younger cats.
- Pleural effusion secondary to congenital cardiac disease is more common in young animals, and pleural effusion secondary to acquired heart disease (including thyrotoxicosis) is more common in middle-aged to older animals.

GENETICS & BREED PREDISPOSITION

- Pyothorax secondary to aspiration of grass awns is most common in hunting/sporting dogs.
- As a component of congestive heart failure, pleural effusion may occur more commonly in specific breeds predisposed to certain cardiovascular diseases.

RISK FACTORS

- Hydrothorax: heart disease (cats > dogs), hypoalbuminemia, neoplasia, lung lobe torsion
- Hemothorax: trauma, intrathoracic neoplasia, anticoagulant toxicity
- Chylothorax: heart disease (cats > dogs), neoplasia, trauma, intestinal lymphangiectasia
- Pyothorax: penetrating injury, inhalation of foreign body, pneumonia, mediastinitis, esophageal perforation (septic); feline infectious peritonitis (FIP) (nonseptic). Higher incidence of FIP in multicat households.

CONTAGION & ZOONOSIS: Based on certain specific causes (e.g., FIP)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Hydrothorax
- Hemothorax
- Chylothorax
- Pyothorax

HISTORY, CHIEF COMPLAINT

- Severity of clinical signs varies with underlying cause, volume of effusion, and rate of fluid accumulation
  - If rate of accumulation is slow, large volumes may be present before clinical signs are apparent (especially cats).
- Restrictive breathing pattern, tachypnea, orthopnea/general discomfort, dyspnea (e.g., abdominal component of respirations) noted by owners
- Lethargy, exercise intolerance
- Cough
- Signs related to underlying disease:
  - Chronic cough
  - Weight loss
  - Inappetence

- Abdominal effusion
- Diarrhea
- Other signs of trauma
- Exercise intolerance

PHYSICAL EXAM FINDINGS: In general for pleural effusion:

- Dyspnea, including wide chest excursions, possibly abducted elbows when standing, extension of the neck, reluctance to lie in lateral recumbency, anxious facial expression, and abdominal lift (cats). These animals typically have a prolonged inspiratory phase and very short expiratory phase.
- Muffled heart and lung sounds ventrally
- Normal to increased bronchovesicular lung sounds (breath sounds) dorsally
- Ventral hyporesonance with thoracic percussion; a fluid line may be detected.
- Other signs associated with specific underlying cause

ETIOLOGY AND PATHOPHYSIOLOGY

- Etiology and fluid classification reflect basic pathophysiologic mechanisms of effusion formation:
  - Reduced plasma colloid oncotic pressure (hydrothorax: pure transudate)
    - Hypoalbuminemia: protein loss (renal: glomerulonephritis [GN], amyloidosis; gastrointestinal [GI]: inflammatory bowel disease, lymphangiectasia, neoplasia, others; vasculitis: infectious or noninfectious) or synthetic failure (chronic hepatopathy, portal vascular anomalies)
  - Increased capillary hydrostatic pressure (hydrothorax: usually modified transudate)
    - Congestive heart failure, Budd-Chiari-like syndromes
    - Thoracic or mediastinal neoplasia
- Reduced lymphatic drainage/lymphatic obstruction (hydrothorax, chylothorax, or pyothorax: modified transudate to exudate):
  - Thoracic or pulmonary neoplasia
  - Chylothorax
- Increased vascular permeability (pyothorax: exudate):
  - Pyothorax
  - FIP
- Disruption of vascular integrity or hemostatic abnormalities (hemothorax):
  - Rupture of neoplastic mass
  - Coagulopathy
  - Trauma
- Respiratory dysfunction can reflect hypoventilation and ventilation/perfusion mismatch

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Physical examination can provide a suggestion of pleural effusion. Presence of the effusion can be confirmed via imaging (thoracic radiographs, thoracic ultrasound) or thoracocentesis. Thoracocentesis and fluid analysis can provide more precise information on the nature of the fluid and perhaps the etiology.

DIFFERENTIAL DIAGNOSIS

- Other pleural space disease:
  - Masses
  - Pneumothorax
  - Constrictive/fibrosing pleuritis (can occur concurrently with pleural effusion—often chylothorax or pyothorax—and typically causes very rounded lung lobe contours that may be difficult to distinguish radiographically from those caused by pleural effusion).
- Pulmonary parenchymal or airway disease
- Thoracic wall disease
- Diaphragmatic hernia
- Neuromuscular disease

INITIAL DATABASE

- In animals with pleural effusion causing severe dyspnea, some clinicians prefer to perform thoracocentesis first and then take thoracic radiographs.

    - Advantages of centesis first: therapeutic value (removal of effusion), diagnostic value (fluid analysis, improved radiographic visualization of parenchymal structures)
    - Advantage of radiographs first: safety (confirms pleural effusion; can identify displacement of cardiac silhouette, to be avoided during centesis)
- Thoracic radiographs; radiographic signs of pleural effusion vary with fluid volume and can include:
    - Interlobar fissures:
        - Approximately 100 mL of fluid is present in a medium-sized dog if fissure lines are evident.
        - Small volumes may be better appreciated on ventrodorsal views.
    - Impaired heart visualization, especially on dorsoventral view
    - Retraction ("scalloping") of lungs from thoracic wall with interposed fluid opacity
    - On lateral radiographs, increased opacity dorsal to the sternum and ventral scalloping of lung margins. The lateral view is prone to misinterpretation, and standard two-view thoracic radiography is recommended in all cases.
    - Blunting of lung margins at costophrenic angles (ventrodorsal view)
    - Obscured diaphragm
    - Widened mediastinum
    - Fractured ribs, diaphragmatic hernia, and other orthopedic injuries may be present if traumatic etiology.
    - Pyothorax and chylothorax may cause constrictive pleuritis, preventing full expansion of lungs after thoracocentesis. The lung lobes appear rounded in contour.
    - Evaluation of radiographs post thoracocentesis for underlying pulmonary disease as visualization of intrathoracic structures improves
- Clinicopathologic abnormalities depend on etiology; possibilities include:
    - CBC:
        - Inflammatory leukogram
        - Thrombocytopenia
        - Anemia
    - Biochemical panel:
        - Hypoalbuminemia
        - Hypoglobulinemia or hyperglobulinemia
        - Hypoglycemia
        - Hypocholesterolemia
        - Azotemia
        - Electrolyte abnormalities
        - Increased liver enzyme activities
        - Hypercalcemia possible with mediastinal lymphoma
    - Urinalysis:
        - Proteinuria
- Thoracocentesis (see p. 1338):
    - Fluid in EDTA (lavender top) and plain (red top) tubes for analysis; prepare fresh smears.
    - If pyothorax is suspected, a culture and sensitivity (C&S) is indicated (aerobic and anaerobic in all cases):
        - Most common canine isolates are *Peptostreptococcus, Bacteroides* spp., *Escherichia coli, Klebsiella pneumoniae, Enterobacter, Fuso-bacterium, Pasteurella* spp., *Actinomyces* spp., and *Nocardia* spp.
        - Most common in cats are *Bacteroides* spp., *Pasteurella* spp., *Peptostreptococcus, Fusobacterium* spp., and *Actinomyces* spp.
    - Measurement of effusion triglyceride and cholesterol concentration if chylothorax suspected
    - An effusion albumin/globulin ratio of >0.8 makes FIP unlikely (exception: if protein clot forms in vitro; false negative).
- Thoracic ultrasonography:
    - Often performed before thoracocentesis to improve the acoustic window, unless the animal is uncomfortable/dyspneic during restraint for the examination
    - Can identify mediastinal masses, consolidated lung lobes, pulmonary masses, and abdominal organs in the thoracic cavity with hernias
    - Can help identify localized fluid for sampling

ADVANCED OR CONFIRMATORY TESTING

Based on nature of effusion and diagnostic test results to date.

- Hydrothorax: pure transudate (effusion [total protein] <2.5 g/dL)
    - Urine protein/creatinine ratio
    - Liver function tests
    - Possibly intestinal biopsies (surgical or endoscopic) if protein-losing enteropathy suspected
- Hydrothorax: modified transudate (effusion [total protein] 2.5-5 g/dL; no cytologic evidence of infection or hemorrhage)
    - Thoracic ultrasound exam
    - Echocardiography, especially if there are signs of cardiac disease
    - CT for masses or pulmonary disease
    - Fine-needle aspirates and cytologic examination of lung or mass if lesion is identified

- Thoracoscopy or thoracotomy for pleural or lung biopsy
- Chylothorax:
  - Lymphangiography is occasionally performed to identify the site of disruption of the thoracic duct if an underlying cause (e.g., congestive heart failure, intestinal lymphangiectasia) has not been identified.
  - Echocardiography (especially cats) if there are signs of cardiac disease
  - CT scanning to check for masses
  - Thoracotomy/thoracoscopy
- Hemothorax:
  - Coagulation profile (PT, PTT, platelet count)
    - If abnormal, toxin screens may sometimes be performed.
    - If normal, imaging (ultrasound and/or CT scan) is indicated, and thoracoscopy/thoracotomy may be warranted if a mass lesion is identified or suspected.
- Pyothorax:
  - Careful examination of skin and haircoat (especially in long-haired pets, possibly including extensive shaving of hair over the thorax to improve visualization) for evidence of penetrating injury/foreign body.
  - Postcentesis/postdrainage thoracic radiographs or CT scan to identify masses, foreign bodies
  - Exploratory thoracotomy is indicated if an intrapleural foreign body is suspected. Thoracotomy may improve outcome in dogs with pyothorax, because pyothorax is often secondary to a migrating foreign body.

TREATMENT

TREATMENT OVERVIEW

Thoracocentesis is commonly needed acutely to improve respiratory function. Ultimately, identification and correction of the underlying disease provides the best chance for resolution of effusion.

ACUTE GENERAL TREATMENT

- Oxygen supplementation if dyspnea is present
- Minimize stress
- Thoracocentesis (seep. 1338)
- For pyothorax: bilateral (assuming bilateral involvement) thoracostomy tubes (see p. 1230) or thoracotomy and thoracic lavage/drainage:
  - Lavage through large-diameter chest tubes with sterile, warm (body temperature) isotonic fluids (10-20 mL/kg) 2-4 times a day for 5-7 days.
  - Drain thoracostomy tubes regularly.
  - Minimize risk of iatrogenic pneumothorax with thoracostomy tubes with clamps on tubes, three-way stopcocks, bandaging, and Elizabethan collars.
  - Analgesia as necessary; cats are often uncomfortable with thoracostomy tubes.
  - Removal of tubes when fluid production <2 mL/kg/d, and cytologic analysis (gram stain ideally) of fluid suggests it is sterile.
- For hemothorax:
  - Blood transfusion if severe anemia
  - Both plasma transfusion (see p. 1347) and vitamin K, 2.5-5 mg/kg SQ in multiple sites q 12 h, if anticoagulant rodenticide toxicity (see p. 83) is identified or suspected as the cause of hemothorax
- Support of circulation and respiratory function if effusion results from trauma

CHRONIC TREATMENT

- For some, correction of the underlying disorder may resolve effusion without thoracocentesis.
- With hypoalbuminemia, cardiac disease, vasculitis, or immune-mediated disease, therapy must be directed at the underlying cause.
- For pyothorax, antimicrobials are necessary but are generally ineffective without proper drainage.
  - Empirical choices based on Gram stain findings and common organisms (see previous paragraphs and Pyothorax, p. 956)
  - If filamentous organisms *(Actinomyces* or *Nocardia*) are identified, ampicillin (22 mg/kg IV q 8 h) and trimethoprim-sulfonamide (30 mg/kg PO q 12 h) are suitable choices.
  - Modify antimicrobial choices based upon results of C&S.
  - If using trimethoprim-sulfonamide, a physical exam and monitoring of tear production, hematologic parameters (including CBC), and liver function are indicated.
  - Administer antibiotics for 1 to 2 months.
  - Consider thoracotomy if there is a poor response to medical therapy over a few days or if pyothorax recurs after antibiotics are discontinued.

        - Some studies suggest better and more rapid resolution with early surgical intervention.
        - Submit any excised tissue for histopathologic examination.
- For hemothorax, consider thoracotomy if there is no evidence of coagulopathy, thrombocytopenia, or trauma and if there is poor/no response to medical treatment.
- Chemotherapy may be indicated when pleural effusion is neoplastic in origin. Confirmation of type of neoplasm (cytologic or histopathologic) is necessary.
- The use of vascular access ports attached to intrathoracic Jackson-Pratt drains has been described for chronic effusions refractory to therapy of the underlying disease.
- Pleuroperitoneal shunts can be used for chronic effusions (see p. 1542) but can have many associated complications.
- Thoracic omentalization has been described in combination with chemotherapy for the long-term treatment of neoplastic pleural effusion in a cat.

POSSIBLE COMPLICATIONS

- Iatrogenic pneumothorax and hemothorax from thoracocentesis or thoracostomy tube
- Constrictive/fibrosing pleuritis from pyothorax or chylothorax
- Disseminated intravascular coagulation (DIC) or systemic inflammatory response syndrome from pyothorax
- Recurrence of pyothorax if migrating foreign body remains or if inappropriate antibiotics are used
- Complications of thoracocentesis (and corresponding precautions) include:
    - Lung laceration (less likely if needle is introduced and withdrawn in linear fashion, without side-to-side or rotatory motions once the needle tip is in the pleural space) and subsequent pneumothorax
    - Reexpansion pulmonary edema; less likely if large-volume effusions are withdrawn periodically over several hours rather than all at once, and more likely with chronic effusions
    - Pleural shock: a sudden bradycardia of vagal origin caused by needle contact with the pleura (no prevention; responds to immediate administration of atropine 0.04 mg/kg IV)
    - Bronchopleural fistula: when constrictive/fibrosing pleuritis prevents further lung expansion during thoracocentesis and ongoing fluid withdrawal creates excessive negative pressure in the pleural space, a rupture of the bronchial wall into the pleural cavity may occur (possibly less likely to occur if large-volume effusions are withdrawn periodically over several hours rather than all at once, especially if lung lobes are very round on radiographs, suggesting constrictive/fibrosing pleuritis).

RECOMMENDED MONITORING

- Thoracic radiographs
- Daily cytologic examination and Gram stain of chest tube fluid withdrawn from pyothorax cases to assess antimicrobial response

PROGNOSIS AND OUTCOME

- Varies with cause and severity of underlying disease
- Pleural effusion may worsen the short-term prognosis of the underlying disease by potentially causing acute respiratory compromise.

PEARLS & CONSIDERATIONS

COMMENTS

- If pleural effusion is suspected, clinicians can consider thoracocentesis, which can be both diagnostic and therapeutic, before thoracic radiographs.
    - Drainage of only some fluid can improve respiratory function.
    - First obtain dorsoventral view, which is often sufficient to confirm effusion.
    - Alternatively, a very brief ultrasound evaluation may provide an initial confirmation of pleural effusion, justifying centesis. Radiographs may then be taken more safely after centesis.
    - Thoracic percussion also helps identify pleural effusion and supports preradiograph thoracocentesis.
- Ultrasonography can rapidly demonstrate pleural effusion in sternal recumbency or standing, with minimal restraint and stress.
- Cats with pleural effusion can be easily stressed by radiographs, so consider thoracocentesis early.
- Hemothorax usually develops from trauma, coagulopathies, or neoplasia.
- Grass awns can be located in multiple sites (including the pericardial sac) in dogs with pyothorax.
- Retrosternal fat and interindividual variation may give the false impression of pleural effusion on lateral radiographic projections of animals without pleural effusion. For this reason, and to determine whether the effusion is unilateral or bilateral,

standard two-view thoracic radiography is always indicated when pleural effusion is suspected or known to be present.

PREVENTION

Avoid trauma and exposure to anticoagulant rodenticides.

TECHNICIAN TIPS

- Animals with larger-volume pleural effusions can be very fragile and susceptible to stress with handling. Therefore minimal handling is important.
- Supplemental oxygen can be very helpful in a dyspneic patient with a pleural effusion.
- Avoid dorsal recumbency (ventrodorsal view) for radiographs in animals with pleural effusions.
- The basics for an emergency thoracocentesis include clippers, skin preparation materials, a butterfly needle or needle with an extension set, three-way stopcock, and syringes.
- The complications of thoracocentesis include pneumothorax and hemothorax. If your patient suddenly develops a high respiratory rate or effort after pleural drainage, alert the attending physician as soon as possible.

SUGGESTED READING

Cahalane AK, et al: Use of vascular access ports with intrathoracic drains for treatment of pleural effusion in three dogs. J Am Vet Med Assoc 230:527, 2007.

AUTHOR: GRAHAM SWINNEY

EDITOR: RANCE K. SELLON

Platelet Dysfunction

BASIC INFORMATION

DEFINITION

A hemostatic defect caused by impaired platelet activation response. Platelet dysfunction is broadly classified as acquired or hereditary.

SYNONYMS

Thrombocytopathia, thrombopathia

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Acquired: depends on the underlying disease or treatment
- Hereditary: dogs and cats of both sexes; severe defects typically manifest by 1 year of age

GENETICS & BREED PREDISPOSITION

- All hereditary traits are autosomal, with recessive or unknown expression pattern.
- Affected dog breeds: basset hound, boxer, cocker spaniel, collie, German shepherd, Great Pyrenees, Landseer Newfoundland, otterhound, spitz
- Affected cat breeds: Persian cat, domestic shorthaired cat

RISK FACTORS: Acquired platelet dysfunction is associated with systemic disease (anemia, uremia, liver failure, hyperproteinemia), drug therapy (nonsteroidal antiinflammatory drugs [NSAIDs], heparin, plasma expanders, sulfonamides), and disseminated intravascular coagulation.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Acquired:
  - Mild to moderate bleeding tendency accompanying a primary disease or drug therapy
  - Hematuria, epistaxis, melena, persistent posttraumatic bleeding
- Hereditary: recurrent mucosal bleeds and ecchymoses, prolonged bleeding from loss of deciduous teeth or minor wounds, blood loss anemia after surgery or trauma

PHYSICAL EXAM FINDINGS

- Petechiae and ecchymoses
- Abnormal bleeding from traumatic/surgical wounds and catheter and venipuncture sites
- Mucosal hemorrhage (epistaxis, gingival hemorrhage, melena, hematuria)

ETIOLOGY AND PATHOPHYSIOLOGY

- Acquired: often multifactorial due to intrinsic changes in platelet metabolism or extrinsic alterations in blood viscosity:
  - Platelet effects of NSAIDs such as aspirin are irreversible (i.e., effects last as long as the platelet lifespan-several days), whereas others (e.g., colloids/plasma expanders) inhibit platelet function only during the time of administration.
- Hereditary defects: pathophysiologic classification:
  - Membrane glycoprotein (GP) disorders. Most common is thrombasthenic thrombasthenia (fibrinogen receptor [GP IIb/IIIa] defects)
  - Secretory granule (storage pool) defects
  - Signal transduction defects
  - Platelet procoagulant deficiency

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Thrombocytopenia and von Willebrand disease are the most common acquired and hereditary primary hemostatic defects, respectively. Along with ruling out these disorders, disorders of the coagulation cascade (coagulation profile), and vascular integrity as causes for clinical signs mentioned above, clinicians should consider platelet dysfunction.

DIFFERENTIAL DIAGNOSIS

- Thrombocytopenia
- Hereditary or acquired coagulation factor deficiencies
- von Willebrand disease
- Vasculopathy or erosive/infiltrative vessel defect
- Defect of fibrinolysis

INITIAL DATABASE

- Physical exam (including funduscopic and rectal exam) to differentiate systemic versus localized or focal site of hemorrhage
- Platelet count: usually normal
- Coagulation screening tests (e.g., activated partial thromboplastin time [APTT], prothrombin time [PT], activated clotting time [ACT]): usually normal
- CBC, serum biochemistry profile, urinalysis to define acquired disorders. Avoid cystocentesis
- Thorough history of drug or dietary supplement administration

ADVANCED OR CONFIRMATORY TESTING

- Buccal mucosal bleeding time: usually increased (normal: 2-4 minutes)
- Platelet morphology review
- Point-of-care hemostasis analyzer: the Platelet Function Analyzer (PFA100 [Dade Behring]) is a tabletop instrument that measures platelet adhesion and aggregation in whole-blood samples. The test endpoint (closure time) is sensitive to platelet adhesion and aggregation defects in dogs, but anemia, thrombocytopenia, and low plasma von Willebrand factor levels also cause prolonged closure time.
- Platelet testing for classification of hereditary defects (may require referral):
    - Clot retraction
    - Platelet aggregation and secretion studies
    - Flow cytometry
    - Electron microscopy
- Mutation detection test (basset hound, Landseer Newfoundland, spitz, otterhound, Great Pyrenees)

TREATMENT

TREATMENT OVERVIEW

- Control active bleeding with medical or transfusion therapy.
- Avoid invasive procedures pending correction of acquired disease (or transfusion):
    - For an acquired dysfunction:
        - Identify and correct underlying disease condition
        - Discontinue or substitute drug therapy
        - Platelet transfusion (although rarely needed)
    - For a hereditary dysfunction:
        - Transfuse sufficient platelets to support hemostasis

ACUTE GENERAL TREATMENT

- Control superficial sites of hemorrhage (gingival or cutaneous wounds).
    - Direct pressure, wound glue, suture, bandage
- Replace red blood cells (RBCs) for severe blood loss anemia (see p. 1347). Adjust initial doses based on hematocrit (Hct) and ongoing loss.
    - Fresh whole blood (e.g., 12-20 mL/kg IV)

- Packed RBCs (e.g., 6-12 mL/kg IV)
- Bovine hemoglobin polymer (Oxyglobin): cats, up to 10 mL/kg; dogs, up to 30 mL/kg). Measure hemoglobin, not hematocrit, to monitor effect.

- Initiate platelet replacement to control systemic bleeding: platelet-rich plasma has a short shelf life (days) and is less widely available and more expensive compared to other blood components. The half-life of transfused platelets is shorter than the half-life of RBCs, but it is still longer than most clotting factors and von Willebrand factor. A single platelet-rich plasma (PRP) transfusion may supply sufficient platelets to form a hemostatic plug, so in vivo half-life is not necessarily a limitation of the product.
  - Fresh whole blood (12-20 mL/kg IV)
  - Platelet-rich plasma (6-12 mL/kg IV; >5 × 10^9 plat/kg IV)

CHRONIC TREATMENT

- For hereditary dysfunction:
  - Avoid invasive procedures unless essential.
  - Do not administer drugs with antiplatelet effects.
  - Administer a perioperative transfusion to supply platelets.
- For prophylactic treatment:
  - Give platelet-rich plasma to animals with clinically severe hereditary platelet function disorders (i.e., showing or having shown overt clinical signs of bleeding) before any surgical procedure.
  - Consider additional transfusion(s) at 2- to 8-hour intervals; these may be needed for major surgery or if excessive hemorrhage is noted.
  - Administer desmopressin acetate (DDAVP; 1 mg/kg SQ); this may be sufficient to prevent abnormal bleeding due to acquired platelet dysfunction if invasive procedures must be performed. The need for additional transfusions is based on falling hematocrit and/or abnormal bleeding from the surgical site.

BEHAVIOR/EXERCISE

Dogs and cats with hereditary thrombopathias should be managed to prevent injuries (e.g., no access to sharp toys, bones, no unobserved outside activity).

DRUG INTERACTIONS

Judicious use or avoidance of drugs with antiplatelet or anticoagulant effects (e.g., NSAIDs, sulfonamides, heparin, warfarin, clopidogrel, plasma expanders, cytotoxic drugs, estrogens)

RECOMMENDED MONITORING

- Physical exam to monitor external blood loss and petechiae/ecchymoses
- Serial hematocrit and plasma protein determinations to help identify internal or chronic hemorrhage

PROGNOSIS AND OUTCOME

- Acquired dysfunction: good prognosis if underlying disease or drug therapy is reversed
- Hereditary dysfunction:
  - Depends on severity of defect
  - Repeated transfusions are required to maintain patients having severe defects.
  - Transfusion typically required for any major surgical or traumatic injury

PEARLS & CONSIDERATIONS

COMMENTS

- Acquired platelet dysfunction is common but rarely causes severe spontaneous hemorrhage. Animals that are bleeding severely should be evaluated for other potential underlying causes (anticoagulant rodenticide intoxication, severe thrombocytopenia, etc.).
- Hereditary platelet dysfunction is relatively uncommon but is likely underdiagnosed because of the need for referral to document and classify specific traits. Platelet dysfunction belongs on the differential diagnosis of abnormal bleeding in any young dog or cat after common disorders (thrombocytopenia, von Willebrand disease, coagulopathies) have been ruled out.
- Platelets stick to glass, including the inside of anticoagulant-filled blood collection bottles. Therefore, whole blood given to

replace platelets should be collected in plastic blood bags.
- The differential diagnoses for animals with persistent bleeding and a normal platelet count, normal PT, and normal APTT should include platelet function defects, von Willebrand disease, fibrinolytic defects, and diseased or damaged blood vessels.
- The website addresses for some of the veterinary blood banks operating in North America are http://www.hemopet.com/; http://www.midwestabs.com/; http://www.evbb.com/products.html; http://www.ssabb.com/; and http://www.rrc.mb.ca/abb/.

TECHNICIAN TIPS

- Dogs and cats with platelet dysfunction are at risk for abnormal hemorrhage at venipuncture and catheter sites. As a general rule, peripheral veins-not the jugular vein-should be used for venous access.

CLIENT EDUCATION

- Owners should avoid giving dietary supplements containing fish oils or plant alkaloids to any pet with acquired or hereditary platelet dysfunction.
- Platelet function testing and/or mutation detection tests may be indicated (before breeding or surgery) for breeds or lines with high prevalence of hereditary thrombopathias.

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Plant Toxicoses

AV, Atrioventricular; *CNS,* central nervous system; *CV,* cardiovascular; *GI,* gastrointestinal tract; *V/D,* vomiting/diarrhea.

Some Common Garden and Household Toxic Plants

Botanical Name and Classification	Common Name(s)	Toxic Principle (if Known), Common Clinical Findings, and Species Sensitivity
Plants That Cause Central Nervous System (CNS) Stimulation		
Brunfelsia spp. (see p. 164)	Yesterday-today-and-tomorrow plant	Hopeanine, brunfelsamidine; vomiting/diarrhea (V/D), hyperesthesia, tremor, seizures in dogs
Ipomoea spp.	Morning glory	Lysergic acid; seeds; agitation, tachycardia, ataxia, hallucination; V/D, mostly dogs
Nicotiana spp. (see p. 766)	Tobacco	Nicotine; V/D, lacrimation, anxiety, shaking, agitation, tachycardia, followed by respiratory and cardiovascular (CV) collapse; mostly dogs
Plants That Cause CNS Depression		
Cannabis sativa (seep. 694)	Marijuana, pot, Mary Jane	Delta-9-THC; prolonged sedation, mydriasis, urinary incontinence, bradycardia, hypothermia, hypotension, hyperexcitability; mostly dogs
Macadamia integrifolia (see p. 681)	Macadamia nuts	Unknown toxin(s); depression, hyperthermia, mild tremor, weakness (especially in the hind limbs of dogs), muscular rigidity, ataxia
Plants That Cause Mixed CNS Effects		
Ricinus communis (see p. 180)	Castor bean	Ricin; vomiting, hemorrhagic enteritis, tremor, seizure/coma, death
Hepatotoxic Plants		
Amanita phalloides mushroom (see p. 734)	Death cap	Amatoxins: V/D, depression/lethargy, severe hepatic necrosis and failure, death; mostly in dogs
Cycas spp., *Zamia* spp. (see p. 814)	Sago palm, cycad palm	Cycasin; hemorrhagic gastroenteritis, hepatic encephalopathy, seizures, death
Cardiotoxic Plants		
Convallaria majalis (see p. 175)	Lily of the valley	Cardenolides; typically V/D; cardiac arrhythmias possible
Digitalis purpurea (see p. 175)	Foxglove	Cardiac glycosides; V/D, lethargy, cardiac arrhythmias, hyperkalemia
Kalanchoe spp. (see p. 175)	Kalanchoes	Bufadienolide; V/D, lethargy, cardiac arrhythmias in dogs possible but uncommon
Persea americana	Avocado	Persin; unsubstantiated cardiovascular toxicity reported in South Africa; not reported in the United States; vomiting in some dogs (gastroenteritis +/− pancreatitis, or due to intestinal obstruction from the large stone)
Nerium oleander (see p. 780)	Oleander	Cardiac glycosides (nerioside, oleandrin); V/D, digitoxin-like effect with bradycardia, tachycardia (any type of arrhythmia); hyperkalemia

Botanical Name and Classification	Common Name(s)	Toxic Principle (if Known), Common Clinical Findings, and Species Sensitivity
Phorandendron spp. (seep. 175)	Mistletoe	Toxalbumin, pharatoxin; V/D most common; very rarely bradycardia
Rhododendron spp. (see p. 175)	Rhododendron, azalea	Grayanotoxin; V/D; possible but uncommon conduction disturbances, with hypotension, bradycardia, AV block
Taxus spp.	Yew, Japanese yew	Taxine; V/D more common in dogs; tremor, hypotension, bradycardia, seizures
Plants That Affect the Respiratory System		
Hydrangea macrophylla	Hydrangea	Cyanogenic glycosides; V/D with or without blood; cyanide poisoning unlikely
Prunus spp.	Apple, cherry, bitter almond, plum, apricot, peach, nectarine	Cyanogenic glycosides (seeds); generally only cause V/D; cyanide poisoning unlikely; seeds must be masticated or ingested in large quantities for significant cyanide effect (hyperpnea, agitation, anxiety)
Nephrotoxic Plants		
Hemerocallis spp. (seep. 656)	Day lily	Unknown toxin(s); vomiting, lethargy, acute renal failure in cats at minimal exposures; only mild GI upset in dogs
Lilium spp. (see)	Easter lily, tiger lily, Asiatic lily, rubrum lily, Japanese show lily	Unknown water-soluble toxin(s); all parts toxic; vomiting, lethargy, acute renal failure in cats at minimal exposures; only mild GI upset in dogs
Oxalis spp.	Shamrock	Soluble (absorbable) calcium oxalates; hypersalivation, vomiting, possible renal failure (rare)
Rheum spp.	Rhubarb	Soluble (absorbable) calcium oxalates; hypersalivation, vomiting, possible renal failure (rare)
Vitis spp. (see p. 458)	Grapes and raisins	Unknown toxin(s); V/D, lethargy, acute renal failure, death in dogs
Plants Causing Hemolysis		
Allium spp.	Onion, garlic, chives	*N*-propyl disulfide; V/D, weakness, hemolytic anemia; cats more sensitive than dogs
Plants Affecting the Skin		
Toxicodendron spp.	Poison ivy, poison oak	Urushiol; hyperemia, pruritus possible; small-breed dogs with short-haired coats are more likely to be affected.
Plants Causing Severe Gastrointestinal (GI) Upset with Potential Systemic Effects		
Amaryllis spp.	Amaryllis, Aztec lily, orchid lily, and others	Lycorine; V/D, lethargy; tremors and cardiovascular signs (hypotension) also possible
Colchicum autumnale	Autumn crocus	Colchicine; vomiting, hemorrhagic enteritis, bone marrow suppression, tremor, seizure, death possible
Cycas spp., *Zamia* spp. (see p. 814)	Sago palm, cycad palm	Cycasin; hemorrhagic enteritis, liver necrosis, death
Hemerocallis spp. (seep. 656)	Day lily	Unknown toxin(s); vomiting; acute renal failure in cats, not dogs
Lilium spp. (see p. 656)	Easter lily, tiger lily, Asiatic lilies	Unknown toxin(s); vomiting, acute renal failure in cats, not dogs

Botanical Name and Classification	Common Name(s)	Toxic Principle (if Known), Common Clinical Findings, and Species Sensitivity
Narcissus spp.	Daffodil, jonquil, hyacinth	Lycorine; V/D, lethargy; moderate to severe V/D with ingestion of the bulb; tremors and CV signs (hypotension) possible with large ingestions
Ricinus communis	Castor bean	Ricin; vomiting, hemorrhagic enteritis, tremor, seizure, and coma, death
Vitis spp.	Grapes, raisins	Unidentified toxin(s); V/D, anorexia, lethargy, acute renal failure in 24-72 hours in dogs
Plants Causing Mild to Moderate GI Upset Without Systemic Effects		
Alocasia antiquorum	Elephant ear	Insoluble calcium oxalate crystals; oral irritation, hypersalivation, local inflammation, swelling of mucous membranes of pharynx and tongue; rarely causes dyspnea; may also cause histamine release
Cyclamen spp.	Cyclamen	Terpenoid saponins; hypersalivation, V/D. Cardiac arrhythmia, seizures with large ingestions (especially tuber portion of plant)
Dieffenbachia	Dumb cane	Insoluble calcium oxalate crystals; hypersalivation, V/D, oral pain.
Dracaena spp.	Corn plant, *Dracaena* plants	Saponins; salivation, V/D +/− hematochezia, anorexia
Epipremnum spp.	Golden pothos	Insoluble calcium oxalate crystals; V/D, hypersalivation, oral pain
Euphorbia spp.	Poinsettia	Latex sap; mild V/D (not deadly, as has been historically reported)
Hedera helix	English ivy	Saponins; mostly V/D, rarely agitation, ataxia, weakness
Philodendron spp.	Philodendron	Insoluble calcium oxalate crystals; hypersalivation, V/D, oral pain
Phytolacca americana	Pokeweed	Saponins, oxalates; V/D common, generally not life threatening; ingestion of berries may cause red-colored urine.
Schefflera spp.	Schefflera	Insoluble calcium oxalate crystals; V/D, hypersalivation, renal damage not expected
Schlumbergera bridgesii or *truncata*	Christmas cactus, Easter cactus	Unknown; mild V/D
Spathiphyllum spp.	Peace lily	Insoluble calcium oxalate crystals; hypersalivation, V/D, oral pain
Zantedeschia aethiopica	Calla lily	Insoluble calcium oxalate crystals; hypersalivation, V/D, oral pain

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Plague

BASIC INFORMATION

DEFINITION

A zoonotic infection caused by *Yersinia pestis,* a non-spore-forming, nonmotile, gram-negative bacterium

SYNONYMS

Bubonic plague, yersiniosis

EPIDEMIOLOGY

SPECIES, AGE, SEX: Cats are most susceptible; no age, sex, or breed predilection. Dogs are thought to be resistant to infection.

RISK FACTORS: Cats that hunt and are exposed to wild rodents and fleas are at highest risk for infection.

CONTAGION & ZOONOSIS

- *Y. pestis* is highly contagious and zoonotic; the bacterium is considered a bioterrorism risk.
- Humans are most commonly infected by flea bites. Cats and other domestic species may temporarily harbor infected fleas.
- Although rare, humans may be infected through direct contact with infected cats, rabbits, or rodents.
- Fomites appear to play a minimal role (the organism is sensitive to desiccation, temperatures above 105°F (40°C), and routine disinfectants). It can remain for weeks to months in organic material (e.g., carcasses), with freezing temperatures prolonging survival.
- Hygienic precautions involving gloving, gowning, mask usage, and avoiding contact between discharge/abscess fluid and open cuts or mucosal membranes, and the like, are essential when plague is possible.
- Direct transmission of zoonoses to veterinary personnel and cat owners has occurred via aerosol (from cats with plague-associated pneumonia). Therefore, in addition to flea elimination, precautions involving protection from respiratory secretions of cats should be implemented when plague is considered possible.
- A greater degree of human morbidity and mortality also appears to exist with delayed diagnosis, emphasizing the veterinarian's role in public health.

GEOGRAPHY AND SEASONALITY: Foci of plague occur most commonly in semi-arid, cooler climates usually adjacent to a desert. Plague is endemic in the western part of the United States, including New Mexico, Arizona, California, and Colorado. Plague is seasonal, with most cases occurring during the summer months.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Three geographic variants of plague exist (*Y. pestis* orientalis, antiqua, and mediaevalis) but are of equal virulence. Of greater clinical relevance, three clinical forms of plague can develop in humans and cats: bubonic, septicemic, and pneumonic.

HISTORY, CHIEF COMPLAINT: Cats may have a history of hunting, ingesting wild rodents, or being exposed to rodent fleas. Clinical signs reported by dog and cat owners usually are acute and nonspecific, including lethargy, fever, and depression. Some owners may notice swollen lymph nodes or draining cutaneous wounds.

PHYSICAL EXAM FINDINGS: Cats with plague will typically present with a fever (≥105°F [≥40.6°C]) and depression.

- Bubonic form: cats have enlarged and often abscessed, draining, or painful lymph nodes, (buboes; most commonly the retropharyngeal, cervical and submandibular lymph nodes).
- Septicemic form: cats demonstrate signs of septic shock with evidence of multiorgan involvement. The spleen is most commonly affected in people and the lungs in cats.
- Pneumonic form: cats may cough, sneeze, and have nasal discharge or dyspnea. The pneumonic form commonly occurs as a dissemination of the bubonic or septicemic forms.
- Dogs usually lack evidence of clinical disease.

ETIOLOGY AND PATHOPHYSIOLOGY

- Wild rodents (prairie dogs, squirrels, chipmunks, wood rats, mice) are reservoir hosts.
- Rodent fleas carry the infectious bacteria and transmit the infection to humans and animals through a bite. Domestic species may be infected through ingestion of a reservoir rodent.
- *Y. pestis* replicates within the host mononuclear cells, which carry the organism to the lymph nodes, resulting in the formation of characteristic buboes (abscessed lymph nodes). Alternatively, the infection may develop rapidly into a septicemia with hematogenous spread to multiple organs.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Presumptive diagnosis is made based on physical examination, relevant history, or suspicion of exposure in endemic areas. The local public health department should be contacted if there is suspicion of disease. Samples can be submitted for cytologic examination, Gram stain and culture, but care must be used to avoid zoonotic exposure. Paired titers are diagnostic, but treatment must be initiated before the disease is confirmed.

DIFFERENTIAL DIAGNOSIS

- Tularemia
- Bite wound abscess
- Other causes of systemic bacterial infection
- Feline panleukopenia virus
- Lymphoma (buboes)

INITIAL DATABASE

- CBC: possible marked leukocytosis
- Gram stain of draining material/fluid: gram-negative coccobacilli
- Chest radiographs: diffuse interstitial pattern or development of abscesses
- Aspiration and cytologic examination of enlarged lymph nodes

ADVANCED OR CONFIRMATORY TESTING

- The local public health department can confirm the diagnosis of plague with antigen detection using immunofluorescent antibodies on tissue samples or aspirates.
- Do not attempt an in-house culture of any material from an animal suspected of having *Y. pestis*.
- Serologic confirmation can be made by submitting two samples drawn 10-14 days apart. A 4-fold (or greater) increase in titer is necessary to confirm the diagnosis.
- A PCR test for tissue, blood, or fleas has been established to identify the organism.

TREATMENT

TREATMENT OVERVIEW

Intensive therapy should be started as soon as possible owing to the rapid course of the disease. Gentamicin is the antibiotic of choice but should not be given until the patient is rehydrated and stabilized with intravenous fluid therapy. Care must be used to avoid exposure and development of zoonotic disease. Antibiotic therapy should be continued for 3-4 weeks. Patients should remain hospitalized and isolated because of the contagious and zoonotic risks.

ACUTE GENERAL TREATMENT

- Fluid resuscitation of infected animals that have concurrent dehydration, shock, or other hypovolemic states
- Administration of supplemental oxygen and other critical care measures; these may be necessary depending on the animal's respiratory effort.
- Institution of treatment with the antibiotic of choice (gentamicin, 6 mg/kg IM or IV q 24 h) and brisk rehydration and fluid diuresis as well as monitoring of renal function. Streptomycin has also been used.
- Alternative antibiotics: trimethoprim-sulfonamide, doxycycline, or fluoroquinolones. These may be less effective. Chloramphenicol has been used in animals with the CNS form.
- Surgical incision and flushing of abscessed lymph nodes for drainage (caution because of public health risk)

CHRONIC TREATMENT

Treatment with antibiotics for a minimum of 21 days and continuation beyond resolution of clinical signs

DRUG INTERACTIONS

Gentamicin should not be used in combination with other nephrotoxic, ototoxic, or neurotoxic drugs. Gentamicin must be used carefully when in combination with cephalosporins or nonsteroidal antiinflammatory drugs (NSAIDs) because of renal effects.

POSSIBLE COMPLICATIONS

When zoonosis occurs, veterinary professionals are most commonly affected.

PROGNOSIS AND OUTCOME

- Mortality of cats approaches 50% the pneumonic form is the most lethal. Septicemic form is usually fatal within 1-2 days.
- Cats with spontaneous draining wounds may have better outcomes.
- Cats with previous exposure to plague (via vaccine or natural exposure) may have a shortened disease course.

PEARLS & CONSIDERATIONS

COMMENTS

- Veterinarians who suspect a clinical case of plague should immediately contact the public health department and observe precautions described above.
- People who have been exposed to an infected animal should seek medical advice.

PREVENTION

- Prevent unsupervised outdoor activities.
- Apply a flea preventive to cats and dogs during high-risk months.
- No vaccine is available against plague in animals.

CLIENT EDUCATION

- Inform clients of the increased risk of infectious diseases in outdoor cats.
- Emphasize proper flea and rodent control.
- Dogs may bring plague-infected fleas into households; sleeping with dogs may increase the human risk of acquiring the disease.

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Pituitary Dwarfism

BASIC INFORMATION

DEFINITION

Rare clinical syndrome of congenital deficiency in growth hormone (GH)

SYNONYM

Congenital hyposomatotropism

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs and cats
- Signs usually apparent at 2-3 months of age
- No gender predilection

GENETICS & BREED PREDISPOSITION: Inherited as an autosomal recessive trait in the German shepherd and the Karelian bear dog but also occurs in other dog breeds and in cats

ASSOCIATED CONDITIONS & DISORDERS: Can occur as part of combined pituitary hormone deficiency with concurrent congenital hypothyroidism (cretinism), hypoadrenocorticism (Addison's disease), and hypogonadism

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Poor growth, stunted stature, alopecia

PHYSICAL EXAM FINDINGS

- Stunted stature
- Bilaterally symmetric alopecia affecting the trunk, neck, and caudomedial thighs, with sparing of the head and extremities
- Soft, wooly haircoat
- Possible hyperpigmentation and scaling of exposed skin
- Delayed dental eruption
- Possible open fontanelles

ETIOLOGY AND PATHOPHYSIOLOGY

- Clinical signs result from a deficiency in pituitary production of GH and a resulting deficiency in insulin-like growth factor 1 (IGF-1), which is produced by the liver under the influence of GH.
- Pituitary dwarfism can occur as a result of pressure atrophy of the anterior pituitary gland secondary to congenital cystic enlargement of the craniopharyngeal duct (Rathke's pouch), or due to pituitary hypoplasia secondary to a defect in organogenesis of the pituitary gland.
- Animals with a combined pituitary hormone deficiency may also lack thyroid-stimulating hormone, prolactin, luteinizing hormone, folliclestimulating hormone, and adrenocorticotropic hormone.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis of pituitary dwarfism is based on finding decreased GH or IGF-1 concentrations in conjunction with appropriate clinical signs.

DIFFERENTIAL DIAGNOSIS

See Stunted Growth, p. 1056.

INITIAL DATABASE

- A CBC, serum biochemical profile, and urinalysis should be performed to help rule out other causes of stunted growth.
  - Results are usually normal.
  - Hypercholesterolemia is possible if concurrent hypothyroidism is present.

ADVANCED OR CONFIRMATORY TESTING

- Availability of GH testing is limited.
  - Basal serum GH concentrations may overlap between affected and normal animals and therefore should not be used alone as a confirmatory test.
  - GH stimulation (measurement of GH before and 15, 30, 45, 60, and 120 minutes following administration of clonidine [10 mcg/kg IV], xylazine [100 mcg/kg IV], or GH-releasing hormone [1 mcg/kg IV] is more useful than basal GH concentrations. Potential adverse effects of clonidine and xylazine include sedation, bradycardia, hypotension, and collapse. Confirm the protocol with the laboratory prior to performing the test. Pituitary dwarfs will have no increase in GH.
- Basal serum IGF-1 concentrations are decreased in dogs with pituitary dwarfism and may be useful when GH measurement is not available. Serum IGF-1 levels vary based on breed size; interpretation of results requires consultation with the laboratory performing the assay.
- Screening of animals for combined pituitary hormone deficiency is recommended (see pp. 588 and 573).
- Dermatohistopathologic examination of a skin biopsy shows changes similar to those in other endocrinopathies. A decrease in the quantity and size of dermal elastin fibers suggests pituitary dwarfism.

TREATMENT

TREATMENT OVERVIEW

The goal of therapy for pituitary dwarfism is to normalize serum concentrations of IGF-1 while monitoring closely for adverse effects caused by the treatment. Therapy of concurrent hypoadrenocorticism or hypothyroidism may be required.

CHRONIC TREATMENT

- Exogenous canine GH is not available.
- Human GH is not effective because dogs form antibodies against it.
- Porcine GH has been used in dogs but can be difficult to obtain.
  - An initial dose of 0.1 IU/kg subcutaneously three times a week for 4-6 weeks is recommended, with subsequent adjustment of the dose and interval based on clinical response and plasma IGF-1 concentrations.
- With GH therapy, a beneficial response is generally seen within 6-8 weeks.
- Progestins may stimulate mammary GH secretion and can be considered as an alternative treatment in dogs.
  - Medroxyprogesterone acetate (2.5-5 mg/kg SQ q 3 weeks, then q 6 weeks) has been shown to improve clinical signs in affected dogs.
  - Proligestone, a synthetic progestin, has been used successfully in 3 dogs at an initial dose of 10 mg/kg SQ q 3 weeks.
  - The efficacy of progestin therapy in affected cats is unknown.

POSSIBLE COMPLICATIONS

- GH supplementation may cause hypersensitivity reactions, carbohydrate intolerance, and overt diabetes mellitus.
- Progestin therapy may cause pyoderma, cystic endometrial hyperplasia in intact females, acromegaly, and diabetes mellitus.

RECOMMENDED MONITORING

- Periodically measure serum glucose and urine glucose levels to monitor for development of serum hyperglycemia and glucosuria associated with diabetes mellitus.
- GH-induced diabetes mellitus can be permanent if GH supplementation is not promptly discontinued.

PROGNOSIS AND OUTCOME

Even with treatment, the long-term prognosis for dogs and cats with pituitary dwarfism is guarded and dependent on maintenance of normal IGF-1 concentrations and avoidance of complications of GH or progestin therapy.

PEARLS & CONSIDERATIONS

COMMENTS

A DNA test (4 mL EDTA blood; cost: $130 U.S./100 Euro) is available through the University of Utrecht to identify unaffected carriers of the mutated gene that leads to pituitary dwarfism in the German shepherd breed; this will allow for the removal of identified carrier dogs from breeding programs.

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Pinnal Diseases

Additional Images Available on Website

BASIC INFORMATION

DEFINITION

Diseases affecting the skin, cartilage, or other tissues of the pinna (externally visible part of the ear). Disorders may affect only the pinna or be part of a more widespread dermatologic disease.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Depends on underlying cause

GENETICS & BREED PREDISPOSITION: Breed predispositions exist for some pinnal diseases:

- Acquired pattern alopecia (see p. 846): dachshund, Boston terrier, Italian greyhound
- Ear margin seborrhea: dachshund
- Sebaceous adenitis (see p. 1007): standard poodle, Akita, Samoyed
- Canine familial dermatomyositis (see online chapter: Dermatomyositis): Shetland sheepdog, collie
- Primary seborrhea (see p. 255): cocker spaniel
- Actinic keratoses, squamous cell carcinoma (see p. 1045), hemangioma: light-colored cats
- Color dilution alopecia (seep. 233): Doberman pinscher, many others
- Canine leproid granuloma syndrome: boxers and other short-coated dogs
- Pigmented viral plaques: pug, miniature schnauzer
- Psoriasiform-lichenoid dermatosis: English springer spaniel
- Hereditary lupoid dermatosis: German shorthair pointer (seep. 271)

CONTAGION & ZOONOSIS: Contagious and zoonotic etiologies affecting the pinna include dermatophytes, *Sarcoptes, Notoedres,* and *Otodectes. Demodex gatoi* and lice are also contagious but not zoonotic.

GEOGRAPHY AND SEASONALITY: A distinct geographic distribution exists for leishmaniasis, notoedric mange, *Demodex gatoi* infestation, and canine leproid granuloma syndrome.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Some conditions are pruritic or painful; others only alter pinnal appearance.
- Clients may note folding of a previously erect pinna.
- Lesions may be limited to the ear or more widespread.
- Some conditions have a predilection for the more densely haired (convex) aspect of the pinna; others are more commonly found on the concave surface.

PHYSICAL EXAM FINDINGS

- Various presentations are seen: crusts, scales, ulcers, alopecia, nodules, plaques, edema, lichenification, pigmentary changes, erythema, hemorrhage, tissue loss, diffuse thickening or deformation of the normal shape of the pinna.
- A full physical and dermatologic examination should be performed in all affected animals.
- Otoscopic examination is indicated, as some pinnal disorders are extensions of a primary process affecting the ear canal.
- Pruritic animals should be assessed for a pinnal-pedal reflex by rubbing or scratching the edge of one pinna and observing for a scratching motion in the ipsilateral hind leg.

ETIOLOGY AND PATHOPHYSIOLOGY

- As the pinna consists of skin and cartilage, a disease process affecting these tissues can result in pinnal lesions.
- Certain diseases are more likely to affect the pinna than other cutaneous sites:
  - Ear margin seborrhea, proliferative and necrotizing feline otitis externa, and aural hematomas are limited to this location.
  - Vasculitis and other ischemic conditions affect the pinna because of its limited collateral blood supply.
  - The feline pinna is prone to both UV-induced damage and frostbite.

- Lesions of canine leproid granuloma syndrome and fly bites have a predilection for this site.
- Conversely, the pinna is a rare location to find pyoderma, otherwise the most common cause of cutaneous crusting in dogs.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Localization of lesions to the pinnae should prompt complete dermatologic and physical examinations; unless the diagnosis is apparent from physical exam alone, cytologic analysis of pinnal lesions via skin scrapings should follow. Further testing is selected based on the list of differential diagnoses (see below).

DIFFERENTIAL DIAGNOSIS

- Parasitic causes:
  - Sarcoptic mange (dogs): positive pinnal pedal reflex, but it may be difficult to find mites on skin scrapings.
  - Notoedric mange (cats): usually easy to find mites on skin scrapings
  - Demodicosis (dogs): may cause erythema in inner pinna, which may be the only affected site
  - Pediculosis (louse infestation)
  - Other: trombiculiasis, fly bites (often *Stomoxys calcitrans,* affecting ear tips or folds), *Otodectes* (primarily affects the ear canal), *Demodex gatoi* (cats)
- Infectious causes:
  - Dermatophytosis (feline > canine)
  - Canine leproid granuloma syndrome: nodules on convex pinna caused by an unidentified species of mycobacteria with a distinct geographic distribution
  - Leishmaniasis (dogs > cats): pinnal scaling and alopecia; infected animals are systemically ill.
  - Pigmented viral plaques: deeply pigmented, scaly plaques
- Hypersensitivity disorders:
  - Atopic dermatitis and food allergy: commonly cause pinnal erythema and pruritus
  - Contact hypersensitivity: most often due to topically applied ear medications (e.g., neomycin, propylene glycol)
  - Mosquito bite hypersensitivity (cats): seasonal; convex pinna is a common site
- Immune-mediated disorders:
  - Pemphigus foliaceus: may resemble pyoderma, which is rare on the pinna. Very common site of lesions in cats.
  - Vasculitis and ischemic dermatopathy: fairly common cause of pinnal lesions in dogs, this diverse group of diseases may be idiopathic, hereditary (e.g., Jack Russell terriers), or iatrogenic (e.g., rabies vaccine-induced). Ulcerative and crusted lesion, often on the distal concave pinna.
  - Less common, also affecting other sites: pemphigus erythematosus, discoid lupus erythematosus, bullous pemphigoid, cold agglutinin disease, alopecia areata
  - Less common, limited to the pinna: proliferative thrombovascular necrosis auricular chondrosis (swollen, misshapen, painful pinnae)
- Hereditary causes:
  - Acquired pattern alopecia: affects dogs (most commonly dachshunds) before 1 year and progresses to complete pinnal alopecia due to diminution of still-active hair follicles
  - Canine familial dermatomyositis: lesions usually present by 6 months of age; immune-mediated cause suspected.
  - Color dilution alopecia: progressive hair loss in blue or fawn dogs
  - Other: primary seborrhea, psoriasiform-lichenoid dermatosis of English springer spaniels, hereditary lupoid dermatosis of German shorthaired pointers, congenital hypotrichosis, black hair follicular dysplasia
- Neoplastic diseases:
  - Squamous cell carcinoma: most common in light-colored cats; often preceded by premalignant actinic keratoses (small areas of crusting and hyperkeratosis). Pinnal lesions on light-colored cats warrant investigation.
  - Histiocytoma and sebaceous gland tumor: the pinna is a common location in dogs.
  - Basal cell tumor: the pinna is a common location in cats.
- Miscellaneous conditions:
  - Aural hematoma (see p. 120): usually straightforward diagnosis. Subcutaneous accumulation of hemorrhagic fluid forming a flocculent pocket within the pinna. Assess for causes of head shaking (e.g., otitis externa).
  - Ear margin seborrhea: pendulouseared dogs, particularly dachshunds. Keratinous deposits on concave and convex pinnal margins; fissures may form in chronic cases. Similar changes can be seen in hypothyroid dogs.
  - Sebaceous adenitis: scaling and follicular casts predominantly in the haired pinna
  - Acquired folding of ear pinnae: associated with iatrogenic hyperadrenocorticism in cats due to topical or systemic steroid use.
  - Proliferative and necrotizing otitis externa of cats: highly characteristic presentation of adherent, dark, keratinous debris on the concave aspect of the pinna, usually in young cats
  - Canine sterile eosinophilic pinnal furunculosis
  - Melanoderma and alopecia of Yorkshire terriers (probably a variant of pattern alopecia)

PINNAL DISEASES Pinnal crusting in a cat with pemphigus foliaceus.

INITIAL DATABASE

Varies depending on differential diagnoses but may include:

- None; diagnosis may be presumptive (e.g., aural hematoma, acquired pattern alopecia)
- Skin scrapings (see p. 1248)
- Pinnal-pedal reflex: 82% sensitivity and 94% specificity for canine sarcoptic mange (seep. 1006)
- Cutaneous cytology
- Wood's light examination, fungal culture
- Trichography (demodicosis, color dilution alopecia, pediculosis)
- Fine-needle aspirates from nodular lesions
    - Acid-fast stain of aspirates if mycobacteria suspected
- Skin biopsies
    - Prior to the procedure, advise clients that pinnal biopsies might result in permanent cosmetic changes.
    - Skin biopsies from the pinna can be difficult and may require general anesthesia, so sample other areas of the skin if they are similarly affected.
    - The pinna may be clipped to identify the major blood vessels (to be avoided). Do not clip hair from the biopsy site, however.
    - For a good cosmetic outcome, sample lesions on the edge of the pinna with a thin shave biopsy of the pinnal margin.
    - Larger wedges can be removed, leaving skin distal to the cartilage for closure.
    - With extensive pinnal necrosis, affected tissue may be excised to create a more proximal margin.
    - Use a biopsy punch to sample skin from nonmarginal lesions. Take care not to cut through underlying cartilage; otherwise a permanent hole will result. Allow skin to heal by second intention.
    - Always include crusts in the biopsy.
- CBC, serum chemistry profile, thyroid hormone levels, urinalysis, antinuclear antibody titers, and so forth as appropriate.
- Response to empirical therapy (e.g., *Sarcoptes)*

TREATMENT

TREATMENT OVERVIEW

Varies depending on cause. For aural hematomas, various surgical and medical techniques are described (see p. 120).

PROGNOSIS AND OUTCOME

Varies depending on cause

PEARLS & CONSIDERATIONS

COMMENTS

- Due to the difficulty of collecting diagnostic skin biopsies from the pinna, seek out and sample other affected areas of skin to sample.
- While both diseases are most common in dachshunds, ear margin seborrhea is characterized by scaling and skin lesions, whereas pattern alopecia is not.
- Consider empirical treatment for *Sarcoptes* in dogs with pinnal pruritus, even with negative skin scrapings and no pinnal-pedal reflex.

TECHNICIAN TIPS

The ear margins in dogs bleed easily with trauma, biopsies, and certain diseases. Head shaking greatly exacerbates hemorrhage. A gentle and effective technique to protect the pinnae from this self-trauma uses a surgical stockinette “tube” placed over the head and secured to the forehead by surgical tape. The stockinette may be used in a single layer or doubled over with loose holes cut out for the ears in the bottom layer. The stockinette is placed over the head such that the ears rest in an anatomically normal position; the stockinette must not be tight. The aim is to keep the ears from “flapping” when the head is shaken.

SUGGESTED READING

Matousek JL: Diseases of the ear pinna. Vet Clin North Am Small Anim Pract 34:511, 2004.

AUTHOR: KINGA GORTEL

EDITOR: MANON PARADIS

Pilonidal Cyst

BASIC INFORMATION

DEFINITION

Tubular skin lesion that extends ventrally from dorsal midline, usually as a blind sac but may connect to dura mater; congenital defect

SYNONYMS

Pilonidal sinus, dermoid cyst, dermoid sinus

EPIDEMIOLOGY

SPECIES, AGE, SEX: Young dogs, either sex

GENETICS & BREED PREDISPOSITION: Primarily Rhodesian ridgeback; believed to be hereditary (simple recessive gene)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

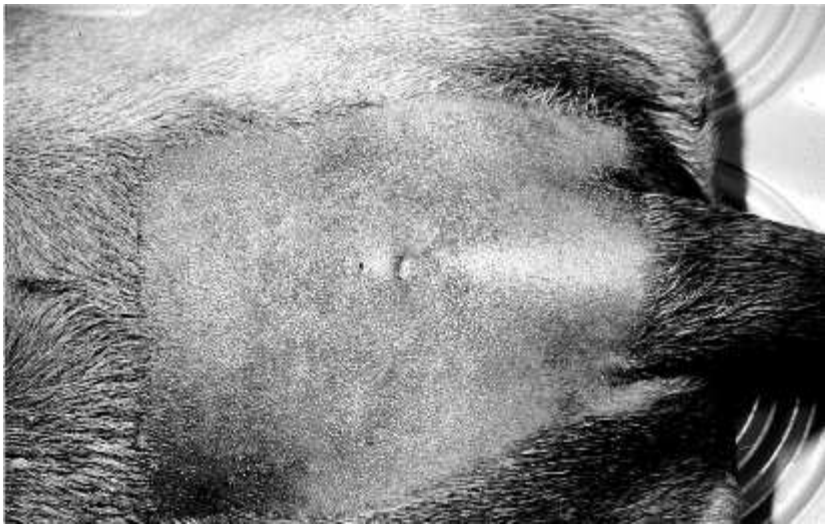
- Single or multiple dermal draining tracts
- Subcutaneous cystic mass(es) along dorsal midline

HISTORY, CHIEF COMPLAINT

- Opening in the skin on dorsal midline, with hair protruding from opening
- Mass in hair on dorsal midline (mass is a concretion of accumulated hair, sebum, and debris overlying the lesion)

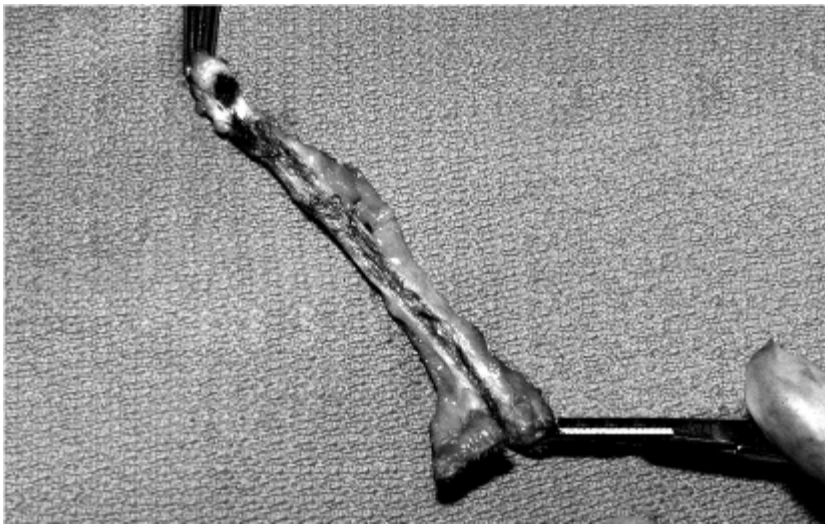
PHYSICAL EXAM FINDINGS

- Single or multiple openings in the skin along dorsal midline:
    - Occurs precisely on the dorsal midline
    - Hair protruding from opening
    - Cord of tissue palpably extending down through subcutaneous tissue toward the spine:
        - May be confined to subcutaneous tissue
        - Can extend to the spine:
            - Cervical sinus often attached to dorsal spinous process of C2
    - Lumen filled with inspissated sebum, exfoliated keratin, hair:
        - May be infected
- Subcutaneous cystic mass and swelling on dorsal midline
- If cyst is infected and connects with the spine:
    - Clinical signs associated with myelitis, meningomyelitis, or encephalitis may be seen:
        - Pain, weakness
        - Neurologic deficits in limbs
        - Seizures



PILONIDAL CYST Dorsal lumbosacral region of a Rhodesian ridgeback dog; cranial is to the left. Appearance of a porelike opening and/or subcutaneous nodule on the dorsal midline skin is the main physical characteristic of a pilonidal cyst.

(Courtesy Dr. Richard Walshaw.)



PILONIDAL CYST Excised pilonidal cyst from same dog. This longitudinal section of the cyst shows its length as well as the haired nature of the cystic tissue. Exterior (skin surface) is at bottom right; other extremity of the cyst *(upper left of image)* was its deepest point, near the spinal cord.

(Courtesy Dr. Richard Walshaw.)

ETIOLOGY AND PATHOPHYSIOLOGY

Congenital neural tube defect:

- Incomplete separation of the skin and neural tube during embryonic development
- Sinus can extend to and connect with dura mater.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is established entirely with signalment (breed) and physical examination findings.

DIFFERENTIAL DIAGNOSIS

- Epidermal inclusion cyst
- Follicular retention cyst
- Sebaceous cyst
- Foreign body
- Abscess
- Hair follicle tumor
- Myiasis

INITIAL DATABASE

Presurgical CBC and serum chemistry profile

ADVANCED OR CONFIRMATORY TESTING

Rarely necessary; physical findings are usually sufficient:

- Fistulography and myelography:
  - If there is concern about connection to the spine and neurologic signs are present
- Histopathologic examination of excised tissue to confirm diagnosis
- Cytologic examination and microbiologic culture and sensitivity (C&S) testing:
  - If infected
  - If connects to spine

TREATMENT

TREATMENT OVERVIEW

Complete excision of sinus tract, and cyst if present, is required.

ACUTE AND CHRONIC TREATMENT

Complete surgical resection: strict aseptic technique is essential if sinus extends to dura mater.

POSSIBLE COMPLICATIONS

- Recurrence due to incomplete excision:
  - Potential problem if extends to and involves dura mater
  - Development of a chronic draining tract
- Postoperative meningitis:
  - If dura mater involved and surgical wound infection occurs

RECOMMENDED MONITORING

- Monitor the incision site for evidence of recurrent draining tract.
- Look for appearance of new lesions:
  - Examine animals for subcutaneous cystic structures.

PROGNOSIS AND OUTCOME

- Excellent with complete excision and no involvement of spinal structures
- Guarded if:
  - Neurologic signs are present prior to surgery
  - Surgical wound infection develops and dura mater is involved

PEARLS & CONSIDERATIONS

COMMENTS

Avoid clipping, shaving, or cutting a mat of hair located on the dorsal midline without first cleaning and carefully examining the area.

Trauma to a pilonidal cyst may lead to subsequent infection and potentially myelitis.

CLIENT EDUCATION

- Common problem in the Rhodesian ridgeback breed
  - Clients should be aware of this problem if considering purchasing a Rhodesian ridgeback
  - Believed to be a heritable defect
- Does occur rarely in other purebred dogs; infundibular keratinizing acanthomas or benign sebaceous adenomas (which can occur anywhere on the body) are much more common, especially in aged dogs. Seepp. 275 , .

SUGGESTED READING

Angarano DW, Swaim SF: Congenital skin diseases. In Bojrab MJ, editor: Disease mechanisms in small animal surgery, ed 2, Philadelphia, 1993, Lea & Febiger.

Hedlund CS: Surgery of the integumentary system. In Fossum TW, editor: Small animal surgery, ed 2, St Louis, 2002, Mosby, pp 194–195.

AUTHOR & EDITOR: RICHARD WALSHAW

Phosphate Enema Toxicosis

BASIC INFORMATION

DEFINITION

Toxicosis due to administration of sodium phosphate enemas in cats and small-breed dogs, resulting in severe hyperphosphatemia, hypernatremia, and hypocalcemia

SYNONYM

Fleet enema toxicosis

EPIDEMIOLOGY

SPECIES, AGE, SEX: Younger animals; cats and small-breed dogs. Small body size produces a disproportionate ratio of enema fluid to body weight.

RISK FACTORS: Constipation, obstipation, colonic disease, and renal disease may increase the risk for problems from administration of sodium phosphate enemas by decreasing sodium and phosphate excretion (renal disease) or enhancing sodium and phosphate absorption (others).

ASSOCIATED CONDITIONS & DISORDERS: Hyperphosphatemia, hypernatremia, hypocalcemia (potentially severe/critical)

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Within 30 minutes to 4 hours of administration of enema, signs that may be apparent include:

- Depression
- Ataxia
- Vomiting
- Diarrhea with or without blood

PHYSICAL EXAM FINDINGS

Common:

- Tachycardia
- Pallor
- Prolonged capillary refill time
- Weakness

Possible:

- Hyperthermia or hypothermia
- Tachypnea
- Tetany
- Seizure

ETIOLOGY AND PATHOPHYSIOLOGY

Source:

Phosphate enemas are available over-the-counter (without a prescription) at pharmacies and in the drug aisles of supermarkets and convenience stores.

Mechanism of Toxicosis:

- Hypernatremia and hyperphosphatemia can occur after administration of sodium phosphate enemas via massive absorption of sodium and phosphate from the colon. Prolonged retention, overdose, colonic disease (dilation or ulceration), or

preexisting electrolyte disturbances as seen with chronic kidney disease increase the risk of toxicosis.
- Hypocalcemia occurs if calcium-phosphorus solubility product is exceeded; phosphorus binds and precipitates calcium, leading to hypocalcemia.
- Hyperosmolality:
  - Hypernatremia
  - Hyperglycemia is only a minor contributor to increased osmolality and is believed to be due to stress release of catecholamines and hypertonicity that alter cellular glucose uptake and metabolism; it can also result from pancreatic insulin release.
- Metabolic acidosis with increased anion gap

DIAGNOSIS

DIAGNOSTIC OVERVIEW

History of administration of an enema to a patient weighing <10 kg, with hyperphosphatemia, hypernatremia, and/or hypocalcemia on a serum biochemical profile taken within 12 hours of enema administration, provide a clinical diagnosis.

DIFFERENTIAL DIAGNOSIS

- Hypernatremia (see p. 559)
- Hypocalcemia (see p. 576)

INITIAL DATABASE

- CBC: generally unremarkable
- Serum chemistry panel; common abnormalities include:
  - Hyperphosphatemia
  - Hypernatremia
  - Hypocalcemia
  - Hyperkalemia or hypokalemia
  - Metabolic acidosis (decreased serum [$HCO3^-$]) with increased anion gap:
    - Anion gap: ([Na^+] + [K^+]) - ([Cl^-] + [$Hco3^-$]); normal = 12-24 mEq/L.
  - Hyperosmolality:
    - Measured directly and also calculated according to formula: 2[Na^+] + blood urea nitrogen (BUN) (mg/dL)/2.8 + glucose (mg/dL)/18; result is in milliosmoles per kilogram.
    - Normally, and in phosphate enema toxicosis, the difference between calculated and measured values (“osmol gap”) should be <10 mOsm/kg.
- Urinalysis: generally unremarkable

TREATMENT

DIAGNOSTIC OVERVIEW

No antidote; treatment aims to correct hypernatremia and hypocalcemia and provide supportive care. Sepsis may occur in animals with compromised colonic mucosa, requiring treatment.

ACUTE GENERAL TREATMENT

- IV fluids to address hypernatremia (see p. 559):
  - Initial choice (assuming <24 h since enema administration): either 5% dextrose in water or 0.45% saline with 2.5% dextrose (with potassium supplementation if hypokalemia is present). Concurrent furosemide (2 mg/kg IV) can increase natriuresis.
  - Initial rate: one to two times the maintenance rate (30-60 mL/lb/day [65-130 mL/kg/day]) plus a dehydration deficit and ongoing losses compensation if applicable; proceed with caution if the patient has heart disease.
  - Adjustment/change in fluid type and rate based on response and results of ongoing monitoring.
- Plain-water enema
  - May help to reduce hypernatremia; the colon has a large surface area and can absorb free water rapidly.
  - Administer 10 mL/kg of plain water as a retention enema (see p. 1258); repeat q 2-4 hours.
- Calcium gluconate if hypocalcemia-associated tetany is present:
  - IV route if tetany is severe and/or if hyperthermia is present concurrently

    - 10% calcium gluconate = 100 mg/mL calcium gluconate. This corresponds to 9.3 mg elemental calcium per milliliter.
    - Give 50-200 mg/kg calcium gluconate (= 0.5-2 mL/kg; typical cat dose = 3 mL) slowly IV over a period of 15-30 minutes with electrocardiogram (ECG) monitoring, administered to effect. Clinical normality usually will not occur immediately; mild to moderate improvement in signs is sought during the infusion, which warrants stopping administration.
    - If heart rate decreases significantly, or if an onset of ST-segment elevation/depression or QT-interval shortening is seen, the infusion must be stopped promptly.
- Calcium gluconate in stable, hypocalcemic patient:
    - 150-250 mg/kg calcium gluconate (1.5-2.5 mL/kg), diluted with two to four times more sterile water and given SQ q 6-8 h
- Phosphate-binding agents (e.g., Amphojel, 64 mg Al(OH)3/ml; or ALternaGEL, 120 mg Al(OH)3/mL):
    - 10-30 mg/kg (or higher) PO q 6-12 h, based on serum phosphorus levels; may cause inappetence
- Antibiotics (e.g., ampicillin, 22 mg/kg IV q 6-8 h; and enrofloxacin, 5 mg/kg diluted 1 : 1 in sterile water and given slowly IV q 12 h [q 24 h in cats]) in cases with history of colonic disease and suspicion or evidence of sepsis due to translocation of enteric bacteria

DRUG INTERACTIONS

- Sodium bicarbonate is not recommended (unless acidosis is severe) because of its hypertonic nature; it may exacerbate hypokalemia and hypocalcemia and may cause metabolic alkalosis.
- Insulin for hyperglycemia is not indicated because spontaneous resolution is expected.

POSSIBLE COMPLICATIONS

Hyperthermia due to ongoing hypocalcemia-induced muscle fasciculations; cerebral edema if hypernatremia is long-standing and then is corrected overly rapidly

PROGNOSIS AND OUTCOME

- Patients treated promptly (when earliest signs are noted or sooner) and thoroughly have a good prognosis: complete recovery is expected.
- Patients for whom treatment is delayed or that develop central nervous system (CNS) dysfunction or complications such as severe hyperthermia due to hypocalcemic tetany have a guarded and potentially poor prognosis, depending on the timing and extent of subsequent treatment.

PEARLS & CONSIDERATIONS

COMMENTS

- Hypernatremia that lasts more than 12-24 hours may need to be treated as a chronic condition (see p. 559). In such cases, the serum sodium level may require slow reduction over 48 hours at a rate of not more than 0.5 mEq/L per hour.
- Avoid administration of phosphate-containing enemas to small patients (<10 kg) or patients with severe obstipation or suspected/known compromise of the colonic wall; marginal or compromised renal function; or preexisting hypernatremia, hyperphosphatemia, or hypocalcemia.
- For injectable calcium, calcium chloride is generally not recommended owing to its potentially severe corrosive effects if it leaks perivascularly/subcutaneously.
- Doses for injectable calcium can be listed in milligrams of elemental calcium (Ca^{2+}) or in milligrams of compound (e.g., calcium gluconate, calcium chloride). It is important to be clear which dose is used to avoid overdosing or underdosing. For example, a 10% calcium chloride (CaCl2) solution has 100 mg/mL calcium chloride, which is 27.2 mg Ca^{2+}/mL CaCl2.

TECHNICIAN TIP

A phosphate enema (Fleet or other brands) is formulated as a clear liquid usually supplied in a transparent, soft plastic bottle and is never appropriate in cats or small dogs. Many safe alternatives (such as DSS enemas or other products made specifically for small animals) are available instead.

SUGGESTED READING

Atkins CE, et al: Clinical, biochemical, acidbase, and electrolyte abnormalities in cats after hypertonic sodium phosphate enema administration. Am J Vet Res 46:4, 1985.

Jorgensen LS, et al: Electrolyte abnormalities induced by hypertonic phosphate enemas in two cats. J Am Vet Med Assoc 187:12, 1985.

AUTHOR: ERIC DUNAYER

EDITOR: SAFDAR A. KHAN

Phobias

BASIC INFORMATION

DEFINITION

Behaviors characterized by persistent and extreme anxiety and avoidance, and occurring only in response to specific triggers. The fear response is out of proportion given the objective threat, is beyond voluntary control, and may be preceded by anticipatory anxiety.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs and cats, any age. As with most behavioral conditions, phobias most commonly develop during social maturity (about 12-36 months in dogs, 24-48 months in cats).

GENETICS & BREED PREDISPOSITION: Predispositions suspected, but modes of inheritance, population and breed variability mostly unproven. Candidate gene regions have been identified that are associated with noise-reactive phenotypes in Australian shepherds, border collies, and German shepherds.

RISK FACTORS: Mild signs may exacerbate quickly after exposure to a trigger of large magnitude.

CONTAGION & ZOONOSIS: A young dog that seems well adjusted and joins a home with a phobic dog may learn (and/or may react to) some of the behaviors associated with the phobia (e.g., reactive barking), especially if these behaviors engender attention.

GEOGRAPHY AND SEASONALITY: Holidays that are celebrated with fireworks, gunfire, or cannon blasts; seasonal thunderstorms

ASSOCIATED CONDITIONS & DISORDERS: Comorbidity of thunderstorm phobia and separation anxiety (see p. 1012) is high.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Thunderstorm phobia
- Noise phobia (single or combination noise types such as booming, metallic, electronic, other noises)
- Neophobia (fear of new objects or circumstances)
- Panic
- Other phobias (e.g., reflective surfaces or floors, nighttime, other animals)

HISTORY, CHIEF COMPLAINT

- Exposure to or anticipation of exposure to discrete triggering events eliciting observable signs of sympathetic arousal (e.g., trembling, shaking, pacing, hypervigilance and scanning of the environment, restlessness, vocalization, mydriasis, piloerection, ptyalism, elimination, anal sac expression, immobility, repeated startle responses and behaviors associated with avoidance)
- The onset may be acute, with or without an identifiable trigger, or may worsen over time. If escape attempts are interrupted, growling, snarling, lunging, or biting may be elicited.
- The aroused state may persist for minutes/hours.
- Clients' chief complaints may only be destructive behavior, excessive vocalization, or house soiling, without awareness of their meaning as markers of anxiety. Since many owners crate their dogs to "resolve" such behaviors, it is important to query owners regarding the reason they do so; otherwise, signs may be missed until the dog escapes the crate, frequently injuring himself/herself in the process.
- Cats may show signs that the owners may misinterpret as "normal," such as frequent and extended hiding out of context with the situations that trigger the behaviors (so-called scaredy cats).

PHYSICAL EXAM FINDINGS

- Generally unremarkable exam findings; damage to teeth, nails, or feet in extreme cases
- Self-inflicted injuries as dogs attempt to break out of crates in which they are confined as "treatment" for anxiety-associated behaviors

ETIOLOGY AND PATHOPHYSIOLOGY

Dogs, like humans, may have susceptibility genes for development of problematic anxieties. Dysfunction or dysregulation of caudate nuclei in the brain has been implicated in some phobic states. Inadequate in utero nutrition has also been associated with heightened reactivity. Cats may remain aroused for 24-48 hours after an event of profound hypothalamic stimulation. The worse the panic, the more insensitive the animal is to routine physical or social stimuli.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A diagnosis of phobia is made using the history: when extreme fear or anxiety (anticipatory fear) is provoked by specific triggers, and the severity of the fearful response is out of context with the risk the trigger represents.

DIFFERENTIAL DIAGNOSIS

- Generalized anxiety disorder
- Separation anxiety
- Learned fear following a traumatic event
- Attention-seeking behavior

INITIAL DATABASE

- CBC, serum chemistry profile, urinalysis: generally unremarkable; to assess systemic illness triggering or contributing to phobic states; also prior to initiating medication (if indicated)
- Perform additional tests based on history and physical exam findings (e.g., feline leukemia virus [FeLV] and feline immunodeficiency virus [FIV] serum assays and serum T4 in most adult cats).

ADVANCED OR CONFIRMATORY TESTING

If signs of neurologic dysfunction are present or develop, a primary behavioral abnormality is virtually never the sole diagnosis; extracranial and intracranial medical disorders should be investigated as appropriate.

TREATMENT

TREATMENT OVERVIEW

The goal is to produce a decreased or ablated response to the inciting trigger as evidenced by a reduction in or elimination of overt signs of sympathetic arousal.

ACUTE GENERAL TREATMENT

- The owner should help the pet avoid all exposure to the panic-inciting stimulus if it has been identified.
- The owner should reward any spontaneous decrease in reactivity to phobic triggers.
- Anxiolytics, specifically the benzodiazepines (BZD) for their quick onset of action and specific panicolytic effects, should be prescribed in combination with other psychotropic medications such as tricyclic antidepressants (TCAs) or selective serotonin reuptake inhibitors (SSRIs).
    - TCA medications:
        - Amitriptyline: dogs, 1-2 mg/kg PO q 12 h for a minimum of 30 days; cats, 0.5-1 mg/kg PO q 12-24 h for a minimum of 30 days. First drug of choice in mild cases without medical contraindications to their use; inexpensive.
        - Clomipramine (Clomicalm): dogs, 2-3 mg/kg PO q 12 h for a minimum of 8 weeks; cats, 0.5 mg/kg PO q 24 h for a minimum of 8 weeks. Most successful when the behaviors have a ritualistic component or elimination component.
    - SSRI medications:
        - Fluoxetine (Prozac, Reconcile): dogs, 1 mg/kg PO q 24 h for 8 weeks minimum; cats, 0.5 mg/kg PO q 24 h for 8 weeks minimum
        - Paroxetine (Paxil); dogs, 1 mg/kg PO q 24 h for 8 weeks minimum; cats, 0.25-0.5 mg/kg PO q 24 h for 8 weeks minimum
        - Sertraline (Zoloft): dogs, 1 mg/kg PO q 24 h for 8 weeks minimum; cats, 0.5 mg/kg PO q 24 h for 8 weeks minimum. Can be successful for situations in which other medications have been less helpful.

- BZD medications:
  - Diazepam or oxazepam: 0.2-0.4 mg/kg PO q 12-24 h for a minimum 30 days
  - Alprazolam: 0.01-0.025 mg/kg PO q 8-24 h or q 4-6 h for panic (dose should be increased to at least 2 mg/dose for a medium-sized dog until effect or sedation before deciding the medication is not effective)
  - Clonazepam (dogs): 0.01-0.05 mg/kg PO q 12-24 h or q 4-6 h for panic as needed.
  - Response to benzodiazepines is very individualized, so constant communication between practitioner and owner to achieve adequate titration of the patient's dose is necessary.

CHRONIC TREATMENT

- Owners should teach dogs to relax while making eye contact with them so that this new behavior can be used when the dog encounters a situation about which it is anxious or unsure. Owners can teach their dogs this behavior over time with positive reinforcement. Owners should learn to monitor facial cues, body postures, pupil size and shape, and respiratory behavior associated with relaxation versus anxiety.
- Avoidance of exposure to the panic-inciting stimulus
- Desensitization to the triggers can be accomplished if two criteria can be met: triggers can be identified and can be reproduced faithfully and in a systematic and incremental fashion.
- Owners should continue offering positive reinforcement to their animals for all relaxed and calm behaviors, particularly in the face of phobic triggers.

DRUG INTERACTIONS

- BZDs, TCAs, and SSRIs can all be combined at lower than normal dosages if needed, but there is potential for sedation, and patient response must be evaluated on a case-by-case basis.
- TCAs and SSRIs should not be given with monoamine oxidase inhibitors (MAOIs), which are found in many flea and tick collars and dips and in some medications to treat cognitive dysfunction.
- Use of SSRIs with tramadol, which has a weak serotonin reuptake inhibiting effect, may increase the risk of serotonin syndrome and should be avoided if possible. If their use together is necessary, starting both at reduced doses, titrating each to effect, and keeping watch for signs of serotonin syndrome reduces but does not eliminate the risk, and the client should be informed.
- TCAs can worsen existing cardiac arrhythmias and should be used with caution in patients with existing hepatic or thyroid disease.
- Paroxetine should be avoided in renal disease. Anecdotal reports of constipation are more common in cats, so owners of feline patients should be cautioned to monitor stool consistency.

POSSIBLE COMPLICATIONS

- Generalization to triggers which are similar to the original stimulus (e.g., a thunderphobic dog begins to respond to firework displays, then reacts to all loud noises in general)
- Phobias are almost always co-morbid conditions, for which all patients should be screened (most common: separation anxiety, panic disorder, and generalized anxiety disorder).
- BZDs have the potential for drug diversion and abuse by clients.

RECOMMENDED MONITORING

- Animals that take BZDs require a physical exam every 6 months in most U.S. states. The potential for human abuse of the drugs warrants vigilance around refills.
- Yearly CBC, serum chemistry profile, urinalysis, and thyroid screen (q 6 months in geriatric pets) if taking psychotropic medications. Cardiac monitoring may be recommended if syncope or other suspected cardiac signs are involved in panic.

PROGNOSIS AND OUTCOME

Prognosis is variable and depends on:

- Timeliness of diagnosis (early diagnosis: prognosis more favorable)
- Maintenance of frequent and thorough communication between clinician and client so treatment can be adjusted according to the animal's response and needs: prognosis more favorable
- Client factors:
  - Diligence of treatment (comprehensive, persistent treatment plan, and follow-up: prognosis more favorable)
  - Client compliance (good compliance: prognosis more favorable)
- If the best outcome is to be obtained, early intervention is essential.
- If the problem has been ongoing for some time before treatment was sought, treatment may well be lifelong, especially if there

are other comorbid anxiety-related conditions.

PEARLS & CONSIDERATIONS

COMMENTS

- Because client observations and reports are critical in data collection, it is important to spend time understanding the clients' use of language. Asking clients to describe what they see their pet do, as opposed to their interpretation of the behavior, is key in obtaining behavioral data.
- The single best tool for evaluating behavior is observation of the behavior itself. Video cameras and webcams make this possible. All practices should have a video camera clinicians can use in the practice and also lend to clients.

PREVENTION

- When selecting breeding stock, clients should assess temperament as well as conformation and medical phenotypes, because genetic predisposition is suspected to be a strong contributor to mood disorder development.
- At the first sign of any fearful behavior, clients should watch for any worsening of the behavior and pay attention to possible triggers that might indicate the development of a phobia.
- Veterinarians should screen for fear and phobias as a routine part of every appointment.

CLIENT EDUCATION

- Most behavioral conditions are due to chemical and functional abnormalities of the brain (areas of the limbic system and prefrontal cortex) and therefore are not willful acts of disobedience by a vengeful pet.
- Treatment of behavioral conditions is an ongoing process, often for the duration of the pet's life. Relapses may occur with treatment discontinuation or with added Stressors.

SUGGESTED READING

Overall KL, et al: Assessing reactivity in three breeds of working dogs: phenotypic determination and associated genotypes. Proceedings of the 2009 International Working Dog Conference, May 12-15, 2009, Ieper, Belgium.

Crowell-Davis SL, et al: Use of clomipramine, alprazolam, and behavior modification for the treatment of thunderstorm phobia in dogs. J Am Vet Med Assoc 22:744–748, 2003.

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Pheochromocytoma

BASIC INFORMATION

DEFINITION

Catecholamine-producing tumors derived from chromaffin cells of the adrenal medulla (most common) or from extraadrenal sympathetic ganglia (paragangliomas)

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs: uncommon; middle-aged/old (mean, 11 years; range, 1-18 years)
- Cats: rare; old (mean, 14.5 years)

ASSOCIATED CONDITIONS & DISORDERS: May occur as part of multiple endocrine neoplasia syndrome

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Ante-mortem diagnosis is challenging because clinical signs are variable, intermittent, and fairly nonspecific.

Dogs:

- Intermittent weakness and collapse are most common. Other clinical signs may include panting/tachypnea, agitation, polyuria and polydipsia (PU/PD), lethargy, vomiting, diarrhea, inappetence/anorexia, sudden blindness, seizures, or sudden death.
- Signs are often episodic and complicated by the high incidence of concurrent disease.
- Many animals show no clinical signs, and the diagnosis is made incidentally during abdominal ultrasonography or necropsy.

Cats:

- PU/PD, lethargy, and anorexia are most common.

PHYSICAL EXAM FINDINGS

- The physical examination is commonly unremarkable.
- When present, abnormalities may include tachypnea, generalized weakness (often episodic), tachycardia and/or cardiac arrhythmias, and pale mucous membranes; epistaxis, muscle tremors, blindness, retinal hemorrhage/detachment, and signs of abdominal pain are also possible.
- An abdominal mass is not usually palpable.

ETIOLOGY AND PATHOPHYSIOLOGY

- Usually solitary, slow-growing, highly vascular tumors. Rare bilateral pheochromocytomas or adrenal pheochromocytomas with a contralateral adrenocortical tumor have been reported.
- Considered malignant, with local invasion (e.g., caudal vena cava) and metastasis to liver and regional lymph nodes most common.
- Clinical signs result from sporadic oversecretion of catecholamines or local tumor invasion and metastasis.
- Excess catecholamines cause arteriolar vasoconstriction and systemic hypertension, cardiac arrhythmias, mydriasis, increased smooth muscle sphincter tone, and increased hepatic gluconeogenesis and glycogenolysis.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A presumptive diagnosis rests on identification of an adrenal mass and concurrent, often transient cardiovascular abnormalities (persistent sinus tachycardia; premature ventricular complexes; systemic hypertension; syncope; pulmonary thromboembolism) in the

affected patient. Definitive diagnosis requires histopathologic examination of the excised adrenal gland.

DIFFERENTIAL DIAGNOSIS

- Adrenal mass:
  - Nonfunctional adrenal mass
  - Adrenocortical neoplasia
- Systemic hypertension—other causes such as kidney, cardiac, hyperadrenocorticism may need to be investigated
- Collapse/weakness; other causes such as hypoglycemia, cardiac or respiratory disease may need to be investigated.
- Sinus tachycardia; other causes such as cardiac disease may need to be investigated.

INITIAL DATABASE

- Diagnosis requires a high index of suspicion because clinical signs are usually episodic and nonspecific; often not suspected until an adrenal mass is found on ultrasound exam or during necropsy.
- CBC, serum biochemical profile, and urinalysis: normal or may show nonspecific changes (mild nonregenerative anemia, mature neutrophilia, increased liver enzymes, hypercholesterolemia, proteinuria).
- Multiple arterial blood pressure (BP) measurements: hypertension (sustained systolic pressure >160 mm Hg and/or diastolic pressure > 100 mm Hg) is well recognized (40% of cases), but normotension does not rule out a pheochromocytoma because tumor catecholamine release is intermittent.
- Abdominal radiographs: low sensitivity for detecting a pheochromocytoma but may reveal a pedrenal mass ± mineralization. May aid in assessment of local extension of the tumor.
- Thoracic radiographs: may show pulmonary metastasis (10% of dogs), cardiomegaly, or pulmonary edema or congestion (rare). Pulmonary thromboembolism (see p. 940) is well recognized with pheochromocytoma and may cause acute cor pulmonale and/or right-sided congestive heart failure.
- Electrocardiogram (ECG): intermittent or sustained tachycardias (sinus tachycardia, ventricular arrhythmias) are common. A 24-hour period of Holter monitoring (see p. 1287) may be needed to document intermittent arrhythmias.
- Abdominal ultrasonography: usually unilateral adrenomegaly with normal-size contralateral adrenal gland; may also identify intraabdominal metastasis or tumor invasion of adjacent structures (see p. 42). Careful evaluation of the regional vena cava using Doppler ultrasound is important to identify any tumor thrombi (basis for anticoagulation; prognosis more guarded); large thrombi are possible.
- Tests for hyperadrenocorticism (see p. 548) should be normal, ruling out adrenocortical tumor.

ADVANCED OR CONFIRMATORY TESTING

- Contrast radiography (nonselective venography or excretory urography) for evaluating tumor invasion of the caudal vena cava or kidney, respectively.
- Abdominal CT or MRI with or without contrast: useful for surgical planning; usually shows an adrenal mass and helps identify any local invasion or distant metastasis.
- Increased serum and urine catecholamines and urinary catecholamine metabolites (e.g., vanillylmandelic acid): confirmatory in humans, but use is limited in veterinary medicine by assay availability, lack of established reference ranges, and expense and inconvenience of 24-hour urine collection. Stress associated with hospitalization has been shown to increase urine catecholamine excretion, so urine collection from dogs and cats with suspected pheochromocytomas should preferably occur at home following a few days of adaptation to the sampling procedure.
- Histopathologic examination and positive immunohistochemical staining for chromaffin granules of the excised tumor: required for definitive antemortem diagnosis.

TREATMENT

TREATMENT OVERVIEW

Initially, medical stabilization of the patient is often necessary, involving judicious blood pressure control and cardiac rate/rhythm management (including into general anesthesia). Surgical excision of the tumor is the treatment of choice for cases where unresectable metastasis is not evident. Concurrent vena caval venotomy is required when caudal vena caval invasion is diagnosed.

ACUTE GENERAL TREATMENT

- An alpha1-antagonist: phenoxybenzamine (0.25 mg/kg PO q 12 h initially, then increased every few days until hypertension controlled); maximum dosage of 1.5 mg/kg PO q 12 h in dogs (cats, maximum 0.5 mg/kg PO q 12 h) can be reached. Treat the animal for 1-3 weeks prior to surgery. Potential side effects may include hypotension (seen clinically as lethargy, weakness, syncope) or adverse drug reactions (e.g., vomiting). Prazosin or amlodipine are alternative treatments.
- Beta-blocker drugs (e.g., atenolol, beginning at 0.5 mg/kg PO q 12 h and titrating up to 1 mg/kg PO q 12 h if needed) may be

used for controlling sinus tachycardia but only after alpha1-adrenergic blockade has been initiated.

CHRONIC TREATMENT

- Careful anesthetic selection is needed to minimize intraoperative complications; isoflurane or sevoflurane are typically used for maintenance. Direct arterial BP and ECG should be monitored during surgery and for at least 24 hours postoperatively.
- If surgical resection is incomplete or not possible, long-term treatment with an alpha1-antagonist is required.

DRUG INTERACTIONS

Avoid administering monoamine oxidase inhibitors and metoclopramide, as both may lead to hypertension in these patients.

POSSIBLE COMPLICATIONS

- Sudden blindness, seizures, or even death from a hypertensive crisis
- Perioperative complications are common and include hypertension, hypotension, arrhythmias, respiratory distress, and hemorrhage. Most animals become normotensive 24-48 hours following surgery.

RECOMMENDED MONITORING

- In hospital: monitor BP and central venous pressure perioperatively.
- After discharge: assess BP and ECG monthly.

PROGNOSIS AND OUTCOME

- Prognosis depends on tumor size, metastasis or local tumor invasion, perioperative complications, and the presence of concurrent diseases, which is common (older animals).
- Animals with a surgically excisable tumor have a guarded to good prognosis. If animals survive the immediate postoperative period, a survival time of 18-24 months is possible.

PEARLS & CONSIDERATIONS

COMMENTS

These tumors are difficult to diagnose antemortem, and perioperative management is complex. Consider referral.

TECHNICIAN TIP

Both preoperatively and immediately postoperatively, these patients may have marked fluctuations in blood pressure and heart rhythm. Close monitoring and preparation for treatment when necessary (monitoring parameters/guidelines should be made clear) are essential.

SUGGESTED READING

Barthez PY, et al: Pheochromocytoma in dogs: 61 cases (1984-1995). J Vet Intern Med 11:272, 1997.

Feldman EC, Nelson RW: Pheochromocytoma and multiple endocrine neoplasia. In Feldman EC, Nelson RW, editors: Canine and feline endocrinology and reproduction, ed 3, Philadelphia, 2004, WB Saunders, pp 440–463.

Maher ER, McNeil EA: Pheochromocytoma in dogs and cats. Vet Clin North Am Small Anim Pract 27:359–380, 1997.

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Phenobarbital: Adverse Effects/Toxicoses

BASIC INFORMATION

DEFINITION

Adverse, unintended effects resulting from repeated therapeutic doses of phenobarbital (chronic exposure) or from an excessively high dose of phenobarbital (acute exposure caused by accidental ingestion/injection of a prescription drug or a dosage miscalculation). Additional information regarding acute barbiturates toxicosis can be found in the online chapter: Barbiturates Toxicosis.

EPIDEMIOLOGY

SPECIES, AGE, SEX: All species and ages; both sexes

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Chronic exposure:
  - Central nervous system (CNS) effects: sedation, lethargy, ataxia; hyperactivity, nervousness
  - Polyuria and polydipsia (PU/PD)
  - Polyphagia, weight gain, indiscriminate ingestions
  - Increased serum liver-associated enzymes without clinical signs of liver disease
  - Decreased serum thyroxine (T4) and free T4; ± mildly increased serum thyroid-stimulating hormone (TSH)
  - Hepatotoxicity
  - Blood dyscrasias (anemia, thrombocytopenia, neutropenia)
  - Superficial necrolytic dermatitis
  - Physical dependency
  - Pancreatitis
  - Generalized hypersensitivity reaction
  - Hyperlipidemia
- Acute overdose: adverse CNS effects (coma, hypothermia, respiratory depression)

HISTORY, CHIEF COMPLAINT: Prescription of or possibility of accidental exposure to phenobarbital. Abnormalities involving any organ system can be caused by phenobarbital.

PHYSICAL EXAM FINDINGS

- Chronic/repeated exposure: one or more of the following may be present:
  - Sedation, ataxia
  - Hyperactivity, nervousness
  - Lethargy, depression
  - Anorexia, vomiting
  - Abdominal pain
  - Icterus, ascites
  - Infection
  - Skin erythema, vesicles, crusted erosions, hyperkeratosis; especially affects footpads; painful
  - Ecchymoses
  - Ulcerations of mouth, mucocutaneous junctions; ear lesions; facial rash; pruritus; swelling of feet and limbs
  - Generalized lymphadenopathy
- Acute overdose
  - Acute onset of CNS depression, ataxia, weakness, hypothermia, hyporeflexia, respiratory depression, cardiac arrhythmias, hypotension, coma, death
    - Time to onset of signs: 15 min to 2 hr. Duration of signs: 24 hr to 8 days or longer (dose-dependent)

ETIOLOGY AND PATHOPHYSIOLOGY

- Sedation, PU/PD, polyphagia: direct CNS effects; common after start of drug and often improves within weeks. Sedation is also common with high serum drug concentrations.

- Hyperactivity, nervousness: often associated with low serum drug concentrations
- Increased serum liver-associated enzymes without clinical liver disease: elevated alkaline phosphatase (ALP) in 50% of dogs; elevated alanine amino-transferase (ALT) in 25% of dogs; can occur within weeks to months. Other liver enzymes are less commonly elevated. Elevated ALP may be due either to liver abnormalities or to benign induction; elevated ALT most likely due to early liver injury.
- Decreased serum T4: occurs in 40% of dogs and is likely due to increased metabolism and excretion of T4; can occur within weeks. Generally not associated with clinical signs of hypothyroidism.
- Hepatotoxicity: uncommon but potentially fatal; occurs in dogs (suspected in cats but not documented) and is unpredictable. Usually associated with long-term treatment (months to years) and high serum drug concentrations (>40 mcg/mL). Unknown if dose dependent or idiosyncratic; histopathologic examination reveals hepatic cirrhosis.
- Blood dyscrasias: uncommon reaction; neutropenia, thrombocytopenia, and/or anemia that often occur within weeks; likely an idiosyncratic or hypersensitivity reaction
- Hypersensitivity reaction: especially in cats, immunologic mechanism; can affect many organs and often occurs within weeks
- Physical dependency: can occur within weeks; abrupt discontinuation of drug can precipitate withdrawal seizures
- Pancreatitis: increased risk with phenobarbital/bromide combination
- Acute overdose: signs are dose dependent (ASPCA Animal Poison Control Center information) as shown in table. Note that any dose leading to coma can cause respiratory failure and death if the animal is not treated intensively.

Signs of Acute Phenobarbital Overdose According to Amount of Drug Intake

Sedation, ataxia	1-2 mg/kg orally (dogs, cats); any dose IV (dogs, cats)
Recumbent	12 mg/kg orally (dogs)
Severe CNS signs	20 mg/kg orally (dogs)
Unconsciousness	65 mg/kg orally (dogs); 6-10 mg/kg IV (dogs; expect cats similar)
Lethal dose	110 mg/kg orally (dogs); 125 mg/kg orally (cats)

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Chronic/repeated exposures: monitor for evidence of liver disease, blood dyscrasias, pancreatitis, and inappropriate serum drug concentrations. Suspect acute overdose if there is history/evidence of excessive exposure and rapid onset of ataxia, sedation, coma, and hyporeflexia.

DIFFERENTIAL DIAGNOSIS

Dependent on adverse effects

INITIAL DATABASE

- Serum biochemical profile, CBC
- Serum phenobarbital concentration

ADVANCED OR CONFIRMATORY TESTING

- Hepatotoxicity: abdominal radiography/ultrasonography; preprandial and postprandial bile acids; coagulation profile; histopathologic evaluation of biopsy
- Decreased T4: serum TSH concentration
- Pancreatitis: abdominal radiography/ultrasonography; pancreas-specific lipase immunoreactivity
- Blood dyscrasias: bone marrow aspirate
- Dermatopathy: dermatohistopathologic examination
- Acute overdose: analysis of blood, stomach contents, urine, feces for drug

TREATMENT

TREATMENT OVERVIEW

For chronic exposures, if adverse effects are sufficiently severe to warrant treatment, a decrease in drug dosage or discontinuation of

the drug as well as supportive care for the patient will be needed. For acute overdoses situations, patient stabilization, decontamination, and supportive care are the cornerstones of treatment.

ACUTE GENERAL TREATMENT

- Chronic/repeated exposure:
  - Sedation, PU/PD, polyphagia: if serum drug concentration is excessive, decrease drug dosage.
  - Hyperactivity, nervousness: if drug concentration is low, increase drug dosage.
  - Increased serum liver-associated enzymes without clinical liver disease:
    - If ALP is elevated but other liver-associated enzymes, albumin, and blood urea nitrogen (BUN) are normal and serum phenobarbital concentration is not excessive, elevation may be due to benign enzyme induction. Monitor animal and serum biochemical profile frequently as well as rule out other causes of elevated ALP (e.g., hyperadrenocorticism, corticosteroids).
    - If ALT is > two times the upper limit of normal, consider decreasing drug dosage and monitor ALT, or can discontinue phenobarbital and initiate alternative anticonvulsant. Discontinue phenobarbital gradually over several weeks to avoid withdrawal-induced seizures. Loading dosages of alternative anticonvulsant may be necessary.
    - If ALT is elevated and BUN and/or albumin are decreased, liver damage is likely. Pursue further diagnostics and discontinue phenobarbital as previously described.
  - Decreased serum T4: initiate supplemental T4 only if the animal has clinical signs of hypothyroidism.
  - Hepatotoxicity: discontinue phenobarbital and initiate alternative anticonvulsant. Rapidity of phenobarbital discontinuation depends on severity of liver disease. If the liver is functional and metabolizing phenobarbital, reduce the dose over several weeks. If the liver is severely affected, causing elevated serum drug concentration due to impaired metabolism, phenobarbital may be abruptly discontinued and an alternative anticonvulsant initiated. Monitor the animal's serum phenobarbital concentration daily and treat liver disease.
  - Blood dyscrasias, hypersensitivity reactions, hepatocutaneous syndrome: discontinue phenobarbital as previously described and initiate alternative anticonvulsant. Treat signs associated with dyscrasia, hypersensitivity, or dermatitis.
  - Pancreatitis: discontinue the combination of phenobarbital and bromide, then initiate monotherapy with phenobarbital or bromide or an alternative anticonvulsant. Treat pancreatitis.
- Acute overdose:
  - Treatment: See online chapter: Barbiturate Toxicoses
  - No specific antidote is available

DRUG INTERACTIONS

Drugs that inhibit drug-metabolizing enzymes (e.g., chloramphenicol, cimetidine) can elevate serum phenobarbital concentration and lead to toxicity. Phenobarbital use may decrease the effect of a number of drugs by inducing enzymes involved in drug metabolism and clearance.

RECOMMENDED MONITORING

- CBC, serum biochemical profile before starting phenobarbital; repeat these tests after 1-2 months and every 6-12 months or when the animal is ill.
- Monitor the serum phenobarbital concentration 2 weeks after the start of drug and every 6-12 months or when the animal is ill or has recurrence of seizures.

PROGNOSIS AND OUTCOME

- With milder adverse effects, prognosis is generally good.
- With serious adverse effects (hepatotoxicity, blood dyscrasias), prognosis can be good if phenobarbital is discontinued early; otherwise, the condition can be fatal.
- Hypersensitivity reactions can resolve within days to weeks of discontinuing the drug.

PEARLS & CONSIDERATIONS

COMMENTS

- Liver failure can cause a rapid rise in serum phenobarbital concentration secondary to impaired drug metabolism.
- Serum liver-associated enzymes can increase transiently after seizure activity.

TECHNICIAN TIPS

Hyperlipidemia is common in patients receiving phenobarbital, and it can interfere with several serum biochemical analyses and drug analyses. Animals should ideally be fasted for at least 12 hours prior to blood collection. Some animals receiving phenobarbital will have a persistent hyperlipidemia, and longer fasting periods may be needed. Alert the attending veterinarian if serum sample is lipemic.

PREVENTION

- Maintain serum phenobarbital concentration within the therapeutic range to decrease the risk of adverse effects (dogs 15-40 mcg/mL; cats 23-30 mcg/mL). Multiply mcg/mL by 4.31 to convert to µmol/L.
- Base drug dosage alterations on serum drug concentration. Variation in metabolism of phenobarbital exists between individual animals, resulting in poor correlations between oral dosage of drug and serum drug concentration.

SUGGESTED READING

Berendt M: Epilepsy. In Vite CH, editor: Braund's clinical neurology in small animals—localization, diagnosis, and treatment. New York, 2004, International Veterinary Information Service, www.ivis.org.

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Petroleum Distillates/Turpentine Toxicosis

BASIC INFORMATION

DEFINITION

- Toxicosis caused by any of a number of hydrogen- and carbon-containing (HC) chemicals originating from distillation of crude oil/petroleum; a few compounds originate from steam distillation of plants.
- Toxicosis is usually due to accidental dermal or oral exposure to HC-containing products and is manifested by repeated vomiting, retching, vocalization, lethargy, salivation, anorexia, ataxia, and signs of aspiration pneumonia (wheezing, coughing, dyspnea, panting).

SYNONYMS

- Petroleum hydrocarbons toxicosis
- Examples of hydrocarbon-containing products: naphtha, gasoline, kerosene, paint thinners/strippers, engine cleaners/degreasers, diesel fuel, heating fuels, lamp and furniture oils, waxes, lubricating oils, grease, paraffin wax, tar, asphalt
- Plant distillate examples: turpentine, linseed oil

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs are more commonly exposed than cats.
- Because of grooming behavior, topical exposure in cats can lead to clinically significant oral exposure.

RISK FACTORS

- Free-roaming animals are at higher risk for accidental exposures (open garage, workshop, shed, or construction area).
- Fenced dogs may chew into charcoal lighter fluid containers or lick hydrocarbon spills from a garage floor or work area.

GEOGRAPHY AND SEASONALITY: Warmer months involve an increased use of hydrocarbon distillate-containing products outdoors, with increased opportunities for exposure.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Evidence or suspicion of exposure to hydrocarbon-containing product
- Onset of clinical signs generally <1-3 hours after exposure
- Owner may note salivation, vomiting, retching, excessive licking motions, and coughing.

PHYSICAL EXAM FINDINGS

- Presence of product on the feet, muzzle, or on the trunk
- Hydrocarbon/distillate smell on the coat or breath
- Dermal discomfort (tender and inflamed interdigital skin or other exposed areas)
- Hyperirritability, agitation, pacing, and crying/whimpering
- Oral exposure: hypersalivation, vomiting, excessive licking motions, hacking, retching, panting, wheezing, coughing, crackling lung sounds
- Ocular: blepharospasm, blepharitis

ETIOLOGY AND PATHOPHYSIOLOGY

- The physical and chemical properties of a particular hydrocarbon determine its toxicity. Hydrocarbons with lower boiling points (more flammable), lower viscosities (“thinner”), and lower surface tensions are more dangerous owing to an increased ability to penetrate lipid membranes (increased systemic absorption) and increased ability to spread over larger surface areas (providing an increased risk of aspiration).

- Volatile hydrocarbons damage nerve endings and solubilize subdermal/submucosal fat, resulting in acute, generalized pain and discomfort. Systemic absorption can result in dissolution of cellular lipids and cell necrosis with generalized systemic inflammation and congestion. Some specific hydrocarbons can cause more direct organ damage (e.g., benzene causes bone marrow toxicity).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

History (known or suspected exposure) and clinical signs, particularly when a volatile scent of petroleum distillates is present, are the major components of the diagnosis. If the patient vomits, the simple spot test can confirm ingestion of petroleum distillates.

DIFFERENTIAL DIAGNOSIS

- Acute gastrointestinal (GI) viral and bacterial diseases
- Acute upper and lower respiratory infections (respiratory toxicosis)
- Allergic or other dermatitides (topical toxicosis)
- Organophosphate or carbamate insecticides, zinc phosphide

INITIAL DATABASE

- CBC: leukocytosis, neutrophilia; possibly septic changes if pneumonia complication; possible hemoconcentration
- Serum biochemistry profile: hypoglycemia possible
- Urinalysis: unremarkable
- Baseline chest radiograph if respiratory involvement (aspiration)
- Pulse oximetry or arterial blood gas measurement if respiratory involvement (aspiration)

ADVANCED OR CONFIRMATORY TESTING

- Simple spot test: vigorously mix warm water and vomitus; distillates will come to the surface; clinicians will note characteristic odor of volatile distillates (e.g., gasoline, charcoal lighter fluid).
- Confirmatory analysis of the distillate is possible but is usually of academic interest and not useful in terms of clinical management; collect samples in airtight containers and refrigerate.

TREATMENT

TREATMENT OVERVIEW

Do not induce vomiting or give activated charcoal; risk of aspiration outweighs benefit. Dermal decontamination (bathing the animal with a dishwashing liquid) is important to decrease continued exposure. Treat pain (especially with skin lesions) and aspiration as needed.

ACUTE GENERAL TREATMENT

- Emesis, gastric lavage, and administration of activated charcoal are contraindicated; increased risk of aspiration.
- Oxygen supplementation (see p. 1318) if the animal is showing respiratory distress
- Mechanical ventilation may be necessary, depending on oxygen concentration and delivery (see p. 1362).
- IV fluid support (may begin with 0.9% NaCl; adjustment based on electrolytes, hydration, etc.) to maintain hydration and perfusion; forced diuresis is not effective at eliminating toxins more rapidly.
- Pain control if needed (opioids such as buprenorphine, 0.005-0.02 mg/kg IM, SQ, IV, or fentanyl patch) because dermal exposure in particular can be painful.
- Corticosteroids: controversial; sometimes considered in aspiration pneumonia, but there is an increased risk of infection; avoid prolonged use.
- Early prophylactic antibiotic use is controversial; hydrocarbon pneumonitis has been reported to be of low risk for bacterial pneumonia complication.
- Broad-spectrum antibiotics: amoxicillin with clavulanate, 12-20 mg/kg PO q 12 h; second- or third-generation cephalosporins (e.g., cefoxitin, 30 mg/kg IV q 8 h to q 6 h); or fluoroquinolones (e.g., enrofloxacin, 5 mg/kg IM or diluted 1:1 in saline and given slowly IV q 12 h or q 24 h in cats) for secondary bacterial pneumonia
- Dermal decontamination, which consists of bathing (including haircoat and feet) with a mild liquid dishwashing detergent solution and rinsing thoroughly.

CHRONIC TREATMENT

If aspiration pneumonitis: oxygen supplementation, mechanical ventilation as necessary.

POSSIBLE COMPLICATIONS

Aspiration and chemical pneumonitis

RECOMMENDED MONITORING

- Chest radiographs as needed
- Arterial blood gas and Pao2 monitoring in animals that are compromised
- CBC and serum biochemistry profile
- In animals with a pulmonary condition, tracheal aspirate for Gram stain and/or culture can assist with antibiotic selection.

PROGNOSIS AND OUTCOME

- Good for cases in which no aspiration pneumonitis/pneumonia develops
- Guarded if aspiration occurs; update as needed

PEARLS & CONSIDERATIONS

COMMENTS

- Most commercial or industrial products containing a petroleum distillate carry a rather stern warning: “May be harmful or fatal if swallowed.” This warning is not specific to the individual product and does not automatically imply a poor prognosis. It is more useful to consider the volatility of the product when reasoning out the relative clinical risk to the animal, with greater volatility carrying a higher risk.
- Risk of aspiration pneumonitis/pneumonia from viscous or solid petroleum distillates including motor oil, transmission oil, waxes, other lubricating oils, grease, paraffin wax, and asphalt is very low. Most of these exposures result in mild self-limiting vomiting, lethargy, and diarrhea.
- Petroleum distillates are listed here in terms of their volatility: tar (least volatile); paraffin wax, lubricating oil, fuel oil, mineral seal oil, kerosene (intermediate); mineral spirits, gasoline, petroleum naphtha, petroleum ether (most volatile).

TECHNICIAN TIP

With petroleum distillates intoxications, “routine” decontamination measures (emesis, charcoal, gastric lavage) are contraindicated.

CLIENT EDUCATION

Owners should keep all products under lock and key and out of reach of pets. Childproof containers are not animal proof.

SUGGESTED READING

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1ST EDITION AUTHOR: MICHAEL KNIGHT

Petechiae and Ecchymoses

BASIC INFORMATION

DEFINITION

Manifestations of disorders of the platelet and/or blood vessel wall (primary hemostasis) that can result in bleeding in the skin or mucous membranes to a degree that is out of proportion to the trauma. Petechiae are pinpoint hemonhages, whereas an ecchymosis is a large area of hemorrhage that a layperson would describe as a bruise.

SYNONYMS

Bruising, hemorrhagic diathesis

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dependent on underlying cause:

- Young, purebred animals: von Willebrand disease, thrombasthenia, thrombopathia
- Young to middle-aged animals: infectious diseases, trauma
- Middle-aged animals: acquired immune-mediated diseases
- Older animals: neoplasia

GENETICS & BREED PREDISPOSITION

- von Willebrand disease (Doberman pinscher, Airedale, German shepherd, Scottish terrier, Chesapeake Bay retriever, and many other breeds; cats: Himalayan)
- Thrombopathia: basset hounds
- Thrombasthenia: otterhounds
- More common in dogs than in cats

RISK FACTORS

- Thrombocytopenia:
  - Immune-mediated disease: young to middle-aged, small to medium female dogs
  - Rickettsial disease: dogs living in or traveling to endemic areas
  - Bone marrow disease
- Thrombopathia/thrombasthenia:
  - Previous/current administration of nonsteroidal antiinflammatory drugs (NSAIDs)
  - Metabolic diseases: uremia, liver disease, paraproteinemia/hyper-globulinemia
- Vascular disease:
  - Hyperadrenocorticism
  - Drug reaction
  - Rocky Mountain spotted fever

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Nasal hemorrhage
- Pinpoint to large areas of bleeding on skin and mucous membranes
- Bruising
- Melena
- Hematuria

PHYSICAL EXAM FINDINGS

- Epistaxis
- Melena: from swallowing blood

- Petechiae, ecchymoses, hematochezia, and hematuria

ETIOLOGY AND PATHOPHYSIOLOGY

The conditions described will all cause capillary hemonhage and, unlike clotting factor defects, will result in frank hemorrhage:

- Thrombocytopenia:
  - Immune-mediated disease: idiopathic disease, systemic lupus erythematosus (SLE), drug reaction
  - Rickettsial disease: ehrlichiosis, Rocky Mountain spotted fever
  - Bone marrow disease: neoplasia, aplastic anemia, infectious (fungal, rickettsial, or viral)
  - Disseminated intravascular coagulation (DIC)
- Thrombopathia:
  - Congenital: von Willebrand disease, thrombasthenia, thrombopathia
  - Acquired: NSAIDs, hyperglobulinemia (ehrlichiosis, multiple myeloma), uremia, DIC
- Vascular disease:
  - Vasculitis: immune-mediated and rickettsial diseases
  - Vascular hemostatic defect:
    - Heightened permeability: hyperadrenocorticism
    - Reduced vessel strength: Ehlers-Danlos syndrome
    - Lack of contraction

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Barring severe trauma, petechiae or ecchymoses indicate a vascular wall, platelet, or severe coagulation factor problem leading to excessive bleeding. The history should seek to identify causes (e.g., intoxication), and the physical exam is essential for triage (to determine whether internal bleeding may be placing vital structures at risk). A platelet count is always indicated and a coagulation profile should be performed.

DIFFERENTIAL DIAGNOSIS

- Trauma resulting in areas of bruising
- Hemolytic uremic syndrome
- Cutaneous vasculopathy of greyhounds
- Cutaneous hemangioma or hemangiosarcoma

INITIAL DATABASE

- CBC:
  - Anemia if sufficient hemorrhage has occurred
  - RBC fragmentation suggests DIC or other vascular disease.
  - Thrombocytopenia
  - Neutrophilia: nonspecific stress, infection, neoplasia
  - Pancytopenia: bone marrow disease
- Urinalysis (avoid cystocentesis until coagulation status is known):
  - Usually normal
  - Isosthenuria with kidney disease
  - Hematuria
  - Proteinuria (e.g., with ehrlichiosis)
- Serum biochemistry profile:
  - Hypoproteinemia: if enough hemorrhage has occurred
  - Elevated urea with normal creatinine: gastrointestinal (GI) bleeding
  - Azotemia with renal disease or prerenal causes
  - Hyperglobulinemia with ehrlichiosis, multiple myeloma
  - Elevated alkaline phosphatase (ALP) activity with hyperadrenocorticism

ADVANCED OR CONFIRMATORY TESTING

- Other laboratory tests:
  - Coagulation profile: prolonged times with DIC; normal with thrombocytopenia and thrombopathia
  - von Willebrand factor analysis

- Buccal mucosal bleeding time (see p. 1222)
- Antinuclear antibody test for SLE
- Platelet function testing
- *Ehrlichia* and Rocky Mountain spotted fever titers, PCR

- Other diagnostic procedures:
  - Bone marrow aspiration biopsy: with pancytopenia
  - Skin biopsy: vascular disease, cutaneous lesions

TREATMENT

TREATMENT OVERVIEW

Treatment of the primary cause and support (e.g., blood transfusions) if necessary until treatment response

ACUTE GENERAL TREATMENT

- Restriction of patient's activity or stimuli that precipitate hemorrhage episodes
- Discontinuation of any medications that may alter platelet function
- Blood or platelet transfusions with severe anemia

CHRONIC TREATMENT

- Immunosuppressive therapy for immune-mediated thrombocytopenia
- von Willebrand disease: plasma or cryoprecipitate for acute bleeding
- Hyperglobulinemia: plasmapheresis
- Vasculitis: doxycycline for rickettsial disease; prednisone for primary immune-mediated diseases

POSSIBLE COMPLICATIONS

- Anemia and collapse state
- Hemorrhage into vital organs

RECOMMENDED MONITORING

- Platelet count with thrombocytopenia
- Clinical signs

PROGNOSIS AND OUTCOME

Dependent on cause

PEARLS & CONSIDERATIONS

COMMENTS

- Petechial hemorrhage is not a diagnosis but a clinical sign. Its presence should prompt a diagnostic workup early on to avoid catastrophic hemorrhage if the underlying cause is left unchecked.
- Pure secondary hemostatic defects (e.g., coagulation factor deficiency) do not typically cause spontaneous petechiae/ecchymoses, but venipuncture and other manipulations can allow subcutaneous bleeding, causing iatrogenic ecchymoses in these cases.

CLIENT EDUCATION

Recurrence of clinical signs

SUGGESTED READING

Callan MB: Epistaxis and hemoptysis. In Ettinger SJ, Feldman EC, editors: Textbook of veterinary internal medicine, ed 6,

Philadelphia, 2005, WB Saunders, pp 232–235.

AUTHOR: REMO LOBETTI

EDITOR: ETIENNE CÔTÉ

Persistent Müllerian Duct Syndrome

BASIC INFORMATION

DEFINITION

Persistent Müllerian duct syndrome (PMDS) is an uncommon condition characterized by the presence of paired uterine tubes, uterine horns, uterine body, cervix, and cranial vagina in a male dog or cat.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs and cats; present at birth

GENETICS & BREED PREDISPOSITION: Miniature Schnauzers, basset hounds, and Persian cats. PMDS is an autosomal recessive condition.

ASSOCIATED CONDITIONS & DISORDERS: Urinary tract infections, prostatitis, fever of unknown origin, pyometra

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Affected animals may show no clinical signs; persistence of female tubular reproductive tract may be an incidental finding during ultrasound examination or exploratory surgery in a male animal. PMDS may also be associated with urinary tract infection, prostatitis, or fever of unknown origin due to pyometra or infected uterus masculinus.

PHYSICAL EXAM FINDINGS: Normal external male genitalia; 50% are cryptorchid.

ETIOLOGY AND PATHOPHYSIOLOGY

Normally, Müllerian inhibitory substance (MIS) secreted by embryonic testes prevents the development of the Müllerian ducts into uterine tubes, uterus, cervix, and cranial vagina. PMDS patients are genetically (XY) male but lack MIS receptors, so embryonic regression of the müllerian duct system does not occur.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Definitive diagnosis of PMDS requires karyotype and abdominal ultrasonography and/or exploratory surgery to confirm that the patient is genetically male with bilateral testes and retention of all Müllerian duct-derived organs.

DIFFERENTIAL DIAGNOSIS

Cystitis, prostatitis, fever of unknown origin, male pseudohermaphrodite

INITIAL DATABASE

CBC only; chemistry panel if clinical signs are present

ADVANCED OR CONFIRMATORY TESTING

Karyotype, abdominal ultrasound, abdominal exploratory surgery

TREATMENT

TREATMENT OVERVIEW

Treatment of PMDS depends on the clinical signs produced by the retention of Müllerian duct-derived organs. If the retained uterus is infected, it must be treated as a pyometra (see p. 954).

ACUTE GENERAL TREATMENT

Affected animals should undergo simultaneous castration and hysterectomy.

PROGNOSIS AND OUTCOME

Prognosis is good for normal lifespan after castration and hysterectomy.

PEARLS & CONSIDERATIONS

PREVENTION

PMDS is a hereditary autosomal recessive trait. Affected animals should be castrated. Parents and male and female siblings of affected animals can be latent carriers and should be eliminated from breeding stock.

CLIENT EDUCATION

As for Prevention, above

SUGGESTED READING

Romagnoli S, Schlafer DH: Disorders of sexual differentiation in puppies and kittens: a diagnostic and clinical approach. Vet Clin North Am Sm Anim Pract 36:573, 2006.

AUTHOR: JAMES FLANDERS

EDITOR: MICHELLE A. KUTZLER

Persistent Frenulum

BASIC INFORMATION

DEFINITION

Persistence of a thin membrane of tissue between the ventral tip of the penis and the corpus of the penis or the inner prepuce

SYNONYMS

Ventral deviation of the penis (phallo-campus), balanopreputial fold

EPIDEMIOLOGY

SPECIES, AGE, SEX: Male dogs and cats; the condition is present at birth.

GENETICS & BREED PREDISPOSITION: Cocker spaniels may be predisposed.

RISK FACTORS: Prepubertal castration (see Etiology)

ASSOCIATED CONDITIONS & DISORDERS: Posthitis, infertility (intromission failure)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Spontaneous
- Iatrogenic

HISTORY, CHIEF COMPLAINT: Licking at the penis, inguinal urine scalding due to urine dripping, painful erection, difficulty breeding

PHYSICAL EXAM FINDINGS: Ventral curvature of the distal penis, with the presence of a thin band of tissue between the ventral tip of the penis and the corpus of the penis or the inner fold of the prepuce (dogs). In cats, the remnant is ringlike rather than a band, since the penis separates from the prepuce (during embryonic growth) in a circumferential manner rather than a linear, longitudinal manner like the dog.

ETIOLOGY AND PATHOPHYSIOLOGY

The frenulum is a remnant of the balanopreputial fold, which normally dissolves during postnatal development under the influence of androgens (near puberty). Prepubertal (early age) castration will prevent or diminish the dissolution of this attachment.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Most cases of persistent frenulum go undiagnosed or are incidental findings during urethral catheterization.

DIFFERENTIAL DIAGNOSIS

Preputial adhesion secondary to trauma or infection

INITIAL DATABASE

Physical examination of the penis following complete preputial retraction

TREATMENT

TREATMENT OVERVIEW

Treatment is necessary if there is urine dribbling, balanoposthitis (inflammation of the penis and prepuce), or if the animal is intended for breeding.

ACUTE GENERAL TREATMENT

The ventral band (dog) or circumferential attachment (cat) is resected with surgical scissors while the patient is under sedation or light general anesthesia.

CHRONIC TREATMENT

Postoperatively the prepuce may need to be retracted daily to prevent readherence.

BEHAVIOR/EXERCISE

The male should be sexually rested until the mucosal defect is completely healed.

POSSIBLE COMPLICATIONS

Balanoposthitis may develop secondary to the persistent frenulum or following resection of the attachment.

RECOMMENDED MONITORING

Monitor for hemorrhage or purulent preputial discharge.

PROGNOSIS AND OUTCOME

Very good prognosis after resection

PEARLS & CONSIDERATIONS

COMMENTS

The heritability of penile frenulum is unknown in the dog and cat but is heritable in other species (bovine, ovine, caprine, porcine).

PREVENTION

If appropriate, delay castration in nonbreeding animals until after puberty (>6 months).

TECHNICIAN TIPS

Difficulty may be encountered during penile exposure for urethral catheterization when a penile frenulum is present.

CLIENT EDUCATION

Delaying castration in nonbreeding animals until after puberty (>6 months) will prevent the iatrogenic occurrence of a persistent frenulum.

SUGGESTED READING

Romagnoli S, Schlafer DH: Disorders of sexual differentiation in puppies and kittens: a diagnostic and clinical approach. Vet Clin North Am Small Anim Pract 36:572, 2006.

AUTHOR: JAMES FLANDERS

EDITOR: MICHELLE A. KUTZLER

Peritonitis, Septic

BASIC INFORMATION

DEFINITION

Peritonitis is the local or generalized inflammation of the peritoneum; a diagnosis of septic peritonitis is based on identification of toxic neutrophils with intracellular bacteria within abdominal fluid.

EPIDEMIOLOGY

SPECIES, AGE, SEX: There is no species or sex predilection; younger animals that are prone to ingesting foreign material and older animals with gastrointestinal (GI) masses that can perforate are predisposed.

RISK FACTORS: Gastrointestinal surgery, gastric dilation and volvulus with gastric resection

ASSOCIATED CONDITIONS & DISORDERS: Neoplasia, linear foreign body, gastric dilation and volvulus

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPE

- GI perforation
- Non-GI perforation of an abdominal organ (e.g., pyometra, prostatic abscesses, hepatic abscess)

HISTORY, CHIEF COMPLAINT

- Lethargy
- Collapse
- Vomiting

PHYSICAL EXAM FINDINGS

- Tachycardia and signs of hypovolemic or septic shock
- Signs of abdominal pain (may be disproportionately subtle for the degree of inflammation or conversely may be mimicked by apprehension and abdominal guarding when no pain is there)
- Ascites
- Fever
- Altered mentation
- Injected mucous membranes/hyperemia

ETIOLOGY AND PATHOPHYSIOLOGY

- Bacteria gain access to the abdominal cavity. This occurs most frequently via perforation of the intestinal tract, although other internal sources (genitourinary tract, liver) and external sources (penetrating trauma) are possible.
- Infection within the abdominal cavity causes localized inflammation, with cellular inflammation and fibrin production.
- The peritoneum responds with increased vascular permeability, cellular infiltration with leukocytes and macrophages, and fibrin deposition.
- With increases in vascular permeability, interstitial fluid may accumulate rapidly.
- Substantial quantities of electrolytes, plasma proteins, and red blood cells (RBCs) may extravasate and be lost through third spacing in the abdominal cavity.
- This loss may progress to the point of causing hypovolemia, dehydration, severe hemoconcentration, septicemia, and metabolic alterations.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis of septic peritonitis, regardless of the underlying cause, is based upon demonstration—typically via cytologic evaluation of fluid obtained by abdominocentesis—of intraperitoneal toxic degenerative neutrophils containing intracellular bacteria.

DIFFERENTIAL DIAGNOSIS

Differentiation from other causes of abdominal pain or distension (e.g., acute abdomen [see p. 28], sterile ascites, neoplasia, sterile pancreatitis)

INITIAL DATABASE

- CBC, serum chemistry panel, urinalysis with culture
  - Urine sample obtained by urethral catheterization if possible; cystocentesis may inadvertently retrieve septic ascitic fluid.
- Abdominal radiographs: may document free intraabdominal air
  - Highly suggestive/specific for septic peritonitis unless air is result of prior abdominal surgery in the preceding week
- Abdominal ultrasound
- Abdominocentesis with fluid analysis, cytologic examination, and culture and sensitivity (C&S; both aerobic and anaerobic)

ADVANCED OR CONFIRMATORY TESTING

- Clotting profiles (prothrombin time and activated partial thromboplastin time) are useful because many animals with septic peritonitis are septic and thus have coagulopathy.
- Abdominocentesis (see p. 1193) and diagnostic peritoneal lavage (see online chapter: Diagnostic Peritoneal Lavage) have been shown to be safe and reliable in evaluating a septic peritonitis:
  - Abdominocentesis: see p. 1193
  - Diagnostic peritoneal lavage: aseptic placement of a large-bore (12- to 14-G) 5¼-inch (12 cm) catheter with additional side holes into the abdomen, followed by instillation of 20 mL/kg body weight of warm (body temperature) sterile saline into the peritoneum using an IV administration set, allowing the fluid to flow with gravity. The patient is then carefully rolled from side to side to mix the fluid. Finally, a sample is recovered for cytologic examination and C&S.
- The diagnosis of bacterial peritonitis is based on the presence of toxic degenerate neutrophils with intracellular bacteria in the abdominal fluid.
  - In most cases, the glucose level of the abdominal fluid is at least 20 mg/dL (1.1 mmol/L) lower than that of the peripheral blood glucose level.

TREATMENT

TREATMENT OVERVIEW

- Patient stabilization
- Identification and correction of underlying cause

ACUTE GENERAL TREATMENT

- Initial treatment must be directed toward stabilization of the metabolic consequences of peritonitis.
- IV crystalloid fluids (60-90 mL/kg), plasma (10-15 mL/kg), or whole blood may be necessary to maintain cardiac output.
  - Hematocrit to be maintained above 21%
- Exploratory laparotomy is warranted as soon as possible.
  - Stabilization of the patient as much as possible preoperatively
  - Repair of the lesion
  - Biopsy of affected tissues and intraoperative cultures
  - Lavage
  - Closed-suction drainage (warranted in almost all cases)
  - Open abdominal drainage if extensive contamination is present
- Broad-spectrum antimicrobial therapy; recommendations include:
  - Ampicillin, 22 mg/kg IV q 6 h; + gentamicin, 6 mg/kg IV q 24 h
    - Gentamicin q 24 h is less nephrotoxic than q 12 h or q 8 h.
    - Gentamicin should not be initiated until the animal is both hydrated and producing urine.
  - Ampicillin, 22 mg/kg IV q 6 h; + enrofloxacin, 10 mg/kg IV q 24 h
    - Enrofloxacin IV should be diluted in saline; use is off label.
    - Avoid enrofloxacin at this dose in cats (permanent retinopathy possible).
  - Cefazolin, 22 mg/kg IV q 8 h; + gentamicin or enrofloxacin (according to dosage just presented); + metronidazole, 10 mg/kg IV q 8 h

- Hospital-acquired infections (e.g., dehiscence of enterotomy sites) should be treated based on the sensitivity pattern of the hospital's pathogenic flora.

POSSIBLE COMPLICATIONS

- Sepsis
- Multiple organ dysfunction syndrome
- Dehiscence at site of prior repair
- Hypoalbuminemia

RECOMMENDED MONITORING

- Hydration status
- Serum total protein and albumin levels
- Serum electrolytes
- Serum/blood glucose level
- Blood pressure
- Renal function/urine output
- Central venous pressure
- Adequacy of pain control

PROGNOSIS AND OUTCOME

The reported mortality rate for dogs and cats with septic peritonitis ranges from 20%-70%. The clinician should inform the owner of the mortality rate prior to surgery.

PEARLS & CONSIDERATIONS

COMMENTS

- Gastric perforations may result in a large amount of free intraabdominal air without fluid.
- Linear foreign bodies are particularly prone to perforation.

PREVENTION

Good surgical technique is required for abdominal surgery.

SUGGESTED READING

Bentley A, Otto CM, Shofer FS: Comparison of dogs with septic peritonitis: 1988-1993 versus 1999-2003. J Vet Emerg Crit Care 17(4):391–398, 2007.

Culp WT, Zeldis TE, Reese MS, et al: Primary bacterial peritonitis in dogs and cats: 24 cases (1990-2006). J Am Vet Med Assoc 234(7):906–913, 2009.

Ruthrauff CM, Smith J, Glerum L: Primary bacterial septic peritonitis in cats: 13 cases. J Am Anim Hosp Assoc 45(6):268–276, 2009.

AUTHOR: DANNA M. TORRE

EDITOR: ELIZABETH ROZANSKI

Peritonitis (General)

BASIC INFORMATION

DEFINITION

Inflammation of the peritoneum

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Any species, breed, age, or sex
- Cat: feline infectious peritonitis (FIP)

RISK FACTORS

- Abdominal trauma:
  - Blunt
  - Penetrating
- Intraabdominal surgery:
  - Gastrointestinal (GI) procedures
- Inflammatory/infectious disease of abdominal organ(s):
  - Cholecystitis/cholangiohepatitis
  - Prostatitis/prostatic abscess
  - Pancreatitis
  - Pyometra
- Cat:
  - Environment conducive to transmission of FIP

CONTAGION & ZOONOSIS: Cat: transmission of coronavirus FIP is mainly fecal-oral; mutation of coronavirus from less pathogenic form to FIP variant is necessary to cause clinical FIP.

ASSOCIATED CONDITIONS & DISORDERS

- Sepsis/septic shock
- Coagulopathy/disseminated intravascular coagulation (DIC)
- Systemic inflammatory response syndrome
- Acute respiratory distress syndrome
- Multiple organ dysfunction

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES:

Primary versus secondary:

- Primary:
  - Peritoneal inflammation or infection without preexisting intraabdominal condition:
    - FIP
    - Rare occurrence of bacterial (mycobacteria) and protozoal primary infections
- Secondary:
  - Peritoneal inflammation or infection caused by intraabdominal pathologic condition:
    - Disruption of hollow viscus
    - Penetrating trauma
    - Organ inflammation/ischemia
    - Iatrogenically induced

Nonseptic versus Septic:

- Nonseptic:
  - Peritoneal inflammation caused by mechanical trauma:
    - Intraabdominal surgery
  - Sterile foreign material:
    - Urine
    - Bile
    - Iatrogenically introduced (e.g., surgical sponge)
- Septic:
  - Contamination and subsequent infection of the peritoneal cavity by an infectious agent:
    - Bacteria; most common cause in dog and cat
    - Virus
    - Protozoa

HISTORY, CHIEF COMPLAINT: History variable depending on underlying cause of peritonitis; may include:

- Known traumatic event
- Ingestion of a foreign object
- Previous abdominal surgery
- Ongoing or recent treatment for intraabdominal organ disease
- Problems urinating or defecating
- Heat cycle in previous month

Chief complaint(s) variable depending on underlying cause of peritonitis; may include:

- Nonspecific complaints:
  - Lethargy, fever, anorexia, vomiting, decreased/no fecal production, diarrhea
- Complaints related to cause of peritonitis:
  - Wound(s) in abdominal area
- Urination:
  - Straining to urinate
  - Decreased/no urine production
  - Blood in urine
  - Developing jaundice
  - Vaginal discharge
- Complaints related to developing peritonitis:
  - Abdominal discomfort:
    - Reluctance to lie down or uncomfortable when lying down
    - “Praying posture”
    - Pain on handling/touching abdomen:
      - May only be subtle (especially in cats)
      - Abdominal distension

PHYSICAL EXAM FINDINGS: Findings related to peritoneal inflammation:

- Nonspecific findings:
  - Lethargy, fever, dehydration
- Specific findings:
  - Pain on abdominal palpation:
    - Localize to specific region of abdomen if possible
    - May be absent or not dramatic:
      - Even in face of significant peritoneal inflammation
      - Especially in the cat
  - Abdominal distension:
    - Fluid
    - Mass

Findings related to underlying cause of peritonitis:

- Evidence of abdominal trauma:
  - Wound(s)
  - Contusions
  - Disruption of the abdominal wall
  - Linear foreign body (see p. 407) caught around tongue base. Clinicians should apply dorsal pressure with thumb externally between mandibles to raise tongue for proper sublingual examination.

- Incision line from previous abdominal surgery
- Icterus
- Hematuria, pyuria
- Purulent or hemorrhagic vaginal discharge
- Findings related to developing sepsis
- Hyperemia or injected mucous membranes
- Increased or decreased capillary refill time
- Tachycardia, tachypnea
- Hyperdynamic or hypodynamic pulse

ETIOLOGY AND PATHOPHYSIOLOGY

- Peritoneal inflammation; vasculitis, increased capillary permeability
- Movement of large volumes of fluid into peritoneal cavity:
  - Severe hypovolemia or hypovolemic shock
  - Accompanying loss of protein and electrolytes
- Development of coagulation abnormalities due to release of inflammatory mediators and cytokines:
  - Hypercoagulable or hypocoagulable state
  - DIC
- If septic, bacterial translocation into the bloodstream:
  - Bacteremia
  - Sepsis or septic shock

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is suspected based on presenting history and physical examination findings. Confirmation requires demonstration of inflammation in intraabdominal fluid and evaluation of the fluid to determine the cause of the peritonitis.

DIFFERENTIAL DIAGNOSIS

- Pain, abdominal; need to rule out nonperitonitis causes:
  - Organ enlargement
  - Organ inflammation
- Pain, nonabdominal; need to rule out:
  - Spinal:
    - Intervertebral disk disease
    - Trauma
  - Pelvic:
    - Fracture/dislocation
  - Thoracic:
    - Trauma related: rib fractures, diaphragmatic hernia
    - Intrathoracic disease: pleural pain
  - Limbs:
    - Joint pain/polyarthritis
- Abdominal distention, fluid:
  - Associated with peritonitis:
    - Refer to fluid analysis for an animal with peritonitis.
  - Not associated with peritonitis:
    - Transudate; modified transudate; hemorrhage
- Abdominal distension, mass:
  - Nonperitonitis causes of abdominal mass:
    - Organ enlargement: hepatomegaly, splenomegaly
    - Cyst formation: paraprostatic cyst

INITIAL DATABASE

- CBC, evidence of:
  - Regenerative left shift: inflammation
  - Degenerative left shift: sepsis
- Serum biochemistry profile:

- Evidence of cause of peritonitis:
  - Azotemia: uroabdomen versus dehydration (postrenal versus prerenal, respectively)
  - Hyperbilirubinemia: bile peritonitis
- Assessment of organ function and pathophysiologic effects of the peritonitis:
  - Electrolyte imbalance:
    - Hypokalemia: fluid loss, no intake
    - Hyperkalemia: uroabdomen, anuria, acidosis
  - Hypoproteinemia:
    - Leakage into peritoneal cavity
    - Decreased production
  - Altered blood glucose concentration:
    - Hypoglycemia or hyperglycemia
    - Blood/peritoneal fluid concentration: blood glucose = 20 mg/dL higher than peritoneal fluid glucose may be predictive of septic peritonitis
  - Lactate:
    - Blood/peritoneal fluid lactate concentration difference >2 mmol/L may be predictive of septic peritonitis in the dog
  - Hyperbilirubinemia:
    - Bile leakage: bile peritonitis

- Urinalysis:
  - Avoid cystocentesis in animals with peritonitis; catheter preferable (indwelling may be desired for monitoring critical cases; contrast cystography for uroperitoneum, etc.)
- Whole-abdomen clipping of hair: if possibility of penetrating wound with (e.g., stick, projectile) or without (e.g., tooth, claw) retention of penetrating object
- Survey abdominal radiographs:
  - Findings suggestive of peritonitis:
    - Fluid, causing loss of serosal detail
    - Free gas:
      - Mottling throughout viscera or “gas cap effect” (clearest with horizontal beam radiograph)
    - Ileus
    - Mass(es)
- Ultrasound examination:
  - Integrity of organs
  - Evaluate mass(es)
  - Confirm presence of fluid and obtain sample for analysis (see below)
- Abdominal fluid analysis:
  - Obtain by ultrasound guidance:
    - Preferable to blind abdominocentesis or diagnostic peritoneal lavage
  - Analysis:
    - Glucose, lactate concentrations (see previous)
    - Urea nitrogen, creatinine concentrations:
      - Fluid/blood creatinine concentration ratio = 2:1 highly predictive of uroabdomen in the dog
    - Bilirubin concentration:
      - Compare to serum: fluid bilirubin concentration > serum concentration highly suggestive of bile peritonitis
    - Electrolytes:
      - Fluid/blood potassium concentration ratio = 1.4:1 highly predictive of uroabdomen in the dog
  - Cytologic examination:
    - Neutrophils:
      - Inflammation: increased count, nondegenerative, no intracellular bacteria
      - Septic peritonitis: increased count, toxic changes, intracellular bacteria
    - Plant material: GI leakage
    - Bacteria: Gram stain to aid choice of antibiotic therapy pending culture results
  - Microbiologic culture and sensitivity (C&S) testing:
    - Aerobic and anaerobic

ADVANCED OR CONFIRMATORY TESTING

- Contrast radiographic studies:
  - Uroabdomen: cystography (lower urinary tract) or excretory urography (upper urinary tract; less commonly indicated) to confirm site of disruption prior to surgery
- Coagulation profile: DIC

TREATMENT

TREATMENT OVERVIEW

- Patients with primary peritonitis (e.g., FIP) require supportive care and specific medical treatment of the underlying cause.
- Patients with secondary peritonitis require surgical exploration of the abdomen with:
  - Surgical correction of the cause
  - Peritoneal lavage and possible drainage
  - Intensive postoperative care
- Some cases (e.g., severe pancreatitis) may have elements both favoring and disfavoring surgical exploration, and consultation with an internist and a surgeon should be considered for optimal planning.

ACUTE AND CHRONIC TREATMENT

- Correction of fluid and electrolyte abnormalities:
  - Hypovolemia
  - Hypokalemia or hyperkalemia:
    - Uroabdomen, hyperkalemia:
      - Potassium-free fluids: 0.9% NaCl (seep. 55)
- Blood products if necessary (see p. 1111):
  - Whole blood (if anemia or bleeding disorder)
  - Packed red cells (if anemia)
  - Fresh frozen plasma (if hypoproteinemia or coagulopathy)
- Appropriate antimicrobial therapy if septic:
  - Empirical therapy (aerobic and anaerobic coverage):
    - Second-generation cephalosporin:
      - Cefoxitin, 22 mg/kg IV q 2 h during the perioperative period, then q 6 h
    - Combination therapy:
      - Metronidazole, 10-15 mg/kg IV q 12 h; enrofloxacin, 2.5-5 mg/kg (diluted 1:1 in sterile saline and given via slow IV q 12 h); and ampicillin, 22 mg/kg IV q 6 h
  - Ultimately based on culture results
- Surgical exploration of abdomen to identify and correct underlying cause of peritonitis if appropriate (e.g., evidence of septic peritonitis; hemorrhage in the absence of systemic bleeding disorder)
  - Thorough lavage of the abdominal cavity
- Consideration of need for postoperative drainage of the abdominal cavity:
  - Specific sites within the abdomen; drain placement:
    - Pancreatic abscess
    - Prostatic abscess
    - Necrotizing cholecystitis
  - Entire abdominal cavity:
    - Open abdominal drainage
    - Closed suction drainage
- Postoperative intensive care with continuous monitoring of animal until peritonitis has resolved

NUTRITION/DIET

- Feeding tue placement if anorexia (seepp. 1267 ,)
- Coax-feeding (see p. 1377)

POSSIBLE COMPLICATIONS

See Peritonitis, Septic, ; Feline Infectious Peritonitis, p. 383; other relevant topics

RECOMMENDED MONITORING

Dependent on cause of peritonitis; see Peritonitis, Septic, ; Sepsis and Septic Shock,p. 1014; Systemic Inflammatory Response Syndrome, ; Multiple Organ Dysfunction Syndrome,p. 732.

PROGNOSIS AND OUTCOME

Variable; dependent on underlying cause

PEARLS & CONSIDERATIONS

TECHNICIAN TIPS

Peritonitis patients (septic) are often in a critical state and require intensive care. Technicians treating and caring for these patients should be familiar with and competent in a number of intensive patient care techniques:

- Fluid and blood component therapy
- Intensive patient monitoring including blood pressure, CBC and serum biochemistry profile, blood gases, urine output
- Nutritional support
- Analgesia

SUGGESTED READING

Bonczynski JJ, Ludwig LL, Barton LJ, et al: Comparison of peritoneal fluid and peripheral blood pH, bicarbonate, glucose, and lactate concentration as a diagnostic tool for septic peritonitis in dogs and cats. Vet Surg 32:161–166, 2003.

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Kirby BM: Peritonitis. In Slatter, editor: Textbook of small animal surgery, ed 3, Philadelphia, 2003, WB Saunders, pp 421–429.

Schmiedt C, Tobias KM, Otto CM: Evaluation of abdominal fluid: peripheral blood creatinine and potassium ratios for diagnosis of uroperitoneum in dogs. J Vet Emerg Crit Care 11(4):275–280, 2001.

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Peritoneopericardial Diaphragmatic Hernia

BASIC INFORMATION

DEFINITION

- Embryologic malformation of the diaphragm, resulting in communication between peritoneal and pericardial cavities and allowing herniation of cranial abdominal organs and omentum into the pericardial space (from most to least common: liver, gallbladder, small intestine, spleen, stomach)
- Can result in vascular compromise or obstruction of herniated organs and (rarely) cardiac tamponade

SYNONYMS

Pericardioperitoneal diaphragmatic hernia, pericardial diaphragmatic hernia, PPDH

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs and cats
- Age at diagnosis highly variable (30% diagnosed at >4 years of age)
- No sex predilection

GENETICS & BREED PREDISPOSITION

- Not known if hereditary but reported in littermates
- Predisposed breeds: weimaraners, cocker spaniels; Persians, Himalayans, domestic longhair cats

RISK FACTORS: Prenatal injury, possibly systemic illness or toxin exposure affecting pregnant dam

ASSOCIATED CONDITIONS & DISORDERS

- Cranioventral abdominal hernias
- Caudal sternal abnormalities (pectus excavatum, malformed or absent sternebrae)
- Ventricular or atrial septal defects, pulmonic stenosis, pericardial cysts
- Polycystic kidney disease in cats

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Often incidental finding with no clinical signs
- Nonspecific signs (lethargy, anorexia, pyrexia, weight loss)
- Respiratory signs (dyspnea, tachypnea, coughing)
- Gastrointestinal (GI) signs (vomiting, diarrhea)
- Rarely, signs of cardiac tamponade and right heart failure (weakness, collapse, ascites)

PHYSICAL EXAM FINDINGS

- May be normal
- Displaced or absent apical cardiac impulse on thorax
- Muffled or displaced heart sounds
- Cardiac murmur if congenital cardiac defect is also present
- Palpable sternal or cranial abdominal defects
- Inability to palpate cranial abdominal organs if herniated into pericardial space
- Borborygmi (GI sounds) over heart

ETIOLOGY AND PATHOPHYSIOLOGY

- Abnormal development of septum transversum (forms ventral portion of the diaphragm) ± pleuroperitoneal folds (form dorsolateral diaphragm), resulting in an hourglass-like shape of the joined peritoneal and pericardial cavities (that should instead be separate body cavities)
- PPDH is always a congenital abnormality, not an acquired one.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Definitive diagnosis can be made on the basis of history, physical exam, and thoracic radiographs alone if characteristic radiographic findings are seen, including heterogeneous radiopacities (gas and/or fat) within an enlarged cardiac silhouette and concurrent loss of distinct diaphragmatic border.

DIFFERENTIAL DIAGNOSIS

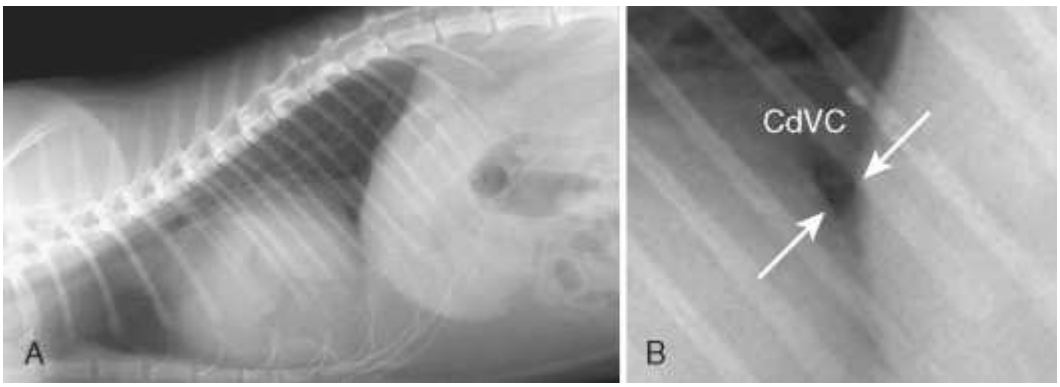
- Other causes of generalized cardiomegaly:
  - Pericardial effusion
  - Congenital or acquired cardiac diseases
- True diaphragmatic hernias do not involve the presence of abdominal viscera in the pericardial space.

INITIAL DATABASE

- CBC and serum biochemistry panel: no characteristic abnormalities
- Thoracic radiographs: o Cardiomegaly
  - Silhouetting of the caudal cardiac border with the diaphragm
  - Discontinuity of the diaphragm
  - Presence of irregular and heterogeneous radiopacities (soft tissue, fat, gas) within cardiac silhouette
  - Dorsal mesothelial remnant on lateral view in cats: curvilinear soft-tissue opacity ventral to caudal vena cava, representing dorsal aspect of hernia
  - Sternal deformities
- Abdominal radiographs:
  - Small or absent liver
  - Cranial displacement or absence of stomach or spleen
  - GI gas pattern extending from abdomen into pericardial space

ADVANCED OR CONFIRMATORY TESTING

- Ultrasound: fat or abdominal organs within the pericardial sac, ± small amount of pericardial effusion and discontinuity of diaphragm
  - Consolidation of the accessory lung lobe can be an extremely misleading impostor for PPDH ultrasonographically; fluid-filled bronchi appear identical to portal veins, and atelectatic lung mimics liver parenchyma. If any uncertainty exists (e.g., clinical features inconsistent with PPDH, such as previously normal thoracic radiographs), a radiologist's evaluation of the thoracic radiographs is strongly recommended.
- Upper GI barium series: may confirm presence of GI segments in pericardial space; often not required for diagnosis
- Positive contrast peritoneography: 2 mL/kg of water-soluble, iodinated radiopaque contrast agent such as iohexol injected aseptically into peritoneal cavity, followed by elevation of the animal's caudal end and thoracic radiography (contrast may flow into pericardial cavity). Often not required for diagnosis; many false negatives (omental/visceral plugging of the hernia).



PERITONEOPERICARDIAL DIAPHRAGMATIC HERNIA A, Lateral radiograph of thorax and cranial abdomen of a cat with

peritoneopericardial diaphragmatic hernia (PPDH). Note cardiomegaly, irregular soft-tissue and fat opacities over the heart, indistinct ventral diaphragm, and small liver. **B**, Magnified view of **A**, showing dorsal mesothelial remnant *(between the arrows),* which is characteristic of PPDH. *CdVC,* Caudal vena cava.

(Courtesy Dr. Stephanie Nykamp.)

TREATMENT

TREATMENT OVERVIEW

Surgical correction is generally indicated to eliminate clinical signs and prevent vascular compromise or obstruction of organs.

ACUTE GENERAL TREATMENT

- Oxygen supplementation if the patient is dyspneic
- Surgical correction via laparotomy: return of all abdominal organs to correct location and closure of the diaphragmatic defect
- Assessment of liver function prior to general anesthesia in order to choose anesthetic protocol accordingly
- It may be appropriate not to pursue surgical repair in some cases (e.g., geriatric animal without clinical signs, small incidentally discovered PPDH).

POSSIBLE COMPLICATIONS

- If the PPDH is left uncorrected, the risk of hepatic or splenic incarceration, bowel obstruction, or (rarely) cardiac tamponade, and right heart failure persists.
- Surgical complications: difficulty ventilating, hypotension, reexpansion pulmonary edema

PROGNOSIS AND OUTCOME

- Excellent prognosis with surgical correction
- Left with an uncorrected PPDH, the patient may remain free of clinical signs, but there is always a risk of complications as listed above.

PEARLS & CONSIDERATIONS

COMMENTS

- PPDH is the most common congenital pericardial disorder in dogs and cats.
- PPDH is a congenital defect (failure of complete separation of the pericardial and abdominal cavities) in contrast to a true diaphragmatic hernia, which is almost always acquired as a result of trauma.
- PPDH is an important rule-out for cardiomegaly and in young animals with cranial abdominal or sternal defects.

SUGGESTED READING

Fossum TW: Surgery of the lower respiratory system: pleural cavity and diaphragm. In Fossum TW, editor: Small animal surgery, ed 3, St Louis, 2007, Mosby Elsevier, pp 896–929.

Reimer SB, Kyles AE, Filipowicz DE, et al: Long-term outcome of cats treated conservatively or surgically for peritoneopericardial diaphragmatic hernia: 66 cases (1987-2002). J Am Vet Med Assoc 224:728, 2004.

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Perirenal Pseudocysts

BASIC INFORMATION

DEFINITION

Collection of fluid (usually transudate, but sometimes urine) between the renal capsule and kidney that is rare in cats and extremely rare in dogs. Pseudocysts may be unilateral or bilateral.

SYNONYMS

Perinephric pseudocyst, capsulogenic renal cyst, capsular cyst, pararenal pseudocyst, capsular hydronephrosis, pseudohydronephrosis

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Rare in cats, extremely rare in dogs
- Older cats; some reports have shown male cats to be overrepresented.

RISK FACTORS

- Chronic kidney disease (transudative pseudocysts)
- Trauma, obstruction, neoplasia of renal pelvis or ureter, causing urine leakage (uriniferous pseudocysts)

ASSOCIATED CONDITIONS & DISORDERS

- Chronic kidney disease
- Urinary tract infection

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Usually abdominal enlargement/abdominal mass (noted by owner or incidental finding during exam)
- Less frequently: weight loss, vomiting, anorexia, polyuria, and polydipsia

PHYSICAL EXAM FINDINGS: Palpable abdominal mass (renomegaly; common but depends on size of cyst) ± thin body condition

ETIOLOGY AND PATHOPHYSIOLOGY

- Incompletely understood pathophysiology
- Lack of epithelial lining in fibrous sacs means that these are not true cysts.
- Renal interstitial fibrosis may impair venous and lymphatic drainage, causing transudate to escape the renal parenchyma and accumulate under the capsule, forming a transudative pseudocyst.
- Uriniferous pseudocysts may form when damage to the renal parenchyma, pelvis, or ureter allows urine to leak between the renal capsule and renal parenchyma.
- The distinction between transudative and uriniferous pseudocysts may be useful with respect to initial management. Transudative pseudocysts suggest chronic kidney disease (International Renal Interest Society [IRIS] stage 2-4, consider appropriate treatment), whereas uriniferous pseudocysts suggest physical disruption of the integrity of the kidney or proximal ureter (identify and correct source of leakage).

DIAGNOSIS

DIAGNOSTIC OVERVEIW

Ultrasonographic identification of hypoechoic fluid between the renal capsule and parenchyma strongly supports the diagnosis but does not usually identify a cause.

DIFFERENTIAL DIAGNOSIS

For enlarged kidneys: perinephric abscess, renal lymphoma or other neoplasia, ureteral obstruction with hydronephrosis, feline infectious peritonitis, hematoma, polycystic kidney disease, and compensatory hypertrophy (Note: abscess, other neoplasia, ureteral obstruction, hematoma, and compensatory hypertrophy: more commonly unilateral than bilateral)

INITIAL DATABASE

- CBC: possibly nonregenerative anemia of chronic kidney disease
- Serum biochemistry profile: usually evidence of mild to moderate renal failure (e.g., azotemia, hyperphosphatemia)
- Urinalysis: isosthenuric or minimally concentrated urine specific gravity
- Urine culture: often positive even in the absence of pyuria
- Abdominal radiographs: unilateral or bilateral renomegaly

ADVANCED OR CONFIRMATORY TESTING

- Abdominal ultrasound: method of choice to confirm diagnosis. Transudative and uriniferous pseudocysts are characterized by an accumulation of completely anechoic fluid between renal parenchyma and capsule. Septations, particulate matter in the perirenal fluid, and other variations suggest a diagnosis other than perirenal pseudocysts.
- Excretory urography if ultrasound unavailable. Decreased renal function may result in poor contrast study. Small risk of contrast-induced renal failure.
- If the diagnosis remains in question after ultrasound, aspiration of anechoic/hypoechoic region for cytologic analysis can differentiate pseudocyst from perinephric abscess, hematoma, or lymphoma.
- Concentration of creatinine will be higher in fluid from uriniferous pseudocysts than concurrent serum creatinine concentration.

TREATMENT

TREATMENT OVERVIEW

Transudative pseudocysts may be managed conservatively, with the goal of preventing renal and ureteral compression. Uriniferous pseudocysts may require surgical intervention.

ACUTE GENERAL TREATMENT

- If transudative pseudocyst, percutaneous drainage or surgical intervention
- If uriniferous, identify (i.e., via excretory urography) and correct source of urine leakage.

CHRONIC TREATMENT

- Repeated percutaneous drainage of transudative pseudocysts
- Surgical resection of pseudocyst ± omentopexy
- Treat existing bacterial cystitis, if present (see p. 276).
- With transudative pseudocysts: treat appropriately for chronic kidney disease (see pp. 205 and <207).
- With uriniferous pseudocysts: surgical intervention
- Nephrectomy should be avoided if possible when renal function is compromised. May become necessary if persistent ascites develops after surgical resection of pseudocyst or if there is reason to believe neoplasia is causative (e.g., thick, irregular capsule on one kidney).

NUTRITION/DIET

For animals with chronic kidney disease, a protein-restricted renal diet is appropriate (see pp. 205 and 207).

POSSIBLE COMPLICATIONS

- Urinary tract infection
- Ascites may be a complication of pseudocyst removal, occasionally necessitating nephrectomy.
- Hydrothorax due to pseudocyst has been reported in a single cat.

RECOMMENDED MONITORING

- Monitor as for chronic kidney disease (see pp. 205 and 207).
- Repeat ultrasound examination periodically after percutaneous drainage or surgical pseudocyst removal. Frequency of repeat ultrasound depends on rapidity of fluid reaccumulation.

PROGNOSIS AND OUTCOME

- Prognosis variable, generally in the range of months to years
- Prognosis better if associated chronic kidney disease is IRIS stage 1 or 2, worse if stage 3 or 4.
- Median survival after surgery (capsulectomy): 9 months, with wide range
- Prognosis apparently worse in cats treated with nephrectomy
- No clear generalization regarding prognosis in transudative versus uriniferous pseudocysts

PEARLS & CONSIDERATIONS

COMMENTS

- The choice between surgical removal of transudative pseudocysts and repeated percutaneous drainage depends on severity of underlying kidney disease, concurrent disease, age of the cat, and cost to owner. Cats with severe azotemia, another disease process that makes them a poor anesthetic/surgical candidate, advanced age, or where cost is an issue may be best managed via repeated percutaneous drainage.
- Nephrectomy may result in worsened azotemia in cats and should be reserved for cats that develop persistent ascites after removal of the pseudocyst. Ideally, renal scintigraphy should precede the decision for nephrectomy to determine contribution of kidney to be removed to total glomerular filtration capacity.

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Periodontal Disease

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Plaque-induced inflammation and infection of the gingiva, periodontal ligament, and alveolar bone

SYNONYMS

Gingivitis (inflammation of gingiva), gum disease, periodontitis (inflammation of the periodontium, which includes gingiva, alveolar bone, periodontal ligament, and cementum)

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Most common disease in companion animals; affects all breeds
- Tends to be more common and severe in toy and small-breed dogs
- Occurs in dogs and cats of any age, although the condition is more severe with increasing age

GENETICS & BREED PREDISPOSITION: Toy and small breed dogs are particularly prone to severe alveolar bone loss (relatively large teeth compared to small size of jaws, causing crowding of teeth).

RISK FACTORS: Soft-food diets; lack of dietary abrasion permits rapid accumulation of plaque and calculus.

CONTAGION & ZOONOSIS: Periodontal disease is an infectious disease; however, all clinically normal animals carry the putative causative organisms in their mouths. There is no evidence of dog/cat-to-dog/cat or dog/cat-to-human spread.

GEOGRAPHY AND SEASONALITY: Dogs and cats in less developed parts of the world are less prone to develop severe periodontal disease, because they have a more varied diet that encourages natural chewing activity.

ASSOCIATED CONDITIONS & DISORDERS: Coexists with many other oral conditions and may mask appearance of diseases with a worse prognosis, such as oral neoplasms. Found in almost every animal with stomatitis (see p. 1428). Masks and is masked by gingival hyperplasia.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Severity of inflammation varies relative to extent of plaque and calculus accumulation and to local and general immunologic health. Maxillary fourth premolar and first molar teeth are often the most severely affected teeth.

HISTORY, CHIEF COMPLAINT: Halitosis, teeth stained by calculus; gingiva may be swollen, bleeding, or ulcerated.

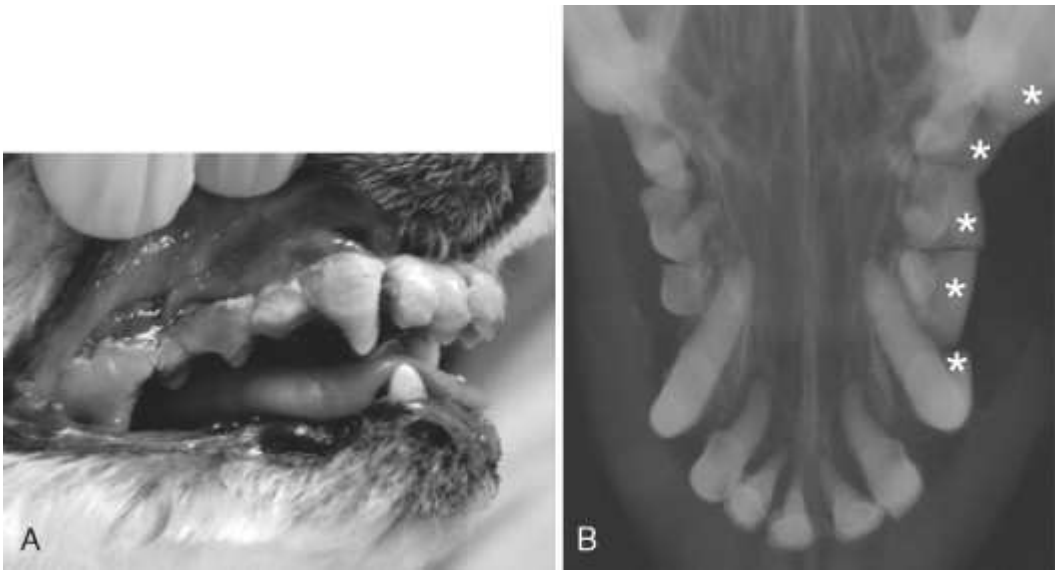
PHYSICAL EXAM FINDINGS: There is often a wide variation in the severity of the disease, which may be apparent when comparing one part of the mouth with another in the same animal.

- Halitosis, plaque, and calculus formation
- Gingivitis, gingival bleeding (on probing or spontaneous), gingival recession (root exposure)
- Involvement of furcation (space between roots of multirooted teeth), periodontal pocket formation
- Horizontal or vertical alveolar bone loss on radiographs
- Perio-endodontic disease on radiographs (extension of periodontal disease to the apical periodontium and pulp involvement)
- Mobile, displaced, and missing teeth
- Pathologic jaw fracture

ETIOLOGY AND PATHOPHYSIOLOGY

- Caused by bacteria in dental plaque at the gingival margin (primarily gramnegative anaerobic rods and spirochetes); exacerbated by accumulation of calculus on the surface of teeth
- Gingival inflammation leads to destruction of the periodontal ligament and resorption of adjacent alveolar bone, causing gradual loss of attachment of the tooth to the jaw.
- Gingiva may recede in step with worsening bone loss, or remain in place with a deepening pocket between the gingiva and

root as bone loss worsens.
- Local disease resolves once the teeth are no longer present (but no regrowth of lost alveolar bone).



PERIODONTAL DISEASE A, Clinical photograph of a dog with severe periodontal disease; note generalized extensive plaque and calculus accumulation. **B**, Radiograph of upper jaw in same patient (labial mounting: rostral is at bottom of image, patient's left is on right of image). Note extensive calculus accumulation *(asterisks)* at the left maxillary teeth (calculus had already been grossly removed on the contralateral side) and generalized alveolar bone loss (particularly visible in the incisor region).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Physical examination of the awake patient provides an initial diagnosis. Full extent of the disease becomes apparent when radiographs are taken and/or on periodontal probing.

DIFFERENTIAL DIAGNOSIS

- Any other oral disease; periodontal disease is almost always present when other oral diseases are present.
- Oral tumors (see pp. 786 and 788) may appear as ulcerated gingival lesions, but unlike tumors, periodontal disease is typically symmetric, and teeth with greater amounts of plaque and calculus deposition are more severely affected.
- Familial gingival hyperplasia of bulldogs, boxers, collies, and some other medium-large dogs; gingiva is firm and symmetric, often irregular in surface contour and may partly or completely cover the tooth crowns. Usually not inflamed or ulcerated (except where extent of overgrowth results in physical injury of gingiva during chewing).
- The abnormalities in periodontal disease are limited to gingiva and alveolar bone in almost all cases; exceptions are considered to be stomatitis cases (see p. 1051). If there is doubt about whether a case is stomatitis or simply a severe case of periodontal disease, a practical approach is to anesthetize the patient, extract severely affected teeth, scale and polish the remaining teeth, and reexamine the animal in 2-3 weeks. If inflammation or ulceration returns, the case is considered to be a stomatitis case.

INITIAL DATABASE

- Awake oral examination. Is the extent of periodontal disease appropriate for the age and diet of the animal? If the extent of inflammation is more severe than would be expected, distant organ or immune disease may be exacerbating the periodontal disease.
- A general physical examination and CBC, serum chemistry profile, and urinalysis are warranted to ensure that the animal is sufficiently healthy to undergo general anesthesia and to rule out distant organ disease (renal, hepatic) that may be exacerbating the oral disease.

ADVANCED OR CONFIRMATORY TESTING

While the animal is under anesthesia, a detailed oral examination is indicated:

- Visual examination of location, color, and swelling of gingiva
- Gentle insertion of a periodontal probe between the gingiva and crown or exposed root to assess the periodontal pocket depth (distance between gingival margin and bottom of pocket normally no more than 3 mm in a dog and 0.5 mm in a cat) and attachment loss (distance between cementoenamel junction and bottom of pocket). Note: Because of gingival recession occurring as part of periodontal tissue loss, the measured pocket depth may substantially underestimate the quantity of attachment loss.
- Pressure against the side of the tooth determines mobility (assessed on a 0 to 3 [least to most] mobility index)
- Dental radiographs are indicated to ensure that remaining bone is healthy, especially when advanced therapy of severely involved teeth is under consideration.

TREATMENT

TREATMENT OVERVIEW

- Removal of the cause: accumulated dental plaque and calculus
- For severely affected teeth: diagnosis and triage of the extent of disease followed by addressing abnormalities of surrounding bone to stabilize the tooth (if owner is willing to provide long-term home oral hygiene following treatment) or extract the tooth
- Prevention of subsequent accumulation of dental plaque and calculus to avoid progression of periodontal disease around remaining teeth

ACUTE GENERAL TREATMENT

- Scaling and polishing of all teeth, accompanied by examination of every tooth to assess extent of bone loss and gingiva present
- For severely affected but retainable teeth (those with periodontal pockets deeper than 5 to 6 mm and mobility of 1 to 2), many procedures are available. Which procedure is selected depends on whether the gingival cuff around the tooth is intact, whether the furcation is exposed, extent of bone surrounding the root, and experience of and equipment and materials available to the veterinarian. Options include periodontal flaps or gingival grafts to enhance the gingiva around the tooth and various bone augmentation techniques.
- When more than 50% of the root length (in a single-rooted tooth) or more than 60% of any root in a multirooted tooth is no longer attached to the surrounding alveolar bone or mobility is 2, scaling and polishing are unlikely to provide effective removal of calculus attached to root surfaces; involved therapy or extraction is indicated. When mobility index for a tooth is 3, extraction is the only practical treatment.
- The only guaranteed effective treatment for the animal is extraction; dogs and cats manage very well without teeth.

CHRONIC TREATMENT

Home oral hygiene (tooth brushing, oral rinses, appropriate chewing toys and treats, dry food) to prevent further development of periodontal disease

DRUG INTERACTIONS

Gingival hyperplasia can result from long-term phenytoin or cyclosporine therapy.

POSSIBLE COMPLICATIONS

- Traumatic lesions (typically chronic granulomatous areas) of the caudal buccal mucosa or sublingual tissue, resulting from abnormal chewing patterns; the lesions may need to be excised as part of comprehensive periodontal treatment.
- Distant organ disease from periodontitis-related bacteremia or systemic release of inflammatory or bacterial degradation products
- Pathologic mandibular fracture due to extensive bone loss around teeth in toy breed dogs
- Damage to adjacent organs (jaw, eye, tongue) during extraction procedures
- Oronasal fistula (see p. 795)

RECOMMENDED MONITORING

Periodic reexaminations:

- 1 month and 2 to 3 months following involved periodontal surgical procedures to ensure that tissues are responding as expected and that home oral hygiene performed by owner is effective (if not, rescaling of teeth and adjustments in homecare regimen should be considered).
- There is a recommended maximum of 6 months between reexaminations following less involved periodontal surgery, and a

maximum of 1 year between reexaminations following scaling and polishing.

PROGNOSIS AND OUTCOME

- Prevention of periodontal disease by plaque and calculus control is very effective.
- Treatment of severe lesions is more problematic as severity of bone loss around the root increases; it is very difficult to create new bone once resorption has occurred, and a tooth that is unstable (mobile) because of insufficient bone surrounding the root(s) will lose more bone as the pressure from the angled, mobile tooth is concentrated on specific areas of bone. Very mobile teeth should always be extracted.
- If teeth have been lost or are extracted because of severe periodontal disease, the tooth that would normally occlude against the missing tooth will be more at risk of plaque and calculus accumulation than teeth with occluding partners present.

PEARLS & CONSIDERATIONS

COMMENTS

- This is a preventable disease if the patient is started on a home oral hygiene program following eruption of permanent teeth.
- The importance of periodontal disease as an insult to the rest of the body is a topic of research; an association has been proven, and the hypothesized cause and effect relationship are under study.
- Meanwhile, an effective prevention program should be built into every animal's wellness program from a young age.
- Oral examination, including assessment of areas of the mouth most severely affected by periodontal disease (maxillary fourth premolars and first molars), does not take much time. Clinicians should perform this examination whenever an animal is brought for a veterinary appointment for any reason.
- The Veterinary Oral Health Council (VOHC) provides a standard for efficacy of products marketed as controlling plaque and calculus accumulation and awards its seal of acceptance to products that have been shown to meet its standards.

PREVENTION

Home oral hygiene (see p. 1243): owner education about the combination of brushing or rubbing the tooth surfaces, the use of oral health care products, and offering pets nutritionally complete diets formulated to reduce plaque and calculus accumulation.

TECHNICIAN TIPS

Proper tooth brushing can easily be demonstrated to owners and is a vital part of long-term maintenance of oral health.

CLIENT EDUCATION

Clinicians should teach owners about methods of prevention, as described previously.

SUGGESTED READING

Harvey CE: Management of periodontal disease: understanding the options. Vet Clin North Am Small Anim Pract 31:819, 2005.

Holmstrom SE, Frost P, Eisner E: Veterinary dental techniques, ed 3, Philadelphia, 2004, WB Saunders, pp 176–338.

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Perineal Hernia

BASIC INFORMATION

DEFINITION

Weakness and separation of the muscles of the pelvic diaphragm allowing prolapse of tissue/organs

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Primarily dogs; highest incidence in middle-aged and geriatric intact male dogs
- Rare in cats

GENETICS & BREED PREDISPOSITION

- Dogs: reported in many different breeds and mixed breeds
- Cats: possible history of megacolon, feline lower urinary tract signs/disease (FLUTS/D, FUS), or previous perineal surgery

RISK FACTORS

- Older, intact, male, dog
- Any condition that causes tenesmus:
    - Prostatomegaly
    - Constipation

ASSOCIATED CONDITIONS & DISORDERS

- Prostatomegaly
- Constipation

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Tenesmus, constipation
- Unilateral or bilateral perineal swelling lateral to the anus
- Dysuria:
    - Bladder entrapment

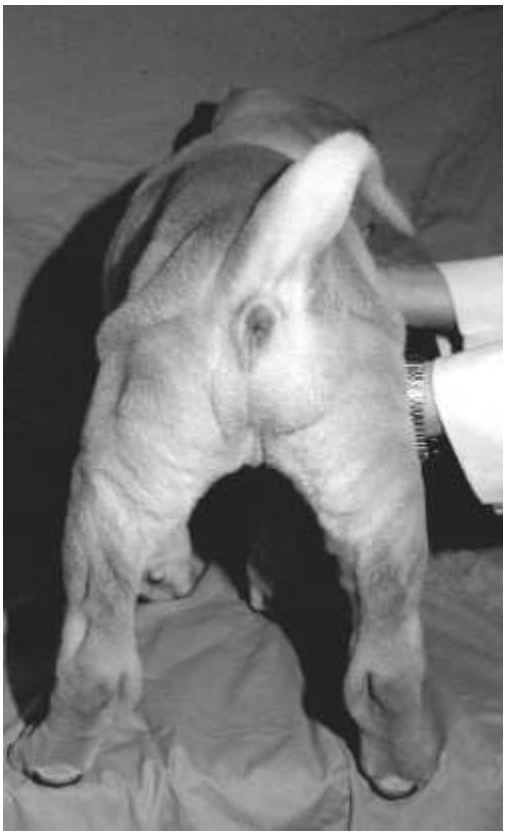
PHYSICAL EXAM FINDINGS

- Unilateral or bilateral swelling in perineal region, lateral and possibly ventral to the anus; may contain:
    - Rectal sacculation packed with feces o Prostate
    - Bladder
    - Fat
- Rectal palpation: diagnostic test of choice
    - Defect or separation in muscles of the pelvic diaphragm on affected side(s)
    - Rectal sacculation

ETIOLOGY AND PATHOPHYSIOLOGY

- Unknown; possible association with:
    - Tenesmus
        - Constipation, obstipation
        - Prostatomegaly
        - Rectal abnormalities
    - Stranguria

- Congenital or acquired weakness of the muscles of the pelvic diaphragm
  - Effect of androgens on muscles
- Neurogenic atrophy of the muscles of the pelvic diaphragm



PERINEAL HERNIA Soft tissue swelling immediately to the right of the anus in a young shar-pei dog; characteristic of a perineal hernia.

(Courtesy Dr. Richard Walshaw.)

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Perineal hernia may be suspected based on history or incidental finding of a subcutaneous perianal protrusion. Confirmation is obtained on rectal palpation.

DIFFERENTIAL DIAGNOSIS

- Colorectal mass
- Pelvic neoplasia
- Prostatic cyst/abscess
- Perianal neoplasia

INITIAL DATABASE

- CBC, serum biochemistry profile, urinalysis:
  - Presurgical screening
  - Bladder entrapped in hernia (postrenal azotemia)
  - Elevated white blood cell count, ± left shift if abscess, cellulitis, strangulation/ischemia of entrapped organs
- External perineal and rectal palpation:
  - Unilateral versus bilateral
  - Contents of hernia:
    - Fecal-filled rectal sacculation
    - Fat

        - Pelvic/abdominal organ (prostate, bladder)
    - Important to rule out neoplasia, prostatic cyst/abscess

ADVANCED OR CONFIRMATORY TESTING

- Survey abdominal and pelvic radiographs:
    - Position and size of bladder and prostate
    - Contents of hernia
- Ultrasound examination:
    - Position and morphology of bladder and prostate:
        - Underlying prostatic disease

TREATMENT

TREATMENT OVERVIEW

Surgical repair of the perineal hernia (perineal herniorrhaphy) is necessary to achieve a good functional outcome. Therapeutic goals are:

- Repositioning of herniated organs
- Reconstructing pelvic diaphragm:
    - Often a bilateral problem requiring bilateral herniorrhaphy:
        - One side often more obvious than other, but on careful palpation, clinician may note weakening of the pelvic diaphragm.
        - The internal obturator flap technique is the recommended surgical procedure for repair of perineal hernia (high success rate, low rate of recurrence).
- Preventing recurrence by resolution of underlying causes of tenesmus:
    - Castration to decrease size of prostate

ACUTE GENERAL TREATMENT

- Emergency treatment to relieve urinary obstruction caused by a retroflexed urinary bladder:
    - Perineal cystocentesis
    - Indwelling catheter
- Relief of constipation:
    - Manual evacuation of rectal sacculation
    - Stool softeners/dietary management

CHRONIC TREATMENT

- Prevention of postoperative tenesmus
    - Dietary management
    - Stool softeners
- Identification of cause of constipation; appropriate treatment
- Identification of cause of prostatomegaly; appropriate treatment
- Cystopexy may be needed to maintain position of bladder in abdomen.

NUTRITION/DIET

Postoperatively:

- Prevent tenesmus, constipation, and diarrhea
- Gastrointestinal diet to produce formed but soft stool
- Stool softener (psyllium mucilloid) as needed for pain-free defecation and no tenesmus

POSSIBLE COMPLICATIONS

- Complications associated with perineal hernia:
    - Urinary obstruction
        - Retroflexed bladder
    - Urinary incontinence or bladder atony
        - Damage to pelvic nerves/detrusor muscle

    - Constipation/obstipation
        - Rectal sacculation
- Complications associated with perineal herniorrhaphy:
    - Recurrence (10%)
    - Incisional dehiscence and infection (6%-26%)
    - Sciatic nerve entrapment (rare)
    - Tenesmus or rectal prolapse
        - Compression of rectal sacculation (8%-13%)

RECOMMENDED MONITORING

History and physical examination findings consistent with recurrence: perineal swelling, tenesmus, and dysuria

PROGNOSIS AND OUTCOME

- Good to excellent outcome with successful herniorrhaphy and no other concurrent diseases
- Fair to poor if the patient cannot undergo surgical correction, if there is recurrence after appropriate surgical correction, and/or if cannot resolve cause of tenesmus/dysuria

PEARLS & CONSIDERATIONS

COMMENTS

- Perineal hernia may be a hormonally related disease in the male dog.
- Herniorrhaphy plus castration is the treatment of choice.
- Diagnosis and elimination of underlying causes of tenesmus are important for a successful outcome.

PREVENTION

- Prevention of tenesmus plays a role in retarding the development or progression of perineal hernia.
- Castration reduces or eliminates the risk of benign prostatomegaly.
- Appropriate diets with increased fiber may help manage constipation.

TECHNICIAN TIPS

Important points regarding postoperative care:

- Maintain appropriate level of analgesia/sedation:
    - Pain control
    - Prevention of tenesmus: undue strain on surgical repair
- Perianal/perineal hygiene:
    - Maintain clean surgical site to decrease risk of wound infection.
    - Especially after defecation
    - Hot pack the area to decrease swelling and ease discomfort.

CLIENT EDUCATION

- Prevention and control of risk factors such as constipation, prostatomegaly, and colitis
- Surgery is the definitive treatment for perineal hernia.

SUGGESTED READING

Szabo S, Wilkens B, Radasch RM: Use of polypropylene mesh in addition to internal obturator transposition: a review of 59 cases (2000-2004). J Am Anim Hosp Assoc May-Jun;43(3):136–142, 2007.

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Pericarditis

BASIC INFORMATION

DEFINITION

Non-neoplastic inflammation of the parietal or visceral pericardium; produces either fibrosis and fusion of the two layers, resulting in pericardial thickening, or adherence to the epicardium, causing constriction or increased intrapericardial fluid formation (effusion) that leads to cardiac tamponade. See also p. 855 and online chapter: Pericarditis, Infectious

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Species: dog ≫ cat
- Idiopathic benign pericarditis is the second most common cause of pericardial effusion in the dog (after hemangiosarcoma).

GENETICS & BREED DISPOSITION: Dogs: golden retriever, German shepherd, Saint Bernard, Great Pyrenees, bull mastiff, Lhasa apso, shih tzu

RISK FACTORS

- Dog: thoracic infections, bacteremia, viral diseases, fungal diseases, trauma, migrating foreign bodies (porcupine quills, foxtail plant awns)
- Cat: FIP virus, *Bartonella* spp. infections, trauma, fungal disease

CONTAGION & ZOONOSIS: FIP transmission cat to cat; systemic mycoses: common-source infection, including zoonoses

ASSOCIATED CONDITIONS & DISORDERS: Idiopathic benign pericarditis: associated with immune complex diseases, chronic inflammatory diseases

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Chronic loss of stamina
- Acute cardiac tamponade
- Recurrent fever
- Development of ascites or pleural effusion

HISTORY, CHIEF COMPLAINT

- Exercise intolerance, weight loss, episodic weakness, lethargy, anorexia, dyspnea, acute collapse, ascites
- Associated with gradual accumulation of pericardial fluid or constriction (restriction) of cardiac filling, leading to tamponade

PHYSICAL EXAM FINDINGS

- Tachycardia, muffled heart sounds, thready/weak pulse, abdominal distension
- In some cases: jugular distension, pulsus paradoxus, positive hepatojugular reflux
- Recurrent fever, pleural effusion

ETIOLOGY AND PATHOPHYSIOLOGY

Idiopathic Benign Pericardial Effusion:

- Unknown etiology
- Generally associated with increasing amounts of sanguineous, inflammatory fluid from damaged blood vessels, lymphatics, mesothelial cells, and microvilli of the serosal layer of the pericardial sac
- The pericardial sac gradually becomes distended.

- When intrapericardial pressures exceed right atrial filling pressures, tamponade develops, which in turn usually produces overt clinical signs.

Infectious Pericarditis:

- Associated with multiple bacterial, fungal, or viral diseases resulting in inflammation, fibrosis, thickening of the pericardium, and epicarditis, with or without accompanying effusion, resulting in either pericardial effusion and tamponade or constrictive pericarditis.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Echocardiography is indispensable, particularly in cases of pericarditis with little or no effusive component to create radiographic changes in size or shape of the cardiac silhouette.

DIFFERENTIAL DIAGNOSIS

Idiopathic Benign Pericardial Effusion:

- Major differential is cardiac hemangiosarcoma
- Other forms of pericardial disease causing effusion

Infectious Pericarditis:

- Major differentials are other forms of pericardial effusion, including idiopathic benign pericardial effusion, hypoalbuminemia, and CHF (especially in the cat).
- Major differentials in the constrictive form are other causes of pleural effusion and ascites. Constrictive pericardial disease is a frequent sequela to idiopathic pleural effusion in the cat.

INITIAL DATABASE

- CBC: may show mild anemia, monocytosis, lymphocytosis, mild neutrophilia
- Serum biochemistry profile: usually unremarkable
- Should screen for immune-mediated disease (antinuclear antibody, rheumatoid factor, Coombs' test, thyroid profile, serum protein electrophoresis)
- Electrocardiogram (ECG): electrical alternans (25% of the time), diminished R-wave amplitudes (50% of the time)
- Thoracic/abdominal radiographs: enlarged globoid cardiac silhouette possible (80% of time), caudal vena caval distension, hepatomegaly, ascites, pleural effusion
- Constrictive pericarditis may not influence the size or shape of the cardiac silhouette.
- Echocardiography: anechoic fluid surrounding heart; may see fibrin tags in fluid, thickened pericardial sac (occasionally), no tumor mass seen

ADVANCED OR CONFIRMATORY TESTING

- Pericardial fluid cytologic examination:
  - Especially to exclude infectious pericardial effusion and lymphoma
  - Cytologic examination alone is highly unreliable: 74% of malignancies are not detected, and 13% of benign cases are wrongly identified as malignant.
- Pericardial fluid pH: controversial. One study indicated pericardial pH = 7.0 as highly indicative of neoplasia and pericardial pH < 7.0 as highly indicative of benign effusion; another study showed no statistical ability to differentiate etiology on basis of pH of pericardial fluid.
- Elevated serum troponin-I concentration is inconsistent with benign disease and rather suggests hemangiosarcoma. This blood test may be performed locally at a human hospital (human assay is accurate in dogs) or may be performed in referral veterinary laboratories.
- Lack of evidence for neoplasia of liver or spleen on abdominal ultrasound
- Contrast CT scan and cardiac MRI: investigational

TREATMENT

TREATMENT OVERVIEW

If pericardial effusion is present echocardiographically, cytologic analysis of the effusion, bacterial culture, fungal serology, and PCR testing when appropriate should be performed prior to considering subtotal (hemi-) pericardectomy. If constrictive pericarditis is present (minimal to no effusion, structurally normal heart, normal vena caval structure without thrombi, and right-sided congestive heart failure all coexisting), medical treatment alone is seldom effective, and subtotal pericardectomy including histopathologic evaluation of excised pericardium should be pursued (elevated risks).

ACUTE GENERAL TREATMENT

- Pericardiocentesis (seep. 1325)
- Diuretics are contraindicated in acute pericardial effusion/cardiac tamponade.
- If an infectious etiology has been ruled out (effusion cytologic examination ± culture): corticosteroids, initially at immunosuppressive doses, taper to antiinflammatory dosage in 2 weeks.
- Treat primary infection when identified.
- Surgical subtotal pericardectomy for constrictive pericarditis when confirmed

CHRONIC TREATMENT

- Repeat pericardiocentesis
- Subtotal pericardectomy with histopathologic examination

POSSIBLE COMPLICATIONS

- Effusive forms may progress to constrictive pericarditis.
- Extension of the disease process to the thorax
- Failure to recognize or resolve systemic disease

RECOMMENDED MONITORING

Follow-up echocardiography 24 hours after initial pericardiocentesis and monthly thereafter

PROGNOSIS AND OUTCOME

Idiopathic Benign Pericardial Effusion:

- Often favorable with initial pericardiocentesis and corticosteroid therapy
- Usually favorable following subtotal pericardectomy

Infective Pericarditis:

- Often poor, especially if evidence of disease beyond the pericardium
- Difficult removal of the pericardium if epicardial adhesions present

PEARLS & CONSIDERATIONS

COMMENTS

- Echocardiography is the cornerstone of diagnosis of pericardial effusion; cytologic analysis of centesed effusion is the determining test for identifying infectious versus noninfectious pericardial disease.
- Subtotal pericardectomy may lead to development of pleural effusion; initially, postsurgical management may require chest drainage/thoracocentesis.
- Following initial pericardiocentesis, monthly follow-up echocardiograms are advised to evaluate resolution of effusion or subsequent visualization of tumor mass not seen on initial evaluation.
- If effusion/tamponade returns following initial pericardiocentesis, subtotal pericardectomy (either by thoracotomy or thoracoscopy [seep. 1340]) can yield results that are superior long term compared to repeated pericardiocentesis.
- Differentiation from mesothelioma may be extremely difficult until late in the course or without pericardial tissue histopathologic examination.
- Serum cardiac troponin-I concentrations are easily assessed at many local human hospitals (human assay is valid in the dog).

- Follow-up echocardiography is important in management of constrictive forms.
- Effusive bacterial forms may benefit from intrapericardial antibiotics.

CLIENT EDUCATION

- Clinicians should inform clients that the condition may spontaneously recur after apparent cure.
- Some animals require long-term steroid therapy, risking complications such as iatrogenic hyperadrenocorticism.

SUGGESTED READING

Edwards NJ: The diagnostic value of pericardial fluid pH determination. J Am Anim Hosp Assoc 32(1):63–67, 1996.

Fine DM, Tobias AH, Jacob KA: Use of pericardial fluid pH to distinguish between idio-pathic and neoplastic effusions. J Vet Intern Med 17(4):525–529, 2003.

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EDITOR: ETIENNE CÔTÉ

Pericarditis, Infectious

BASIC INFORMATION

DEFINITION

Inflammation of the parietal and visceral layers of the pericardium due to infectious agent(s); relatively uncommon condition

SYNONYM

Infective pericarditis

EPIDEMIOLOGY

SPECIES, AGE, SEX

- No reported age or sex predilection
- Dogs: causative etiology has been identified in 2% of cases diagnosed with pericardial effusion.
- Cats: causative etiology has been identified in 14% of cases diagnosed with pericardial effusion.

RISK FACTORS

- Local infection (pleural or pulmonary)
- Penetrating trauma
- Migrating foreign body
- Open wounds
- Bacteremia
- Viral infection

CONTAGION & ZOONOSIS

- Feline infectious peritonitis (FIP), cat to cat
- Tuberculous pericarditis, while uncommon, has been reported (postmortem risk for transmitting the disease from dog to human).
- *Coccidioides immitis* (postmortem risk for transmitting the disease from dog to human)

GEOGRAPHY AND SEASONALITY

- *C. immitis* in the southwestern part of the United States
- Grass awn migration in the western part of the United States

ASSOCIATED CONDITIONS & DISORDERS

- Pericardial effusion
- Effusive-constrictive pericarditis

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Virulence of the infectious agent and rate and magnitude of fluid accumulation determine the clinical signs.

HISTORY, CHIEF COMPLAINT

- Weight loss
- Lethargy, weakness
- Dyspnea
- Ascites
- Fever (inconsistent finding)

PHYSICAL EXAM FINDINGS: Reflective of secondary cardiac tamponade or effusive-constrictive pericarditis:

- Jugular vein distension or pulsation
- Weak arterial pulses
- Muffled heart and lung sounds
- Ballotable abdominal fluid wave
- Pale mucous membranes

ETIOLOGY AND PATHOPHYSIOLOGY

- Reported organisms or diseases:
  - *Actinomyces*
  - *Nocardia*
  - *Mycobacterium*
  - *Pasteurella multocida*
  - *C. immitis*
  - *Acremonium*
  - *Leishmania*
  - Tuberculosis
  - Leptospirosis
  - *Streptococcus canis*
  - *Citrobacter* spp.
  - *Pseudomonas* spp.
  - α-hemolytic streptococci
  - Canine distemper virus
- Mixed bacterial infections are common.
- Pathophysiologic examination reflects secondary cardiac tamponade or effusive-constrictive pericarditis:
  - Effusion becomes extensive, and intrapericardial pressure rises.
  - Intrapericardial pressure exceeds intracardiac diastolic pressures, and filling is impaired.
  - Stroke volume is reduced.
  - Central venous pressure increases, and venous return to the right atrium is impaired.
  - Increased venous pressure leads to pleural effusion and ascites. Therefore, pleural effusion or ascites may be due to increased venous pressure or to concurrent infection in those body cavities (cytologic examination to differentiate).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected in an animal that is systemically ill (i.e., weight loss, lethargy) with pericardial effusion +/− right heart failure (pleural effusion and/or ascites); pericardiocentesis with fluid and cytologic analysis and culture and susceptibility are required for confirmation.

DIFFERENTIAL DIAGNOSIS

- Radiographic:
  - Cardiac enlargement from other types of heart disease
  - Normal variation
- Echocardiographic:
  - Pericardial effusion due to other etiology (i.e., neoplastic, idiopathic)
  - Pleural effusion: many causes (see p. 882)

INITIAL DATABASE

- CBC: ± anemia, ± inflammatory leukogram, ± degenerative left shift
- Serum biochemistry panel: elevated liver enzymes, elevated creatine kinase (CK), decreased albumin
- Thoracic radiographs: mildly to severely enlarged, round cardiac silhouette; caudal vena cava distention; pleural effusion; ± abnormal pulmonary parenchyma if source of infection
- Echocardiogram: pericardial effusion which may be hyperechoic, ± thickened pericardium, fibrin, ± hyperechoic densities within pericardial space
- Electrocardiogram (ECG): changes may be present if effusion is severe: low-voltage complexes, electrical alternans, ST-segment changes.

ADVANCED OR CONFIRMATORY TESTING

- Cytologic analysis of the effusion:
  - Serosanguineous or bloody
  - Modified transudate or exudates
  - Protein content is >2.5 mg/dL; often >3.5 mg/dL
  - Neutrophils and erythrocytes are predominant cell types.
  - Others: macrophages, reactive mesothelial cells, degenerative neutrophils, etiologic agent
- Microbial culture of the effusion:
  - Always do both aerobic and anaerobic cultures.
  - Secondary invaders are common with aerobic cultures.
- Histopathologic examination:
  - Lesions dependent on etiology

TREATMENT

TREATMENT OVERVIEW

Treatment consists of pericardiocentesis if pericardial effusion is causing cardiac tamponade, with the goal of delaying or eliminating recurrent effusion. Antibiotic therapy is ideally based on culture and susceptibility results. Aggressive therapy such as continuous chest drainage may be indicated in chronic cases where pericardiectomy +/− epicardial stripping has been performed.

ACUTE GENERAL TREATMENT

- Pericardiocentesis (see p. 1325) if cardiac tamponade is present
- Thoracocentesis (see p. 1338) if respiratory compromise
- Abdominocentesis (see p. 1193):
  - Usually unnecessary
  - Can be performed if ascites is causing discomfort and/or respiratory compromise

CHRONIC TREATMENT

- Subtotal pericardiectomy:
  - Pericardial window not recommended
  - May require epicardial stripping if pericardium is severely thickened
- Continuous chest drainage after the pericardiectomy
- Aggressive antibiotic therapy based on culture and susceptibility

BEHAVIOR/EXERCISE

- Animals will naturally limit their own activity if pericardial effusion with cardiac tamponade is present. Weakness and/or collapse may be observed.

DRUG INTERACTIONS

Diuretics contraindicated if cardiac tamponade is present:

- Contract intravascular volume
- Reduce venous filling pressure and stroke volume

POSSIBLE COMPLICATIONS

- Infectious effusion can lead to constrictive pericarditis.
- Dyspnea due to pleural effusion or ascites

RECOMMENDED MONITORING

- Follow-up exam and echocardiography 24 hours after the pericardiocentesis or sooner if poor perfusion
- Periodic reassessment for recurrent effusion

PROGNOSIS AND OUTCOME

- If treated aggressively with pericardiectomy, continuous chest drainage, and appropriate antibiotics, prognosis is good in acute phase.
- If the animal is systemically ill and treatment is not aggressive, prognosis is poor.

PEARLS & CONSIDERATIONS

COMMENTS

- Infectious pericarditis is a rare cause of pericardial effusion in dogs and cats.
- A normal cardiac silhouette on radiographs, a negative culture, and the absence of fever may exist in patients with infectious pericarditis.
- Some antibiotics achieve high concentrations well in pericardial fluid.

PREVENTION

- Minimize foreign body exposure.
- Treat local infections, wounds, and bacteremia aggressively.
- Minimize viral exposure.

TECHNICIAN TIPS

If heart sounds are difficult to auscultate, pulses are weak and/or variable, and/or mucous membrane color is pale during status checks, alert the attending veterinarian; pericardial disease could be the cause.

CLIENT EDUCATION

- If this disorder is treated aggressively with pericardiectomy, continuous chest drainage, and appropriate antibiotics, prognosis is good in early stages.
- Prognosis worsens with time and degree of fibrosis (pericardial and epicardial scarring).

SUGGESTED READING

Aronson LR, et al: Infectious pericardial effusion in five dogs. Vet Surg 24:402–407, 1995.

Berg RJ, et al: Pericardial effusion in the dog: a review of 42 cases. J Am Anim Hosp Assoc 20:721–730, 1984.

Calvert CA: Cardiovascular infections. In Greene CE, editor: Infectious diseases of the dog and cat, Philadelphia, 1998, WB Saunders, pp 580–581.

AUTHOR: SARAH J. MILLER

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Pericarditis, Idiopathic Sterile

BASIC INFORMATION

DEFINITION

Non-neoplastic inflammatory pericardial effusion of undetermined etiology; frequently accompanied by thickening of the pericardium, epicardial fibrin formation, and adhesions between the serosal layer of the pericardial sac and the epicardium

SYNONYMS

Benign pericardial effusion, idiopathic sterile pericarditis

EPIDEMIOLOGY

SPECIES, AGE, SEX: Canine, more common in males, middle aged and older

GENETICS & BREED DISPOSITION: Dogs: golden retrievers, German shepherd, St. Bernard, Great Pyrenees, mastiff, Lhasa apso, shih tzu.

RISK FACTORS: Associated with immune complex diseases, chronic inflammatory diseases; idiopathic second most common cause of pericardial effusion in the dog

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Chronic loss of stamina, acute cardiac tamponade

HISTORY, CHIEF COMPLAINT

- Exercise intolerance, episodic weakness, dyspnea, acute collapse, ascites
- Associated with gradual accumulation of pericardial fluid leading to tamponade

PHYSICAL EXAM FINDINGS: Tachycardia, muffled heart sounds, thready pulses, jugular distension, pulsus paradoxus, positive hepatojugular reflux, abdominal distension

ETIOLOGY AND PATHOPHYSIOLOGY

- Unknown etiology, may be several causes
- Generally associated with increasing amounts of sanguineous, inflammatory fluid by damaged blood vessels, lymphatics, mesothelial cells, and microvilli of the serosal layer of the pericardial sac
- Gradually the pericardial sac becomes distended; when intrapericardial pressures exceed right atrial (RA) and RA filling pressures, tamponade develops.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on presenting physical signs and confirmation of pericardial effusion with echocardiography. The definitive confirmation of benign disease can be extremely challenging, as cytologic analysis of fluid is often misleading (both false positives and false negatives for malignancy). Some malignancies, particularly mesothelioma and small hemangiosarcoma masses that bleed vigorously, mimic idiopathic benign pericarditis on echocardiographs: hemorrhagic pericardial effusion with no visible mass. In many cases, idiopathic benign pericarditis is either a histologic diagnosis when recurrent effusion prompts subtotal pericardiectomy, or a presumptive diagnosis (albeit imperfect) based on self-resolution of pericardial effusion after one or two centesis procedures.

DIFFERENTIAL DIAGNOSIS

- Major differential is cardiac hemangiosarcoma

- Other forms of pericardial disease
- Often a diagnosis by exclusion where no specific cause of the effusion can be identified.

INITIAL DATABASE

- CBC: may be mild anemia, monocytosis, lymphocytosis, mild neutrophilia
- Serum chemistry: usually unremarkable
- Should screen for immune-mediated disease (ANA, RF, Coombs, thyroid profile, serum protein electrophoresis)
- Electrocardiography (ECG): electrical alternans (25% of cases), diminished amplitudes (50% of cases)
- Thoracic/abdominal radiographs: enlarged globoid cardiac silhouette, vena caval distension, hepatomegaly, ascites, pleural effusion
- Echocardiography: anechoic fluid surrounding heart; may see fibrin tags in fluid, thickened pericardial sac (occasionally), no tumor mass seen

ADVANCED OR CONFIRMATORY TESTING

- Pericardiocentesis: for cytologic analysis and pH (see and ; difficult differentiation from malignancy)
- Lack of evidence of neoplasia of liver, spleen on abdominal ultrasound
- Lack of evidence of thoracic neoplasia on thoracic ultrasound and radiography

TREATMENT

TREATMENT OVERVIEW

Therapeutic goal is relief of effusion/tamponade.

ACUTE GENERAL TREATMENT

- Pericardiocentesis (see p. 1325): fluid is sanguineous, nonclotting, and may contain small fragments of fibrin.
- Verify complete drainage and resolution of tamponade by echocardiography.
- Corticosteroids, initially at immunosuppressive doses (e.g., prednisone, 2-4 mg/kg PO q 24 h), taper to antiinflammatory dose (1-2 mg/kg PO q 24 h) in 2 weeks.

CHRONIC TREATMENT

- Repeat pericardiocentesis
- Partial pericardial fenestration using balloon technique to allow drainage into pleural space
- Subtotal pericardectomy with histopathologic confirmation of inflammation; preferred procedure if more than two repeat pericardiocentesis procedures required

POSSIBLE COMPLICATIONS

May progress to constrictive pericarditis

RECOMMENDED MONITORING

Follow-up echocardiography 24 hours after initial pericardiocentesis and monthly thereafter

PROGNOSIS AND OUTCOME

- Often favorable with initial pericardiocentesis and corticosteroid therapy
- Usually favorable following subtotal pericardectomy

PEARLS & CONSIDERATIONS

COMMENTS

- Subtotal pericardectomy may lead to development of pleural effusion, pleural thickening, and compartmentalization of lung

lobes
- Initial postsurgical management may require chest drainage.
- Following initial pericardiocentesis, monthly follow-up echocardiograms advised to evaluate resolution of effusion or subsequent visualization of tumor mass not seen on initial evaluation
- If effusion/tamponade returns following initial pericardiocentesis, consider subtotal pericardectomy rather than repeated attempts at pericardiocentesis where surgery is an appropriate option, either by thoracotomy or thoracoscopy.
- Differentiation from mesothelioma maybe extremely difficult until late in the course or without pericardial tissue histopathology, as reactive mesothelial cells are a common cytological finding on fluid analysis.

CLIENT EDUCATION

- May spontaneously recur after apparent cure
- Some patients require long-term steroid therapy, leading to development of iatrogenic hyperadrenocorticism

SUGGESTED READING

Kienle RD: Pericardial disease and cardiac neoplasia. In Kittleson MD, Kienle RD, editors: Small animal cardiovascular medicine, St Louis, 1998, Mosby, pp 413–432.

Sisson D, Thomas WP: Pericardial disease and cardiac tumors. In Fox PR, Sisson D, Moise NS, editors: Textbook of canine and feline cardiology, Philadelphia, 1999, WB Saunders, pp 679–701.

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Pericardial Effusion

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Pathologic accumulation of fluid (blood, plasma, neoplastic cells, pus, chyle, or combinations) in the pericardial space

SYNONYM

Pericardial fluid accumulation

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dependent on underlying cause; dogs: older adults (neoplastic, idiopathic)

GENETICS & BREED PREDISPOSITION

- Dogs: golden retrievers, Labrador retrievers, German shepherds, other large breeds (hemangiosarcoma, mesothelioma); boxers, bulldogs (and other brachycephalics), terriers (chemodectoma)
- Cats: rare predispositions. Asian breeds, feline infectious peritonitis (FIP)

RISK FACTORS

- Dogs: mesothelioma associated with asbestosis; speculative link between lymphoma and exposure to volatile chemicals
- Cats: multicat household, FIP

CONTAGION & ZOONOSIS: Cats: FIP (cat-to-cat only)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Incidental/unexpected finding; no clinical signs caused by pericardial effusion:
  - During echocardiography
  - Cardiomegaly on radiographs
  - Electrocardiogram (ECG) changes: electrical alternans or small QRS complexes
- Cardiac tamponade: pericardial effusion is causing overt signs.

HISTORY, CHIEF COMPLAINT

- Acute collapse, usually without loss of consciousness
- Exercise intolerance/episodic weakness
- Abdominal distension
- General discomfort, with or without dyspnea
- Pale mucous membranes

PHYSICAL EXAM FINDINGS

- Tachycardia
- Soft or muffled heart sounds
- Weak pulse
- Abdominal distension possible
- Dyspnea/attenuated lung sounds possible if pleural effusion

ETIOLOGY AND PATHOPHYSIOLOGY

Etiology:

- Primary:
  - Neoplasia (hemangiosarcoma [dogs], heart base tumors [chemodectoma, ectopic thyroid carcinoma], mesothelioma, lymphoma)
  - Idiopathic pericardial effusion (dogs)
  - Left atrial rupture
- Systemic:
  - Congestive heart failure (effusion volume usually very small)
  - Infectious (FIP [cats], bacterial [very uncommon])
  - Anticoagulant intoxication
  - Uremia

Mechanism:

- Rate and volume of fluid accumulation and pericardial distensibility determine onset of clinical signs.
- When overt signs are present as a result of pericardial effusion, cardiac tamponade exists.
- In general, pericardial effusions caused by systemic processes rarely produce cardiac tamponade (exception: anticoagulant intoxication), whereas pericardial effusions caused by primary lesions within the pericardial space commonly produce cardiac tamponade.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Pericardial effusion is suspected in one of two very different contexts: either as an incidental finding during diagnostic testing (typically small volume, no overt clinical signs of right-sided congestive heart failure) or as the cause of clinical signs of cardiac tamponade. Confirmation requires echocardiography; thoracic radiographs, abdominal sonography, and routine complete blood and urine testing are typically necessary to investigate the underlying cause.

DIFFERENTIAL DIAGNOSIS

- Physical:
  - Hypovolemia
  - Hypotension
  - Causes of ascites (seep. 93)
  - Causes of pleural effusion (see p. 882)
- Radiographic:
  - Cardiac enlargement from heart disease
  - Expiratory radiograph
  - Normal variation
- Echocardiographic:
  - Pleural effusion
  - Oblique views
- Specific causes can be determined by etiology (previously described)

INITIAL DATABASE

- Echocardiogram: confirmation of the diagnosis and investigation for right atrial/ventricular (hemangiosarcoma) or periaortic (heart base) masses. Right ventricular diastolic collapse is highly indicative of severe cardiac tamponade; right atrial collapse is less specific.
- Thoracic radiographs: large cardiac silhouette (80% of cases), globoid cardiac silhouette (60% of cases), caudal vena cava enlargement; metastatic lesions, pleural effusion
- CBC, serum biochemistry panel, and urinalysis are usually unremarkable except with systemic disorders.
- ECG: Electrical alternans is unreliable and only found in 50% of dogs with pericardial effusion.
- Prothrombin time if anticoagulant intoxication is suspected

ADVANCED OR CONFIRMATORY TESTING

- Pericardial effusion cytologic examination: useful for lymphoma, infectious causes; otherwise, malignant versus benign is totally unreliable with Cytologie examination.
- Pericardial effusion pH: generally unreliable, much overlap between benign and malignant
- Transesophageal echocardiography
- Serum cardiac troponin-I level: elevation is suggestive of hemangiosarcoma.

- Effusion vascular endothelial growth factor (VEGF) concentration: nondiagnostic

TREATMENT

TREATMENT OVERVIEW

- Removal of pericardial effusion if causing cardiac tamponade
- Delaying or eliminating recurrent effusion is a long-term goal, including correction of the underlying cause of the effusion if possible.

ACUTE GENERAL TREATMENT

- Pericardiocentesis (see p. 1325): if cardiac tamponade is present; contraindicated if coagulopathy is a cause of effusion, unless there are critical circulatory effects (severe/periterminal tamponade).
- Abdominal drainage is usually unnecessary if ascites is secondary to congestion (resorbs in 24-48 hours).
- Treatment of underlying cause if systemic disorder
- Diuretics contract intravascular volume and therefore are contraindicated in treating cardiac tamponade acutely.

CHRONIC TREATMENT

- Management/resolution of systemic disorder if present
- Recurrent pericardiocentesis if needed
- Pericardiectomy if recurrent effusion occurs secondary to idiopathic pericarditis or heart base mass
- Diuretics are indicated if the animal has congestive heart failure (and secondary pericardial effusion) due to myocardial or valvular heart disease; otherwise, chronic diuretic treatment for delaying recurrence of primary pericardial effusion is controversial.

POSSIBLE COMPLICATIONS

- Recurrent effusion; follow-up echocardiography to assess need for recentesis ± pericardiectomy
- Dyspnea from severe pleural effusion or ascites
- Pericardiocentesis-related (seep. 1325)

RECOMMENDED MONITORING

- Follow-up exam and echocardiography 24 hours after the pericardiocentesis (sooner if poor perfusión): assessment for recurrent effusion
- Follow-up exam and echocardiography 2-4 weeks after the pericardiocentesis
- Serial echocardiography and thoracic radiographs as dictated by recurrence

PROGNOSIS AND OUTCOME

- Guarded (average: days to months) with hemangiosarcoma; worse if a mass is seen on the right atrium or if pulmonary metastases exist, but better if nonhemorrhagic ascites is present
- Guarded to fair with heart base tumors, better if pericardiectomy
- Guarded to fair with mesothelioma (months to a year or more)
- Guarded to fair with idiopathic (risk of constrictive pericarditis or of mesothelioma)
- Hemorrhagic effusion that recurs in hours to 1 to 2 days after the pericardiocentesis is rarely benign; prognosis is worse.

PEARLS & CONSIDERATIONS

COMMENTS

- Grossly malignant pericardial effusions and benign pericardial effusions can both appear equally hemorrhagic.
- Normal-looking heart on radiographs does not rule out pericardial effusion.
- If a weak pulse, tachycardia, and muffled heart sounds are all present, pericardial effusion is possible, and an echocardiogram is warranted.

CLIENT EDUCATION

- Clients need to monitor for recurrence of presenting signs as described previously.
- Rapid deterioration is possible; re-checks are necessary.

SUGGESTED READING

Dunning D, et al: Analysis of prognostic indicators for dogs with pericardial effusion: 46 cases (1985-1996). J Am Vet Med Assoc 212:1276–1280, 1998.

Rush JE, et al: Pericardial disease in the cat: a retrospective evaluation of 66 cases. J Am Anim Hosp Assoc 26:39–46, 1990.

AUTHOR & EDITOR: ETIENNE CÔTÉ

Perianal Fistula

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

A chronic inflammatory disease of the tissues surrounding the anus in the dog. The lesions are painful, ulcerative, with sometimes deep, draining tracts adjacent to the anus. The anus itself is not usually involved.

SYNONYM

Anal furunculosis

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs, usually >5 years old; males may be overrepresented.

GENETICS & BREED PREDISPOSITION: German shepherds are by far the most common breed affected. Irish setters may be predisposed. Any breed may be affected.

RISK FACTORS: Possibly broad-based tail, low tail carriage, and increased density of apocrine sweat glands in the perianal region

ASSOCIATED CONDITIONS & DISORDERS: Food allergy has been theorized to be a causative or associated condition resulting in inflammation of the colon or pruritus of the perineum.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Initially the owners may notice a foul odor or observe the dog licking the perianal region excessively. As the lesions progress, the dog may have dyschezia, hematochezia, tenesmus, and fecal incontinence; the dog may engage in self-mutilation. In the severe cases, inappetence, lethargy, and weight loss are also possible.

PHYSICAL EXAM FINDINGS

- In mild to moderate cases, physical examination abnormalities are confined to the perianal region. In more severe cases, the dog may also be in poor body condition. Examination of the perianal region may be very difficult in some patients due to pain, and sedation is often necessary. Visual and digital rectal exams are indicated.
- Visually, the lesions appear as multiple ulcerated, draining tracts that may be superficial or extend deeply into the perianal tissues. The lesions may extend 360° around the anus and involve the ventrum of the tail base.
- Upon rectal palpation, rectal strictures, loss of anal tone, anal sac rupture or abscessation, and/or roughened rectal mucosa may also be found.

ETIOLOGY AND PATHOPHYSIOLOGY

- An immunologic basis is suspected based on clinical improvement with immunosuppressive medications, as well as a few pathologic studies identifying sterile chronic inflammatory changes.
- Secondary bacterial infection is common, often due to fecal microflora or skin contaminants.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

In general, a diagnosis can be made with history and physical examination, including visual examination of the perianal region.

DIFFERENTIAL DIAGNOSIS

- Perianal neoplasia (anal sac adenocarcinoma)
- Anal sac abscessation/rupture
- Trauma, bite wounds

- Perianal hernia (early phase of fistula, prior to ulcerated lesions)

INITIAL DATABASE

- CBC, serum chemistry panel, and urinalysis are often unremarkable; may occasionally have a mature neutrophilia.
- Abdominal radiographs may show evidence of constipation.

ADVANCED OR CONFIRMATORY TESTING

- Colonoscopy may reveal inflammatory colitis (usually lymphoplasmacytic), rectal strictures.
    - Occasionally, rectal balloon dilation or surgery may be needed if the stricture is severe.

TREATMENT

TREATMENT OVERVIEW

Goals of treatment include reducing the size and number of strictures (often to the point of no visible lesions), control of infection, and treatment of colitis if present or rectal stricture if present.

ACUTE GENERAL TREATMENT

- Under sedation or general anesthesia, the hair in the area should be clipped, feces and debris removed, and surrounding tissues cleansed.
- Enemas may be needed if constipation is present.
- Antibiotics (cephalexin, 22 mg/kg PO q 8-12 h for at least 2 weeks) can be helpful to treat secondary infections.

CHRONIC TREATMENT

- Immunosuppression is the initial therapy of choice. Cyclosporine results in a reported 90% success rate. This can be expensive in larger dogs. Starting dose using the emulsion form (Atopica, Neoral, cyclosporine modified generic) is 3-5 mg/kg PO q 12 h for 16 weeks. Ideally, whole-blood trough cyclosporine levels should be run and maintained at 400-600 ng/mL. Adding ketoconazole at 10 mg/kg PO q 24 h allows a reduction in cyclosporine dose to 1 mg/kg PO q 12 h, while achieving similar cyclosporine levels.
- Azathioprine 2 mg/kg PO q 24 h for 2-4 weeks, then tapered, may be an effective alternative in some dogs.
- Prednisone alone may be effective in about 33% of dogs. A starting dose of 2 mg/kg PO q 24 h for 2-4 weeks followed by a taper is recommended. The dose should be tapered to 0.5 mg/kg q 48 h.
- Tacrolimus 0.1% topical applied q 12-24 h resulted in resolution of lesions in 50% of dogs with mild to moderate lesions.
- Stool softeners such as lactulose at 0.25-0.5 mL/kg PO q 12 h are indicated to prevent constipation, assist defecation if strictures are present, and keep stool soft when defecation is painful.
- If appropriate medical management does not resolve the lesions to an acceptable degree, surgery can be considered. Nd: YAG laser and cryotherapy as well as en bloc resection have been reported with variable success rates. Surgical procedures that may be needed include anal sacculectomy, removal of skin overlying the tracts, débridement of diseased tissue, and rectal pull-through for rectal strictures.
- Balloon dilation is recommended as first line of therapy for rectal strictures, because surgical removal of strictures may result in fecal incontinence.

NUTRITION/DIET

Dietary therapy has been used in conjunction with immunosuppression. Novel antigen diets have been recommended because there is a suspected association with food hypersensitivity. Most important, animals should avoid high-fiber (bulking) foods/diets, and owners should feed highly digestible diets that will result in a softer, smaller stool (low-residue diets).

DRUG INTERACTIONS

Ketoconazole decreases metabolism of cyclosporine and can be given for this purpose.

POSSIBLE COMPLICATIONS

- Recurrence of fistulae with discontinuation of immunosuppressive drugs
- Rectal strictures secondary to chronic inflammation
- Constipation secondary to pain or rectal strictures
- Fecal incontinence secondary to chronicity or surgery

RECOMMENDED MONITORING

- Follow-up examinations of the perianal region every 2 weeks until healed, then periodically thereafter to check for recurrence
- Whole-blood trough cyclosporine levels at 2 weeks, then monthly
- CBC when azathioprine is being used

PROGNOSIS AND OUTCOME

- Fair to good prognosis with early treatment
- Long-term prognosis may be guarded with more severe lesions and the need for indefinite medical therapy.

PEARLS & CONSIDERATIONS

COMMENTS

- Improvement on cyclosporine will usually be seen within 4 weeks. If the signs recur once the drug is discontinued, long-term therapy may be needed, with the lowest effective dose determined with a taper.
- Most dogs will respond to medical management but may also require long-term therapy to maintain remission.

PREVENTION

- Recurrent cases may need long-term medications or novel protein diet to prevent recurrences.
- Keeping lesions under control with immunosuppressive medications and diet can help prevent infections, rectal strictures, and constipation.

TECHNICIAN TIPS

These lesions may be painful, and a gentle approach to any manipulation of the anal region (e.g., rectal temperature) is important.

CLIENT EDUCATION

Advise clients on the clinical signs and lesions that warrant early intervention if lesions recur.

SUGGESTED READING

House AK, Guitian J, Gregory SP, et al: Evaluation of the effect of two dose rates of cyclosporine on the severity of perianal fistulae lesions and associated clinical signs in dogs. Vet Surg 35:543–549, 2006.

Lombardi RL, Marino DJ: Long-term evaluation of canine perianal fistula disease treated with exclusion fish and potato diet and surgical excision. J Am Anim Hosp Assoc 44:302–307, 2008.

Paricelli AJ, Hardie RJ, McAnulty JF: Cyclosporine and ketoconazole for the treatment of perianal fistulas in dogs. J Am Vet Med Assoc. 220:1009–1016, 2002.

AUTHOR: LISA MOORE

EDITOR: DEBRA L. ZORAN

Pemphigus Complex

Additional Images Available on Website

BASIC INFORMATION

DEFINITION

A group of autoimmune blistering diseases of the skin and/or mucous membranes characterized by keratinocyte acantholysis (separation from cell-cell detachment), producing varying degrees and depth of cutaneous ulceration, pustules, vesicles, and crusting. Subsets of pemphigus are classified based on the level of blistering in the epidermis. Spontaneous, drug-induced, and paraneoplastic forms are reported. The most common type in dogs and cats is pemphigus foliaceus.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Seen in dogs and cats; more common in middle-aged animals (average age of onset is 5 to 6 years, with a range of 0.5-16 years).

GENETICS & BREED PREDISPOSITION

- Pemphigus foliaceus (PF): Akita, Australian shepherd, chow chow, cocker spaniel, dachshund, Doberman pinscher, Finnish spitz, schipperke (drug-induced PF in Doberman pinscher and Labrador retriever)
- Pemphigus erythematosus (PE): collie and German shepherd
- Canine benign familial chronic pemphigus has been reported in English setters and their crosses and appears inherited (autosomal dominant)

RISK FACTORS: PF and PE may be aggravated by sunlight. Some cases of pemphigus are triggered by drug reactions. Paraneoplastic pemphigus (PNP) in dogs has been associated with underlying lymphoma, thymoma, and (in one case) Sertoli-cell tumor.

GEOGRAPHY AND SEASONALITY: A lower incidence of canine PF exists in the northeastern United States, and a higher prevalence exists in warmer regions. Seasonal exacerbation of lesions may occur during months of increased sunlight exposure.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Subsets of pemphigus are described and listed in decreasing order of frequency:

- Superficial pemphigus complex: PF, PE (a possible local and milder variant of PF), panepidermal pustular pemphigus (PPP; possibly a more extensive subtype of PF).
- Deep variants: pemphigus vulgaris (PV), pemphigus vegetans (PVg), and PNP. A few cases of benign familial pemphigus have also been reported in dogs.

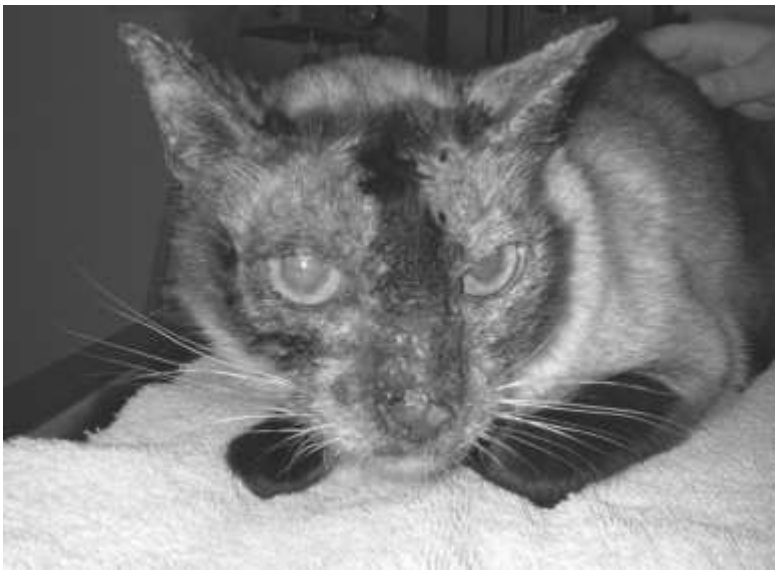
HISTORY, CHIEF COMPLAINT

- PF: progressive multifocal or generalized skin disease, often with facial and footpad involvement. Degree of pain appears to be variable. Pruritus is noted in 30%-50% of the cases. The initial complaint can be lameness due to footpad disease.
- With PV and PNP, disease of the oral cavity is common, and presenting signs include hypersalivation, halitosis, anorexia, and weight loss.
- Fever, anorexia, lethargy, and limb edema are reported in severe cases of pemphigus.

PHYSICAL EXAM FINDINGS

- **PF:** a pustular and crusting dermatitis, with crusts on the trunk and/or the facial area being the most common lesion. Inner pinnae and dorsal muzzle are often the first areas affected, and the disease can stay restricted to the head and face. Other commonly involved areas are the feet, footpads, and nail beds (nail beds are affected more often in cats; it is sometimes the only physical exam abnormality). The disease progresses and becomes generalized or multifocal in most cases. Range of lesions noted includes erythema, pustules, dry honey-colored crusts, scales, alopecia, and erosions bordered by collarettes. Secondary bacterial pyoderma (a third of PF cases) and peripheral lymphadenopathy are common.
- **PE:** a milder form of PF with crusts, erosions, alopecia, and scales restricted to the face
- **PV:** a deep and severe form of pemphigus, presenting with transient flaccid vesicles rapidly replaced by large erosions and ulcers of the mucosal surfaces and mucocutaneous junctions. Affected areas include oral cavity (>70% of cases), inner pinnae, nasal planum, lip margins, genitalia, and anus. Erosions of the nail beds are reported in 14% of cases. A milder form

of PV is reported where lesions are restricted to one body area (nail beds, nasal planum, oral cavity).
- **PVg and PPP:** Severe erosions and ulcerations of the oral cavity, nose, vulva, and haired skin



PEMPHIGUS COMPLEX A 5-year-old male castrated Siamese cat with pemphigus foliaceus affecting the face and pinnae.

(Courtesy Dr. Caroline de Jaham.)

ETIOLOGY AND PATHOPHYSIOLOGY

- Intraepithelial acantholysis (loss of intercellular cohesion between keratinocytes) leading to vesicles/pustules formation due to antikeratinocyte autoantibodies (IgG) binding to components of desmosome complex.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis of PF, the most common form of pemphigus, is suspected in a middle-aged dog or cat presented for evaluation of a progressive crusting and pustular dermatitis that does not typically respond to appropriate systemic antibiotic therapy. The definitive diagnosis requires skin biopsies showing histopathologic changes of acantholysis.

DIFFERENTIAL DIAGNOSIS

- **PF, PE, and PNP:** bacterial folliculitis, demodicosis, dermatophytosis, eosinophilic folliculitis and furunculosis, cornification disorders, cutaneous (discoid) and systemic lupus erythematosus, drug eruptions
- **PV and PPP:** bullous pemphigoid, epidermolysis bullosa acquisita, erythema multiforme, toxic epidermal necrolysis, Stevens-Johnson syndrome, epitheliotropic lymphoma, ulcerative stomatitis, vesicular cutaneous lupus erythematosus, systemic lupus erythematosus.

INITIAL DATABASE

- Cytologic examination of content of intact pustules or of exudate under a crust may strongly suggest pemphigus: intact neutrophils, varying number of eosinophils, and clusters of acantholytic keratinocytes can be seen in most cases, but biopsies are still required because other disorders may present similar findings.
- CBC, serum biochemistry profile: nonspecific changes, mild to moderate leukocytosis with neutrophilia, mild nonregenerative anemia, and hypoalbuminemia

ADVANCED OR CONFIRMATORY TESTING

- Skin biopsies: confirmatory test. Histopathologic findings of acantholysis with pustule formation are diagnostic. Lesional epidermal location is related to depth of autoantibody deposition: subcorneal and intragranular layers in PF and PE; suprabasilar level in PV and PPP; panepithelial in PNP.
- Immunohistochemical and immuno-fluorescent analysis of skin biopsies or serum may be helpful but depends on the

sensitivity of the methods being used; not routinely performed.

TREATMENT

TREATMENT OVERVIEW

The treatment goal is to implement immunosuppressive therapy that will induce and maintain remission of skin lesions without significant or life quality-altering side effects. The therapeutic modalities and response to treatment will vary with the type of pemphigus and the species treated. Cases refractory to initial systemic glucocorticoids should be referred to a dermatologist.

ACUTE TREATMENT

Systemic glucocorticoids alone induce remission in most cases of PE and in a third to half of cases of PF in dogs and in most cats. Other forms of pemphigus are more refractory. Response should be seen within 10-14 days.

- Dogs (initially):
  - Prednisone/prednisolone: 2-4 mg/kg PO q 24 h; *or*
  - Dexamethasone: 0.2-0.4 mg/kg PO q 24 h for more refractory cases
- Cats (initially):
  - Prednisone/prednisolone: 4-8 mg/kg PO q 24 h (prednisolone is preferred in cats); *or*
  - Dexamethasone: 0.2-0.4 mg/kg PO q 24 h; *or*
  - Triamcinolone: 1-2 mg/kg PO q 24 h
- High (shock) dosages of glucocorticoid used in the acute phase in severe cases of PF or PV. Prednisolone sodium succinate, 10 mg/kg IV over 4 hours; or prednisone, 10 mg/kg PO given 1-3 days consecutively. Potential side effects such as gastrointestinal ulceration are increased.

CHRONIC TREATMENT

- The dose of glucocorticoid is slowly reduced on a daily basis over 30-40 days once remission of active skin lesions is attained (2-4 weeks). Lowering to an alternate-day regimen with an ideal maintenance dose of 1 mg/kg q 48 h of prednisone/prednisolone or less is the ultimate goal.
- Concurrent immunosuppressive drugs are used initially in conjunction or added later to glucocorticoids to enhance or maintain adequate immune suppression to induce or maintain remission with fewest/no glucocorticoid adverse effects.
  - Azathioprine: 2.2 mg/kg PO q 24-48 h in conjunction with prednisone/prednisolone; first choice in dogs, contraindicated in cats; *or*
  - Chlorambucil: 0.1-0.2 mg/kg PO q 24-48 h in conjunction with prednisone/prednisolone; first choice in cats; *or*
  - Cyclosporine: 5-10 mg/kg PO q 24 h has shown good effectiveness with prednisone/prednisolone for PF in dogs and cats.
- Alternative immunosuppressive drugs:
  - Tetracycline and niacinamide: milder or localized cases of PF and PE (250 mg of each PO q 8 h for dogs <10 kg; 500 mg of each PO q 8 h for dogs >10 kg) for 2-3 months to achieve remission then gradually decrease to q 12-24 h or alternate days if remission is maintained.
- Topical therapy is indicated as a sole treatment in some localized forms of PF and PE and in conjunction with systemic therapy on persistent focal lesions that remain active despite satisfactory control of the overall disease. Person applying treatment must wear gloves.
  - Potent topical glucocorticoid initially: fluocinolone acetonide, triamcinolone, betamethasone valerate; when adequate response, treatment is changed to l%-2% hydrocortisone for maintenance.
  - Tacrolimus 0.1%: has shown efficacy for treating both PE and PF.

POSSIBLE COMPLICATIONS

- Recurrence of skin lesions with discontinuation of immunosuppressive drugs
- Side effects are common with long-term oral glucocorticoid therapy (signs of iatrogenic hyperadrenocorticism, urinary tract infections, pyoderma).
- Persistent use (daily for >14 days) of potent topical glucocorticoids can create skin atrophy, alopecia, and comedone formation.

DRUG INTERACTIONS

- Ketoconazole potentiates cyclosporine activity; adjust dosage accordingly and monitor serum cyclosporine levels.
- Azathioprine is contraindicated in cats because of a profound myelosuppressive effect in this species.

RECOMMENDED MONITORING

- Semiannual CBC, serum biochemistry profiles, urinalysis, and urine cultures for all patients receiving long-term oral glucocorticoids
- Azathioprine, chlorambucil: CBC monitoring for cytopenias every 2-3 weeks for the first 3 months then q 3-6 months. For azathioprine, also monitor liver and pancreatic enzyme activity.

PROGNOSIS AND OUTCOME

- PF: fair to good prognosis with the majority achieving partial or complete remission with oral glucocorticoid +/− other immunosuppressive drugs. Time to improvement with therapy is 2-6 weeks; time to complete remission is 3-9 months. Mortality (euthanasia) rate in dogs with PF averages 20%-30% within the first year owing to lack of response or adverse effects of treatment, notably glucocorticoids (implying a need to use combination therapy prior to triggering adverse effects that are unacceptable to the owner, deleterious to the patient, or both). Mortality rate in cats with PF: <10% first 6 months of therapy. Persistence of long-term remission of PF after discontinuation of therapy has been reported in 7%-22% of cases.
- PV: 39% mortality (death or euthanasia). Milder variants have better prognosis.
- PNP: poor prognosis

PEARLS & CONSIDERATIONS

COMMENTS

- Response to treatment and prognosis vary with the forms of pemphigus. It is therefore essential to make a specific diagnosis.
- Although acantholytic keratinocytes and neutrophils on skin cytology exams are highly suggestive of pemphigus, clinicians may also see these cells in cases of pustular dermatophytosis *(Trichophyton* spp.) and in some cases of canine pyoderma. Biopsies are indicated for confirmation.
- Clinicians should consider prophylactic antibiotic treatment during initial immunosuppression or (in milder cases) prior to starting immunosuppressive therapy.
- Combination therapy (prednisone and either azathioprine or cyclosporine) as the initial therapy in PF can decrease the maintenance dose of glucocorticoids and reduce side effects.

TECHNICIAN TIPS

Gentle bathing or whirlpool bathing for 10-20 minutes in lukewarm water will help soften the cutaneous crusts, clean and débride the skin, and improve healing in animals afflicted with generalized forms of pemphigus.

CLIENT EDUCATION

Owners of dogs with pemphigus must be well informed of the chronic and typically incurable nature of the disease as well as the potential side effects of immunosuppressive drug therapy.

SUGGESTED READING

Olivry T: A review of autoimmune skin diseases in domestic animals: I—superficial pemphigus. Vet Dermatol 17:291–304, 2006.

Rosenkrantz WS: Pemphigus: current therapy. Vet Dermatol 15:90, 2004.

AUTHOR: CAROLINE DE JAHAM

EDITOR: MANON PARADIS

Pediculosis

BASIC INFORMATION

DEFINITION

Infestation with lice

EPIDEMIOLOGY

SPECIES, AGE, SEX: Affects animals of any age, but young patients are predisposed.

RISK FACTORS: Neglect, overcrowding, poor sanitation

CONTAGION & ZOONOSIS

- Contagious to animals of the same species
- Transmitted by direct contact, grooming instruments, bedding
- Lice are not zoonotic

GEOGRAPHY AND SEASONALITY: Possibly more common in winter. Rare in areas where flea control is routine, fairly common in some areas where fleas are rare (e.g., parts of Canada, Sweden).

ASSOCIATED CONDITIONS & DISORDERS

- Acute moist dermatitis (hot spots)
- Pyoderma
- Anemia, debilitation (young puppies)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Biting versus sucking lice: differentiation is possible via microscopic examination; clinical signs also may be suggestive (e.g., signs of anemia with sucking but not biting lice infestations).

HISTORY, CHIEF COMPLAINT

- Pruritus may be severe and affect several animals.
- Lice or nits (ova) may be seen by owners.
- Weakness (puppies with sucking lice)

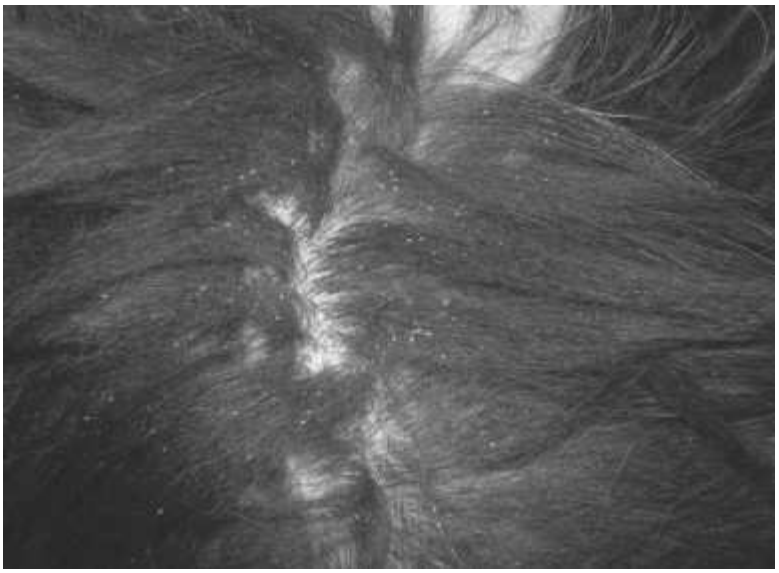
PHYSICAL EXAM FINDINGS

- Unless lice or nits are seen, examination findings are nonspecific.
- Lice accumulate around ears and body openings.
- Lice are smaller than fleas but visible to the naked eye.
- More frequently, small white eggs (nits) are seen on hairs.
- Excoriations, scaling, matted hair, alopecia, and:
    - In dogs, secondary pyoderma and pyotraumatic dermatitis (hot spots)
    - In cats, miliary dermatitis
- Occasionally weakness, pale mucous membranes in puppies (sucking lice)

ETIOLOGY AND PATHOPHYSIOLOGY

- Pediculosis is caused by insects of the suborder Anoplura (sucking lice, which suck host's blood) or Mallophaga (biting lice, which feed on skin debris and hair)
- Dogs: sucking louse *Linognathus setosus* and biting louse *Trichodectes canis*
- Cats: biting louse *Felicola subrostratus*
- Rarely, other louse species
- Lice have a 2-4 week life cycle spent entirely on the host, survive only 2-3 days off host

- Lice may be capable of transmission of *Bartonella* and *Rickettsia* spp. in some animals, but the importance of their role as vectors in dogs and cats is not known



PEDICULOSIS Louse nits attached to hairs on a black dog.

(Courtesy Dr. Kinga Gortel.)

PEDICULOSIS Microscopic examination of dog hair with attached louse nit.

(Courtesy Dr. Kinga Gortel.)

T. canis can act as the intermediate host of the dog tapeworm, *Dipylidium caninum*

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Pediculosis is diagnosed by finding lice or nits on direct physical and microscopic examinations.

DIFFERENTIAL DIAGNOSIS

- Other ectoparasite infestations, particularly fleas, *Sarcoptes, Cheyletiella*
- Various hypersensitivity disorders

INITIAL DATABASE

- Attempt to find and identify ectoparasites, including lice, in pruritic cats and dogs. See p. 1248.
- Direct examination of skin and hair can reveal lice and nits. Aided by adequate lighting and magnification (e.g., loupe).
- Skin scrapings
- Clear tape preparations can trap surface-dwelling ectoparasites: press tape repeatedly onto skin surface, place on a drop of mineral oil and examine like a skin scraping.
- Hair clippings or plucks from areas with suspected nits should be examined microscopically to confirm the diagnosis (see figure).
- Hair and surface samples may be collected using a flea comb and similarly examined.

ADVANCED OR CONFIRMATORY TESTING

Response to therapy can be used but is not specific for pediculosis.

TREATMENT

TREATMENT OVERVIEW

The goals of therapy are eradication of lice from the patient and in-contact animals, and amelioration of associated clinical signs.

ACUTE GENERAL TREATMENT

- Treat the affected pet and same-species in-contact animals.
- Wash the premises, bedding, collars, and grooming equipment at least once.
- Clip matted hair.
- Treat secondary pyoderma (see p. 951).
- Pruritus is reduced in 2-4 weeks; if it is severe, coadministration of antiinflammatory doses of corticosteroids for 1-3 weeks should not interfere with parasiticidal therapy.
- Lice succumb to many parasiticides, some after a single application.
- Nits are more resistant, so repeating treatment after 2-4 weeks is recommended for products without residual efficacy. May not be necessary using some modern topical flea-control preparations.
- All treatments are off label.
- Treatments considered effective for lice (and species studied) include:
    - Fipronil spray and spot-on (biting lice; cats and dogs)
    - Imidacloprid spot-on (biting and sucking lice; dogs)
    - Selamectin spot-on (sucking lice; dogs)
    - Various pyrethrin, carbamate, and (for dogs only) permethrin preparations
    - Lime sulfur dip
    - Ivermectin, 0.2 mg/kg PO or SQ every 2-4 weeks; no longer routinely recommended, as safer alternatives exist
- Follow-up is recommended to ensure complete eradication of lice.
- In weak, anemic puppies, additional supportive care (including blood transfusion) as needed

RECOMMENDED MONITORING

Recheck patients after 4-6 weeks.

PROGNOSIS AND OUTCOME

The prognosis for pets with pediculosis, with the exception of severely anemic or debilitated animals, is excellent.

PEARLS & CONSIDERATIONS

COMMENTS

- Nits attached to hairs may be mistaken for skin scales. Unlike scales, nits are of uniform size and almost impossible to

remove from hair shafts.
- Nits are harder to see on light coats.
- Microscopically, *Cheyletiella* ova may also be seen in association with hair shafts, but they are attached much more loosely.

PREVENTION

Pets regularly receiving topical flea control products are protected from lice. In areas where fleas are not endemic, consider protecting dogs attending grooming, boarding, dog shows, or dog daycare facilities.

TECHNICIAN TIPS

- Clients become understandably concerned about a diagnosis of lice in their pet. They may also inquire whether a household pet could be the source of a human infestation (no). Counsel clients about the highly host-specific nature of this parasite.
- Stress the importance of follow-up to assess efficacy, since all treatments used for pediculosis are administered off label.

SUGGESTED READING

Medleau L, Hnilica KA: Small animal dermatology: a color atlas and therapeutic guide, ed 2, St Louis, 2006, Saunders Elsevier.

AUTHOR: KINGA GORTEL

EDITOR: MANON PARADIS

Pectus Excavatum

BASIC INFORMATION

DEFINITION

Congenital dorsoventral narrowing of the thorax or depression of the sternum dorsally into the thoracic cavity; can cause malpositioning or compression of heart and lungs

SYNONYMS

Chondrosternal depression, funnel chest

EPIDEMIOLOGY

SPECIES, AGE, SEX

- More common in cats than dogs
- No sex predilection
- Defect is present at birth, but affected animals may not present with clinical complications until secondary disease (e.g., acquired heart disease) develops later in life.

GENETICS & BREED PREDISPOSITION: The defect is congenital and can be inherited. Brachycephalic dogs are more commonly affected.

ASSOCIATED CONDITIONS & DISORDERS

- Other congenital defects, such as cardiac defects
- Stunted growth
- Hypoplastic trachea
- “Swimmer's syndrome” (laterally splayed legs as neonate)
- Pneumonia
- Recurrent respiratory infections

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Presentation of defect ranges from mild to severe. Severity of thoracic defect does not always correlate to severity of clinical signs, which may be more a reflection of concurrent defects (e.g., cardiac, respiratory).
- Simple cases of pectus excavatum occur in the absence of other congenital anomalies.

HISTORY, CHIEF COMPLAINT

- In many animals, pectus excavatum is found incidentally, and no clinical signs are present.
- Owners may palpate the defect and seek veterinary advice despite lack of clinical signs.
- When signs occur, they can include:
    - Exercise intolerance
    - Dyspnea
    - Cyanosis
    - Poor growth
    - Cough
    - Inappetence
    - Cachexia
    - Lethargy
    - Weakness
    - Vomiting

PHYSICAL EXAM FINDINGS

- Palpable dorsal defect of caudal sternum, creating sternal concavity
- Dyspnea, tachypnea, and shallow respirations may be evident at rest or with excitement and minimal exertion.
- Auscultation of a heart murmur or muffled heart and breath sounds are possible.
- Affected animals may be small in stature for age or smaller than their littermates and exhibit poor condition.

ETIOLOGY AND PATHOPHYSIOLOGY

Congenital malformation of the sternum and costochondral cartilages causes deformation of the thorax and malpositioning of thoracic organs. The exact etiology is unknown.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is usually straightforward and typically based on physical examination identification of palpable dorsal defect of the caudal sternum that creates sternal concavity. Thoracic radiographs and echocardiography may provide additional details.

DIFFERENTIAL DIAGNOSIS

- Trauma
- Lordosis of thoracic or thoracolumbar spine
- Differentials must include those for associated abnormalities:
    - Cardiac murmurs indicating cardiac defects must be differentiated from murmurs generated through malpositioning of the heart and great vessels.

INITIAL DATABASE

Thoracic radiographs; possible findings include:

- Elevated sternum in caudal thorax
- Malformation of sternum and costochondral cartilages
- Decreased thoracic volume
- Displacement of heart and other structures:
    - The heart may falsely appear enlarged because of abnormal positioning and must be differentiated from other causes of true cardiomegaly. Consultation with a radiologist is often warranted.
    - Complete diaphragm may be difficult to confirm.

ADVANCED OR CONFIRMATORY TESTING

Echocardiography to identify cardiac defects and assess possibility of pleuroperitoneal/pericardioperitoneal hernia; may be very challenging owing to chest malformation

TREATMENT

TREATMENT OVERVIEW

Treatment is aimed at supportive care and manual compressions for young, nonsurgical cases and surgical correction for moderate to severe cases. Goals are maximizing thoracic cavity capacity to allow normal function and activity, treatment of respiratory infections if present, improvement of growth by increasing nutritional plane/assimilation, and identification and management of concurrent defects.

ACUTE GENERAL TREATMENT

- No treatment may be needed for animals without concurrent defects and for whom pectus excavatum is an incidental finding (no clinical signs).
- For severely compromised animals or acute complications:
    - Oxygen supplementation (see p. 1318)
    - Avoidance of exertion, excitement, and stress
    - Treatment with antibiotics if pneumonia or other infections are suspected or confirmed

CHRONIC TREATMENT

- Incidental/mild cases: daily gentle, manual, lateral-to-medial chest compressions until the animal is mature (about 9 months of age) to help flatten the chest as the animal grows. An external compressing stent may be applied. Chest contour may normalize with growth.
    - The benefits of surgical correction in animals with moderate or severe pectus excavatum and no clinical signs have not been established.
- Moderate/severe clinical signs: surgical application of an external splint. Correction in young animals is generally more successful because the costal cartilages and sternum remain pliable, allowing the thorax to reshape.
    - Optimal age for surgery is variable; a minimum of 8 weeks of age has been recommended.
    - Anesthetic management requires the utmost attention and monitoring.
    - Prevention of hypothermia and hypoglycemia in young animals
    - Positive-pressure ventilation
    - Theoretically, reduction of risk for reexpansion pulmonary edema with slow reexpansion of atelectatic lung; often not practical intraoperatively.
    - Avoiding chamber or mask induction if animal is dyspneic

NUTRITION/DIET

High-quality nutritional augmentation benefits animals with poor growth until correction or improvement of the defect.

POSSIBLE COMPLICATIONS

- Surgical complications
- Pneumothorax
- Hemothorax
- Infection
- Reexpansion pulmonary edema

RECOMMENDED MONITORING

- Postoperative monitoring for intrathoracic hemorrhage; immediate postoperative monitoring for pneumothorax
- Monitoring for signs of respiratory infections in untreated or conservatively treated animals

PROGNOSIS AND OUTCOME

- Mild cases without overt clinical signs: excellent prognosis if no other defects are present
- Prognosis of more severe cases depends on nature of concurrent defects.
- Long-term prognosis is excellent in animals that show clinical signs but have no other defects, provided surgery is performed at a young age. Surgery of older animals may require partial sternectomy.

PEARLS & CONSIDERATIONS

COMMENTS

- Severity of signs at maturity is difficult to predict. If corrective surgery is not possible (cost, unavailability), signs may still lessen spontaneously with growth. Thus, euthanasia should be only considered in the most severe cases when surgery is not possible.
- Puppies and kittens with swimmer's syndrome can benefit from early physical therapy.
- The opposite of pectus excavatum is pectus carinatum (protruding sternum).

PREVENTION

- Spaying or neutering of affected animals once they are stable for elective surgery
- Avoidance of breeding animals with pectus excavatum or the relatives of animals with pectus excavatum

TECHNICIAN TIPS

Small-gauge (22 or 23 G) butterfly needles and 3-way stopcocks attached to a syringe are often useful for acute management of pneumothorax or hemothorax if such complications develop postoperatively.

CLIENT EDUCATION

If corrective surgery is not an option, thoracic volume may improve as the animal grows. Outcome is highly variable, and even animals with severe deformities may thrive.

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AUTHOR: CHRISTINE L. WILFORD

EDITOR: RANCE K. SELLON

Pattern Alopecia, Canine

BASIC INFORMATION

DEFINITION

Canine pattern alopecia is a relatively common, likely heritable, noninflammatory alopecic disorder of specific breeds. It encompasses several distinct syndromes.

SYNONYMS

CPA, canine pattern baldness

EPIDEMIOLOGY

SPECIES, AGE, SEX

- These disorders affect dogs of either sex and of any reproductive status.
- Early onset (usually before 1 year of age)

GENETICS & BREED PREDISPOSITION

- CPA, ventral type is seen in dogs with fine, short coats such as dachshunds, Chihuahuas, miniature pinschers, whippets, greyhounds, Boston terriers, and boxers.
- CPA, pinnal type is seen mainly in dachshunds.
- Alopecia and melanoderma of Yorkshire terriers is breed specific.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- The two main forms of CPA are the ventral type, the most common syndrome, and the pinnal type.
- Alopecia and melanoderma of Yorkshire terriers is clinically very similar to CPA, pinnal type, and it is most likely the same disorder.

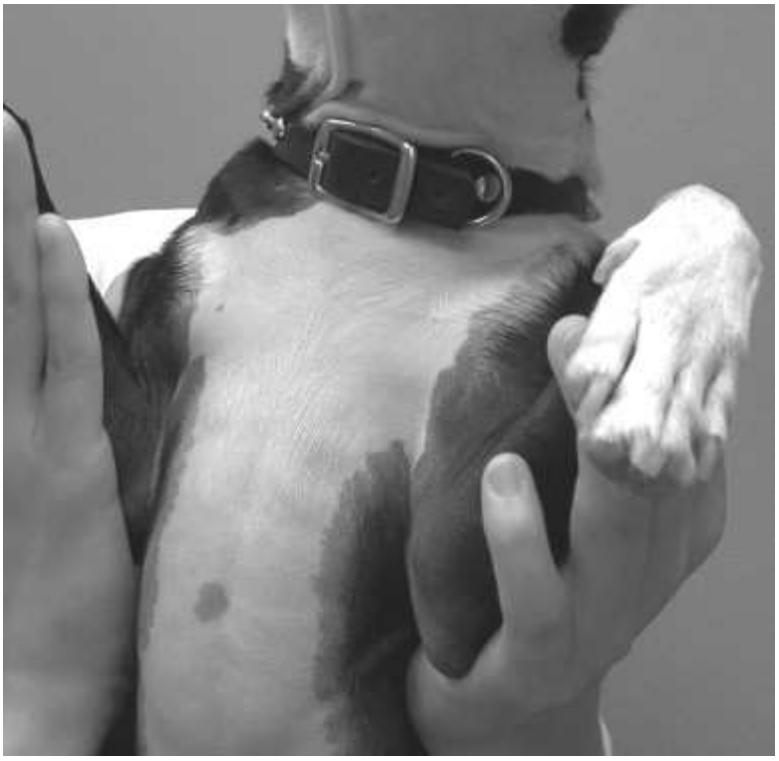
HISTORY, CHIEF COMPLAINT: Dogs born with a normal hair coat are presented for evaluation of a gradual thinning of the coat in specific body areas.

PHYSICAL EXAM FINDINGS

- CPA, ventral type: progressive alopecia developing along the ventral neck, chest, and abdomen, caudomedial aspect of thighs, perineum, and post-auricular regions (base of the ear pinnae)
- CPA, pinnal type: progressive alopecia of the convex aspect of the ear pinnae, starting around 6 months of age
- Alopecia and melanoderma of Yorkshire terriers: alopecia and hyperpig-mentation of the convex aspect of the ear pinnae and the bridge of the nose

ETIOLOGY AND PATHOPHYSIOLOGY

CPA may be an overshoot reaction to artificial selection pressure favoring the fine, delicate coat sought by breeders. Over the last decades, smooth-hair dachshund breeders have been able to significantly decrease the incidence of CPA, ventral type by selective breeding but with the result of dogs generally having a coarser hair coat.



PATTERN ALOPECIA Pattern alopecia (ventral type) in a 2-year-old neutered male Boston terrier. Note loss of hair on ventral neck and chest.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is based on history, dermatologic exam, and exclusion of endocrinopathies and inflammatory diseases such as alopecia areata. The early onset, breed predisposition, and absence of inflammation and pruritus are distinctive.

DIFFERENTIAL DIAGNOSIS

- Endocrinopathies (hypothyroidism, hyperadrenocorticism, hyperestrogenism)
- Follicular dysplasias
- Alopecia areata
- Infectious process (pyoderma, demodicosis, dermatophytosis) in some clinical presentations

INITIAL DATABASE

- History and physical exam findings are generally sufficient.
- Ruling out other differentials may involve thyroid testing, adrenal function testing, and dermatologic diagnostic tests such as skin scraping based on lesion distribution and appearance.

ADVANCED OR CONFIRMATORY TESTING

Skin biopsies: changes are characterized by miniaturization of anagen hair follicles. Biopsies are rarely performed, because biopsy sites often require general anesthesia, biopsy healing may lead to permanent visible scarring, and histopathologic changes can be subtle and wrongly suggestive of endocrinopathies.

TREATMENT

TREATMENT OVERVIEW

The goal is to try to promote hair regrowth if this is the desire of the owner; it may protect the dog from cold climate.

ACUTE GENERAL TREATMENT

Anecdotal evidence exists for the efficacy of melatonin at 3-6 mg/dog PO q 8-12 h for 1-2 months to stimulate hair growth.

PROGNOSIS AND OUTCOME

- Dogs affected by this genetically based dermatosis are healthy otherwise.
- It is not known if dogs initially responding to melatonin will eventually become refractory to this form of treatment.

PEARLS & CONSIDERATIONS

COMMENTS

- The early onset, pattern-linked alopecia, and breed predisposition make the diagnosis straightforward in many cases.
- The main impact of this disorder is usually cosmetic rather than medical.

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AUTHOR & EDITOR: MANON PARADIS

Patent Ductus Arteriosus

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

An arterial shunt between the aorta and pulmonary artery that is normally present in fetuses but should constrict and close within 24 hours after birth. Incomplete closure (patency) results in a variably sized channel whose minimum diameter determines the amount and direction of blood flow through the shunt and hence determines the impact on the patient. It is the most common congenital heart defect in dogs, occurring in 1/1000. It is rare in cats.

SYNONYM

PDA

EPIDEMIOLOGY

SPECIES, AGE, SEX

- All species and any age
- Recognized most frequently in young animals
- Moderate predominance in females
- Occurs much less frequently in cats

GENETICS & BREED PREDISPOSITION

- Any breed
- Sporadic or heritable defect occurring most frequently in small, relatively nonmuscular dog breeds such as Maltese, Pomeranians, Yorkshire terriers, Shetland sheepdogs, and toy and miniature poodles

RISK FACTORS: Inbreeding

GEOGRAPHY AND SEASONALITY:

Breed predispositions may vary due to regional differences in the gene pool.

ASSOCIATED CONDITIONS & DISORDERS

- Arrhythmias
- Congestive heart failure
- Pulmonary hypertension
- Polycythemia

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Type 1: small patent ductus arteriosus (PDA)
- Type 2: medium PDA
- Type 3A: large PDA
- Type 3B: large PDA with congestive heart failure
- Type 4: large PDA with pulmonary hypertension and right-to-left or bidirectional shunt
- An angiographic classification scheme also exists for dogs, wherein PDAs are categorized according to morphology: type I (5%) = gradual tapering from aorta to pulmonary artery; type IIa (most common; 54.5%) = walls of PDA taper gradually until abrupt tapering at pulmonary arterial insertion; type IIb (32.5%) = walls of PDA abrupt tapering at pulmonary arterial insertion; type III (8%) = walls of PDA are parallel for the length of the PDA (tubular).

HISTORY, CHIEF COMPLAINT

- Varies with PDA diameter and age
- Most often recognized as an incidental heart murmur in a young animal presented for vaccination and not showing overt clinical signs
- When clinical signs are present, they include exercise intolerance, failure to thrive, and signs of congestive heart failure.

PHYSICAL EXAM FINDINGS: Vary with PDA diameter:

- Type 1, small:
  - Characteristic focal continuous murmur at left heart base
- Type 2, medium:
  - Type 1 signs

    - Continuous murmur audible at apex
    - Precordial thrill at left heart base
- Type 3A, large:
    - Types 1 and 2 signs
    - Bounding pulses
    - Prominent cardiac impulse at left apex
    - Systolic murmur of mitral regurgitation at left apex
- Type 3B, large with congestive heart failure:
    - Types 1, 2, and 3A signs
    - Dyspnea
    - Pulmonary crackles
    - Ascites (occasionally)
    - Arrhythmias, especially atrial fibrillation, possible
- Type 4, large PDA with pulmonary hypertension:
    - No heart murmur
    - Prominent right apical impulse
    - Split second heart sound
    - Caudal cyanosis
    - Hind limb collapse with exercise

ETIOLOGY AND PATHOPHYSIOLOGY

- The principal cause of PDA in dogs is site-specific hypoplasia of ductus smooth muscle, coupled with reciprocal excess elastic tissue in the wall of the ductus. In varying degree, the hypoplastic smooth muscle does not encircle the lumen, and muscle contraction does not completely constrict the lumen postpartum.
- Typically, pulmonary vascular resistance decreases after birth and postnatal blood flow through the PDA is from the aorta to the pulmonary artery (“left-to-right type”), causing increased flow through the pulmonary circulation, left atrium, left ventricle, and ascending aorta, resulting in enlargement of these chambers and left ventricular hypertrophy. Established left-to-right types very rarely develop enough pulmonary hypertension to cause reversed PDA flow (“right-to-left type”).
- In animals with a large PDA and pulmonary hypertension (type 4, persistent fetal circulation), there is right ventricular hypertrophy; blood flows through the ductus predominantly from the pulmonary artery to the aorta, resulting in caudal cyanosis and secondary polycythemia.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

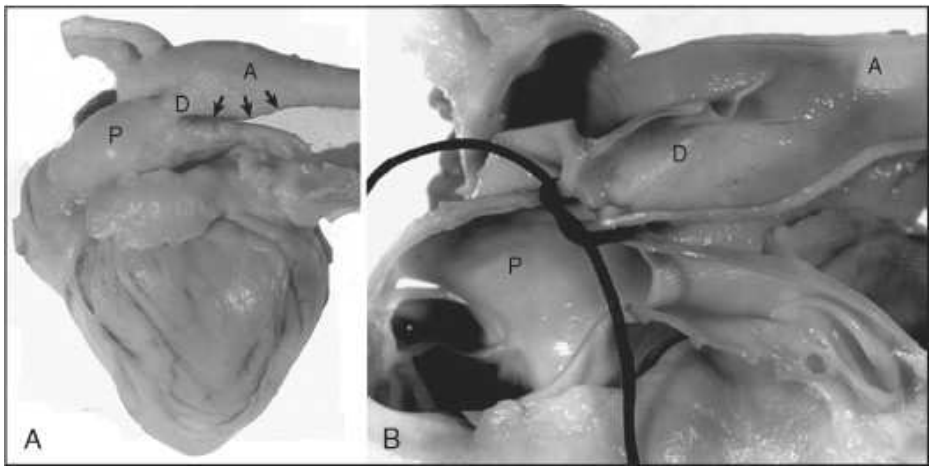
The diagnosis is made easily by palpating a precordial thrill and auscultating a continuous murmur over the left heart base (types 1-3). Chest radiographs reveal the degree of cardiomegaly and the urgency of PDA closure.

DIFFERENTIAL DIAGNOSIS

- Combined abnormalities producing systolic and diastolic heart murmurs, such as a ventricular septal defect and aortic insufficiency due to an unsupported aortic valve cusp
- Aorticopulmonary window
- Arteriovenous fistula
- Bronchial artery flow in chronic heart-worm cor pulmonale
- Tortuous collateral arteries in aortic coarctation or interruption

INITIAL DATABASE

- Thoracic radiographs to assess heart and lung vessel size and lung parenchyma
- Electrocardiogram (ECG) to identify ventricular hypertrophy and arrhythmias
- Packed cell volume to determine presence of anemia or polycythemia



PATENT DUCTUS ARTERIOSUS A, Photograph of heart, aorta *(A),* and pulmonary artery *(P)* in a 4-month-old dog with a PDA *(D)* and ductal-aortic aneurysm *(arrows).***B**, Sagittal section photograph of great vessels and a ligature demonstrating PDA ligation at surgery. Most of the PDA lies within the wall of the aorta in dogs and constitutes a ductal-aortic aneurysm commonly referred to as a *ductus diverticulum.* Typical ridge at pulmonary artery opening limits PDA diameter and determines blood flow through PDA.

(Courtesy Dr. James W. Buchanan, Philadelphia, Pennsylvania.)

ADVANCED OR CONFIRMATORY TESTING

These tests are optional:

- Two-dimensional echocardiography to determine chamber sizes, wall thickness, and contractility and to identify any concurrent cardiac defects
- Color Doppler echocardiography to verify turbulent blood flow in the pulmonary artery
- Spectral Doppler echocardiography to determine flow velocity in the PDA and estimate the aorta/pulmonary artery pressure gradient. If tricuspid and pulmonic insufficiencies are present, respective estimates of right ventricular systolic and pulmonary artery diastolic pressures can be made.

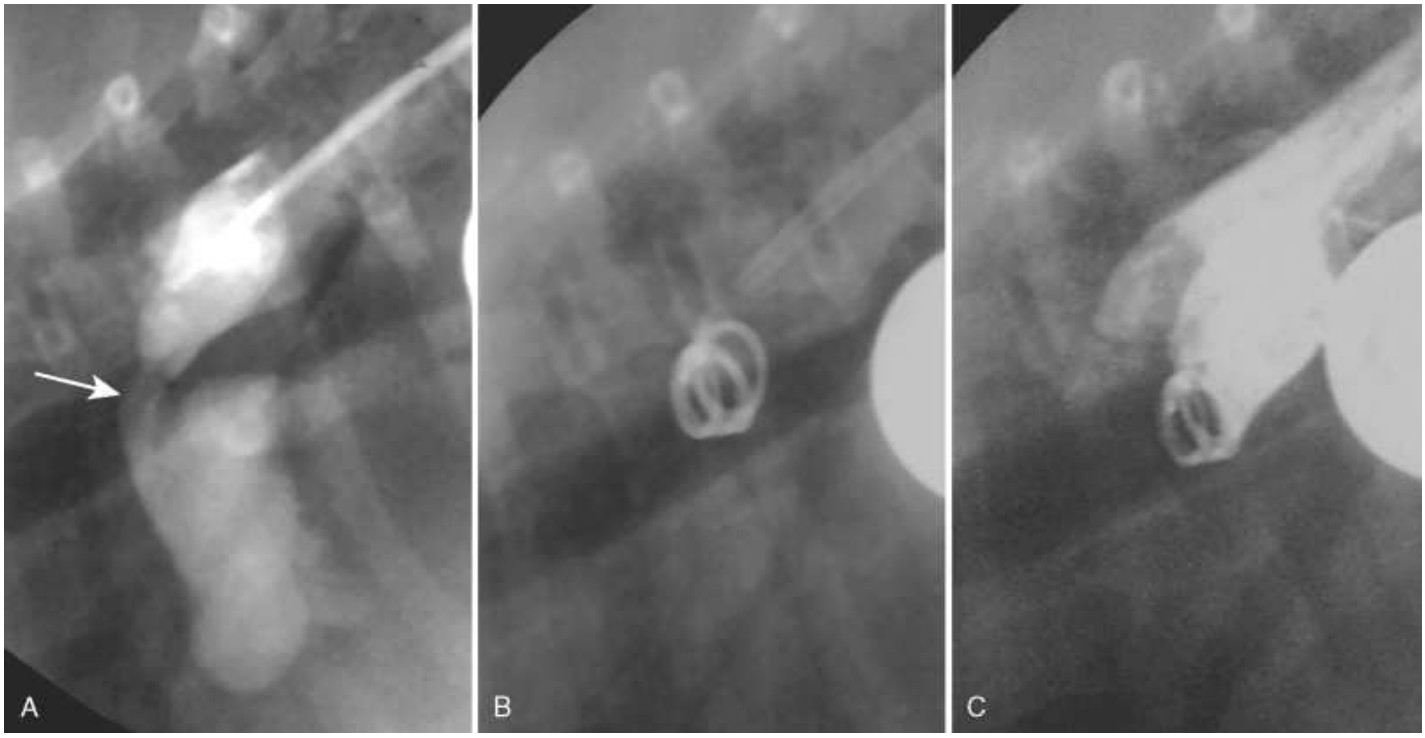
TREATMENT

TREATMENT OVERVIEW

PDA closure is recommended for all left-to-right cases (types 1-3) but contraindicated in right-to-left cases (type 4). In type 4 cases, phlebotomy and/or chemotherapy reduce and maintain hematocrit at 60%-65%, which improves blood flow characteristics.

ACUTE GENERAL TREATMENT

- Type 3B: For large PDA, preoperative diuretic and cage rest to alleviate congestive heart failure, then occlusion of PDA are indicated.
- Types 1-3: surgery or transarterial coil or Amplatz duct occluder to occlude PDA
- Type 4: phlebotomy to reduce polycythemia



PATENT DUCTUS ARTERIOSUS Aortic injection angiograms in a 6-month-old dog with PDA before **(A)** and after **(C)** PDA occlusion with a transarterial coil **(B)**. The *arrow* (panel **A**) indicates the narrowest part of the PDA; a properly deployed coil should be placed on the aortic side of this point (as shown in panels **B** and **C**).

(Courtesy Dr. James W. Buchanan, Philadelphia, Pennsylvania.)

Comparison of PDA Occlusion Methods

	Surgery	Transvascular Device	Favors
Equipment cost	$1000	$500,000	Surgery
Supply inventory	$1000	$10,000	Surgery
Single-use supplies	$100	$500-1500	Surgery
Client charge	$3500	$3500-4500	—
Procedure time	1 hour	1 hour	—
Procedure people	2	2	—
Animal size	Any	Limited	Surgery
PDA shape	Any	Limited	Surgery
Success rate	98%	98%	—
Days in hospital	2-3	1-2	Transvascular device
Postoperative monitoring	++	+	Transvascular device
Animal discomfort	+++	+	Transvascular device
Mortality	<2%	<1%	Transvascular device

CHRONIC TREATMENT

Type 4: hydroxyurea to suppress bone marrow, 20-25 mg/kg PO q 12 h every other day; titrated downward as needed based on resulting hematocrit

POSSIBLE COMPLICATIONS

- Refractory congestive heart failure
- Refractory arrhythmias
- Iatrogenic surgical hemorrhage

- Coil or occludar device embolization into pulmonary artery branch
- Hematoma at transarterial site
- Persistent polycythemia in type 4

RECOMMENDED MONITORING

Nonspecific

PROGNOSIS AND OUTCOME

- Types 1-3A: 98% successful correction and normal lifespan
- Type 3B: 98% initially successful if heart failure and arrhythmia are controlled preoperatively; animal can live for years, but lifespan is usually shortened.
- Type 4: may live for years if polycythemia is controlled

PEARLS & CONSIDERATIONS

PREVENTION

Owners should avoid breeding affected animals.

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AUTHOR: JAMES W. BUCHANAN

EDITOR: ETIENNE CÔTÉ

Patellar Luxation

BASIC INFORMATION

DEFINITION

Medial or lateral displacement of the patella from the femoral trochlear sulcus or groove. Medial patellar luxation is more common in dogs and cats.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Primarily seen in dogs; less frequently in cats
- All ages affected; more common in the young dog

GENETICS & BREED PREDISPOSITION

- Most dog breeds affected; more common in the toy and miniature canine breeds and Newfoundland dogs
- Heritability has been established in toy/miniature poodles and toy spaniels.
- Some reports of increased incidence in Maine coon, Persian, Devon rex and Abyssinian cats

RISK FACTORS

- Malalignment of the quadriceps mechanism (hereditary and developmental causes)
- Trauma to the bone or soft tissues of the hind limb, or neurogenic muscle contracture
- Previous stifle surgery that included lateral arthrotomy with patellar luxation

ASSOCIATED CONDITIONS & DISORDERS

- Cranial cruciate ligament instability (present in 15%-20% of stifles with chronic patellar luxation)
- Hip dysplasia in large dogs

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Medial patellar luxation (MPL): the most common form of PL in dogs and cats
- Lateral patellar luxation (LPL): uncommon. Seen in all breeds; large and giant canine breeds most commonly affected.
- Traumatic luxation: uncommon. Usually the patella displaces medially following retinacular injury.

HISTORY, CHIEF COMPLAINT

- Intermittent, partial to non-weight-bearing lameness of one or both hind limbs
- Transient “skipping” gait (holding hindlimb flexed and nonweightbearing for a few steps at a time) when walking or running with low-grade luxation
- Mechanical lameness due to secondary limb deformity with high-grade luxation
- Weakness in jumping or reluctance to jump
- Sudden lameness or increase in lameness in a stifle with chronic PL suggests recent cranial cruciate ligament rupture.

PHYSICAL EXAM FINDINGS: Grading system:

- Normal:
  - Patella cannot be manually luxated
  - Normal gait
- Grade I:
  - Patella can be luxated manually but spontaneously reduces.
  - No clinical signs of lameness, or occasional “skipping” lameness
- Grade II:

- Spontaneous luxation and reduction of the patella occurs.
- Intermittent “skipping” lameness, or persistent weight-bearing lameness
- Mild to moderate internal (MPL) or external (LPL) tibial torsion
- Mild to moderate medial (MPL) or lateral (LPL) deviation of the tibial crest

- Grade III:
  - Patella remains luxated but can be manually reduced with stifle extension.
  - Persistently abnormal gait: externally rotated stifle, internally rotated pes (bowlegged and pigeon-toed) with MPL, valgus deformity of stifle, external rotation of pes (knock-kneed and cow-hocked) with LPL
  - Moderate to severe tibial torsion and tibial crest deviation
  - Shallow distal femoral trochlear groove may be palpable.
- Grade IV:
  - Patella is permanently luxated and cannot be manually reduced. o Non-weight-bearing hind limb lameness or ambulation in a “crouched” position (inability to fully extend the stifles)
  - Severe internal (MPL) or external (LPL) tibial torsion
  - Severe medial (MPL) or lateral (LPL) deviation of the tibial crest
  - Distal femoral trochlear groove is shallow or absent.

ETIOLOGY AND PATHOPHYSIOLOGY

- Hereditary and developmental skeletal changes that lead to malalignment of the quadriceps mechanism. Which deformity comes first is unknown because many of the changes in high-grade MPL and LPL result from the abnormal directional pull of the quadriceps.
  - Medial patellar luxation:
    - Coxa vara (decreased femoral neck angle)
    - Distal femoral varus
    - Tibial internal torsion
    - Shallow femoral trochlear sulcus
    - Tight, thick medial retinaculum, loose, thin lateral retinaculum
  - Lateral patellar luxation:
    - Coxa valga (increased angle of inclination of the femoral neck)
    - Distal femoral valgus
    - External tibial torsion
    - Tight, thick lateral retinaculum; loose, thin medial retinaculum

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

Diagnosis of patellar luxation is based on physical examination. Radiographs may be normal if taken when the patellas are in place, but they are useful for planning surgical intervention and identifying changes present with concurrent cranial cruciate ligament rupture. However, interpretation of apparent angular and torsional deformities must be done with caution, since natural curvatures of the femur and tibia can give the impression of abnormal conformation.

DIFFERENTIAL DIAGNOSIS

- Aseptic necrosis of the femoral head (Legg-Calvé-Perthes disease): young, small dogs only
- Coxofemoral luxation
- Cranial cruciate ligament rupture
- Osteochondrosis of the stifle
- Immune-mediated polyarthritis
- Lumbosacral compressive disease

INITIAL DATABASE

- Palpation of the stifle joints for patellar instability and cranial cruciate ligament rupture
- Radiographs to characterize the femoral and tibial conformation and joint condition:
  - Lateral and craniocaudal radiographs of the femur, stifle, and tibia
  - Need to include the hip and tarsal joints in higher grades of luxation to better assess angular and torsional deformities. Caution should be taken with positioning (it is often best to take craniocaudal views with the dog held sitting upright and the hind limbs extended, stifles pointed directly upward with no splay), as slight variations from the ideal can cause the femurs to appear falsely angled.

ADVANCED OR CONFIRMATORY TESTING

- Calculation of femoral neck inclination and anteversion angles for LPL in large-breed dogs
- CT scan with three-dimensional reconstruction

TREATMENT

TREATMENT OVERVIEW

- Only animals showing overt clinical signs should have surgery. Patellar luxation usually produces surprisingly little osteoarthritis, which is typically slow to progress.
- In all but very young puppies and kittens, correction of bone deformities, in addition to soft-tissue repairs, will be necessary. A soft-tissue repair that feels stable on the operating table usually allows patellar reluxation by 3 weeks after surgery.
- Concurrent cranial cruciate rupture must be addressed during the PL operation, since cruciate ligament rupture is frequently the chief source of the lameness being treated.

ACUTE GENERAL TREATMENT

- Medical management:
  - Nonsteroidal antiinflammatory, drugs (NSAIDs) in dogs:
    - Carprofen: 2 mg/kg PO q 12 h, *or*
    - Etodolac: 10-15 mg/kg PO q 24 h, *or*
    - Deracoxib: 1-2 mg/kg PO q 24 h (may use 3-4 mg/kg PO q 24 h for first 7 days only), *or*
    - Meloxicam: 0.1 mg/kg PO q 24 h, *or*
    - Tepoxalin: 10 mg/kg PO q 24 h, *or*
    - Other drugs
- Physical rehabilitation for mild patellar luxations (grade I, ± grade II)
  - Exercises to strengthen quadriceps muscle function
- Surgical management
  - Soft-tissue reconstruction:
    - Imbrication of loose and release of tight pericapsular tissues based on direction of luxation; release of the rectus femoris or sartorius muscle for MPL
    - Derotational suture from fabella to patella or tibial tuberosity
  - Trochleoplasty to deepen the femoral trochlear groove:
    - Trochlear chondroplasty in immature dogs
    - Trochlear abrasion sulcoplasty
    - Trochlear recession sulcoplasty (using a wedge or a block technique)
  - Tibial tubercle transposition opposite to direction of luxation
  - Femoral or tibial correctional osteotomies: usually performed when angular deformity is severe (>15○ varus for the distal femur in MPL).
  - Stifle arthrodesis may be performed as a salvage procedure for severe luxations not amenable to other treatments.
  - Concurrent cranial cruciate ligament rupture should be treated along with the MPL; osteotomy techniques such as tibial plateau-leveling osteotomy (TPLO) or tibial tuberosity advancement (TTA) can be modified so that the tibial osteotomy also transposes the tibial tuberosity.

CHRONIC TREATMENT

- Same as in acute cases but may require long-term medical management for the treatment of osteoarthritis
- One of these chondroprotective agents can be used:
  - Polysulfated glycosaminoglycan, 5 mg/kg IM once weekly for 4-6 weeks
  - Pentosan polysulfate, 3 mg/kg SQ once weekly
  - Oral formulations (glucosamine. chondroitin sulfate, hyaluronan, avocado soy unsaponifiables): according to formulation/labeled instructions

NUTRITION/DIET

Weight control

POSSIBLE COMPLICATIONS

- Medical management:
  - Gastrointestinal (GI), hepatic, renal, or other systemic reactions from NSAIDs

    - Continued progression of degenerative joint disease
    - Failure of medical management to control pain
- Surgical management:
    - Patellar reluxation (occurs in 10%-30% of cases, especially if tibial tuberosity transposition has not been done)
    - Implant failure/tibial tuberosity avulsion

RECOMMENDED MONITORING

- Basic laboratory monitoring of animals on NSAID therapy
- Weight, exercise levels, and clinical signs as dictated by the patient
- Postoperative rehabilitation enhances clinical recovery.

PROGNOSIS AND OUTCOME 

- Generally good to excellent for return to normal limb function if appropriate techniques are utilized
- Degenerative joint disease progresses (radiographically, not necessarily symptomatically) despite treatment.

PEARLS & CONSIDERATIONS 

COMMENTS

- Severity of lameness may not correlate with grade of patellar luxation. Animals with grade 2 luxation are often the most painful, as their patellas are repeatedly grinding across the trochlear ridges. Animals with higher-grade luxations are not painful, but rather impeded by joint misalignment.
- Patellar luxation is usually a developmental condition, and the grade of luxation may increase as the animal matures.
- In bilateral luxations, the grade of patellar instability may differ between stifles.
- Soft-tissue stabilization techniques alone are not sufficient to stabilize moderate or severe luxations.
- Trochlear recession sulcoplasty (wedge or block) is the preferred method to deepen the femoral trochlear groove, because it preserves the articular cartilage.
- In older animals with chronic patellar instability and acutely worsening lameness, always rule out concomitant cranial cruciate ligament rupture.

PREVENTION

Screening and control of breeding animals for prevention of patellar luxation

SUGGESTED READING

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Parvoviral Enteritis

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

A viral infection that destroys the crypt cells of the villous epithelium of the small intestine together with lymphocyte depletion and neutropenia, leading to severe enteritis, anorexia, vomiting, hemorrhagic diarrhea, and shock

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs only; parvoviral enteritis almost exclusively affects puppies (<8 months old) and unvaccinated adults. In cats, parvovirus-induced disease is called *panleukopenia* (see p. 822).

GENETICS & BREED PREDISPOSITION:

Suspected predisposition for Doberman pinscher, rottweiler, pit bull, German shepherd, and dachshund breeds; toy poodles and cocker spaniels have below-normal degree of risk.

RISK FACTORS

- Unvaccinated puppies or pups less than 7 weeks of age with poor maternal immunity; unvaccinated dogs are 12.7 times more likely than vaccinated dogs to develop parvoviral enteritis.
- Exposure to high viral loads
- Immunosuppression (systemic illness, cancer chemotherapy)

CONTAGION & ZOONOSIS

- Extremely resistant virus (parvovirus 1 and 2) that can survive more than 7 months in the environment (longer if frozen over winter months) and is resistant to most disinfectants
    - Diluted bleach (1:32 bleach/water) and quaternary ammonium disinfectants (Parvosol, Roccal-D, quats, and others) effectively kill parvovirus.
- Highly contagious to other dogs via the fecal-oral route
    - Fecal shedding begins 4-5 days after exposure (i.e., before the onset of overt clinical illness, which occurs 6-10 days after exposure).
    - Shedding generally occurs for a total of 7-10 days, usually ending by day 14 after exposure.
    - An animal that is discharged after successful treatment of parvoviral enteritis has a low risk of contagion to other dogs through feces it passes, but there is a high risk of contagion through fecal staining on the hair-coat or in feces or vomit produced at home immediately prior to hospitalization.
- Shedding of vaccine-source (attenuated live) parvovirus occurs for several days after vaccination; there is no contagion risk, but the shedding may produce a false-positive reaction on fecal ELISA testing for parvovirus.
- Species-specific; no clinically relevant transmission to cats or other species, and no zoonotic transmission

GEOGRAPHY AND SEASONALITY: Occurs worldwide and year round but is more common in warmer, wetter seasons. Most commonly seen in spring when the majority of puppies are born. However, in a Canadian study, dogs were three times more likely to be admitted with parvoviral enteritis in July, August, or September compared with the rest of the year.

ASSOCIATED CONDITIONS & DISORDERS

- Helminthiasis, giardiasis, coccidiosis, and coronavirus infections may occur concurrently.
- Sepsis likely is prevalent in parvoviral enteritis cases because bacteremia is common: in 90% of dogs that died of parvoviral enteritis, microbial liver or lung cultures revealed growth of *Escherichia coli.*

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Subclinical, mild, moderate, and severe enteritis

HISTORY, CHIEF COMPLAINT

- Onset of signs 3-14 days after exposure (if known)

- Acute onset of lethargy (often first sign), anorexia, vomiting, and diarrhea (often hemorrhagic)

PHYSICAL EXAM FINDINGS

- Mild cases may be unremarkable.
- Moderate and severely affected puppies are typically lethargic, dehydrated (tacky oral mucous membranes), with palpably fluid-filled intestines; abdominal palpation may induce vomiting or retching, and fever and tachycardia are common.
- Severely affected puppies may present in hypovolemic shock, with altered mentation (may be due to septic shock, hypoglycemia) and hypothermia.

ETIOLOGY AND PATHOPHYSIOLOGY

- Exposure is followed by a 3-to 14-day incubation period
- Parvoviral predilection for rapidly dividing cells
- Destruction of intestinal crypt epithelium, causing sloughing of intestinal mucosa, vomiting, diarrhea, and sepsis from translocation of enteric bacteria into the portal circulation
- Lymphocyte depletion and neutropenia
- Glucose and potassium depletion/loss
- Dehydration and sepsis

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on the presence of anorexia, vomiting, diarrhea, lethargy, or a combination of these, typically in a young and usually unvaccinated dog; confirmation requires fecal assay such as a parvovirus ELISA snap test.

DIFFERENTIAL DIAGNOSIS

- Any severe acute gastroenteritis
- Distemper
- Salmonellosis
- Coronaviral enteritis
- Foreign body/intussusception

INITIAL DATABASE

- ELISA test for parvovirus in feces: diagnostic test of choice
  - Sensitive and specific
  - False-positive result possible with recent vaccination (beginning 5 days after vaccination and continuing for 1 week)
  - False-negative result possible with fecal sample obtained outside period of shedding or profusely hemorrhagic diarrhea (diluted or complexed antigen fails to react with test antibody)
- Fecal flotation and fecal wet preparation: concurrent helminthiasis is common.
- CBC: leukopenia (neutropenia) is common and supports the need for broad-spectrum antibiotic treatment. If financial restrictions: hematocrit, total solids, and blood smear as a minimum for hematologic examination.
- Serum biochemistry panel: hypokalemia, hypoalbuminemia, and hypoglycemia are common correctable secondary effects of parvoviral enteritis. Azotemia (often prerenal) and liver enzyme elevations are common. If severe financial restrictions: serum potassium, albumin, and glucose as a minimum for serum biochemistry.
- Urinalysis: generally unremarkable; specific gravity > 1.035 confirms prerenal source of azotemia.
- Abdominal radiography: to avoid misdiagnosis (e.g., identify foreign body) and detect abnormalities secondary to parvoviral enteritis (e.g., obstruction due to intussusception).

ADVANCED OR CONFIRMATORY TESTING

Financial considerations often result in empirical therapy without comprehensive evaluation beyond confirming the diagnosis. In cases of financial restriction, it is considered more important to direct veterinary costs toward treating the pup rather than performing exhaustive diagnostic testing. While doing so carries a risk of missing important information, which the owner must accept, most puppies will recover with supportive care; without treatment, the mortality rate is high.

TREATMENT

TREATMENT OVERVIEW

Treatment goals are rehydration, treatment or prevention of sepsis, correction of potassium and glucose levels, normalization of blood pressure (BP), cessation of vomiting, pain control, + enteral nutrition, and voiding iatrogenic complications (e.g., risk of abscess formation with subcutaneous injections in parvovirus cases [especially with neutropenia]).

ACUTE GENERAL TREATMENT

See table below.

Initial Treatment of Parvoviral Enteritis in Puppies

At admission	• Place IV catheter, administer IV antibiotics (cefazolin, 22 mg/kg IV q 8 h; or ampicillin, 22 mg/kg IV q 6 h). If leukopenia: add enrofloxacin, 7.5-10 mg/kg slow IV q 24 h; or once patient is rehydrated, gentamicin, 6 mg/kg IV q 24 h. Aminoglycosides are contraindicated in hypovolemia/dehydration. • Test: hematocrit/total protein/glucose • crystalloid fluid bolus (e.g., lactated Ringer's solution 60 mL/kg) if hypovolemic shock
First 2 hours	• Calculate fluid needs (i.e., sum of: rehydration + maintenance + ongoing losses for first 12 hours). Note: rehydration (mL) = % dehydration (expressed as a percent [7% is 7]) × body weight in kg × 10. • Maintenance is 65 mL/kg/d (30 mL/lb/d) • Give ¼ to ½ of amount over first 2 hours to correct intravascular volume and blood pressure (warm fluids to body temperature). • Colloids can be used at 10-20 mL/kg IV over 1-4 hours if shock is present or if albumin is low. Recall additional cost of colloids.
After first 2 hours	• Give rest of fluid allotment over next 10 hours. • Test hematocrit + total protein + serum potassium + serum/blood glucose. • Warm patient on heating pad at this point if needed (not before; doing so may dilate peripheral vasculature). • Add glucose to fluids if needed (50 mL of 50% dextrose in 1 liter bag = 2.5% or 100 mL of 50% dextrose in 1 liter bag = 5%). • Plasma or polymerized hemoglobin (Oxyglobin) can be administered as an immunotherapy (plasma) and for oncotic pressure; potentially indicated if plasma albumin < 1.5 mg/dL. • Blood transfusion or polymerized hemoglobin indicated if status worsening and hematocrit < 20%
Approximately 2-3 hours	• Metoclopramide IV constant rate infusion (CRI), 1-2 mg/kg/d, to treat ileus and/or vomiting • Pain control: e.g., buprenorphine, 0.01 mg/kg IV q 6 h • Amikacin/gentamicin IV if not already administered and blood pressure has improved, or enrofloxacin if a concern persists regarding nephrotoxicity • Test: blood pressure, palpate for urine in bladder, confirm capillary refill time < 2 seconds.
Approximately 4-5 hours	• Start to feed (aim for at least ⅓ of requirements over next 24 hours). Some clinicians will advocate feeding despite vomiting. • Calculate energy requirements with formula: kcal = [(body weight (kg) × 30) + 70] × illness factor (1.25-1.5) • See main text for added control of vomiting and diet.
Approximately 12 hours	• Reassess hydration (weigh patient often): continue rehydration as needed. • In pups with large ongoing losses, fluid rates may be very high (5-10 mL/kg/h). Titrate fluid rate to hydration, perfusion, and clinical signs (vomiting and diarrhea).

CHRONIC TREATMENT

- Continuation of IV fluids, antibiotic therapy, pain control, antiemetic treatment, and nutrition as described in table
- Repeated blood, plasma, or synthetic colloid transfusions as often as needed
- To control vomiting after ensuring no obstruction (e.g., intussusception):
    - Step 1: continuous rate infusion (CRI) metoclopramide (as previously described)
    - Step 2: maropitant (Cerenia), 1 mg/kg SQ q 24 h
    - Step 3: add ondansetron, 0.5-1 mg/kg PO or IV q 12-24 h; or dolasetron, 0.6 mg/kg IV q 24 h.
    - Step 4: add prochlorperazine (often given as a suppository).
- Deworming:

- Fenbendazole 50 mg/kg PO q 24 h, 3-5 days (if > 12 weeks old); *or* ○ Ivermectin 0.2 mg/kg SQ once

NUTRITION/DIET

- High-protein, high-calorie foods (e.g., Eukanuba Max Calorie, Hill's Science Diet A/D) diluted with as little water as possible
- It is the author's opinion that a small volume of food is far more important than a low-fat content.

DRUG INTERACTIONS

- Flunixin meglumine is nephrotoxic and gastric ulcerogenic and should be avoided in animals that are hypovolemic.
- Fluoroquinolones (5 mg/kg q 24 h) used for 5-8 days should be safe and *not* cause cartilage problems.
- Ivermectin deworming is not advised in debilitated patients.

POSSIBLE COMPLICATIONS

- Intussusception or rectal prolapse
- Septic arthritis or endocarditis
- Acute respiratory distress syndrome
- Pneumonia (embolic, aspiration, or opportunistic [e.g., canine distemper])

RECOMMENDED MONITORING

- Clinicians should monitor the following at admission, after 2 hours of fluid therapy, and then at least on a daily basis in patients that are still ill:
  - Body weight
  - Blood glucose
  - Hematocrit and total solids
  - Serum potassium
- Pediatric sampling tubes and very small quantities of blood should be used. Once the puppy is eating, monitoring should be curtailed or stopped to avoid overinterpretation of results in an animal that is improving.

PROGNOSIS AND OUTCOME

Good with correct therapy. Following the treatment protocol, a 93%-95% success rate is expected with severely ill, confirmed cases of parvoviral enteritis.

PEARLS & CONSIDERATIONS

COMMENTS

Essential aspects of management include:

- Normalize hydration, potassium, and glucose.
- Control vomiting.
- Control pain.
- Feed early.

TECHNICIAN TIPS

- Become familiar with estimating the volume of fluid on a surface such as the cage floor. This helps in calculating daily fluid requirements.
- Wear gloves and use strict hygiene when handling these patients, not only for contagion prevention but because of their immunocompromised state (often leukopenic); this applies to doctors and anyone else in contact as well.

PREVENTION

- Ensure adequate vaccination status.
- Owners should limit environmental access for puppies until they are fully vaccinated.
- Dogs that survive parvoviral enteritis generally have immunity to reinfection (lifelong).

CLIENT EDUCATION

- Parvovirus remains in the environment for up to 7 months or more. Indoor surfaces should be cleaned and then disinfected with diluted bleach, and only vaccinated adult dogs should be allowed in the dog's immediate environment.
- Serial vaccination of all puppies until at least 12 weeks of age is essential; typical protocols involve vaccination at age 6, 9, 12, and possibly 16 weeks, the latter being for breeds at risk.
- Annual re vaccination of adult, and especially geriatric, dogs with a complete history of vaccinations is controversial, since titers remain high for more than 1 year. The debate over the appropriate interval of vaccination interval in adult dogs remains unresolved, with a recent advisory board recommending vaccination every 3 years.

SUGGESTED READING

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Mohr AJ, et al: Effect of early enteral nutrition on intestinal permeability, intestinal protein loss, and outcome in dogs with severe parvoviral enteritis. J Vet Intern Med 17:791– 798, 2003.

Prittie J: Canine parvoviral enteritis: a review of diagnosis, management, and prevention. J Vet Emerg Crit Care 14(3):167–176, 2004.

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Parturition, Normal

BASIC INFORMATION

DEFINITION

The act or process of giving birth to puppies or kittens

SYNONYMS

- Queening: parturition in the queen (female cat)
- Whelping: parturition in the bitch

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs and cats: adult, female

CONTAGION & ZOONOSIS: *Brucella canis* (see p. 162) and canine herpesvirus 1 (see p. 525) can be shed in lochia (parturient uterine fluids) during term parturition, preterm parturition, and/or abortion.

GEOGRAPHY AND SEASONALITY

- With the exception of the basenji, bitches are nonseasonal, meaning that parturition occurs year round. However, in the basenji, ovulation only occurs in October, and parturition associated with a resulting pregnancy only occurs in December.
- By contrast, queens are seasonal, long-day breeders; estrous cycles cease during October-December (Northern Hemisphere) unless they are exposed to 14 hours of light (natural and artificial). Parturition associated with any resulting pregnancy could be expected about 65 days from breeding (February-December).

ASSOCIATED CONDITIONS & DISORDERS

- Dystocia
- Premature parturition
- Abortion

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Bitch or queen uncomfortable about 60 days after breeding, may have a vaginal discharge

PHYSICAL EXAM FINDINGS

- In the bitch, rectal temperature is normal to low normal (98°F-100°F; 36°C-37°C) in the hours before parturition and increases to normal or slightly higher than normal during parturition. In the queen, rectal temperature is normal to low normal (100.5°F-102.5°F; 37.8°C-39.3°C), with additional variation based on environment, body condition, and other factors.
- Respiration and heart rates are slightly increased to normal.
- Uterine contractions may be visible through the abdominal wall.
- Examiner may be able to palpate fetuses transabdominally.

ETIOLOGY AND PATHOPHYSIOLOGY

- Three stages of labor:
  - Stage 1: cervical dilation, 3-6 hours
  - Stage 2: fetal expulsion, 3-6 hours (depends upon litter size)
  - Stage 3: placental expulsion, occurs at the same time or within minutes of each fetal expulsion (however, two fetuses and then two placentas may be delivered).
- Dystocia may occur for a variety of reasons (see p. 329).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Parturition is identified when a gravid dam is at term gestation and is showing clinical signs of labor or has began delivering fetuses.

DIFFERENTIAL DIAGNOSIS

- Abortion
- Dystocia
- Pseudopregnancy
- Premature birth
- Pyometra

INITIAL DATABASE

- Pups or kittens are present on abdominal palpation
- Confirmation of fetal skeletons in the normal position and not too large for dam's bony pelvis: abdominal radiography after 42 days' gestation
- Evaluation of fetal distress: see p. 162

ADVANCED OR CONFIRMATORY TESTING

Tocodynamometry can be used for monitoring uterine contractility (see p. 162)

PARTURITION, NORMAL A tocodynamometer used for monitoring uterine contractility in bitches.

TREATMENT

TREATMENT OVERVIEW

- Goal: delivery of healthy puppies or kittens without compromising mother's health
- Bitches and queens with normal parturition do not require any treatment.

ACUTE GENERAL TREATMENT

- In normal parturition, treatment is not needed.
- If parturition is not normal, see p. 329.

NUTRITION/DIET

Administration of a calcium carbonate tablet (e.g., Tums) at the onset of parturition may increase the strength of uterine contractions and prevent dystocia secondary to uterine inertia. However, administration of any calcium supplementation prior to parturition is contraindicated.

BEHAVIOR/EXERCISE

Dams can have unrestricted exercise before and during parturition.

POSSIBLE COMPLICATIONS

If the bitch or queen has prolonged abdominal contractions without delivery of a fetus, or appears to be in constant intense pain, she should be evaluated by a clinician (see p. 162).

RECOMMENDED MONITORING

- Clinicians can monitor the puppy or kitten delivery and be available to assist if needed (e.g., if dystocia occurs, if puppies experience distress).
- Clinicians should make sure a placenta is delivered following each fetus.

PROGNOSIS AND OUTCOME

- Good if parturition is normal
- Fair to guarded in cases of dystocia

PEARLS & CONSIDERATIONS

COMMENTS

- As parturition is a normal process, many animal owners and breeders prefer that the female deliver pups or kittens at home in familiar surroundings.
- Oxytocin treatment should be used only if the cervix is open (see p. 162).
- Dark-green colored lochia or postpartum vaginal discharge before the delivery of any pups in the bitch is an indication of premature placental separation. The bitch should be evaluated for fetal viability by abdominal ultrasonography and may require a caesarean section to remove the fetuses.

PREVENTION

Ovariohysterectomy

TECHNICIAN TIP

- Technicians involved in whelping/queening should be familiar with
  - Basic asepsis and hygiene of neonates
  - Normal neonatal responses that indicate viability (versus signs of distress)
  - Normal maternal behavior
  - Neonatal resuscitation

CLIENT EDUCATION

For prepartum bitches, the client should monitor the rectal temperature two to three times daily beginning at 56 days postbreeding. Rectal temperature decreases by 1°F-2°F (0.5-1°C) about 8-12 hours before whelping.

SUGGESTED READING

Johnston S, Root Kustritz M, Olson P: Canine and feline theriogenology, Philadelphia, 2001, WB Saunders.

AUTHORS: MUSHTAQ A. MEMON, MICHELLE A. KUTZLER

EDITOR: MICHELLE A. KUTZLER

Paresis, Hind Limb

BASIC INFORMATION

DEFINITION

Paraparesis is defined as partial loss of motor function to the pelvic limbs. Para-paralysis or paraplegia is a complete loss of voluntary motor function to the pelvic limbs.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Any species, age, or sex can be affected.

GENETICS & BREED PREDISPOSITION

- Young to middle-aged chondrodystrophoid dogs (e.g., basset hounds, dachshunds, beagles) are predisposed to intervertebral disk disease (IVDD), especially Hansen type I.
- Middle-aged to older nonchondrodystrophoid dogs (e.g., German shepherds) are predisposed to IVDD, especially Hansen type II.
- German shepherds (geriatric) are over-represented in degenerative myelopathy.

CONTAGION & ZOONOSIS: In some cases where underlying etiology is infectious (e.g., rabies)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Hind limb paresis or paralysis can present as difficulty or inability to use the hind limbs due to weakness, ataxia (incoordination), or spasticity (limb stiffness caused by a neurologic lesion). Weakness suggests a lower motor neuron or neuromuscular lesion, whereas spasticity and ataxia suggest an upper motor neuron lesion.

HISTORY, CHIEF COMPLAINT: Inability to walk on the hind leg(s)

PHYSICAL EXAM FINDINGS

- Assessment of the femoral pulse; if absent, consider aortic thromboembolism as a diagnosis.
- Palpation of the bones of limbs, pelvis (including rectal exam in dogs), and vertebral column for fractures/luxations
- Fundic exam: for evidence of multifocal/diffuse central nervous system (CNS) inflammation
- Neurologic injuries: physical findings depend on severity of lesion.
- Gait varies from mild hind limb ataxia to a nonambulatory status without deep pain perception.
- Spinal reflexes (e.g., patellar):
  - Hyporeflexia: lesion in L4-S2 spinal cord segments
  - Hyperreflexia: lesion in T3-L3 spinal cord segments
- Spinal hyperpathia (back pain on palpation):
  - Presence: may indicate IVDD, neoplasia, or trauma
  - Absence: may indicate embolism or degenerative cord process
- Muscle tone:
  - Increased (spasticity): lesion in T3-L3 spinal cord segments
  - Decreased: lesion in L4-S2 spinal cord segments

ETIOLOGY AND PATHOPHYSIOLOGY

- IVDD (see p. 1571):
  - Degenerative disk changes lead to herniation of the nucleus pulposus into the spinal canal.
    - Hansen type I disk rupture: focal, acute myelopathy
    - Hansen type II disk rupture: chronic, progressive disk (annulus) bulging into the spinal canal; chronic, slowly progressive myelopathy
    - Concussive type III disk rupture: high velocity rupture that leaves little residual compression
- Fibrocartilaginous embolization (see p. 392):
  - Herniation of disk material into vertebral body and entrance into the venous plexus
- Degenerative myelopathies (see p. 286:
  - Progressive, diffuse degeneration of spinal cord myelin and axons

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Patients with weakness or motor dysfunction confined to the pelvic limbs most likely have neurologic or orthopedic disease. Definitive diagnosis begins with neurologic and orthopedic exams and usually requires advanced spinal cord imaging (myelogram, CT, MRI)

DIFFERENTIAL DIAGNOSIS

- Acute, nonprogressive: orthopedic intervertebral disk rupture, fracture/luxation, fibrocartilaginous embolism, aortic thromboembolism
- Acute progressive: intervertebral disk rupture (type I), hemorrhagic myelomalacia, neoplasia, infectious/inflammatory (distemper myelitis; bacterial, protozoal, or fungal myelitis; granulomatous meningoencephalitis; feline infectious peritonitis; diskospondylitis)
- Chronic progressive: IVDD (type II), degenerative myelopathies, neoplasia, infectious/inflammatory (as previously stated)

INITIAL DATABASE

- CBC, serum biochemistry panel, urinalysis: may reflect stress or underlying infectious cause (less common)
- Complete orthopedic (see p. 1315), neurologic (see p. 1311) and cardiovascular evaluation to rule out concurrent disease
- Spinal radiographs to evaluate animal for bony lesions such as fracture, neoplasm, or infection

ADVANCED OR CONFIRMATORY TESTING

- Myelogram, CT, or MRI (seepp. 1306 ,1233 , and 1302): spinal cord compression secondary to IVDD or neoplasia or changes consistent with infection
- Cerebrospinal fluid (CSF) analysis (): evidence of infection, inflammation, exfoliating neoplasia
- Serum or CSF titers: to assess for infectious etiologies, especially if initial CSF analysis suggests active inflammation
- CSF culture if indicated by cytologic examination report

TREATMENT

TREATMENT OVERVIEW

Treatment should address the underlying cause: surgical decompression if a compressive lesion is found (IVDD, neoplasia, granuloma, etc.) or medical management as indicated (antibiotics, antiinflammatory medication, antifungal medication). The main goal of treatment is pain relief and resolution of neurologic dysfunction.

ACUTE GENERAL TREATMENT

- Acute traumatic spinal cord injuries (no spinal cord compression): consider initial methylprednisolone (30 mg/kg IV, then 15 mg/kg IV 2 and 4 hours later; if no improvement, consider surgical intervention).
  - Must be given within the first 8 hours to be effective
  - Further evaluation to determine need for surgery
  - Dexamethasone is contraindicated, as there is no evidence of efficacy, and gastrointestinal side effects can be severe.
- Pain secondary to intervertebral disk rupture with no neurologic deficits: consider nonsteroidal antiinflammatory drug (NSAID) at appropriate dose OR tapering course of prednisone (start at 0.5 mg/kg PO q 12 h and decrease by 50% every 5 days) and methocarbamol (20 mg/kg PO q 8 h) for 2 weeks and strict cage confinement for 4 weeks.
- Animals that have neurologic deficits should be evaluated with advanced imaging (myelogram, CT, MRI), followed by surgical decompression if indicated; referral to veterinary surgeon or neurosurgeon is recommended.

CHRONIC TREATMENT

Nursing care:

- Preventing pressure sores, urinary tract infections, muscle atrophy
- Hygiene: providing clean, dry, well-padded bedding
- Performing manual urinary bladder expression or catheterization if not voiding normally
- Performing physical rehabilitation exercises as indicated (seep. 1329)

POSSIBLE COMPLICATIONS

- Methylprednisolone may cause gastrointestinal (GI) ulceration.
- Ascending myelomalacia from severe cord injury is somewhat unpredictable and has a grave prognosis.

RECOMMENDED MONITORING

- Reevaluation of animal's neurologic function at 4-week intervals; duration of reevaluation is based on the animal's progress.
- If the dog remains nonambulatory after weeks or months, without signs of improvement in limb function, a canine cart is an option.

PROGNOSIS AND OUTCOME 

- Based on preoperative neurologic exam and underlying disease
- Acute spinal lesion in an animal with good deep pain perception: fair to excellent for return to near-normal neurologic function with surgery
- If deep pain perception is not present: prognosis is guarded to poor if surgical lesion is addressed in the first 8 hours and poor to grave if after 8 hours.
- Chronic spinal cord compression in an animal with good deep pain perception: guarded to good prognosis, depending on number of lesions and duration of clinical signs, with a prospect of a longer recovery with surgical decompression.
- Nonsurgical spinal cord disease has a variable prognosis depending on underlying etiology.

PEARLS & CONSIDERATIONS 

COMMENTS

Immediate referral to a surgeon or neurosurgeon is warranted for an animal that is decompensating neurologically.

TECHNICIAN TIPS

Care should be taken when moving these patients, especially if clinical signs are acute and history of trauma is unknown.

Two technicians per patient and/or rigid support are recommended.

CLIENT EDUCATION

- Prognosis often guarded, depending on preoperative neurologic examination; potential for prolonged postoperative nursing care.
- It is essential to respect a recommendation of a period of cage rest/confinement.

SUGGESTED READING

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Paresis, Forelimb

BASIC INFORMATION

DEFINITION

- Monoparesis: partial loss of motor function to one limb; voluntary movement but will not initiate gait and unable to support weight
- Monoplegia/paralysis: complete loss of motor function to one limb
- Mononeuropathy: disease or injury of a peripheral nerve or its nerve roots

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Weakness, lameness, or inability to use a forelimb

ASSOCIATED DISEASES & DISORDERS

- Horner's syndrome
- Loss of ipsilateral cutaneous trunci (panniculus) reflex
- Self-mutilation/trauma to affected limb

PHYSICAL EXAM FINDINGS

- Lower motor neuron (LMN) signs to the affected limb: weakness and decreased muscle tone
- Variable degree: mild forelimb lameness to complete loss of sensory and motor function
- Denervation atrophy of forelimb musculature, usually within 7-10 days of nerve injury. Differentiate from disuse atrophy, which is slower to develop and generally less severe.
- Nerve root signature: lameness and pain of affected forelimb caused by entrapment of a nerve root within the brachial plexus (see pp. 149 and)
- Suspicion of neoplasia if chronic progressive monoparesis, nerve root signature, and denervation atrophy
- Variable exam findings also may include:
    - Horner's syndrome (ipsilateral); common with traumatic injuries to the brachial plexus
    - Loss of cutaneous trunci (panniculus) reflex (ipsilateral); may be seen with brachial plexus injuries
    - Palpable mass in axilla; uncommon
    - Dysesthesia/paresthesia of limb and secondary self-trauma
    - Traumatic injury/fracture

ETIOLOGY AND PATHOPHYSIOLOGY

- Central nervous system (CNS):
    - Lesions affecting spinal cord segments C6-T2 can cause LMN forelimb signs.
    - Flaccid forelimb monoparesis
    - Basis: injury to LMN cell bodies that innervate forelimb musculature
    - Usually associated with upper motor neuron signs to ipsilateral pelvic limb
- Peripheral nervous system:
    - Spinal/peripheral nerve disorders cause sensory and motor dysfunction distal to the lesion (permanent nerve damage or temporary, self-resolving trauma called neurapraxia).
        - Trauma: brachial plexus avulsion and radial nerve injury as examples
        - Neoplasia: commonly affected are brachial plexus and dorsal nerve roots
- Cervicothoracic spinal cord, nerve roots, sympathetic trunk: Horner's syndrome (ipsilateral)
- Lateral thoracic nerve (C8, T1) disruption causes ipsilateral loss of the panniculus reflex.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A complete orthopedic and neurologic exam (including distribution of sensory loss) is the best means of differentiating musculoskeletal disease from neural involvement. Electromyography and nerve conduction can also aid in confirming the diagnosis

of a nerve injury, determining the distribution, estimating the prognosis and monitoring recovery, though these procedures are uncommonly performed. Advanced imaging (MRI, CT) and/or surgical exploration and biopsy may be necessary to achieve a definitive diagnosis.

DIFFERENTIAL DIAGNOSIS

- CNS
  - Trauma
  - Vascular
  - Neoplasia
  - Infectious
  - Inflammatory
- Peripheral nervous system
  - Trauma
  - Vascular
  - Neoplasia
  - Inflammatory

INITIAL DATABASE

- CBC, serum biochemistry panel, urinalysis: generally unremarkable
- Orthopedic (see p. 1315) and cardiovascular evaluation: rule out concurrent diseases
- Neurologic exam (gait, posture, spinal reflexes; seep. 1311)
  - Distribution and severity of sensory loss aids in localizing the injury to a particular nerve or within 2-3 spinal cord segments: most important test for establishing prognosis for peripheral nerve injuries.
- Forelimb, spinal radiographs (bone fractures, luxations, neoplasia, or infection)

ADVANCED OR CONFIRMATORY TESTING

- Myelogram (see p. 1306) or MRI (see p. 1302) to localize unilateral spinal cord compression (intervertebral disk disease [IVDD] or neoplasia)
- MRI or CT scan to evaluate for nerve/nerve sheath tumors
- Electrodiagnostics (electromyography [EMG], motor nerve conduction [see online chapter: Electromyography and Nerve Conduction Velocity]) to localize the dysfunctional spinal cord segment, nerve root, or peripheral nerve
  - EMG used for determining if LMN, myelin, or muscle fibers are the site of the lesion. Fibrillation potentials, positive sharp waves, and fasciculations can be seen beginning 5 days after denervation.
  - Nerve conduction will be polyphasic and prolonged with LMN disease (with severe loss of myelin sheath) and absent with avulsion injury (or injury resulting in wallerian degeneration).
- Surgical exploration (based on imaging results):
  - Biopsy, histopathologic examination for suspected neoplasia o Evaluation of type, extent, and severity of nerve injury

TREATMENT

TREATMENT OVERVIEW

- Short-term treatment is dictated by the etiology, anatomic localization, and severity of the lesion/injury. Long-term treatment may involve appropriate medications, physical rehabilitation, protection of affected limb from trauma, and an adequate duration of supportive care to allow for recovery/reinnervation.

ACUTE GENERAL TREATMENT

- CNS
  - Trauma; intervertebral disk herniation (see pp. 1039 and)
  - Vascular (see p. 392)
  - Neoplasia; treatment based on tumor type, location, and invasiveness
  - Infectious (e.g., diskospondylitis [])
- Peripheral nervous system
  - Trauma (see pp. 149 and 1016)
  - Surgical management: referral to neurosurgeon for primary nerve repair (lacerated/entrapped nerve). Carpal arthrodesis or transposition of a flexor tendon may be helpful in radial nerve injury.
  - Vascular: ischemic thromboembolic neuromyopathy involving the subclavian or brachial artery
    - Pain management, anticoagulation therapy, treatment of underlying heart disease

- Neoplasia: surgical recommendations depend on the type, location, and invasiveness of the tumor.
- Inflammatory: brachial plexus neuritis (hypertrophic, chronic or idiopathic). Medical management may include prednisolone, chlorambucil versus supportive care only.

CHRONIC TREATMENT

- Physical rehabilitation (see p. 1329); the animal should continue treatment for 3-6 months or until it shows signs of reinnervation.
- Adequate protection of an affected limb to prevent secondary trauma and self-mutilation

POSSIBLE COMPLICATIONS

- Failure to regain adequate function of affected limb
- Local recurrence of nerve root tumors
- Persistent trauma, self-mutilation, or contracture of paretic limb, necessitating amputation

RECOMMENDED MONITORING

- Monitoring of limb daily for signs of trauma or self-mutilation
- Serial neurologic examinations for up to 6 months to evaluate limb for reinnervation
- Serial electrodiagnostics to monitor recovery
- Monitoring for evidence of recurrence of nerve root tumor by physical exam and MRI or CT scan if indicated

PROGNOSIS AND OUTCOME

- Largely depends on the neurologic exam at presentation and response to treatment
- Central
  - Intervertebral disk herniation:
    - Fair to excellent if good deep pain perception
    - Guarded to poor with poor deep pain sensation if addressed within 8 hours
    - Poor to grave if poor deep pain sensation and addressed after 8 hours
  - FCE:
    - Approximately 50% chance for return to function of limb
  - Neoplasia:
    - Guarded to poor based on surgical accessibility and follow-up care
- Peripheral
  - Brachial plexus avulsion:
    - Generally poor; often requires amputation
    - Guarded to fair if deep pain sensation is present
  - Brachial plexus neuritis:
    - Guarded but recovery is possible
  - Peripheral nerve injuries:
    - Fair to good for mild neurologic deficits, sharp lacerations with prompt surgical repair and short distance from site of injury to end organ
    - Guarded to poor for severe neurologic deficits; stretching, crushing, and avulsion injuries; contaminated wounds with delayed surgical repair; and large distance from site of injury to end organ (>12 inches/>30 cm)
  - Ischemic thromboembolic neuromyopathy
    - Prognosis more favorable for forelimb emboli
  - Nerve sheath tumors:
    - Guarded to poor because local recurrence is common

PEARLS & CONSIDERATIONS

COMMENTS

Brachial plexus avulsions with severe traction on the nerve roots may cause damage to the spinal pathways, resulting in pelvic limb deficits that are generally ipsilateral but can be bilateral.

TECHNICIAN TIPS

Fractures or luxations can cause damage to peripheral or spinal nerves. Use caution when manipulating a patient that has suspected fractures or luxations so as to avoid secondary nerve injuries.

CLIENT EDUCATION

- Clinicians should inform clients of prognosis, expected duration of forelimb paresis, and potential for failure to regain adequate function of limb, which necessitates amputation.
- Clinicians should perform or recommend physical rehabilitation techniques.

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Paraquat and Diquat Toxicoses

BASIC INFORMATION

DEFINITION

Paraquat and diquat are herbicides with corrosive properties, causing acute gastrointestinal (GI) signs, abdominal pain, and oral mucosal ulcerations when ingested. Delayed pulmonary toxicity (pulmonary fibrosis) occurs with paraquat toxicosis, and central nervous system (CNS) effects can occur with diquat.

SYNONYMS

Paraquat: 1,1′-dimethyl-4,4′-bipyridinium or N,N′-dimethyldipyridyl dichloride

Diquat: 9,10-dihydro-8a,10a-diazoniaphenanthrene dibromide or ethylene dipyridylium dibromide

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs are more commonly involved than cats.

GEOGRAPHY AND SEASONALITY: Accidental poisonings are more common during growing seasons; paraquat has been used year round for malicious poisonings in dogs.

CONTAGION/ZOONOSIS: Paraquat penetrates transcutaneously in animals and humans; users and veterinary personnel should wear gloves and protective clothing.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Known/suspected exposure to paraquat or diquat herbicide
- Clinical signs within hours to days after exposure; with acute ingestions, neurologic signs may occur within 2-6 hours, whereas the respiratory effects are seen in 3-5 days
- Paraquat: vomiting (all cases), lethargy, anorexia, diarrhea, ataxia; eventually, tachypnea and respiratory distress are apparent.
- Diquat: vomiting, lethargy, anorexia, diarrhea, ataxia

PHYSICAL EXAM FINDINGS

- Paraquat: initially, patient may experience oral, esophageal, and gastric irritation leading to ulceration; abdominal pain; dermatitis if topical contact. Patient may then experience hypotension, arrhythmias, weakness, and disorientation/depression due to cerebral edema. Onset of cough, dyspnea, and hemoptysis may occur 3-14 days after ingestion.
- Diquat: oral/pharyngeal mucosal ulceration, oliguria/anuria, dermal irritation/burns, weakness, coma; rarely, arrhythmias, seizures, and dyspnea due to noncardiogenic pulmonary edema.

ETIOLOGY AND PATHOPHYSIOLOGY

- Paraquat concentrates in lung tissue (type I and II pneumocytes). Free radicals are produced, causing cellular injury (especially pulmonary, GI, renal, and erythrocytic). Cell wall injury leads to mononuclear macrophage activation and, notably, pulmonary fibrosis, which can be fatal 3-14 days after ingestion. Paraquat is a restricted-use pesticide (RUP) owing to its toxicity; only certified applicators can purchase and use the product.
- The mechanism of diquat toxicity is similar, but diquat does not accumulate in the lungs (no pulmonary fibrosis); instead, diquat may cause cerebral hemorrhage, coma, and renal failure.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The clinical diagnosis is made from history and physical exam: observed or suspected exposure, typically in a patient with fresh oral ulcers. Delayed pulmonary effects (3-5 days from paraquat) and CNS signs (hours after exposure to diquat) help support the diagnosis during/after treatment. Definitive diagnosis is possible through toxicologic analysis of vomitus, bait, blood, plasma, or other tissues (liver) within 48 hours of exposure.

DIFFERENTIAL DIAGNOSIS

- Toxicosis involving any caustic or corrosive agent (acids, alkali, cationic detergents, potpourri)
- Kidney disease/renal failure (uremic ulcers)

INITIAL DATABASE

- Paraquat:
  - CBC: neutrophilia, monocytosis, lymphopenia
  - Serum biochemistry panel: moderate increases in blood urea nitrogen (BUN), aspartate aminotransferase, and alanine aminotransferase in 24-96 hours and slight increases in total protein, creatinine, cholesterol, and bilirubin
  - Urinalysis: myoglobinuria (from rhabdomyolysis); proteinuria, hematuria (acute renal injury)
  - Thoracic radiographs: initially normal, progressing to noncardiogenic pulmonary edema (marked interstitial lung pattern); pneumomediastinum is a common, early finding.
- Diquat: serum biochemistry panel shows BUN, creatinine elevations (within 24-96 hours) and liver enzyme elevations

ADVANCED OR CONFIRMATORY TESTING

- Analysis of vomitus, bait, plasma, blood, tissues, urine: samples must be obtained within 48 hours of exposure, because initial excretion is rapid; contact the laboratory first.
- Histopathologic lesions:
  - Paraquat: marked pulmonary edema, hemorrhage, congestion, eventually fibrosis; mild hepatic congestion, degeneration; mild renal tubular degeneration, glomerulonephritis
  - Diquat: myocardial necrosis, cerebral hemorrhages, renal tubular damage

TREATMENT

TREATMENT OVERVIEW

Since no antidote exists for either substance, treatment is general and supportive.

ACUTE AND CHRONIC TREATMENT

- Decontamination of the animal:
  - Paraquat:
    - Emesis: induction of vomiting (see p. 1364) as soon as possible after ingestion, even though paraquat can be irritating or corrosive to the esophagus; the possible benefits of early removal outweigh the potential risks.
    - Fuller's earth or bentonite (either is a preferred choice over activated charcoal, because they bind paraquat/diquat more effectively, but most clinics do not carry them) or activated charcoal (1-4 g/kg q 4-8 h) can be used as an adsorbent and are most useful if given PO within 4 hours of exposure. Multiple doses are recommended.
    - Clinicians should bathe the entire patient if there is any dermal exposure. Paraquat is absorbed well through abraded or injured skin (wear protective clothing).
    - With ocular exposures, irrigate eyes with copious amounts of tepid water for at least 15 to 30 minutes (see p. 250).
  - Diquat
    - Induction of vomiting is usually not recommended unless the patient has been exposed to a very large dose of the toxin.
    - Activated charcoal, bentonite clay, or Fuller's earth: same dosage as for paraquat
    - With dermal exposure, the animal's skin should be immediately washed with soap and water. Diquat can be absorbed through damaged or injured skin, resulting in systemic poisoning. Absorption through intact skin is minimal.
    - Ocular exposures: same treatment as for paraquat
- Supportive care:
  - IV fluids as indicated to correct hypovolemia, electrolyte changes associated with vomiting
  - Control pain as needed (e.g., for dogs/cats: buprenorphine, 0.005-0.03 mg/kg IV, IM, or SQ q 6-12 h; or fentanyl patch).

- Ascorbic acid (antioxidant), 20-30 mg/kg IM, IV, or PO q 8 h, may be useful.
- Avoid supplemental oxygen therapy because it increases the formation of superoxide free radicals.
- Control vomiting as needed with maropitant, 1 mg/kg SQ q 24 h; or metoclopramide, 0.1-0.4 mg/kg SQ or IM q 6 h.
- Treatment of ventricular arrhythmias (see p. 1165), seizures (see p. 1009), secondary infections, oral ulcers (see), gastric ulcers (see), and renal complications (see p. 31) as needed.
- Positive-pressure ventilation (see p. 1362) may be used, but lung lesion may become (or may already be) irreversible.

POSSIBLE COMPLICATIONS

- Paraquat: pneumothorax, pneumopericardium, and subcutaneous emphysema
- Diquat: pneumonia, renal failure

RECOMMENDED MONITORING

- Paraquat: baseline thoracic radiographs and blood gases and serial monitoring for several days (CBC and renal and liver panels)
- Diquat: renal values (monitor for 3-4 days with large ingestions) and monitor CBC, liver enzymes, and electrolytes.

PROGNOSIS AND OUTCOME

- Paraquat: outcome appears to be related to dose and early intervention (decontamination of animal); poor prognosis for affected animals showing any clinical signs; those that survive the acute toxicosis often succumb to chronic pulmonary fibrosis.
- Diquat: good prognosis with early and aggressive treatment

PEARLS & CONSIDERATIONS

COMMENTS

- Paraquat LD50 (dogs, oral) 25-50 mg/kg
- Diquat LD50 (dogs, oral) 100 mg/kg
- Concentration of diquat in most ready-to-use weed and grass killer products is <1%. Systemic effects from these products is highly unlikely with casual exposure (e.g., dog walking through the sprayed area when it was still wet or dog licking the grass after spray) unless large amounts have been ingested from the container.

TECHNICIAN TIP

As with most ingestions of toxic material, knowing which toxin is involved allows for accurate treatment and prognostication. Therefore, clients telephoning because their dogs or cats have ingested a foreign substance should be encouraged to bring the container or label along with the patient.

PREVENTION

Keep animals away from all herbicides until dry; dipyridyl herbicides are rapidly and completely inactivated in the soil.

CLIENT EDUCATION

Follow label directions on all herbicides.

SUGGESTED READING

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Paraphimosis

BASIC INFORMATION

DEFINITION

Inability to retract the penis into the prepuce

SYNONYM

Penile protrusion

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Young, intact male dogs > castrated male dogs; rare in cats
- 4 months to 13 years of age (average: 2.9 years)

GENETICS & BREED PREDISPOSITION

- Boxer, Chihuahua, cocker spaniel, Doberman, German shepherd, German short-haired pointer, Great Pyrenees, Labrador retriever, poodle, and mixed-breed dogs
- Boxers (n = 4), poodles (n = 2), and mixed-breed dogs (n = 12) have had more than one case reported.

RISK FACTORS

- Developmental preputial anomalies (e.g., small preputial opening, aplastic or hypoplastic prepuce, hypospadias [urethra opening is on the ventral penis or perineum], male pseudohermaphroditism)
- Infectious (e.g., transmissible venereal tumor, balanoposthitis)
- Neurologic deficits associated with posterior paresis (e.g., intervertebral disk disease [IVDD], spinal tumors)
- Trauma (e.g., os penis fracture)

CONTAGION & ZOONOSIS

Transmissible venereal tumor preventing penile retraction

ASSOCIATED CONDITIONS & DISORDERS

- Balanoposthitis: inflammation of the glans penis (balanitis) and preputial mucosa (posthitis)
- Phimosis: inability to extrude the penis from the prepuce (paraphimosis occurs 14 times more frequently than phimosis in the dog)
- Priapism: prolonged penile erection with or without sexual arousal

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Acute paraphimosis usually resolves within 12 hours; chronic paraphimosis may be intermittent or continuous.

HISTORY, CHIEF COMPLAINT: History may include recent mating, penile or preputial trauma, masturbation, balanoposthitis, neurologic disease, and/or promazine tranquilizer administration.

PHYSICAL EXAM FINDINGS

- Protrusion of the penis from the prepuce: extent of penile protrusion can vary from only the apex to the entire length of the penis.
- Penile mucosa may be erythematous, dry, inflamed, edematous, ischemic, and painful, which may lead to self-mutilation. Chronic protrusion of the penis may lead to excoriation and subsequent cornification of the mucosa.

ETIOLOGY AND PATHOPHYSIOLOGY

- Most commonly associated with a relatively stenotic preputial orifice or with ineffective preputial musculature that cannot effectively retract the penis into the prepuce; hair ring or scar tissue also possible.
    - Following sexual excitement or copulation, the engorged penis may become entrapped outside the prepuce, causing penile strangulation, congestion, and paraphimosis.
    - Cranial preputial muscles (paired muscles originating from the cutaneous trunci) draw the prepuce cranially, normally about 1 cm beyond the tip of the penis.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Paraphimosis is diagnosed conclusively on physical exam alone. Additional testing may help elucidate the cause, although in dogs roughly 30% of cases are idiopathic.

DIFFERENTIAL DIAGNOSIS

- Balanoposthitis
- Phimosis
- Priapism

INITIAL DATABASE

Neurologic exam (see p. 1311) with specific attention to posterior peripheral motor and sensory function.

ADVANCED OR CONFIRMATORY TESTING

- Electromyographic testing and/or histopathologic evaluation of cranial preputial muscles: to identify abnormal function or cellular architecture; rarely necessary
- Radiographs: to identify concomitant os penis fracture

TREATMENT

TREATMENT OVERVIEW

Paraphimosis is an emergency condition. Immediate treatment should protect the penile mucosa, prevent additional swelling (edema, inflammation) and trauma, and return the penis within the prepuce as quickly as possible. The underlying cause is then addressed to reduce the risk of recurrence.

ACUTE GENERAL TREATMENT

- Conservative: reduction of penis size via topical cold compresses, topical hyperosmotic solutions (e.g., sugar, honey), and systemic antiinflammatory therapy (e.g., prednisolone sodium succinate [SoluDeltaCortef] 10 mg/kg slow IV bolus)
- Passage of urinary catheter: to ensure patency of urethra
- If paraphimosis occurred secondarily to promazine-induced priapism, benztropine mesylate (0.015 mg/kg IV) should be administered as soon as possible (i.e., within 6 hours of onset of clinical signs).
- Removal of hair from around the preputial orifice
- Manual replacement of the penis in the preputial sheath using lubrication and gentle digital pressure. If unsuccessful, emergency surgical intervention is required.

CHRONIC TREATMENT

Surgical intervention:

- Attempt manual reduction under general anesthesia.
- If unsuccessful, incisional enlargement of preputial orifice and retraction of penis within prepuce
- Options for preserving reduction: purse-string suture at the preputial orifice, preputial orifice narrowing, preputial lengthening (preputioplasty), preputial advancement, preputial muscle myorrhaphy, and phallopexy. None entirely eliminates the possibility of recurrence.

- Chronic paraphimosis can be eliminated with amputation of the penis and concurrent scrotal urethrostomy.
- Castration is often performed in conjunction with surgical correction of paraphimosis, but castration alone is not successful in correcting paraphimosis.

BEHAVIOR/EXERCISE

Affected intact males should be separated from estrous females for at least 4 weeks afterward. Efforts should be made to prevent excessive licking of the penile and prepuce that may result in self-mutilation.

POSSIBLE COMPLICATIONS

- Erection and ejaculation may be impaired following longstanding paraphimosis.
- Balanoposthitis secondary to phimosis may occur following surgical retention of the penis within the preputial cavity.
- Urethral stricture formation and recurrent urinary tract infections may result following penile amputation.

PROGNOSIS AND OUTCOME

The prognosis is good to guarded for the resolution of paraphimosis, depending on the severity and duration of clinical signs.

PEARLS & CONSIDERATIONS

COMMENTS

Dogs with developmental preputial conditions associated with paraphimosis should not be used for breeding.

PREVENTION

- Hairs around the preputial orifice should be kept short in long-haired dogs.
- Following mating or semen collection, application of a topical lubricant to penile mucosa around the preputial opening will prevent inversion of the prepuce during detumescence (natural resolution of erection and penile retraction).

PARAPHIMOSIS Ventral caudal abdomen of a longhaired male dog; cranial is to the top of the image. Following semen collection for an infertility evaluation, this dog developed paraphimosis secondary to inversion of the prepuce during detumescence. This was resolved quickly with application of a topical lubricant to penile mucosa near the preputial opening and gently sliding the prepuce over the swollen glans penis.

CLIENT EDUCATION

Paraphimosis may occur as a learned behavior secondary to penile licking (masturbation). Owners should be cautioned not to promote paraphimosis by positive behavioral reinforcement.

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Paraneoplastic Syndromes

BASIC INFORMATION

DEFINITION

Pathologic change in structure or function which develops secondary to and distant from a primary neoplasm. Certain paraneoplastic syndromes (PNS) occur very frequently, whereas others are rare. PNS mostly commonly arise secondary to hormonal or other cytokine factors produced by the tumor. In some instances, the PNS can be more harmful than the physical tumor.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Both canine and feline patients may experience PNS. In most cases, there is no sex predilection, with few exceptions (e.g., feline acromegaly in association with pituitary adenomas occurs more commonly in males).

GENETICS & BREED PREDISPOSITION

- PNS are rarely directly induced by genetic factors, with occasional exceptions (e.g., nodular dermatofibrosis associated with autosomal dominant heritable mutation of Birt-Hogg-Dube gene in German Shepherds). Affected dogs commonly develop bilateral renal cysts or cystadenocarcinomas. Female dogs may also develop uterine leiomyoma.
- Certain purebreds are predisposed to individual cancers, so incidence of PNS will be relatively higher (e.g., boxer has higher incidence of T-cell lymphoma; boxer, pug, Labrador retriever have higher incidence of mast cell tumors).

RISK FACTORS: Individual PNS associated with specific tumors:

- Hypercalcemia: T-cell lymphoma, anal sac apocrine gland adenocarcinoma, and parathyroid adenoma most common. Also reported sporadically with malignant melanoma, squamous cell carcinoma, mammary adenocarcinoma, thyroid carcinoma, bronchoalveolar carcinoma, multiple myeloma, and others.
- Cachexia: multiple tumor types
- Hypoglycemia: beta-cell tumor (insulinoma), gastrointestinal leiomyosarcoma, hepatocellular carcinoma most common; others sporadically
- Gastroduodenal ulceration: mast cell tumor (MCT), pancreatic gastrinoma (Zollinger-Ellison syndrome)
- Erythrocytosis: renal tumors, nasal fibrosarcoma
- Disseminated intravascular coagulopathy: hemangiosarcoma, acute leukemia, lymphoma
- Hyperviscosity syndrome: multiple myeloma, lymphoma, leukemia, primary polycythemia
- Hyperadrenocorticism: pituitary adenoma, primary adrenocortical adenoma/carcinoma
- Cardiac arrhythmias/altered blood pressure: pheochromocytoma, hemangiosarcoma
- Anemia: hemangiosarcoma, lymphoma, leukemia, multiple myeloma, estrogen-producing tumors (Sertoli cell), other chronic neoplasia
- Thrombocytopenia: lymphoma, leukemia, multiple myeloma, hemangiosarcoma
- Leukocytosis: lung tumor, renal transitional cell carcinoma (TCC)
- Peripheral neuropathy: many tumors
- Alopecia: pancreatic carcinoma
- Hypertrophic osteopathy: lung tumor (primary or metastatic), Sertoli cell tumor, renal TCC, nephroblastoma, adrenocortical carcinoma
- Myasthenia gravis: thymoma
- Acromegaly: pituitary adenoma (cats), mammary adenocarcinoma (dogs)
- Superficial necrolytic dermatitis (hepatocutaneous syndrome): glucagonoma

ASSOCIATED CONDITIONS & DISORDERS

- Chronic hypercalcemia can result in renal failure via tubular mineralization and ischemic damage.
- Hyperglobulinemia/hyperviscosity syndrome can lead to coagulopathy and hypertension, resulting in retinal detachment, seizures, renal infarction, cerebral/pulmonary thromboembolism, congestive heart failure.
- Hypoglycemia usually causes depression, ataxia, and seizures.
- Gastroduodenal ulceration from excessive histamine-induced gastric hydrochloric acid (HCl) production results in melena, hematemesis, and anemia.
- Pancytopenia predisposes patients to opportunistic infections and spontaneous hemorrhage.
- Myasthenia gravis-induced megaesophagus predisposes to aspiration pneumonia.
- Hypertrophic osteopathy causes fever and lameness.

- Hyperadrenocorticism may predispose to thromboembolism.
- Acromegaly commonly causes insulin resistance, hypertrophic cardiomyopathy, and renal failure.
- Hepatocutaneous syndrome results in superficial necrolytic dermatitis of skin, paw pads.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Hypercalcemia: most common clinical signs include polyuria and polydipsia (PU/PD). Patients may also be lethargic with inappetence, vomiting from renal failure.
- Cachexia: patient has profound loss of lean body mass, often despite normal appetite.
- Hyperviscosity syndrome: presenting clinical signs depend on organ system(s) affected: seizures, blindness, syncope, dyspnea.
- Hypoglycemia: depression, ataxia, and seizures
- Gastroduodenal ulceration: anorexia, melena, hematemesis
- Myasthenia gravis: regurgitation, dyspnea, weakness/collapse
- Hypertrophic osteopathy: lameness, lethargy
- Hyperadrenocorticism: PU/PD, polyphagia, bilaterally symmetric hair loss, muscle wasting, pot-bellied appearance, comedones
- Acromegaly: PU/PD, weight gain, enlarged head and limbs
- Peripheral neuropathy: cranial nerve deficits, altered proprioception, urinary/fecal incontinence
- Superficial necrolytic dermatitis: ulcerated cutaneous lesions, cracked/painful paw pads

PHYSICAL EXAM FINDINGS: Dependent on tumor type; see History, Chief Complaint

ETIOLOGY AND PATHOPHYSIOLOGY

- Hypercalcemia: due to excessive parathyroid hormone (PTH) production by parathyroid adenomas or humoral production of PTH-related peptide (PTHrp) and other cytokines (interleukin [IL]-1, transforming growth factor [TGF]-β), prostaglandins, and receptor activator of nuclear factor κB ligand (RANKL)
- Cachexia: complex metabolic derangement due to altered cytokine milieu (especially increased IL-1β, IL-6, tumor necrosis factor [TNF]-a), increased anaerobic glycolysis, and misappropriation of nutrients
- Hypoglycemia: due to excessive insulin or insulin-like growth factor 1 (IGF-1) production
- Gastroduodenal ulceration: most commonly result of hyperhistaminemia leading to excessive gastric acid in mast cell tumors and rarely hypergastrinemia in pancreatic gastrinoma
- Erythrocytosis: due to excessive production of erythropoietin (Epo)
- Bleeding disorder: due to antibody coating of platelets, platelet loss/sequestration/consumption, or inappropriate activation of the secondary coagulation cascade
- Hyperviscosity syndrome: due to excessive immunoglobulin production and subsequent antibody coating of red blood cells, leading to aggregation
- Hyperadrenocorticism: due to excessive cortisol production in adrenal glands; most commonly due to excessive ACTH release from pituitary tumors but may also be primarily produced by adrenal tumors, or rarely ectopically
- Cardiac arrhythmias/altered blood pressure: due to excessive catecholamine production, hypoxia, sepsis
- Cytopenias: due to hemorrhage, chronic inflammation, immune-mediated hemolysis, hormone-induced suppression, myelophthisis
- Leukocytosis: due to excessive production of granulocyte-macrophage colony stimulating factor (GM-CSF) or G-CSF
- Myasthenia gravis: due to antibody production targeted against acetylcholine receptors at neuromuscular junctions
- Acromegaly: due to excessive growth hormone (GH) production

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Definitive diagnosis of PNS requires observation of associated clinical signs, documentation of syndrome with laboratory testing when applicable, and confirmation of underlying cancer.

DIFFERENTIAL DIAGNOSIS

- Hypercalcemia: granulomatous disease, hypoadrenocorticism, renal secondary hyperparathyroidism, hypervitaminosis D, young/growing, spurious, osteogenic disease
- Cachexia: intestinal parasites, poor-quality diet, inadequate feeding, malabsorptive/maldigestive disorder
- Hypoglycemia: sepsis, iatrogenic (insulin overdose), spurious/old sample

- Gastroduodenal ulceration: nonsteroidal antiinflammatory medications (NSAIDs), corticosteroids, foreign body, toxin ingestion
- Erythrocytosis: hemoconcentration, breed-related variation (greyhounds, sled dogs)
- Bleeding disorder: anticoagulant rodenticide ingestion, sepsis, idiopathic immune-mediated thrombocytopenia
- Hyperadrenocorticism: iatrogenic (corticosteroid administration)
- Cardiac arrhythmias/altered blood pressure: primary cardiac disease, renal failure
- Cytopenias: infectious disease (especially *Rickettsiae)*
- Myasthenia gravis: hypothyroidism, hypoadrenocorticism, lead intoxication, esophagitis, idiopathic

INITIAL DATABASE

CBC, serum chemistry panel, urinalysis, coagulation profile, thoracic radiographs, abdominal ultrasound, tumor aspiration/biopsy to confirm neoplasia

ADVANCED OR CONFIRMATORY TESTING

- Hypercalcemia: measure PTH/PTHrp and ionized calcium to identify inappropriate function of hormone axis; parathyroid gland ultrasound to identify tumor; bone marrow aspiration to identify sequestered neoplasia.
- Hypoglycemia: measure serum insulin. Concentration should be below reference range; if level is high or within reference range with concurrent hypoglycemia, this suggests inappropriate function of the hormonal feedback axis.
- Pancytopenia: bone marrow aspiration to evaluate for infiltrative disease versus maturation arrest of cell lines
- Hyperviscosity syndrome: serum/urine protein electrophoresis to document monoclonal gammopathy
- Hyperadrenocorticism: urine cortisol/creatinine ratio, ACTH stimulation test, dexamethasone suppression test, endogenous ACTH to identify inappropriate function of pituitary-adrenal hormone axis.
- Myasthenia gravis: measure serum acetylcholine receptor antibody titer to prove autoimmunity.
- Acromegaly: measure serum GH, IGF-1 to confirm inappropriate hormone secretion.

TREATMENT

TREATMENT OVERVIEW

The severity of a PNS tends to parallel the status of the neoplasm. Direct treatment of the primary tumor (surgical excision, chemotherapy, or radiation therapy) should be the ultimate goal and usually causes resolution of the PNS. However, in some cases, the patient may be debilitated by the PNS and initially unable to undergo definitive therapy. Other supportive measures include the following:

- Hypercalcemia: saline diuresis, loop diuretics, corticosteroids, bisphosphonates, calcitonin to reduce serum calcium to normal range and/or to alleviate clinical signs
- Hyperviscosity syndrome: phlebotomy, plasmapheresis to reduce serum globulins to normal range
- Gastroduodenal ulceration: gastroprotectants (histamine receptor antagonists, proton pump inhibitors, coating agents, prostaglandin analogues) to reduce gastric HCl production; antiemetics, antidiarrheals as needed
- Myasthenia gravis: cholinesterase inhibitors and/or immunosuppressive therapy to improve esophageal muscular tone; upright feedings versus permanent gastrostomy tube to reduce risk of aspiration
- Cytopenias: blood product transfusion as needed; prophylactic antibiotics to prevent opportunistic infection in neutropenic patients
- Hypoglycemia: dextrose, corticosteroids, and diazoxide to increase serum glucose concentration; small frequent meals with complex carbohydrates to prevent spikes in serum glucose
- Seizures: anticonvulsant medications, corticosteroids, and mannitol as needed for increased intracranial pressure
- Hypertrophic osteopathy: analgesic medications such as NSAIDs, opioids, bisphosphonates as needed

PROGNOSIS AND OUTCOME

Usually dependent on individual tumor type, although some PNS influence long-term prognosis:

- Hypercalcemia shortens survival in lymphoma +/− anal sac apocrine gland adenocarcinoma.
- Myasthenia gravis: megaesophagus shortens survival in thymoma.
- Gastroduodenal ulceration: patients with MCT and clinical signs have shorter survival.

PEARLS & CONSIDERATIONS

COMMENTS

- Recrudescence of a PNS can indicate cancer relapse.
- If cause for hypercalcemia cannot be determined based on history and baseline diagnostic testing, consider bone marrow aspiration to investigate occult neoplasia.

TECHNICIAN TIPS

- PNS can cause clinical signs not typically associated with individual cancer types.
- Understanding the dynamic behavior of PNS can be helpful in distinguishing recurrence of cancer from treatment-related complications.

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Paraneoplastic Syndromes, Cutaneous

BASIC INFORMATION

DEFINITION

Uncommon non-neoplastic skin lesions that serve as markers for internal neoplasia

SYNONYMS

Exfoliative dermatitis, nodular dermatofibrosis, paraneoplastic alopecia, paraneoplastic pemphigus

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Paraneoplastic alopecia: older cats (7-16 years)
- Exfoliative dermatitis: middle-aged to old cats
- Nodular dermatofibrosis: middle-aged dogs (3-9 years)
- Paraneoplastic pemphigus: dogs

GENETICS & BREED PREDISPOSITION: Nodular dermatofibrosis: German shepherds, autosomal dominant inheritance

ASSOCIATED CONDITIONS & DISORDERS

- Paraneoplastic alopecia (cats): pancreatic carcinoma, bile duct carcinoma, hepatocellular carcinoma
- Exfoliative dermatitis (cats): thymoma
- Nodular dermatofibrosis (dogs): renal cystadenocarcinomas/cystadenomas, polycystic kidneys, concurrent uterine leiomyoma
- Paraneoplastic pemphigus (dogs): lymphoma, Sertoli cell tumor, mammary carcinoma

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Paraneoplastic alopecia: progressive alopecia, weight loss, lethargy, excessive grooming. The alopecia may be noted as the first manifestation (harbinger) of internal neoplasia. Internal disease is often advanced at the time of presentation, but the chief complaint commonly relates to alopecia.
- Exfoliative dermatitis: scaling dermatitis; alopecia; brown, waxy deposits noted on the skin
- Nodular dermatofibrosis: cutaneous nodules on the limbs, head
- Paraneoplastic pemphigus: anorexia, ptyalism, erosive/ulcerative skin and mucosal lesions

PHYSICAL EXAM FINDINGS

- Paraneoplastic alopecia: nonpruritic symmetric alopecia on ventrum, legs, face, and neck; glistening skin; fur epilates easily; dry, fissured footpads; erythema; scale; + dehydration, emaciation
- Exfoliative dermatitis: nonpruritic scaling dermatitis on pinnae, head, generalized; variable alopecia; brown, waxy deposits around mucocutaneous areas, nail beds; variable erythema
- Nodular dermatofibrosis: nonpainful, firm cutaneous nodules on extremities; also present on the head, neck, ventral trunk
- Paraneoplastic pemphigus: depressed attitude; ulcers and erosions of the oral mucosa, mucocutaneous junctions

PARANEOPLASTIC SYNDROMES, CUTANEOUS Paraneoplastic alopecia in a 14-year-old cat with pancreatic adenocarcinoma.

(Copyright Dr. Manon Paradis.)

ETIOLOGY AND PATHOPHYSIOLOGY

- Paraneoplastic alopecia: pathogenesis may involve cytokine production, leading to atrophy of hair follicles.
- Exfoliative dermatosis: a tumor-induced immune-mediated process has been suggested.
- Nodular dermatofibrosis: collagen production within the skin may be stimulated by growth factors produced by the renal tumors; lesions develop separately through a common genetic abnormality, or simultaneous fibrosis of the skin and kidneys results in collagenous nevi and renal outflow obstruction.
- Paraneoplastic pemphigus: cross-reactivity between tumor antigen and self-antigen or secretion of excessive immunostimulatory cytokines may be involved.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The association between cutaneous lesions and internal neoplasia should be remembered (but not overinterpreted) to avoid under-and overdiagnosis of these syndromes. Diagnosis of the different cutaneous paraneoplastic syndromes is confirmed with skin biopsy and dermatohistopathologic evaluation. The histologic diagnosis of the skin lesions then suggests which underlying metabolic derangement or internal neoplasm to pursue as the cause of the paraneoplastic disorder.

DIFFERENTIAL DIAGNOSIS

- Paraneoplastic alopecia: demodicosis, dermatophytosis, endocrine (hyperadrenocorticism, hyperthyroidism, hypothyroidism), immune-mediated (alopecia areata), neoplasia, telogen effluvium
- Exfoliative dermatosis: demodicosis, infectious agents (dermatophytosis, bacterial infections, feline leukemia virus [FeLV] infection), hypersensitivities, cutaneous drug reactions, autoimmune disorders, neoplasia (cutaneous lymphoma)
- Nodular dermatofibrosis: primary cutaneous neoplasms
- Paraneoplastic pemphigus: pemphigus vulgaris, bullous pemphigoid, systemic lupus erythematosus, erythema multiforme, toxic epidermal necrolysis, cutaneous lymphoma

INITIAL DATABASE

- CBC, serum biochemical panel, and urinalysis. Nonspecific changes may be noted.
- FeLV and feline immunodeficiency virus (FIV) serologic examination is indicated in all cats, but these neoplasms are not expected to be associated with seropositive status.
- Paraneoplastic alopecia:
    - Dermatohistopathologic examination: hair follicle atrophy, telogenization, hyperkeratosis, or hypokeratosis
    - Abdominal ultrasonography: liver or pancreatic lesions due to neoplasia
- Exfoliative dermatosis:
    - Dermatohistopathologic examination: cell-poor interface dermatitis with apoptotic keratinocytes in the stratum basal and stratum spinosum layers
    - Thoracic radiographs/ultrasound: mediastinal mass

- Nodular dermatofibrosis:
  - Dermatohistopathologic examination: nodular areas of collagenous hyperplasia
  - Abdominal imaging: renal cysts, renal masses (neoplasms), or uterine masses (neoplasms)
- Paraneoplastic pemphigus:
  - Dermatohistopathologic examination: intraepithelial acantholysis, apoptotic keratinocytes, vacuolar interface dermatitis
  - Abdominal and thoracic imaging: masses (primary neoplasm, metastases)

ADVANCED OR CONFIRMATORY TESTING

- Paraneoplastic alopecia:
  - Exploratory laparotomy with pancreatic, liver or biliary tract biopsies
- Exfoliative dermatosis:
  - Fine-needle aspiration of the mediastinal mass and cytologic examination
  - Core biopsies of the mediastinal mass
- Nodular dermatofibrosis:
  - Biopsy of renal masses
- Paraneoplastic pemphigus:
  - Biopsy of tumor
  - Indirect immunofluorescence testing: Positive on stratified and nonstratified squamous epithelia
  - Western blot analysis; target antigen proteins include envoplakin (210 kD), periplakin (190 kD), desmoglein lll (130 kD), and an unidentified antigen (170 kD)

TREATMENT

TREATMENT OVERVIEW

The goal of treatment is to resolve the primary neoplasm if possible, since control or resolution of the cutaneous lesions is ultimately dependent on control or resolution of the underlying internal neoplasm. Palliative care for dermatologic lesions should be provided.

ACUTE GENERAL TREATMENT

- Paraneoplastic alopecia: surgical excision of neoplasm, if possible
- Exfoliative dermatosis: surgical excision of thymoma
- Nodular dermatofibrosis: unilateral nephrectomy is rarely curative but is indicated if renal cysts are severe; bilateral renal disease is common.
- Paraneoplastic pemphigus: none reported

CHRONIC TREATMENT

Nodular dermatofibrosis: surgical excision of collagenous nevi until end-stage renal failure develops

PROGNOSIS AND OUTCOME

- Paraneoplastic alopecia: grave; euthanasia due to advanced disease
- Exfoliative dermatosis: guarded; outcome depends on complete thymoma removal
- Nodular dermatofibrosis: poor for long-term survival; slowly progressive renal disease; average lifespan: 9 years of age
- Paraneoplastic pemphigus: grave unless neoplasm can be removed; euthanasia for failure to respond to immunosuppression

PEARLS & CONSIDERATIONS

COMMENTS

- Cutaneous clinical signs represent the “tip of the iceberg.”
- Internal disease is often advanced at the time of presentation.
- Earlier recognition may improve outcome in some cases (at least in thymoma).
- Nodular dermatofibrosis may precede clinical signs of renal disease by 3-5 years and does not warrant immediate consideration of euthanasia.

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Papillomas, Oral and Cutaneous

BASIC INFORMATION

DEFINITION

Benign tumors of the skin and oral cavity caused by site-specific papilloma viruses (see p. 786)

SYNONYMS

Lentiginosis profuse, papillomas, pigmented epidermal nevi, verrucae, warts

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Young dogs (6 months to 4 years) or immunocompromised adults
- Cutaneous papillomas are more often seen in males, likely due to their aggressive interactive behavior.

GENETICS & BREED PREDISPOSITION

- Cutaneous papillomas: cocker spaniels, Kerry blue terriers
- Pigmented sessile papillomas: miniature Schnauzers and pugs

RISK FACTORS

- Young and immunologically naive individuals with damaged skin or mucous membranes
- Immunosuppressed individuals (chronic use of glucocorticoids and/or oral cyclosporine)

CONTAGION & ZOONOSIS: Contagious to other dogs via direct and indirect (fomite) contact but not to humans or cats

ASSOCIATED CONDITIONS & DISORDERS

- Hyperadrenocorticism
- Squamous cell carcinoma (SCC)
- Bowen's disease (SCC in situ, cats)

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Oral: owner-observed intraoral nodule(s); oral discomfort, dysphagia, halitosis, and ptyalism
- Cutaneous: owner-observed cutaneous growth that often involves a distal extremity and may bleed if scratched or chewed upon; occasional lameness (footpad)

PHYSICAL EXAM FINDINGS

- Canine oral papilloma virus (COPV) presents with multiple growths in the oral cavity (a few millimeters to 1 cm in diameter). Initially develop as smooth white nodules before progressing to gray pedunculated masses with fronds.
- In contrast, cutaneous lesions are normally solitary and can either present as:
    - Pedunculated growth with multiple fronds; found anywhere on the body (head, eyelids, and feet most commonly affected); rarely >1 cm diameter
    - Inverted papilloma with a small pore opening (ventral trunk and abdomen most common); typically 1-2 cm diameter
    - Pigmented sessile plaques/nevi/lentigines dispersed in numbers from 3 or 4 up to 80, involving the ventral neck, trunk, and medial surfaces of limbs of pugs and miniature schnauzers (autosomal dominant inheritance)
    - Multiple papillomas affecting the footpads of dogs (digital keratomas). Firm, hyperkeratotic, hornlike growths that occur on multiple footpads, sometimes resulting in lameness as the primary presenting complaint.

PAPILLOMAS, ORAL AND CUTANEOUS Multiple papilloma on the lips and oral cavity in a weimaraner.

(Copyright Dr. Manon Paradis.)

ETIOLOGY AND PATHOPHYSIOLOGY

- Papilloma viruses (PV) are host specific and fairly site specific, nonenveloped, double-stranded DNA viruses that induce proliferative cutaneous and mucosal tumors in dogs.
- Infection requires inoculation via breaks in the epidermal or mucosal barrier by means of direct contact with other infected dogs or iatrogenic transmission through use of contaminated instruments.
- Replication: PV attaches to cell receptors and undergoes endocytosis. Viral DNA (vDNA) makes its way to the nucleus and establishes a pool of vDNA in basal cells. Amplification of vDNA in differentiated cells and virion maturation in nucleus and infected cells are immortalized by PV infection. Reactivation of the latent PV occurs if the patient is immunocompromised naturally or iatrogenically. Early genes stimulate cell hyperplasia followed by benign tumor formation showing as warts.
- Incubation period is 1-8 weeks; regression typically occurs in 1-5 months, and lesions may persist for 24 months or more.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is primarily visual, at least for the oral papillomas. Biopsy and histopathologic examination may be necessary for diagnostic confirmation of cutaneous papillomas.

DIFFERENTIAL DIAGNOSIS

- Oral papilloma:
  - Fibromatous epulis
  - Transmissible venereal tumor
  - SCC, especially if ulcerated
- Cutaneous papilloma:
  - Pedunculated with fronds: sebaceous adenoma/hyperplasia
  - Pigmented: melanomas
  - Inverted: intracutaneous cornifying epitheliomas

INITIAL DATABASE

- Oral papillomatosis: clinical appearance is characteristic, followed by biopsy for dermatohistopathologic examination if a definitive diagnosis is desired (uncommon).
- Cutaneous papillomatosis is not as clinically evident and thus requires dermatohistopathologic examination to diagnose the lesion.
- Cytologic evaluation of smears may identify koilocytes, a type of dysplastic squamous cell found in potentially precancerous lesions with the following characteristics: nuclear enlargement (two to three times normal size), irregularity in the nuclear contour (occasionally), hyperchromasia, perinuclear clearing.
- Dermatohistopathologic evaluation of biopsies reveals fingerlike projections into the dermis and parakeratotic hyperkeratosis, inclusion bodies in keratinocytes.

ADVANCED OR CONFIRMATORY TESTING

- Virtually never needed in the clinical setting
- Immunohistochemistry: avidinbiotin complex method to detect papilloma virus group-specific antigen in tissue
- PCR to identify cutaneous papillomas
- Electron microscopy is the gold standard for diagnosis but is primarily used for research or publication purposes.

TREATMENT 

TREATMENT OVERVIEW

Because of frequent spontaneous regression, benign neglect can be an option in mild and early cases. In face of persistent or numerous lesions, various treatment options are available. Clinicians should also identify and correct any underlying cause of immunosuppression.

ACUTE GENERAL TREATMENT

- Lesions may regress spontaneously within 1-2 months.
- Some reports claim that crushing of 5 to 15 tumors may induce spontaneous regression.
- Azithromycin (suspension, tablet, and injectable), 10 mg/kg, q 24 h for 10 days, has been recently reported to result in clinical remission within 10-15 days, possibly as a result of an antiviral essential factor binding and/or immunomodulatory components.
- Surgical removal: especially if compromising normal body function (e.g., airway obstruction, dysphagia) using CO^2 laser ablation, excision, cryosurgery, or electrosurgery.
- Discontinue use of systemic glucocorticoids or cyclosporine, particularly if oral or cutaneous disease recurs or persists.

CHRONIC TREATMENT

- Interferon (IFN), either at immunostimulatory low doses of 30,000 IU/mL-0.1 mL (3000 IU) PO q 24 h OR high doses given at 1-1.5 million IU/m^2 SQ q 48-72 h for 4-8 weeks pending response
- Imiquimod 5% (Aldara) is a topically applied, human-approved immunomodulator that activates toll-like receptors and upregulates interleukin (IL)-6, IL-12, tumor necrosis factor (TNF)-α, IFN-α and IFN-γ. Also activates Langerhans cells and provides antiproliferative and antiviral effects at an application rate of two to three times weekly to affected areas; irritation is anticipated as part of the immune response against the virus and can sometimes be difficult to differentiate from resolving lesions.
- Vaccines (autologous, fractional) are currently experimental. Contact your local veterinary dermatologist for updates regarding this option.

RECOMMENDED MONITORING

- If benign neglect is chosen, clinicians should monitor lesions for ulceration, purulent exudation, and proliferation of growths, any of which might mandate intervention.
- Clinicians should monitor for abnormal persistence (e.g., development into large, ulcerated mass), which could warrant biopsy because of the potential for malignant transformation of affected cells to SCC.

PROGNOSIS AND OUTCOME 

- Prognosis usually good

- Spontaneous regression is likely, with subsequent lifelong immunity.

PEARLS & CONSIDERATIONS

COMMENTS

Once thought to be more of a nuisance often treated by benign neglect with spontaneous regression, persistent lesions should be addressed sooner to minimize the potential metaplasia to SCC.

PREVENTION

Owners should separate dogs with oral papillomatosis from other susceptible individuals.

CLIENT EDUCATION

Contagious to other dogs but not to humans and cats

SUGGESTED READING

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Panting

BASIC INFORMATION

DEFINITION

- Rapid, shallow breathing with a small tidal volume, usually with the mouth open
- It is a normal and very common thermoregulatory mechanism in dogs, and rare in cats.
- Excessive panting occurs with elevated ambient temperature, exercise, or anxiety (e.g., a visit to the veterinarian's office) in dogs or in the absence of severe ambient temperature elevations in cats.

SYNONYMS

Hyperpnea, hyperventilation, polypnea, tachypnea

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dependent on underlying cause
- Common in normal dogs (thermoregulation, anxiety) but rare in normal cats, except in stressful situations (e.g., car ride)
- Older cats (hyperthyroidism)
- Middle-aged to older dogs, with mild female predominance (hyperadrenocorticism)

RISK FACTORS: Common and physiologic condition with emotional stress in both dogs and cats

GEOGRAPHY AND SEASONALITY: Summer (normal thermoregulation in dogs)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Normal panting due to elevated ambient temperature or anxiety versus inappropriate panting due to underlying disease

HISTORY, CHIEF COMPLAINT

- Increased amount of panting or panting at inappropriate times
- Increased with elevated environmental temperatures and/or humidity
- Perceived evidence of pain
- Glucocorticosteroid or narcotic drug administration
- Polyuria, polydipsia, polyphagia, weight gain (canine hyperadrenocorticism)
- Polyphagia, weight loss, hyperactivity (feline hyperthyroidism)
- Seizures, abnormal mentation (brain disease)
- Exercise intolerance, lethargy, coughing, dyspnea (cardiac or respiratory disease)

PHYSICAL EXAM FINDINGS

- Rapid (200-400 breaths/min), shallow breathing without evidence of respiratory distress
- Elevated body temperature if fever or hyperthermia
- Signs of pain
- Truncal hair loss, pot-bellied appearance, hepatomegaly (canine hyperadrenocorticism)
- Enlarged thyroid, tachycardia, heart murmur, or gallop heart sound (feline hyperthyroidism)
- Neurologic deficits (brain disease)
- Heart murmur, tachyarrhythmia (cardiac disease)
- Harsh lung sounds, wheezing (bronchial disease)
- Obesity

ETIOLOGY AND PATHOPHYSIOLOGY

- Primary means of thermoregulation in dogs via evaporative cooling within the mouth and nasal passages; passage of air,

blood flow, and secretions are increased in these areas during panting.
- Muscular work of breathing is minimally increased during panting.
- Causes respiratory alkalosis only if prolonged or severe.
- Hyperthyroidism rarely causes panting at rest but commonly with any stress. Possible reasons include respiratory muscle weakness, increased carbon dioxide production, and chemical thermogenesis.
- Hyperadrenocorticism and glucocorticosteroid administration may cause panting because of respiratory muscle weakness, muscle wasting, hepatomegaly, and abdominal fat deposition.
- Pure agonist narcotics commonly cause dose-dependent panting that is independent of route of administration.
- Cardiac disease and tachyarrhythmias may lead to panting due to anxiety or angina.
- Animals with pheochromocytoma may pant because of epinephrine induced chemical thermogenesis.
    - A similar mechanism may be inferred for anxiety-associated panting.
- Hypocalcemia may lead to panting, most likely because of anxiety and pain caused by tetany.
- Obese animals fail to lose as much heat through evaporation and radiation, which increases the need for heat loss through panting. Furthermore, the tidal volume may be reduced due to fat deposition in the thorax, further increasing the respiratory rate.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Complete history and physical examination findings can help determine whether panting is normal (thermoregulation or anxiety) or a sign of disease, and aid in ranking the importance of additional tests, which can be varied and extensive.

DIFFERENTIAL DIAGNOSIS

- Elevated ambient temperature, hyperthermia
- Fever
- Anxiety, nervousness
- Pain
- Narcotic administration
- Glucocorticosteroid therapy
- Hyperadrenocorticism
- Hyperthyroidism
- Hypocalcemia
- Pheochromocytoma
- Cardiac disease, tachyarrhythmia
- Feline bronchial disease
- Brain disease
- Obesity

INITIAL DATABASE

- Blood pressure: moderate-severe hypertension possible with hyperthyroidism or pheochromocytoma; mild hypertension possible with severe anxiety
- CBC: possible erythrocytosis, thrombocytosis, leukocytosis, lymphopenia, and eosinopenia in dogs with hyperadrenocorticism
- Serum biochemical profile: elevated alkaline phosphatase (ALP) and cholesterol in dogs with hyperadrenocorticism; elevated liver enzymes in cats with hyperthyroidism; hypocalcemia
- Urinalysis: low specific gravity and/or proteinuria in dogs with hyperadrenocorticism
- Serum T^4: elevated in cats with hyperthyroidism
- Thoracic radiographs: heart enlargement + pulmonary edema, pleural effusion with cardiac disease; bronchiolar lung pattern, lung hyperinflation in feline asthma

ADVANCED OR CONFIRMATORY TESTING

- Arterial blood gas may show respiratory alkalosis (diminished carbon dioxide, elevated pH) in animals with severe panting.
- Hyperadrenocorticism screening via urine protein/creatinine ratio, adrenocorticotropic hormone (ACTH) stimulation, or low-dose dexamethasone suppression tests if history and initial database are suggestive
- Abdominal ultrasound to locate adrenal mass(es)
- Electrocardiogram and echocardiogram to confirm cardiac disease
- Bronchial wash cytologic evaluation to confirm feline asthma
- Brain CT scan or MRI

TREATMENT

TREATMENT OVERVIEW

Clinicians should treat the underlying condition to eliminate excessive panting.

ACUTE GENERAL TREATMENT

Clinicians should:

- Reduce anxiety.
- Control pain if present.
- Decrease ambient temperature if elevated.
- Ensure adequate hydration in animals with elevated body temperature and provide external cooling (e.g., cool water bath, fan, cool water enema, or gastric lavage) in animals with a body temperature above 106○F (41.1○C).
- Discontinue or decrease dose of narcotic or glucocorticosteroid therapy if possible.
- Manage underlying cause (± antiarrhythmic therapy) for tachyarrhythmias.
- Administer calcium supplementation for hypocalcemic animals.
- Manage underlying cause (± antihypertensive medication) for hypertensive animals with hyperthyroidism or pheochromocytoma.
- Eliminate or control underlying trigger (± glucocorticosteroid and bronchodilator therapy) for feline bronchial disease.

CHRONIC TREATMENT

Clinicians should:

- Start cats with hyperthyroidism on oral or topical methimazole and/or schedule them for radioactive iodine therapy.
- Treat hyperadrenocorticism with mitotane, trilostane, or adrenalectomy.
- Perform an adrenalectomy for animals with pheochromocytoma.

NUTRITION/DIET

Initiate program for weight loss if the animal is obese.

POSSIBLE COMPLICATIONS

Bronchodilator therapy may worsen primary cardiac disease.

PROGNOSIS AND OUTCOME

Highly variable, owing to range of severity of underlying causes

PEARLS & CONSIDERATIONS

COMMENTS

Any panting cat should be evaluated for underlying disease. An exception is cats that only pant under predictable conditions of stress (e.g., car ride), the panting has not progressed in severity to resting dyspnea, and an initial physical exam has revealed no abnormalities.

TECHNICIAN TIPS

Obtaining complete historical and physical examination information can assist in determining whether a patient is panting because of normal reasons (thermoregulation, anxiety) or because of underlying illness.

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Panosteitis

BASIC INFORMATION

DEFINITION

A spontaneous, self-limiting painful condition of diaphyseal and metaphyseal portions of long bones commonly diagnosed in young, large breed dogs

SYNONYMS

Enostosis, juvenile osteodystrophy, eosinophilic osteomyelitis, eosinophilic panosteitis, juvenile osteomyelitis, osteomyelitis of young German shepherd dogs

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Young (5 months to 2 years), medium-and large-breed dogs
- Occasionally seen in younger or older dogs and in small breeds
- More common in males than females

GENETICS & BREED PREDISPOSITION

- German shepherds have been reported to be at highest risk.
- Basset hounds may be overrepresented.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- The hallmark chief complaint is acute, shifting limb lameness of variable severity that typically lasts 1-3 weeks (each leg).
- Systemic signs (e.g., anorexia, lethargy) occasionally can be severe and may require nutritional and physical support.

PHYSICAL EXAM FINDINGS

- Orthopedic examination demonstrates pain on deep palpation/firm digital pressure of the diaphyseal and metaphyseal (midshaft and distal, respectively) portions of affected bones.
- Frequency: ulna (42%), radius (25%), humerus (14%), femur (11%), and tibia (8%)
- Fever, depression, and anorexia can be seen in more severe (unusual) cases.

ETIOLOGY AND PATHOPHYSIOLOGY

- Panosteitis has an unknown etiology.
- Infectious agents (bacteria, canine distemper virus, modified live viral vaccines) have been suspected but never proven to cause panosteitis.
- Other suggested inciting causes include localized vascular congestion, metabolic diseases, genetic diseases, parasitism, hyperestrinism, and hemophilia.
- Panosteitis is associated with excessive bone remodeling after the death of intramedullary adipocytes and hematopoietic cells. Cell death is attributed to vascular congestion, but the true cause remains unknown.
- The necrotic marrow cells are replaced with fibrous tissue. Woven bone is formed within the fibrous tissue. Endosteal bone formation is a prominent histologic finding with panosteitis.
- Periosteal bone formation is occasionally noted.
- Eventually, endosteal bone resorption occurs, and normal vascularity and marrow adipose tissue are reestablished.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Panosteitis is typically a mild, self-limiting condition and should be a primary consideration in any lame dog < 2 years of age. Panosteitis may occur in a single bone or limb or as a recurrent "shifting leg" lameness. It is suspected from signalment, history, and physical exam, and is confirmed radiographically.

DIFFERENTIAL DIAGNOSIS

Infectious diseases (septic arthritis, osteomyelitis), immune-mediated arthropathies, and other developmental bone diseases (hypertrophic osteodystrophy, ununited anconeal process, osteochondrosis, hip dysplasia, etc.)

INITIAL DATABASE

- Anamnesis and physical examination:
  - Pain during deep palpation of the affected bone (diaphysis or metaphysis)
- Radiography:
  - Diagnostic test of choice
  - Characteristic radiographic lesions:
    - Patchy areas of increased intramedullary opacity
    - Increased radiographic lucency near the nutrient foramen of the bone
    - Increased periosteal bone formation
- Characteristic lesions may not be present during acute phase of the disease.
- Radiographs of other nonpainful limbs may also have characteristic lesions.
- CBC, serum biochemical panel, and urinalysis, as indicated by presence of systemic signs

ADVANCED OR CONFIRMATORY TESTING

Nuclear scintigraphy may be used if radiographs are inconclusive.

TREATMENT

TREATMENT OVERVIEW

Generally, no specific therapy is required, but clinicians should provide analgesia during acute phase of panosteitis to permit the dog to have normal activity with minimal discomfort and maintain appetite.

ACUTE GENERAL TREATMENT

- Supportive care as required; hospitalization is rarely needed.
- Nonsteroidal antiinflammatory drugs (NSAIDs) generally provide adequate analgesic relief for dogs with panosteitis.
  - Carprofen: 2 mg/kg PO q 12 h, *or*
  - Etodolac: 10-15 mg/kg PO q 24 h, or
  - Deracoxib: 1-2 mg/kg PO q 24 h, *or*
  - Meloxicam 0.1 mg/kg PO q 24 h, *or*
  - Firocoxib 5 mg/kg PO q 24 h
  - Misoprostol (synthetic prostaglandin E 1 analog; 2-5 mcg/kg PO q 8-12 h) can be given to decrease the risk of gastrointestinal ulceration.
- There is no indication for the use of glucocorticoids in panosteitis.
- Use of opioid analgesics for discomfort is rarely required but can be considered in patients that have a contraindication to the use of NSAIDs.
  - Butorphanol: 1-4 mg/kg PO q 4-6 h. *or*
  - Tramadol: 1-4 mg/kg PO q 6-8 h

CHRONIC TREATMENT

- Seldom required, since this is a self-limiting condition
- An occasional severe case will require use of stronger analgesics (opioids), nutritional support (i.e., feeding tube placement), or short-term hospitalization.

NUTRITION/DIET

- A well-balanced maintenance diet should be recommended if the patient is not already receiving this.

- Use of additional supplements have not been shown to alter the course of panosteitis and could further complicate the development of other orthopedic conditions.

BEHAVIOR/EXERCISE

Limited activity in patients that are painful

DRUG INTERACTIONS AND CONTRAINDICATIONS

- Gastric ulceration and other side effects may rarely occur with use of NSAIDs; clinicians should be familiar with specific product information and inform owners of possible side effects and actions to be taken if side effects are encountered (i.e., discontinue medication, veterinary evaluation, etc.).
- Corticosteroids should not be used in patients receiving NSAIDS; increases risk of gastric ulceration.

POSSIBLE COMPLICATIONS

- Most complications arise from treatment rather than disease.
- Gastrointestinal (GI) hemorrhage, ulceration, and perforation (NSAIDs).
- Liver toxicity or failure and renal dysfunction are possible with NSAIDs.
- Coagulation abnormalities are rare with most NSAIDs.

RECOMMENDED MONITORING

- Radiographic examination when other legs become affected
- Repeated evaluation in dogs with protracted lameness to rule out other developmental bone diseases
- CBC (blood loss anemia), biochemical profile (changes in liver or renal parameters), and urinalysis (urine specific gravity, sediment for evidence of real casts) are recommended with long-term NSAID usage.

PROGNOSIS AND OUTCOME 

- Disease may last several weeks to months.
- The condition may shift among limbs.
- Long-term prognosis is very good; seldom causes permanent disability.

PEARLS & CONSIDERATIONS 

COMMENTS

- Panosteitis should be a primary differential diagnosis in any young dog with acute onset of lameness.
- Panosteitis is “self-limiting” in most cases.
- Panosteitis may repeatedly flare up over several months.
- Panosteitis is most common in dogs prone to other developmental orthopedic conditions. If the patient does not improve with supportive care, other underlying conditions should be ruled out.
- Nutraceuticals and vitamin supplementation have not been shown to decrease clinical signs, duration, or severity of panosteitis.

CLIENT EDUCATION

- Clients should be reminded that panosteitis is a self-limiting condition and will resolve with minimal treatment in the majority of dogs.
- There are potential side effects of NSAID use in dogs:
    - Long-term use of NSAIDs may require concurrent administration of gastroprotectants.
- Panosteitis can mask other developmental orthopedic conditions.

SUGGESTED READING

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AUTHOR: D. MICHAEL TILLSON

EDITOR: JOSEPH HARARI

Pannus (Chronic Superficial Keratitis)

BASIC INFORMATION

DEFINITION

A typically bilateral, progressive, immune-mediated, inflammatory disease of the cornea characterized by infiltration of vessels and granulation tissue and/or pigmentation

SYNONYMS

CSK, degenerative pannus, German shepherd pannus, Uberreiter's syndrome

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs only
- Age of onset: 2-5 years of age; depends on breed and altitude

GENETICS & BREED PREDISPOSITION

- Primarily affects large-breed dogs; may occur in any breed
- Breed predisposition: German shepherd, greyhound, Belgian Tervuren, Belgian sheepdog, dachshund, border collie, Shetland sheepdog, Siberian husky, Scotch collie, Australian shepherd, miniature pinscher, pointer, dalmatian, English springer spaniel, Airedale terrier

RISK FACTORS

- Ultraviolet radiation exposure

GEOGRAPHY AND SEASONALITY: Increased incidence and severity of disease in geographic regions with high altitude (i.e., elevation of 4500 feet [1500 m] or higher) and intense sunlight. Dogs that live at lower altitudes respond better to therapy (e.g., dogs living in the southeastern part of the United States are less severely affected and respond better to therapy than dogs living in the Rocky Mountains).

ASSOCIATED CONDITIONS & DISORDERS: Lymphocytic/plasmacytic conjunctivitis

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Early chronic superficial keratitis (CSK): lesions occur in the lateral to latero ventral cornea.
- Chronic CSK: entire cornea may be affected
- CSK may present as a:
  - Vascular form
  - Pigmentary form
  - Combination of vascular and pigmentary forms in same eye or between eyes

HISTORY, CHIEF COMPLAINT

- Corneal discoloration: rapidly or slowly progressive; reddish and/or brown film covering surface of the eyes
- Progressive loss of vision

PHYSICAL EXAM FINDINGS

- Typically bilateral; often symmetrical
- Generally nonulcerative, pinkish-red, vascularized, and/or pigmentary superficial corneal lesions commencing in the lateral to ventrolateral cornea; progressively involving the medial, ventral, and dorsal aspects of the cornea, including the central

cornea
- Conjunctivitis present in most cases
- Multifocal white, crystalline lipid deposits often present at the leading edge of the corneal lesions (see p. 245)
- ± Third eyelid involvement as evidenced by pink proliferative lesions and depigmentation along leading edge of third eyelid
- Early CSK:
  - Vascularization and/or pigmentation at lateral to ventrolateral cornea adjacent to limbus
  - Progresses centrally
- Chronic CSK:
  - Fleshy lesion (i.e., granulation tissue) with corneal vascularization and/or pigmentation
  - Entire cornea may be affected, predisposing the animal to blindness

ETIOLOGY AND PATHOPHYSIOLOGY

- Immune-mediated disease
- Ultraviolet radiation exposure at high altitude potentiates the disorder.
- Tissue-specific antigens in the cornea are altered with ultraviolet radiation exposure.
- Dogs with CSK develop a hypersensitivity response to corneal proteins, predisposing them to chronic inflammation.
- CSK is a more rapidly progressive and severe disease in young dogs (<3 years of age).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is based on the clinical presentation of typically bilateral corneal vascularization and pigmentation in large-breed dogs.

DIFFERENTIAL DIAGNOSIS

Other causes of CSK:

- Corneal vascularization (see p. 254)
- Corneal pigmentation (see p. 246)

INITIAL DATABASE

Complete ophthalmic examination (see p. 1313), including:

- Schirmer tear test (typically normal with CSK)
- Fluorescein dye application (typically no corneal dye retention with CSK, but there may be with secondary corneal ulceration)
- Intraocular pressures normal (15-25 mm Hg) with CSK
- Careful examination of the conjunctiva and cornea

ADVANCED OR CONFIRMATORY TESTING

- Usually not required; CSK is diagnosed by clinical findings, signalment of dog, and ruling out other causes of corneal vascularization and pigmentation.
- Cytologic examination of corneal and conjunctival swabs/scrapings reveals lymphocytes and plasma cells.
- If a keratectomy is performed, histopathologic findings consist of lymphocyte, plasma cell, macrophage, and melanocytic cell infiltrations with corneal vascularization and fibroplasia.

TREATMENT

TREATMENT OVERVIEW

The treatment goal is to suppress the disease process with intensive initial treatment and to keep the disease in remission with maintenance therapy.

ACUTE GENERAL TREATMENT

- Topical corticosteroids (dexamethasone 0.1% solution or ointment, or prednisolone acetate 1% suspension) q 6-8 h for 3 weeks, followed by slow reduction to a maintenance dose

- Cyclosporine-A (CsA) 0.2% ointment or 0.5%-2% solution topically q 12 h; or tacrolimus 0.02%-0.03% ointment or aqueous suspension q 12 h

CHRONIC TREATMENT

- Requires lifelong therapy
- Maintenance therapy consists of topical corticosteroids and/or CsA or tacrolimus once or twice a day.
- Maintenance of remission is possible in some dogs with one daily application of CsA.
- For nonresponsive and severe cases, clinicians can consider:
    - Adjunctive subconjunctival injections of corticosteroids (e.g., methylprednisolone acetate, 4-12 mg; or triamcinolone acetonide, 4-12 mg [dose dependent on size of dog]) q 2-3 weeks
    - Referral to veterinary ophthalmologist for:
        - ß-irradiation (i.e., strontium-90)
        - Superficial keratectomy

POSSIBLE COMPLICATIONS

- Corneal ulceration (see p. 250); if it occurs, clinicians should discontinue corticosteroid for the animal and commence/continue CsA or tacrolimus until corneal ulcer has healed.
- Granuloma at site of subconjunctival corticosteroid injection

RECOMMENDED MONITORING

- Response to therapy is monitored every 3-4 weeks initially then every 4-6 weeks.
- Once stable, the patient is reevaluated every 3-6 months.

PROGNOSIS AND OUTCOME

- CSK is a chronic disorder that typically responds to intensive medical therapy.
- Maintenance therapy is needed to keep the disease in remission.

PEARLS & CONSIDERATIONS

COMMENTS

- A common error in treatment is lack of intensive therapy in the early stages of disease.
- The disease should be treated pro-actively with topical corticosteroids, ± CsA or tacrolimus, and the frequency should be slowly reduced over weeks to reach a maintenance therapy.
- CSK is a chronic disease that requires lifelong treatment.

PREVENTION

- Owners should limit exposure of pets to ultraviolet light.
- They should also avoid breeding affected or closely related dogs.

CLIENT EDUCATION

- CSK is an immune-mediated disease that is manageable but not curable.
- Lifelong treatment is required.

SUGGESTED READING

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AUTHOR: PHILLIP A. MOORE

EDITOR: CHERYL L. CULLEN

Panniculitis

BASIC INFORMATION

DEFINITION

Inflammation of the subcutaneous adipose tissue. Panniculitis is different from cellulitis, which is an acute, diffuse, and suppurative inflammation of loose connective tissue, particularly the deep subcutaneous tissues, and sometimes muscle, most commonly resulting from infection of a wound, ulcer, or other skin lesion.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Uncommon in dogs and cats

GENETICS & BREED PREDISPOSITION: Sterile nodular panniculitis: dachshunds, golden retrievers, collies, and miniature poodles

RISK FACTORS

- Outdoor pets (penetrating foreign body, bite wound): infectious panniculitis
- Immunocompromised cat (e.g., feline leukemia virus [FeLV], feline immunodeficiency [FIV]) or dog (e.g., iatrogenic hyperadrenocorticism): greater risk of dissemination of infectious organisms
- Unbalanced diets low in antioxidants (e.g., low levels of vitamin E)
- Recurrent pancreatitis: panniculitis and steatitis (inflammation of body fat)
- Pancreatitis or pancreatic carcinomas: mineralizing fat necrosis/panniculitis

CONTAGION & ZOONOSIS

- Dermatophytic granulomatous panniculitis: *Microsporum canis* and *Trichophyton mentagrophytes* are potentially contagious to other animals and are zoonotic.
- Sporotrichosis: risk of cat-to-human transmission is extremely high; dog-to-human transmission not yet reported.
- Blastomycosis, coccidioidomycosis, histoplasmosis: risk of zoonosis by aerosol from culture plates; in-house culture is always contraindicated.

GEOGRAPHY AND SEASONALITY: Sporotrichosis outbreak in Brazil; Blastomycosis, p. 138; Histoplasmosis, p. 538; Coccidioidomycosis, ; Pythiosis and Lagenidiosis, p. 960; Protothecosis, p. 926.

ASSOCIATED CONDITIONS & DISORDERS: Interscapular panniculitis may be a precursor of vaccine-associated fibro-sarcoma in cats.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Acute to chronic onset of single or multiple subcutaneous nodules or draining tracts, potentially with accompanying systemic signs such as anorexia and lethargy.

PHYSICAL EXAM FINDINGS

- Lesions typically involve the trunk and may be single or multifocal.
- Subcutaneous nodules to swellings may become cystic and painful, especially prior to rupturing or developing draining tracts.
- Panniculitis and subsequent fat necrosis are characterized by an oily yellow-brown to blood-tinged discharge.
- Lesions often heal with crusting and scarring.

ETIOLOGY AND PATHOPHYSIOLOGY

- Panniculitis is caused by inflammation and/or infection of the panniculus (subcutaneous fat) with subsequent oxidative damage to the lipocytes.
- Result: release of lipids into subcutis, where the lipids undergo hydrolysis to glycerol and fatty acids
- The fatty acids are potent inflammatory agents, resulting in further inflammation and granulomatous reactions.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Panniculitis has several etiologies but is initially suspected based on physical finding of subcutaneous swellings/nodules that may or may not be painful or have developed draining tracts. Biopsies for histopathologic confirmation and/or bacterial and fungal cultures are generally indicated for diagnosis.

DIFFERENTIAL DIAGNOSIS

- Infectious: bacterial/botryomycosis, actinomycotic, systemic and subcutaneous fungal, dermatophytic pseudomycetomas, feline leprosy, atypical mycobacteria, *Chlamydia* spp., *Bartonella* spp.
- Immune-mediated: lupus profundus, erythema nodosum, drug eruption, insect bite
- Idiopathic: sterile nodular panniculitis
- Trauma with or without foreign body reaction
- Nutritional: vitamin E deficiency (feline nutritional pansteatitis)
- Pancreatitis or pancreatic adenocarcinoma
- Postinjection reaction: corticosteroids, vaccine (rabies)
- Neoplastic: multicentric mast cell tumors, cutaneous lymphoma
- Deep pyoderma/abscess
- Cutaneous cysts
- Drug reaction

INITIAL DATABASE

- Cytologic examination; infectious organisms:
  - Gram-positive branching filamentous organisms: *Actinomyces* sp. (nonacid-fast); *Nocardia* sp. (partially acid-fast)
  - Diff-Quik: fungi possible (systemic mycoses)
  - Acid-fast bacilli: atypical mycobacteria, feline *M. lepraemurium*
  - Organisms may be noted within foamy macrophages.
- Full-thickness (skin plus subcutaneous fat) biopsy, and the panniculus must be included; consider double-punch technique.
- Histopathologic analysis:
  - Identify one of the three possible histopathologic patterns: septal (interlobular connective tissue septa affected; most common in cats); lobular (fat lobules affected); and diffuse (both the lobules and septa involved; most common in dogs).
  - Qualify cellular infiltrate.
  - Identify infectious organisms (special stains).
  - Severity of lesions (necrosis, fibrosis, vasculitis)

ADVANCED OR CONFIRMATORY TESTING

- Clinicians should aseptically submit part of a biopsy specimen for tissue maceration and culture.
- They should also notify the laboratory of suspected organisms (to make adjustments to culture media selection and incubation times and for precautions taken especially with systemic mycoses):
  - Bacterial culture and sensitivity testing
  - Rapid-growing atypical mycobacterial culture
  - Fungal culture (not usually for systemic mycoses; other tests are safer).
  - Negative cultures support a diagnosis of sterile nodular panniculitis, lupus profundus.
- Serologic evaluation: systemic mycoses
- Antinuclear antibody to help rule in lupus profundus
- Direct fluorescent antibody testing for *Sporothrix* antigen
- Abdominal ultrasound: pancreatic diseases may be a contributing factor (rare).

TREATMENT

TREATMENT OVERVIEW

Because panniculitis is caused by a variety of etiologies, selection and duration of treatment are dependent on identification of the specific cause.

ACUTE AND CHRONIC TREATMENT

- Surgical excision of solitary lesions
- Appropriate antifungal, antibacterial, or antimycobacterial treatment if indicated
- Sterile panniculitis (rabies vaccine-induced, sterile nodular, lupus profundus)
    - Vitamin E (10-20 IU/kg PO q 8-12 h) may control mild cases.
    - Tetracycline and niacinamide, 500 mg of each for dogs > 10 kg, or 250 mg of each for dogs < 10 kg, PO q 8 h until improvement (about 2-3 months), then tapering gradually
    - Pentoxifylline, 10-30 mg/kg PO q 8 h until resolved, then tapering gradually
    - Prednisone, 2.2 mg/kg PO q 24 h, or methylprednisolone for dogs, 1.6 mg/kg PO q 24 h; or prednisolone for cats, 4.4 mg/kg PO q 24 h until resolution (about 2-6 weeks), then gradually tapering
    - Azathioprine, 2 mg/kg PO q 24 h (dogs); or chlorambucil, 0.1-0.2 mg/kg PO q 24 h (cats and small dogs): corticosteroid-sparing alternatives for long-term treatment. After a 4-to 8-week lag phase associated with both of these medications, dosage may be q 48 h (or less frequent) on alternate days of glucocorticoid use (if still required).
- Dietary elimination trial: adverse food reaction may be a trigger in immune-mediated panniculitis (rare).

DRUG INTERACTIONS

Clinicians should adjust dosage or minimize combination therapy with drugs that alter cytochrome P450 and/or p-glycoprotein activity (e.g., ketoconazole).

POSSIBLE COMPLICATIONS

Glucocorticoid side effects (iatrogenic hyperadrenocorticism)

RECOMMENDED MONITORING

- Schirmer tear test if long-term use of sulfa-based drugs
- CBC, platelet count, serum chemistry profile, and urinalysis typically after 2-4 weeks (initially) to q 3-6 months (when stable) if using immunosuppressive agents

PROGNOSIS AND OUTCOME 

- Variable, from guarded to good; healed lesions may leave scars.
- Most cases of panniculitis involve lengthy treatment (months).
- Amputation may be a serious consideration to prevent further spread of the disease should traditional therapies provide minimal improvement in a lesion localized to one limb.

PEARLS & CONSIDERATIONS 

COMMENTS

- A complete diagnostic workup to identify the underlying etiology leads to the most appropriate and successful treatment plan and outcome.
- More commonly a medically treated condition rather than a surgically managed disorder
- Clinicians should review the complexity of the differential diagnoses with clients, and ensure they are willing to pursue prolonged treatment before starting extensive diagnostic testing beyond histologic confirmation.
- Clinicians should obtain and freeze extra serum for future diagnostic tests based on histologic findings.

TECHNICIAN TIP

In some cases, a biopsy punch may not reach the hypodermis (subcutaneous fat), impeding proper diagnosis. Therefore, wedge biopsy may be preferred if panniculitis is suspected.

PREVENTION

- Weight loss for obese animals. Reduces amount of fat to which the body can react; may allow medication discontinuation.
- Owners should minimize pets' access to high-risk areas (swamps, riverbeds) and should rinse/bathe the pet after high-risk area exposure.
- Owners can give their pets routine vitamin E antioxidant.

CLIENT EDUCATION

- Extensive diagnostic testing can be involved; need to determine infectious versus immune-mediated cause.
- Treatment is generally lengthy, especially when addressing atypical mycobacteria, *Actinomyces, Nocardia,* and intermediate/systemic fungal infections; but with appropriate therapy, the prognosis in most cases is positive. Healed lesions may leave scars, however.

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AUTHOR: ANTHONY YU

EDITOR: MANON PARADIS

Panleukopenia, Cat

BASIC INFORMATION

DEFINITION

Highly contagious parvoviral infection of cats that typically causes severe, sometimes fatal, acute gastroenteritis and leukopenia. No longer common, owing to effective vaccination protocols.

SYNONYMS

Feline infectious enteritis, feline parvovirus (FPV)

EPIDEMIOLOGY

SPECIES, AGE, SEX

- All Felidae: domestic housecats, tigers, lions, cheetahs
- Also affects raccoons, ferrets, mink, civet cats
- Can affect all susceptible cats, primarily kittens <1 year old; most infections (>75%) are subclinical.

RISK FACTORS

- Unvaccinated cats > 6 weeks old
- Vaccinated kittens 8-20 weeks old, when maternal antibodies wane but may still neutralize vaccine-induced antibodies
- Pregnant queens receiving modified live-virus vaccines: risk of kittens with cerebellar hypoplasia
- Diagnosed most frequently in dense feral or shelter populations (frequent new animals, lower vaccination rates)

CONTAGION & ZOONOSIS

- Highly contagious to other cats; quarantine/isolation required
- Virus is shed in all body secretions, primarily feces. Virus extremely stable in the environment (up to 1 year). Susceptible cats infected by exposure to infected feces, secretions, or fomites. Can also be transmitted in utero.
- Does not infect dogs or humans, but cats are susceptible to canine parvovirus 2 (CPV-2) antigenic subtypes, which cause the same clinical course as FPV.

GEOGRAPHY AND SEASONALITY: Worldwide

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Classical feline enteritis: kittens and susceptible adults
- Silent abortion/fetal death: queens (first trimester)
- Central nervous system (CNS) form: kittens infected in utero in second or third trimester or up to 9 days postpartum
    - Virus infects replicating neurons.
    - Neurologic signs are nonprogressive, and affected kittens can still make good pets.

HISTORY, CHIEF COMPLAINT

- Classic enteritis, acute onset:
    - Sudden death, “fading kitten syndrome”
    - Vomiting, anorexia, and/or diarrhea
    - Extreme lethargy or depression, hiding
- In utero infection:
    - Queening of mummified fetuses
    - Ataxia and intention tremors noted once kittens start to walk (10-14 days old)
    - Altered mentation and dullness (usually not noted until several weeks old)
    - Seizures

PHYSICAL EXAM FINDINGS

- Classic enteritis; kitten is infected with FPV:
  - Fever or hypothermia in severe cases
  - Marked dehydration or hypovolemic shock
  - Vomiting, diarrhea
  - Thickened bowel loops, abdominal discomfort
- CNS form; mother was infected with panleukopenia virus when pregnant:
  - Cerebellar ataxia, hypermetria, intention tremors
  - Optic nerve hypoplasia, dark foci/folding/streaking of retina
  - Mental dullness, behavior abnormalities

ETIOLOGY AND PATHOPHYSIOLOGY

- Single-stranded nonenveloped DNA virus
- Replicates in rapidly dividing cells; clinical signs reflect destruction of these cells:
  - Lymphoid tissue: lymphopenia, lymph node necrosis
  - Bone marrow: panleukopenia, occasionally other short-lived cell lines (thrombocytes)
  - Intestinal mucosal crypt cells: damage results in malabsorptive diarrhea, increased permeability, increased risk for bacterial translocation.
  - Nervous system: cerebellar hypoplasia, hydrocephalus, hydranencephaly, retinal dysplasia from destruction of developing neural tissue

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Confirmatory FPV laboratory testing is not readily available; diagnosis is typically based on history, signalment, clinical signs, and initial laboratory findings. Severe gastroenteritis with neutropenia in a 3-to 5-month-old kitten is sufficiently suggestive of FPV infection to proceed with treatment, contagion precautions, and prognostication.

DIFFERENTIAL DIAGNOSIS

- Gastroenteritis:
  - Foreign body
  - Other bacterial or viral infections (coronavirus, *Salmonella* spp., *Clostridium* spp.)
  - Inflammatory bowel disease
  - Neoplasia
  - Toxin ingestion
- Leukopenia:
  - Feline leukemia virus (FeLV)
  - Salmonellosis

INITIAL DATABASE

- CBC: mild anemia unless severe gastrointestinal (GI) bleeding; leukopenia, especially neutropenia, is typical, but normal leukogram does not rule out FPV; thrombocytopenia due to bone marrow suppression or disseminated intravascular coagulation (DIC).
- Serum biochemistry profile: often unremarkable; prerenal azotemia, increases in alanine aminotransferase/aspartate aminotransferase/bilirubin possible
- Coagulation panel: may see evidence of DIC
- Radiographs: typically unremarkable

ADVANCED OR CONFIRMATORY TESTING

- Confirmatory diagnostic tests for enteric FPV exist (e.g., serologic titers, immunofluorescent antibody testing, PCR assay, and virus isolation), but are often labor-or time-intensive, expensive, and not readily available.
- Canine parvoviral fecal ELISA test kits can reliably detect FPV antigen. As with vaccination in puppies, false-positive results can occur within 2 weeks of vaccination with modified live feline panleukopenia vaccine.
- Since definitive antemortern diagnosis of the CNS form is not realistically possible, the practitioner should rely on history, signalment, and neurologic exam to point to in utero or perinatal FPV infection.
- Histologic findings are also similar to those of canine parvovirus.

TREATMENT

TREATMENT OVERVIEW

There is no specific antiviral drug for FPV infection, so comprehensive supportive care is required to carry the patient through the acute episode of enteritis. There is no treatment that will change the course of the neurologic form.

ACUTE GENERAL TREATMENT

Supportive care:

- IV crystalloids/colloids to correct shock, dehydration, and electrolyte abnormalities
- Broad-spectrum antibiotics (e.g., ampicillin, 22 mg/kg IV q 8 h; and gentamicin, 4 mg/kg IV q 24 h, only when hydration is normal) to combat secondary bacterial infections
- Withholding of food/water during acute episode to decrease crypt cell division and subsequent viral replication
- Antiemetics (e.g., metoclopramide 0.2-0.4 mg/kg SQ q 8 h or 1-2 mg/kg/d as an IV contrast rate infusion)

CHRONIC TREATMENT

Cats that recover are immune for life.

NUTRITION/DIET

- Appetite stimulants (cyproheptadine, 2 mg per cat PO q 12 h; or mirtazapine, 3.75 mg PO q 72 h); or enteral tube feeding during recovery period if anorexia persists. Trickle feeding of a liquid diet through a nasogastric tube after acute enterocyte destruction has stopped may improve gut healing and hasten return of appetite.
- Vitamin B^{12}, 0.25 mg IM or SQ per cat once

RECOMMENDED MONITORING

Repeat CBC: rebound leukocytosis (24-48 h). If leukopenia persists, clinicians should rule out other causes (e.g., FeLV).

PROGNOSIS AND OUTCOME

- Guarded (short-term) for acute gastroenteritis
- Guarded to good for kittens with cerebellar hypoplasia, depending on ability to compensate for deficits; neurologic signs are not treatable but are also nonprogressive.
- Grave to poor for kittens with fore-brain signs

PEARLS & CONSIDERATIONS

COMMENTS

- Kittens cannot have both neurologic signs and signs of enteritis simultaneously from panleukopenia, because neurologic signs occur from in utero infection of the dam.
- Routine vaccination has profoundly decreased the incidence of disease. Disease is maintained due to persistence of FPV in the environment and birth of susceptible animals in unvaccinated populations.

PREVENTION

Modified live vaccines (MLV) are preferred because they are rapid and provide more effective immunity. Clinicians should administer the vaccine after the kitten is 8 weeks old to avoid inactivation by maternal antibodies, then 2 and 4 weeks after first vaccination, and again 1 year later. Initial vaccinations probably provide lifelong immunity, but clinicians should revaccinate triennially per American Association of Feline Practitioners. MLV is contraindicated in pregnant queens or kittens < 4 weeks old.

TECHNICIAN TIPS

Because the virus is easily spread via fomites (towels, bowls, shoes) and persists up to 1 year, a strict isolation protocol is essential

in these cases (e.g., disposable gowns, booties, and gloves; monitoring equipment such as stethoscopes and thermometers cannot leave the isolation area). Disinfection of the environment or fomites requires 1:32 diluted sodium hypochlorite (bleach), formaldehyde, or glutaraldehyde.

CLIENT EDUCATION

Breeders should vaccinate new, susceptible cats 1 week prior to introduction to cattery.

SUGGESTED READING

Greene CE, Addie DD: Feline parvovirus infections. In Greene CE, editor: Infectious diseases of the dog and cat, ed 3, St Louis, MO, 2006, Saunders Elsevier, pp 78–88.

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Pancreatitis, Dog

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Pancreatitis is an inflammatory condition of the pancreas. It can be acute or chronic, which can only be differentiated histopathologically.

EPIDEMIOLOGY

SPECIES, AGE, SEX: There are no known age or sex predilections.

GENETICS & BREED PREDISPOSITION: Miniature schnauzers appear to be more commonly affected. As in some humans with hereditary pancreatitis, a mutation of the SPINK gene may be responsible.

RISK FACTORS

- Dietary indiscretion
- Blunt abdominal trauma
- Hypercalcemia
- Pancreatic hypoperfusion
- Pharmaceuticals: potassium bromide, phenobarbital, L-asparaginase, azathioprine, trimethoprim-sulfa, and others
    - There is little evidence that corticosteroids cause pancreatitis in dogs, and pancreatitis or a history of pancreatitis are not considered contraindications for corticosteroid use.
- Severe hypertriglyceridemia and disorders of lipid metabolism

ASSOCIATED CONDITIONS & DISORDERS: Peritonitis (in severe cases)

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- History of dietary indiscretion (often high-fat foods)
- Anorexia and vomiting are most common (reported in 91% and 90% of patients in one study, respectively).
- Weakness
- Abdominal pain is reported in more than 50% of dogs with pancreatitis.
- Diarrhea is reported in about 33% of dogs with pancreatitis.

PHYSICAL EXAM FINDINGS

- Abdominal pain
- Dehydration
- Fever
- Possible icterus

ETIOLOGY AND PATHOPHYSIOLOGY

- The cause of pancreatitis is unknown in many dogs.
- There is a common pathogenetic pathway, regardless of the initiating cause. Any number of insults can lead to premature activation of trypsinogen to trypsin. Trypsin, in turn, activates more trypsinogen and other pancreatic zymogens. Prematurely activated pancreatic digestive enzymes lead to local and systemic damage. This process also leads to recruitment of inflammatory cells and cytokine release, causing further systemic changes.
- In general, premature activation of pancreatic digestive enzymes leads to initiation of pancreatitis, while the inflammatory response leads to progression of the disease and systemic complications.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Measurement of serum pancreatic lipase immunoreactivity (now measured by Spec cPL) is the most sensitive and specific laboratory test currently available for pancreatitis, but the diagnosis rests on a combination of clinical signs, diagnostic imaging results, and pancreas-specific serologic tests.

DIFFERENTIAL DIAGNOSIS

- Primary acute or chronic gastrointestinal disorders: infectious, inflammatory, neoplastic, toxic, mechanical, or other
- Acute or chronic metabolic or systemic disorders: hepatic, renal, adrenal, thyroid (less likely), reproductive, or central nervous system (CNS) disease

INITIAL DATABASE

- CBC findings are variable and nonspecific: most commonly observed changes are thrombocytopenia, neutrophilia with a left shift, and anemia.
- Findings on a serum chemistry profile are variable and nonspecific: hypochloremia, hypophosphatemia, elevated hepatic enzyme activities, azotemia, hyperbilirubinemia, hypoalbuminemia, hypoglycemia, or hyperglycemia. Results from a serum chemistry profile are most useful in assessing the patient for systemic complications and ruling out other disorders with overlapping clinical signs.
- Abdominal radiographs are not useful in diagnosing pancreatitis but are useful in ruling out other differential diagnoses of pancreatitis.

ADVANCED OR CONFIRMATORY TESTING

- Abdominal ultrasound is useful for the diagnosis of canine pancreatitis:
  - Diagnostic criteria: enlargement of the pancreas, fluid accumulation around the pancreas, pancreatic mass effect, hypoechoic pancreas (necrosis), hyperechoic peripancreatic fat, or dilated pancreatic duct.
  - Resolution of equipment and operator expertise have increased significantly over the last 2 decades.
  - Clinicians must exercise caution not to overdiagnose pancreatitis.
- Serum amylase and lipase activities have been used for the diagnosis of pancreatitis for several decades.
  - Measurements of serum amylase or serum lipase activities are neither sensitive (approximately 50% sensitivity) nor specific (approximately 50% specificity) for pancreatitis and are thus clinically not very useful.
- SNAP cPL is a patient-side test for immediate rule out of canine pancreatitis. A negative SNAP cPL test should prompt the clinician to evaluate the patient for other differential diagnoses. A positive SNAP cPL should be confirmed by measurement of a Spec cPL test.
- Serum canine pancreatic lipase immunoreactivity (cPLI) concentration (now measured by the Spec cPL assay):0 Measures the concentration of pancreatic lipase in serum (many other lipases contribute to serum lipase activity measurement).
  - Reference range: <200 µg/L
  - Cutoff value for pancreatitis: 400 µg/L
  - Highly specific for exocrine pancreatic function
  - Highly sensitive for both acute and chronic pancreatitis
  - One-time measurement does not allow assessment of disease severity, but serial measurements do allow for monitoring of disease progression in a specific patient.

TREATMENT

TREATMENT OVERVIEW

- Treat the underlying cause if identified.
- Treat clinical signs that cause morbidity (e.g., pain, vomiting, anorexia).
- Identify and treat complications.
- Nutritional support

ACUTE GENERAL TREATMENT

- If the clinician can identify an underlying cause, it should be treated appropriately. For example, the drug history of the animal should be carefully assessed, and if the animal has been treated with any medication that has been implicated in causing pancreatitis, the medication should be discontinued. In addition, medications the animal does not necessarily need should be discontinued or switched to a different class of drug with the same or similar effect.
- The mainstay of pancreatitis therapy is supportive care. This includes aggressive fluid therapy and careful monitoring for any signs of ensuing complications. Once a complication has become established in an animal, treatment of such a complication

becomes increasingly difficult.

- Providing supportive therapy for effects of pancreatitis that cause morbidity is also important. Foremost, analgesia is very important.
  - Abdominal pain is a key clinical sign in people with pancreatitis and should be assumed to be present in any dog with pancreatitis, whether or not this is clinically apparent. Analgesia can be achieved with intermittent dosing or continuous rate infusion. Acceptable options include one of the following:
    - Meperidine: 5-10 mg/kg IM or slow IV as needed (q 1-4 h); short half-life can be limiting.
    - Butorphanol: 0.2-0.7 mg/kg SQ, IM, or IV q 3-6 h
    - Fentanyl: 0.01-0.04 mg/kg SQ, IM, or IV once, then as a constant rate infusion at 0.003-0.006 mg/kg/h; alternatively, may be administered as transdermal patch, which takes >12 hours to be effective.
    - Buprenorphine: 0.01-0.02 mg/kg IM or IV
  - Antiemetic therapy can be important. Metoclopramide antagonizes dopamine at the receptor site, which may have a negative impact on pancreatic perfusion and therefore is not the drug of first choice. Dolasetron and ondansetron are 5-HT^3 serotonergic receptor antagonists that have much stronger antiemetic properties than metoclopramide. Dolasetron and ondansetron can be safely used in the dog. Dolasetron can be used at dosages of 0.3-0.6 mg/kg IV, SQ, or PO q 12-24 h. Maropitant is an NK^1 receptor antagonist which has both peripheral and central antiemetic properties (1 mg/kg SQ q 24 h or 2 mg/kg PO q 24 h). Patients can be treated with a 5 HT^3 and an NK^1 inhibitor simultaneously.
- Dogs with severe pancreatitis (associated with dehydration, electrolyte and acid-base abnormalities, disseminated intravascular coagulation [DIC], and/or other systemic complications) should receive plasma transfusions on a daily basis (10 mL/kg given IV for 1-2 hours). While there is little scientific evidence that plasma administration is clinically useful in human patients with pancreatitis, many veterinary gastroenterologists feel that there appears to be a clinical benefit. One recent retrospective study of dogs with acute pancreatitis showed no benefit from plasma administration.
- Antibiotics have failed to show any benefit in human patients with pancreatitis. In addition, dogs with pancreatitis rarely have the infectious complications of pancreatitis commonly seen in humans with the condition. Thus, antibiotic therapy should only be implemented when there is a specific suspicion for a concurrent infectious disease or an infectious complication of pancreatitis.
- There is no evidence that any other therapeutic strategy is clinically efficacious in dogs with pancreatitis.

CHRONIC TREATMENT

- Dogs with chronic pancreatitis should be evaluated for potential risk factors for pancreatitis. An 18-hour fasting serum triglyceride concentration should be measured, and treatment measures should be employed in hyperlipidemic animals to keep the serum triglyceride concentration below 500 mg/dL (see p. 1398). Also, a serum calcium concentration should be measured and a detailed drug history taken. Dietary measures are important in the successful treatment of dogs with chronic pancreatitis (see below). Antioxidants may also be of benefit.
- Measurement of serum Spec cPL concentration can be used to objectively monitor animals with pancreatitis.

NUTRITION/DIET

- Recommending nothing per os (NPO) for the animal was once standard therapy for dogs with acute pancreatitis. However, nutritional support, preferably enteral nutritional support, can have beneficial effects in animals with pancreatitis. NPO should only be chosen in animals for which vomiting cannot be controlled.
- If the patient vomits and has to be kept NPO for several days, total or partial parenteral nutrition (TPN or PPN; see p. 1322) should be considered for nutritional support. Alternatively, jejunostomy tube placement surgically or via endoscopy (see) can be used for nutritional support.
- Dogs with pancreatitis should be fed an ultra low-fat diet. Care should also be taken to avoid any treats that may be high in fat.

DRUG INTERACTIONS

Any drugs implicated in causing pancreatitis should be avoided. However, corticosteroids, formerly implicated in causing pancreatitis, probably pose little risk of leading to worsening of pancreatitis in the dog.

POSSIBLE COMPLICATIONS

- A pancreatic pseudocyst (an encapsulated fluid collection in the region of the pancreas) rarely develops in dogs with pancreatitis. Little is known about appropriate management in dogs. In humans, pancreatic pseudocysts are carefully monitored and are only drained if they increase in size.
- Pancreatic abscesses have only been reported in approximately 40 dogs. Most of these were not infected. Surgical removal may be the best option. Aggressive antibiotic therapy should be instituted after draining the abscess, at least until culture results show absence of any infectious organisms.
- Pancreatitis can lead to extrahepatic biliary obstruction. In most cases, the obstruction will resolve with supportive care.

However, some patients will need surgery to reroute the bile duct.
- Systemic complications may include DIC, thrombocytopenia, acute renal failure, pleural effusion, pulmonary emboli, myocarditis, peritonitis, and aspiration pneumonia.

RECOMMENDED MONITORING

- Short-term monitoring: CBC, chemistry profile, coagulation panel, Spec cPL
- Ultrasound is of little value in monitoring short-term progress.
- Long-term monitoring: Spec cPL

PROGNOSIS AND OUTCOME

- The prognosis for dogs with pancreatitis is directly related to the severity of disease. Mild disease without pancreatic and systemic complications carries a good prognosis. Severe disease with pancreatic (e.g., pancreatic necrosis, pancreatic pseudocyst, pancreatic abscess, or other) or systemic (e.g., renal failure, pulmonary failure, DIC, or other) complications carries a poor to grave prognosis.
- There is no commonly accepted scoring system that would allow prediction of the outcome of the disease in a specific animal. Such scoring systems are routinely utilized in human patients with pancreatitis.

PEARLS & CONSIDERATIONS

COMMENTS

- Pancreatitis is being diagnosed with increasing frequency in dogs. A recent study has shown histopathologic changes of the exocrine pancreas in most dogs that died for any reason, suggesting that subclinical exocrine pancreatic disease and, more specifically, inflammation are common in dogs. However, at this point, the clinical importance of subclinical pancreatic inflammation in dogs is unknown.

PREVENTION

- Avoiding high-fat foods and treats may prevent pancreatitis, especially in animals that have had previous episodes of pancreatitis.
- Eliminating risk factors will aid in the prevention of pancreatitis.

SUGGESTED READING

Steiner JM: Exocrine pancreas. In Steiner JM, editor: Small animal gastroenterology, Hannover, 2008, Schlütersche-Verlagsgesellschaft mbH, pp 283–306.

Xenoulis PG, Suchodolski JS, Steiner JM: Chronic pancreatitis in dogs and cats. Compend Contin Educ Vet 30(3):166–180, 2008.

AUTHOR: JÖRG M. STEINER

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Pancreatitis, Cat

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Pancreatitis is an inflammatory condition of the pancreas. It can be acute or chronic, which can only be differentiated histopathologically. In contrast to acute pancreatitis, chronic pancreatitis is associated with permanent changes such as pancreatic fibrosis and/or atrophy.

EPIDEMIOLOGY

SPECIES, AGE, SEX: There are no known age or sex predilections for feline pancreatitis.

RISK FACTORS

- Blunt abdominal trauma
- Hypercalcemia
- Pancreatic hypoperfusion
- Pharmaceuticals: organophosphates and others
    - Corticosteroids are no longer implicated in causing pancreatitis in humans, and there is no evidence that they cause pancreatitis in cats.
- Infections: *Toxoplasma gondii,* hepatic fluke infestation *(Amphimerus pseudofelineus),* possibly feline infectious peritonitis (FIP), and others

ASSOCIATED CONDITIONS & DISORDERS

- Feline pancreatitis often concurrently occurs with cholangitis and inflammatory bowel disease (termed “triaditis” when inflammation is present in all three sites), but a cause-and-effect relationship between these conditions has not been demonstrated.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Acute or chronic
- Mild (not associated with systemic or pancreatic complications) or severe (associated with systemic or pancreatic complications)

HISTORY, CHIEF COMPLAINT: Vague complaints are typical:

- Lethargy
- Anorexia
- Vomiting occurs only in approximately 33% of cases.

PHYSICAL EXAM FINDINGS: Vague findings:

- Lethargy
- Dehydration
- Hypothermia
- Abdominal pain is only reported in approximately 25% of cases.
- Possible icterus

ETIOLOGY AND PATHOPHYSIOLOGY

- The causes for feline pancreatitis are not well defined. Several risk factors (see previous paragraphs) have been identified.
- There is a common pathogenetic pathway regardless of the initiating cause. Any number of insults can lead to premature activation of trypsinogen to trypsin. Trypsin, in turn, activates more trypsinogen and other pancreatic zymogens. Prematurely activated pancreatic digestive enzymes lead to local and systemic damage, which in turn leads to recruitment of inflammatory

cells and cytokine release, leading to further systemic complications.
- In general, premature activation of pancreatic digestive enzymes leads to initiation of pancreatitis, while the inflammatory response leads to progression of the disease and systemic complications.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Serum feline pancreatic lipase immunoreactivity concentration (fPLI), now measured by a commercially available assay, Spec fPL, is the most sensitive and specific laboratory test currently available for feline pancreatitis. However, it should be noted that integration of all clinical data available will afford the most accurate diagnosis.

DIFFERENTIAL DIAGNOSIS

- Primary acute or chronic gastrointestinal (GI) disorders: infectious, inflammatory, neoplastic, toxic, mechanical, or other conditions
- Acute or chronic metabolic or systemic disorders: hepatic, renal, adrenal, thyroid, systemic, or (less likely) central nervous system (CNS) or heart-worm disease

INITIAL DATABASE

- CBC findings are variable and nonspecific: most commonly observed changes are anemia and leukocytosis.
- Findings on a serum chemistry profile are also variable and nonspecific: increased serum hepatic enzyme activities, hyperbilirubinemia, hypercholesterolemia, hyperglycemia, azotemia, hypokalemia, hypocalcemia, and hypoalbuminemia. Results from a serum chemistry profile are very useful in assessing the patient for systemic complications of pancreatitis and ruling out other disorders with overlapping clinical signs.
- Abdominal radiographs are not useful for diagnosing pancreatitis but are useful for ruling out other differential diagnoses of pancreatitis.

ADVANCED OR CONFIRMATORY TESTING

- Abdominal ultrasound is useful for the diagnosis of feline pancreatitis:
    - Diagnostic criteria: enlargement of the pancreas, fluid accumulation around the pancreas, pancreatic mass effect, hypoechoic (necrosis) or, less common, hyperechoic (fibrosis) pancreas, hyperechoic peripancreatic fat, or dilated pancreatic duct
    - Resolution of equipment and operator expertise have increased significantly over the last 2 decades.
    - Clinicians should exercise caution and avoid overdiagnosing pancreatitis.
- Serum amylase and lipase activities are not useful for the diagnosis of feline pancreatitis.
- Serum feline trypsinlike immunoreactivity (fTLI) is highly specific (abnormally high value indicates pancreatitis with a high degree of accuracy) but not very sensitive (only 30%-60% of feline pancreatitis cases have an abnormal fTLI result).
- Serum feline pancreatic lipase immunoreactivity (Spec fPL [Idexx Laboratories, Portland, Maine]) concentration.
    - Measures concentration of pancreatic lipase in serum (many other lipases contribute to total serum lipase activity).
    - Reference range: 0.1-3.5 µg/L
    - Cutoff value for pancreatitis: 5.4 µg/L
    - Highly specific for exocrine pancreatic function
    - Highly sensitive for both acute and chronic pancreatitis
    - One-time measurement does not allow assessment of disease severity, but serial measurements do allow for monitoring of disease progression in a specific animal.

TREATMENT

TREATMENT OVERVIEW

- Treatment of the underlying cause if identified
- Treatment of clinical signs that cause morbidity (e.g., abdominal pain, vomiting)
- Identification and treatment of systemic and pancreatic complications
- Nutritional support

ACUTE GENERAL TREATMENT

- If an underlying cause can be identified, it should be treated accordingly. Examples:
  - The drug history of the animal should be carefully assessed; if the animal has been treated with any medication that has been implicated in causing pancreatitis, the medication should be discontinued.
  - In addition, medications the patient requires for a concurrent condition should be switched to a different class of drug with the same or similar effect.
- The mainstay of pancreatitis therapy is supportive care. This includes intensive but judicious fluid therapy and careful monitoring for any signs of ensuing complications. Once a complication has established itself in a patient, treatment of such a complication becomes increasingly difficult.
- Supportive therapy for signs that cause morbidity is also important. Foremost, analgesia is very important.
- Abdominal pain is a key clinical sign in people with pancreatitis and should be assumed to be present in any cat with pancreatitis, whether the sign is clinically apparent or not. Analgesia can be achieved with intermittent dosing or continuous rate infusion. Acceptable options include one of the following:
  - Meperidine: 2-4 mg/kg IM, as needed; short half-life or adverse effects can be limiting.
  - Butorphanol: 0.1-0.4 mg/kg SQ, IM, or IV
  - Morphine: 0.05-0.2 mg/kg q 2-6 h SQ or IM; may cause dysphoria or nausea
  - Fentanyl: 0.002-0.003 mg/kg IV once, then if needed, as a constant rate infusion: 0.001-0.004 mg/kg/h IV
  - Buprenorphine: 0.005-0.01 mg/kg IM or IV
- Antiemetic therapy can be important. Metoclopramide antagonizes dopamine at the receptor site, which may have a negative impact on pancreatic perfusion and therefore is not the first drug of choice. Dolasetron and ondansetron are 5-HT^3 serotonergic receptor antagonists that have much stronger antiemetic properties than metoclopramide. Dolasetron and ondansetron can be safely used in the cat. Dolasetron can be used at dosages of 0.3-0.6 mg/kg IV, SQ, or PO q 12-24 h. Maropitant is an NK^1 receptor antagonist, which has both peripheral and central antiemetic properties and can be used at 1 mg/kg SQ or PO q 24 h. Patients can be concurrently treated with a 5 HT^3 and an NK^1 inhibitor.
- Recommending nothing per os (NPO), nothing taken orally, was once standard therapy for cats with pancreatitis. However, nutritional support, preferably enteral nutritional support, can have beneficial effects in animals with pancreatitis. Thus, NPO should only be ordered for cats in which vomiting cannot be controlled. In animals that are eating and not vomiting, a low-fat diet should be offered in small amounts and given multiple times a day. If the animal vomits and has to be kept NPO, total or partial parenteral nutrition (TPN or PPN; see p. 1322) should be considered for nutritional support. If the animal is not vomiting but has prolonged anorexia, tube feeding (nasogastric, esophagostomy, or percutaneous endoscopic gastrostomy tube; see , , ,) is warranted. Nutritional support is especially important in cats. Many cats with pancreatitis have been partially or fully anorectic for some time before presentation and are thus at increased risk for secondary hepatic lipidosis.
- Antibiotics have failed to show a reproducible benefit in human patients with pancreatitis. In addition, infectious complications, which are a common cause for morbidity and mortality in human patients with severe pancreatitis, are extremely rare in cats with pancreatitis. Thus, antibiotic therapy should only be implemented when there is a specific suspicion for a concurrent infectious disease or an infectious complication of pancreatitis.
- Glucocorticoid therapy may be helpful, especially if there is concurrent histologically confirmed inflammatory bowel disease and/or cholangiohepatitis.
- There is no evidence that any other therapeutic strategy is clinically efficacious in cats with pancreatitis.

CHRONIC TREATMENT

- Cats with chronic pancreatitis often have concurrent inflammatory conditions such as inflammatory bowel disease (IBD) and/or cholangitis (known as “triaditis” when inflammation is present in all three sites). While there is little scientific evidence to suggest that these concurrent conditions cause pancreatitis, oftentimes the overall health of the cat will improve as these conditions are being appropriately diagnosed and managed.
- Serum calcium and fasting triglyceride concentrations should be measured in cats with pancreatitis, and conditions causing abnormalities in these parameters should be managed if present.
- While there is little evidence that high-fat diets are a cause of pancreatitis in cats, it still seems prudent to place cats with pancreatitis on a low-fat diet.
- Measurement of serum fPLI concentrations can be used for objectively monitoring animals with pancreatitis.
- Many cats with chronic pancreatitis have a lymphocytic infiltration of the pancreas. This is similar to humans with autoimmune pancreatitis. Thus, if no risk factors are identified and the patient does not improve spontaneously, a therapeutic trial with corticosteroids can be undertaken. A baseline serum fPLI concentration is measured, and prednisolone, 2 mg/kg PO q 12 h, is then given for 10 days. A second serum fPLI concentration measured at this point indicates whether to stop treatment (fPLI the same or higher) or continue on a tapering schedule based on positive response (fPLI lower).

DRUG INTERACTIONS

Any drugs implicated in causing pancreatitis should be avoided. However, corticosteroids, formerly implicated in causing pancreatitis, probably pose little risk of leading to worsening of pancreatitis in cats.

POSSIBLE COMPLICATIONS

- Pancreatic abscessation has only been reported in a single cat.

- Pancreatitis can lead to extrahepatic biliary obstruction. Most of these obstructions will resolve with supportive care. A small number of these cats need surgery to reroute the bile duct.
- Systemic complications may include disseminated intravascular coagulation (DIC), thrombocytopenia, acute renal failure, pleural effusion, and peritonitis. These are rare in cats.

RECOMMENDED MONITORING

- Short-term monitoring: CBC, chemistry profile, coagulation panel, fPLI
- Ultrasound is of little value in monitoring short-term progress.
- Long-term monitoring: fPLI

PROGNOSIS AND OUTCOME

The prognosis for cats with pancreatitis is directly related to the severity of disease. Mild disease without pancreatic and systemic complications carries a good prognosis. Severe disease with pancreatic (such as pancreatic necrosis, pancreatic pseudocyst, pancreatic abscess, or other) or systemic (such as renal failure, pulmonary failure, DIC, or other) complications carries a poor to grave prognosis.

PEARLS & CONSIDERATIONS

COMMENTS

Pancreatitis is diagnosed with increasing frequency in cats. In addition, autoimmune pancreatitis has been described with increasing frequency in humans. It is intriguing to speculate that at least some cats with chronic pancreatitis have a similar condition and, like humans with autoimmune pancreatitis, may benefit from corticosteroid administration (see above).

PREVENTION

There is no known prevention for pancreatitis in cats.

SUGGESTED READING

Xenoulis PG, Suchodolski JS, Steiner JM: Chronic pancreatitis in dogs and cats. Compend Contin Educ Vet 30(3):166–180, 2008 Mar.

Steiner JM: Exocrine pancreas. In: Steiner JM, editor: Small animal gastroenterology, Hannover, 2008, Schlütersche-Verlagsgesellschaft GmbH, pp 283–306.

AUTHOR: JÖRG M. STEINER

EDITOR: KEITH P. RICHTER

Pancreatic Adenocarcinoma

BASIC INFORMATION

DEFINITION

- Most commonly a malignant, highly metastatic epithelial tumor of the pancreas, of ductular or acinar origin

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Uncommon tumor of dogs and cats (<0.5% of all cancers)
- Older dogs and cats (dogs median age 9.2 years; cats 8-18 years)
- More common in female dogs; no gender predilection in cats

GENETICS & BREED PREDISPOSITION

- Airedale terriers and spaniel breeds may be at higher risk.
- No breed predilection in cats

RISK FACTORS

- Unknown
- Experimentally, *N*-ethyl-*N*′-nitro-*N*-nitrosoguanidine administered intraductally has been shown to induce pancreatic adenocarcinoma.

ASSOCIATED CONDITIONS & DISORDERS

- Paraneoplastic alopecia in cats
- Bile duct obstruction
- Secondary pancreatitis
- Carcinomatosis with or without ascites and metastasis to distant sites
- Diabetes mellitus (reported in two cats)
- Exocrine pancreatic insufficiency secondary to pancreatic duct obstruction (rare)
- Superficial necrolytic dermatitis/hepatocutaneous syndrome (in dogs)

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Typically vague and nonspecific: anorexia, weight loss, lethargy, vomiting, constipation, diarrhea, abdominal distension (mass, ascites), and paraneoplastic alopecia (cats)
- Owners may note icterus if the neoplasm is occluding the common bile duct.
- Signs related to metastasis: ascites, dyspnea, lameness/bone pain
- Signs related to effects of hepatocutaneous syndrome on paws (dogs): reluctance to walk or signs of paw pain when walking

PHYSICAL EXAM FINDINGS

- Abdominal mass and/or ascites
- Icterus if common bile duct obstruction
- Dyspnea due to pleural effusion or pulmonary metastasis
- Necrolytic pododermatitis due to superficial necrolytic dermatitis (dogs)

ETIOLOGY AND PATHOPHYSIOLOGY

- Etiology unknown
- Clinical signs related to local disease (mass), metastatic disease (carcinomatosis and systemic), and metabolic effects

- The majority of cases have already metastasized to regional or distant sites before the diagnosis can be made.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis may be suspected with vague nonspecific clinical signs. In some cases, there is a palpable abdominal mass, ascites (associated with carcinomatosis) and/or icterus (associated with extrahepatic biliary obstruction). Confirmation is based on detection of a pancreatic mass, (usually with ultrasound or at exploratory laparotomy in an older patient) and cytologic or histopathologic examination of smears or tissue specimens, respectively, from the mass.

DIFFERENTIAL DIAGNOSIS

- Pancreatitis: primary pancreatitis or pancreatitis secondary to the tumor
- Pancreatic pseudocyst
- Pancreatic abscess
- Pancreatic nodular hyperplasia
- Other pancreatic tumors (islet cell tumor, adenoma, sarcoma, and lymphoma)

INITIAL DATABASE

- CBC, serum biochemical profile, and urinalysis:
  - Can be unremarkable
  - Variable neutrophilia, anemia, hyper-bilirubinemia, azotemia, hyperglycemia, and elevations in hepatic enzymes
  - Serum lipase activities: marked hyperlipasemia may be a noninvasive indicator and biochemical marker for neoplasia of the pancreas; an activity greater than 25 times normal is probably diagnostic for exocrine pancreatic carcinoma.
- Abdominal radiographs: nonspecific; may reveal cranial abdominal mass effect and/or loss of abdominal organ detail due to ascites
- Thoracic radiographs (three views): to evaluate for pulmonary metastasis
- Abdominal ultrasound (high yield):
  - In most cases, a soft-tissue mass can be identified in the region of the pancreas. It may not be possible to conclusively identify the mass as pancreatic in origin on the ultrasound exam.
  - Benign pancreatic nodular hyperplasia, a common incidental finding in cats, must be considered when pancreatic nodules are identified. There is a tendency for neoplastic lesions to manifest as a single larger lesion and for nodular hyperplasia to manifest as multiple smaller lesions, although there can be overlap of the imaging findings for both entities.
  - Allows identification of metastatic lesions (liver “target lesions,” peritoneal masses, lymphadenopathy) and ascites, but not specific for pancreatic adenocarcinoma
  - Metastases are already present in a majority of cases of pancreatic adenocarcinoma and may be visible ultrasonographically.
  - The presence of gross metastatic disease (e.g., on ultrasound) must not be overinterpreted, because benign lesions such as hepatic nodular regeneration/hyperplasia, accessory splenic tissue, and others can be present and should not be misidentifted as metastases.

ADVANCED OR CONFIRMATORY TESTING

- Cytologie or histologic diagnosis is essential, owing to the inability to differentiate grossly between pancreatic adenocarcinoma, chronic pancreatitis, and pancreatic nodular hyperplasia.
- Cytologie evaluation of ascites may reveal neoplastic cells in some cases (neoplastic cells may not exfoliate).
- Ultrasound-guided percutaneous fine-needle aspirate for Cytologie examination (variable yield; neoplastic cells may not exfoliate; differentiation between neoplastic lesions and nodular hyperplasia may be difficult).
- Ultrasound-guided percutaneous core biopsy, laparoscopic biopsy, or surgical biopsy for histopathologic evaluation of tissue.
- Pancreatic lipase immunoreactivity (PLI): has not been evaluated with pancreatic neoplasia; increased levels would be expected if there is secondary pancreatitis.
- Abdominal CT scan or MRI (surgical planning and staging)

TREATMENT

TREATMENT OVERVIEW

- Surgical excision of the tumor may be palliative but is not indicated if metastasis is present (majority of cases).
- Aggressive surgical procedures (complete pancreatectomy or pancreatico-duodenectomy) have been described, but they carry high operative morbidity and mortality without meaningful cure rates.

ACUTE GENERAL TREATMENT

- Supportive therapy if there is secondary pancreatitis
- Surgery is indicated for solitary masses without evidence of metastasis, although a high metastatic rate makes this situation uncommon.
- Palliative surgery if there is intestinal or biliary obstruction

CHRONIC TREATMENT

- Chemotherapy or radiation therapy: no effective chemotherapy or radiation therapy protocols have been described.
- Gemcitabine (Gemzar) is approved for the treatment of pancreatic adenocarcinoma in people, and although cures are rare, gemcitabine has improved survival times in human patients. A recent case series of cats with pancreatic adenocarcinoma that underwent surgery and/or chemotherapy reported a median survival time of 3.8 months, with a range of 1 day to 17 months.
- Palliation of pain with analgesics

POSSIBLE COMPLICATIONS

Postoperative pancreatitis; preoperative and perioperative octreotide (Sandostatin, Novartis; 5 meg/kg SQ q 8 h) may be protective.

PROGNOSIS AND OUTCOME

- Very poor to grave
- Survival time of more than 1 year is rare.

PEARLS & CONSIDERATIONS

COMMENTS

- Pancreatic adenocarcinoma is an aggressive malignancy with high potential for metastasis and generally no effective treatment.
- Must be differentiated from non-neoplastic pancreatic lesions. It is important to have a Cytologie or histologic diagnosis, because chronic pancreatitis may closely resemble pancreatic adenocarcinoma.
- Animals with solitary masses without evidence of metastasis are candidates for surgery.

SUGGESTED READING

Seaman RL: Exocrine pancreatic neoplasia in the cat: a case series. J Am Anim Hosp Assoc 40:238–245, 2004.

Withrow SJ: Cancer of the gastrointestinal tract: exocrine pancreatic cancer. In Withrow SJ, Vail DM, editors: Small animal clinical oncology, ed 4, St Louis, 2007, Saunders Elsevier, pp 479–480.

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Palm (Cycad/Sago) Toxicosis

BASIC INFORMATION

DEFINITION

Acute, potentially fatal toxicosis occurring from ingesting cycad palm leaves, seeds, bark, or roots and characterized by vomiting and diarrhea, anorexia, lethargy, acute liver failure (2-3 days later), coagulopathies, and neurologic signs

SYNONYMS

Cycad palm/plant: sago palm (true synonyms); includes *Zamia floridana, Cycas revoluta,* and *C. circinalis*

EPIDEMIOLOGY

SPECIES, AGE, SEX: All animals are susceptible; most poisoning cases reported in dogs instead of cats.

RISK FACTORS: Presence of palm in the pet's environment.

GEOGRAPHY AND SEASONALITY

- Ornamental plants, indoor; in the southern part of the United States and in Hawaii, sago palms are frequently used for landscaping.
- Intoxication occurs mostly in summer months. Availability of indoor ornamental sago palms makes intoxication possible throughout the year.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Exposure to sago palm (any part of the plant)
- Within 24 hours, onset of vomiting, diarrhea, lethargy, and anorexia; chewed leaves, seeds, plant material may be in vomitus.
- Ataxia, weakness, or seizures
- Occurrence or recurrence of lethargy, anorexia, vomiting 2-3 days after ingestion, due to acute hepatic injury/failure.

PHYSICAL EXAM FINDINGS

- As above (see History, Chief Complaint)
- Signs of abdominal pain
- Weak pulse associated with hypovolemia or dehydration
- Petechiae, ecchymoses
- Hypovolemic shock (depressed mentation, weakness/collapse, poor perfusion)
- Central nervous system (CNS) signs: ataxia, seizures

ETIOLOGY AND PATHOPHYSIOLOGY

- Sago palms (cycad plants) are palmlike plants in the family Cycadaceae. These are woody, coarse plants with leaves originating from a thickened stem and are found in dry sandy soils of tropical and subtropical regions throughout the world.
- *C. revoluta* is the species most commonly involved in poisoning cases.
- Toxins: cycasin and methylazoxymethanol, a neurotoxic amino acid, and an unidentified high molecular-weight compound.
- The glucose molecule on cycasin is hydrolyzed by the gut bacterial enzyme alpha-glycosidase, yielding sugars and methylazoxymethanol, which then alkylates DNA and RNA. This process causes hepatotoxic, teratogenic, carcinogenic, and gastrointestinal (GI) effects.
- Azotemia can occur secondary to decreased renal perfusion resulting from systemic hypotension/hypoperfusion.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is based on history/evidence of exposure to plant, and presence of vomiting, anorexia, lethargy, and diarrhea within 24 hours. High serum liver enzyme levels 2-3 days after exposure offer further support. There is no definitive diagnostic test.

DIFFERENTIAL DIAGNOSIS

- Mushroom *(Amanita)* poisoning
- Blue-green algae toxicosis
- Idiopathic chronic hepatitis
- Viral hepatitis (canine hepatitis virus)
- Iron toxicosis in dogs

INITIAL DATABASE

- CBC:
  - Leukocytosis (reported: 3500-34,000 cells/µL)
  - Thrombocytopenia: mild and due to blood loss
- Serum biochemistry panel:
  - Increased alanine aminotransferase (ALT; range 128-10,000 IU/L)
  - Increased alkaline phosphatase (ALP; 218-3931 IU/L)
  - Hyperbilirubinemia (reported: 1.03-10 mg/dL; reference range 0-0.3 mg/dL)
  - Hypoproteinemia
  - Azotemia (prerenal and/or renal)
- Coagulation profile: increased pro-thrombin time, partial thromboplastin time due to liver damage
- Urinalysis: glucosuria, bilirubinuria, hematuria possible

ADVANCED OR CONFIRMATORY TESTING

Histopathologic lesions of liver may include marked focal centrolobular and midzonal coagulation necrosis.

TREATMENT

TREATMENT OVERVIEW

In patients showing clinical signs (GI. CNS), initial treatment is aimed at stabilization (seizure control, antiemetics, respectively). Signs of hepatic dysfunction should prompt treatment/prophylaxis for hepatic encephalopathy. Patients who are thought or known to have ingested this plant but where no clinical signs are apparent should undergo decontamination (induction of vomiting and administration of activated charcoal). Goals of treatment are decontamination of the animal as soon as possible, control of CNS and GI signs, treatment of liver injury, and provision of supportive care.

ACUTE GENERAL TREATMENT

- Decontaminating the animal:
  - Emesis (see p. 1364): only in animals not showing clinical signs; may remain effective within a couple of hours of ingestion
  - Gastric lavage (see p. 1281) only if a very large dose has been ingested and emesis cannot be induced (e.g., comatose animal)
  - Activated charcoal 1-4 g/kg PO; airway protected with cuffed endotracheal tube if animal is unconscious
- Controlling CNS and GI signs:
  - Seizures:
    - Diazepam 0.5-2 mg/kg IV as needed
    - Other anticonvulsants if refractory (see p. 1425)
  - Vomiting, gastric ulceration:
    - Control severe vomiting with metoclopramide (0.1-0.4 mg/kg PO, SQ, or IM q 6 h); or with maropitant, 1 mg/kg SQ q 24 h or 2 mg/kg PO q 24 h for up to 5 days
    - GI protectants, such as famotidine (0.5-1 mg/kg IV q 12-24 h) or sucralfate (0.5-1 g for a dog or 125-250 mg for a cat) PO q 8-12 h if evidence of gastric ulceration
- Treating signs of liver damage (see p. 503):
  - Clinicians should monitor and treat secondary effects of acute hepatic failure, such as hepatic encephalopathy (see p. 501), coagulopathy/bleeding tendencies (see), and hypoproteinemia (see).
  - If serum levels of liver enzymes are elevated or signs of liver dysfunction are present, oral antibiotics (e.g., neomycin, 10-20 mg/kg PO q 6-8 h) and lactulose (15-30 mL PO q 6-8 h [dogs]; 0.25-1 mL PO q 8-12 h [cats]) may help reduce the risk of hepatic encephalopathy (see p. 501).

- S-adenosyl-L-methionine (SAM-e), 18 mg/kg PO q 48-72 h
- Vitamin K[1;] 3 mg/kg PO, IM, or SQ, ± blood transfusions if hemorrhage
- Consider using *N*-acetylcysteine (Mucomyst), 140 mg/kg PO or IV (use a 5-micron filter for IV use) followed by 70 mg/kg PO for 5-7 treatments. Efficacy for treating sago palm toxicosis has not been determined.

- Supportive care
  - IV fluids (may require dextrose supplementation if hypoglycemia)

CHRONIC TREATMENT

SAM-e 18 mg/kg PO every other day to third day for 1-3 months if evidence of persistent liver insult (e.g., serum ALT and/or bilirubin elevation)

POSSIBLE COMPLICATIONS

Chronic liver disease (cirrhosis/fibrosis)

RECOMMENDED MONITORING

- CBC
- Serum biochemistry profile, especially liver enzymes (baseline, 24, 48, 72 hours)
- Coagulation panel (prothrombin time [PT], activated partial thromboplastin time [APTT])
- Hematocrit

PROGNOSIS AND OUTCOME

- Poor prognosis if evidence of severe liver injury
- Good prognosis with early and intensive treatment

PEARLS & CONSIDERATIONS

COMMENTS

- All sago palm exposures should be taken seriously because the overall mortality rate in dogs can be 33%.
- All parts are considered toxic, and seeds concentrate more toxins; one to two ingested seeds potentially can be lethal in a medium-sized dog.
- Clinical signs of toxicosis can last from a few days to several weeks depending on the severity of liver injury.

TECHNICIAN TIP

- Be aware of the biphasic nature of this intoxication: initial clinical signs occur within hours of ingestion of the plant, and after initial recovery, a second clinical syndrome (due to liver failure) should be anticipated, monitored, and treated, 2-3 days after the first.

PREVENTION

Owners should keep pets out of areas where sago palm plants are growing.

SUGGESTED READING

Albretsen JC, et al: Cycad palm toxicosis in dogs: 60 cases (1987-1997). J Am Vet Med Assoc 213(1):99–101, 1998.

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Pallor

BASIC INFORMATION

DEFINITION

Pale mucous membranes

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs and cats of any age and either sex

GENETICS & BREED PREDISPOSITION: Rare hereditary hemolytic anemias in Abyssinian, Siamese, and Somali cats and in poodle, basenji, and beagle dogs CONTAGION & ZOONOSIS: Feline leukemia virus-associated anemia (cat to cat)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Anemia: perfusion is adequate, but circulating red blood cell (RBC) mass is low.
- Shock: perfusion is inadequate, but circulating RBC mass is normal.

HISTORY, CHIEF COMPLAINT

- Weakness
- Tachypnea
- Collapse
- Those due to underlying disease:
    - History of trauma in hypovolemic shock
    - Coughing and dyspnea with cardiogenic shock
    - Lethargy and anorexia with septic shock
- Pale mucous membranes (uncommon as an owner-reported chief complaint)

PHYSICAL EXAM FINDINGS

- Pale mucous membranes of the gingiva, tongue, conjunctiva, anus, penis, and/or vulva
- Tachypnea, cool mucous membranes, tachycardia, and weakness may be seen with either anemia or shock.
- Capillary refill time (CRT):
    - Unless there is severe anemia, CRT should be normal (<2 sec) in an anemic animal that is not in shock.
    - Animals in shock typically have a prolonged CRT.
- Visualization of stool via rectal examination may identify fresh blood or melena in cases with gastrointestinal (GI) hemorrhage.
- Palpation of the extremities (pinnae, paws) reveals a cool temperature with poor perfusion (e.g., shock) but not with anemia alone.

ETIOLOGY AND PATHOPHYSIOLOGY

- Severe blood loss or severe anemia can lead to shock, so both conditions may exist in the same animal.
- Anemia causes pallor due to blood with diminished hemoglobin (i.e., decreased red blood cells) traversing through easily seen capillary beds, creating a pale red color in the mucous membranes.
- Shock leads to poor perfusion of blood through capillary vessels, thus causing pallor. Shock is a peracute condition, but the underlying cause may be chronic in nature.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Initially, distinguishing the cause of pallor between anemia and shock can be completed via physical examination and blood pressure (BP) and packed cell volume (PCV) measurement. Then additional testing can provide a specific diagnosis.

DIFFERENTIAL DIAGNOSIS

There are two major forms of anemia: regenerative and nonregenerative.

- Regenerative anemia:
  - Blood loss/hemorrhage:
    - Trauma
    - Parasitic infestation
    - Coagulopathy
    - GI disease (ulceration, mass, inflammation, infiltration)
    - Abdominal or intrathoracic mass
  - Hemolysis:
    - Primary immune-mediated
    - Fragmentation (disseminated intravascular coagulation [DIC], hemangiosarcoma, heartworm disease, vasculitis)
    - Toxicoses (zinc, acetaminophen, onions)
    - RBC parasites *(Babesia, Bartonella, Cytauxzoon, Mycoplasma* spp.)
    - Hereditary (pyruvate kinase or phosphofructokinase deficiency)
- Nonregenerative anemia:
  - Bone marrow disease (aplastic anemia, myelodysplasia, myelofibrosis, myeloproliferative disorder)
  - Chronic kidney disease
  - Anemia of chronic disease
  - Feline leukemia virus (FeLV) infection

There are four major types of shock:

- Cardiogenic shock:
  - Severe atrioventricular (AV) valvular endocardiosis
  - Cardiac tamponade secondary to pericardial effusion
  - Dilated cardiomyopathy
  - Hypertrophie cardiomyopathy
  - Heartworm disease
  - Severe dysrhythmia
- Hypovolemic shock:
  - Dehydration
  - Blood loss
  - Hypoadrenocorticism
  - Intoxications
- Traumatic shock
- Septic shock

INITIAL DATABASE

- PCV will help differentiate anemia from shock in most cases. Unless the animal was anemic beforehand, cases of acute shock should have a normal PCV, including those with acute blood loss. Anemic animals, by definition, have a diminished PCV.
- BP is usually diminished in cases of shock. Unless the anemia is severe or acute, BP is typically normal in anemic animals.
- CBC, biochemical profile, and urinalysis are warranted in most cases of pallor to assist in determining the underlying cause.

ADVANCED OR CONFIRMATORY TESTING

- Reticulocyte count to characterize type of anemia
- Evidence of saline-diluted RBC agglutination on a slide suggests an immune-mediated hemolytic anemia, as would a positive Coombs' test result.
- Thoracic radiographs to look for evidence of primary heart disease, trauma (e.g., rib fractures, lung contusions), or an infectious focus causing sepsis (e.g., pneumonia)
- Abdominal radiographs and/or ultrasound to visualize fluid (e.g., blood loss, congestive heart failure), neoplasia, and metallic (zinc) objects in the GI tract
- Cytologie and/or histopathologic examination of bone marrow to help characterize the amount of regeneration in persistently anemic animals and look for evidence of primary bone marrow disease (e.g., neoplasia, FeLV).

TREATMENT 

TREATMENT OVERVIEW

Stabilization of the animal (e.g., blood transfusion for severely anemic patients, intravenous fluids for those in shock) while the cause of pallor is determined and corrected if possible.

ACUTE GENERAL TREATMENT

- Determined by the underlying cause
- Patients with severe anemia or acute blood loss may require transfusion of RBC ± plasma (see p. 1347).
- Hypovolemic, traumatic, and septic shock cases are usually treated with vigorous intravenous crystalloids, + colloids (see pp. 1591 and 1592).
- Cardiogenic shock requires supplemental oxygen and attempts to improve perfusion, such as with pericardiocentesis (if cardiac tamponade) and medications (e.g., positive inotropes, antidysrhythmics).

CHRONIC TREATMENT

Depends on the underlying cause

RECOMMENDED MONITORING

- PCV in patients with anemia
- CRT and BP in cases of shock

PROGNOSIS AND OUTCOME

- Determined by the underlying cause
- Many cases of pallor come with a guarded to poor prognosis (e.g., DIC, hemangiosarcoma, FeLV, cardiogenic shock, chronic kidney disease), but others may respond much better with proper therapy (e.g., trauma, parasitic infection, hypoadrenocorticism).

PEARLS & CONSIDERATIONS

COMMENTS

- Because there are many causes of pallor, the clinician especially needs to be aware of the differential diagnoses and methods to distinguish anemia from shock.
- Most causes of pallor are serious, thus requiring timely workup and therapy.

TECHNICIAN TIP

Strive to recognize pallor in hospitalized and outpatient cases, and assist in distinguishing anemia from shock via physical examination, PCV and BP measurement.

SUGGESTED READING

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Pain

BASIC INFORMATION

DEFINITION

An unpleasant sensory or emotional experience associated with actual or potential tissue damage

EPIDEMIOLOGY

SPECIES, AGE, SEX: Animals of any species, age, or sex may experience pain, although pain thresholds and response characteristics may vary.

ASSOCIATED CONDITIONS & DISORDERS: Pain intensity does not always correlate with degree of tissue damage. In some cases, there may be no obvious evidence of tissue disruption, and persistence of pain may indicate abnormal processing of input in the central nervous system (CNS). The following are some associated conditions and disorders:

- Trauma
- Surgery
- Degenerative disease processes
- Inflammatory disease processes
- Neoplasia

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Physiologic versus pathologic
- Acute versus chronic
- Somatic versus visceral versus neuropathic

HISTORY, CHIEF COMPLAINT

- Humans can verbally report pain as their primary complaint, whereas animals cannot.
- An animal's history will vary depending on the type of pain (i.e., acute versus chronic) and may include an inciting injury.

PHYSICAL EXAM FINDINGS

- Behavioral signs of pain vary considerably among individuals. Common pain-related behaviors in dogs and cats include:
  - Postural changes: arched/hunched back, drooped head
  - Temperament changes: aggression, hiding
  - Vocalization: moaning, howling, purring (cats)
  - Locomotor changes: reluctance to move, lameness
  - Others: no interest in food or play, failure to groom
- Physiologic signs associated with stress response (tachycardia, tachypnea, mydriasis, hypertension) may accompany pain but are nonspecific. Clinical signs associated with chronic pain may be very subtle.

ETIOLOGY AND PATHOPHYSIOLOGY

- A noxious stimulus activates specialized nerve endings called *nociceptors.*
- Nociceptors transduce noxious chemical, mechanical, or thermal stimuli into electrochemical potentials that are transmitted via sensory nerves from affected tissue to spinal cord.
- In the spinal cord dorsal horn, incoming first-order peripheral neurons synapse with ascending spinal neurons that extend to the brainstem.
- Incoming noxious input is modulated at the level of the dorsal horn by other incoming sensory information, descending inhibitory nerve impulses, or pharmacologic interventions.
- In the brainstem, incoming second-order neurons synapse with third-order neurons that form tracts extending to numerous locations within the brain where pain perception ultimately occurs.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Since pain is a sensation, animals may experience it without expressing appreciable manifestations of it. Therefore, attentive physical examination and especially repeated evaluations to detect early or subtle changes are cornerstones of diagnosis of pain, especially in stoic animals.

DIFFERENTIAL DIAGNOSIS

- Since animals cannot self-report pain, the veterinarian must accurately identify it when it is present.
- Pain must be differentiated from:
  - Distress associated with other factors (restraint, restrictive bandaging, confinement, separation from owners)
  - Dysphoria associated with drugs used to treat pain (particularly opioids, dissociative agents)
- Once a presumptive diagnosis of pain is made, veterinarians should investigate the underlying cause.
- Differential diagnoses of common causes listed under Associated Conditions and Disorders.

INITIAL DATABASE

- Recognition of pain in animals is subjective.
- Veterinarians should follow a routine for evaluation. The veterinarian should:
  - Evaluate the animal's signalment, history, and previous physical exam findings.
  - Observe the animal's behavior from a distance (preferably unobserved by the animal).
  - Observe the animal's behavior during interaction prior to extensive palpation and examination.
  - Gently palpate the body region of interest and evaluate the animal's response.
- Perform serial evaluations and record findings in the animal's medical record.
- Pain should be evaluated as the fourth vital sign (in addition to temperature, pulse, and respiration).
- No predictable changes in routine laboratory tests specifically indicate pain.

TREATMENT

TREATMENT OVERVIEW

- Improve the animal's quality of life while addressing underlying cause of pain if possible.
- If pain is intractable, euthanasia may be most humane option.

ACUTE GENERAL TREATMENT

- Depends on species, pain intensity, underlying cause
- Acute pain most often is managed pharmacologically.
- Pharmacologic treatment involves one or more of the following:
  - Opioids: morphine, hydromorphone, oxymorphone, fentanyl, buprenorphine, butorphanol
  - Nonsteroidal antiinflammatory agents (NSAIDs): carprofen, meloxicam, deracoxib
  - Local anesthetics (regional anesthesia techniques, see p. 1299), lidocaine, bupivacaine
- Utilize the following treatment strategies: *multimodal analgesia,* which is a combination of multiple analgesic drugs or techniques to target different points along the pain pathway; *preemptive analgesia,* which is the administration of analgesic agent(s) prior to noxious insult (i.e., surgery).

CHRONIC TREATMENT

- Dietary changes and nonpharmacologic treatment (e.g., physiotherapy, acupuncture) may be beneficial.
- Pharmacologic treatment involves one or more of the following given by the oral route:
  - Nonsteroidal antiinflammatory drugs
  - Opioids (doses may need to be increased if pain intensifies)
  - Adjunctive analgesic agents (tramadol, gabapentin, amantadine) may be added if conventional analgesics fail to manage pain adequately.

DRUG INTERACTIONS

- Opioids reduce anesthetic requirements significantly.

- Certain opioids (e.g., meperidine) may interact with monoamine oxidase-B inhibitors (e.g., selegiline [L-deprenyl] or amitraz) and produce “serotonin syndrome.”
- There is a significantly increased risk of gastrointestinal toxicosis possible when NSAIDs and glucocorticoids are administered concurrently.

PROGNOSIS AND OUTCOME

- Acute pain expected to resolve within period of normal tissue healing
- When pain persists beyond normal course, veterinarians should suspect persistent disease, injury, or CNS changes and consult a specialist.

PEARLS & CONSIDERATIONS

COMMENTS

For challenging cases, veterinarians should seek advice from a veterinary pain specialist (i.e., an anesthesiologist, surgeon, oncologist, or internist with advanced training in pain management).

PREVENTION

Veterinarians should institute preemptive analgesic protocols when appropriate.

SUGGESTED READING

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Roundworm Infection

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Infection with a small intestinal round-worm *(Toxocara* or *Toxascaris* spp.)

SYNONYMS

Toxocariasis, ascarid infection, infection with *Toxocara cants* (dog) or *T cati* (cat), infection with *T. leonina* (dogs and cats), visceral larva migrans (zoonosis); ascarids

EPIDEMIOLOGY

SPECIES, AGE, SEX: Young puppies and kittens < 6 months old most commonly infected. Clinically significant disease is uncommon in adult dogs and cats. *T. cants* affects dogs, *T. cati* affects cats, and *T. leonina* affects both dogs and cats.

RISK FACTORS: Young animals and pregnant dogs and cats are more susceptible.

CONTAGION & ZOONOSIS: Unembryonated *Toxocara* spp. eggs are passed in the host's feces. Embryonation in the environment produces second-stage larvae in the eggs, which are infective (via ingestion) to humans, dogs, and cats. Infection with *Toxocara* spp. is the most common cause of human visceral and ocular larva migrans. *T leonina* is not zoonotic.

GEOGRAPHY AND SEASONALITY: *Toxocara* spp. are found worldwide, with a higher incidence in lower socio-economic communities.

ASSOCIATED CONDITIONS & DISORDERS: Commonly found in association with other intestinal parasites. Intussusception and, with very large worm burdens, intestinal obstruction are possible.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Intestinal infection is most common.
- Aberrant migration of larvae (visceral, ocular) is rare.

HISTORY, CHIEF COMPLAINT

- Commonly unremarkable; the parasite is discovered incidentally during a routine fecal examination, or infection is never detected.
- Intestinal: in overt cases, presence of worms in feces or diarrhea, a pot-bellied appearance in young puppies or kittens, or occasional vomiting with or without worms may prompt the owner to seek veterinary attention.

PHYSICAL EXAM FINDINGS: Typically, no physical abnormalities are noted, as above. It has been speculated that essentially all puppies have *Toxocara.*

ETIOLOGY AND PATHOPHYSIOLOGY

- *T. cants* transmission: mainly transplacental from dam to puppies
- *T. cants* (puppies) or *T. cati* (kittens): transmammary transmission possible; principal route in cats
- Fecal-oral transmission and ingestion of other paratenic or transport hosts such as rodents: additional routes of infection
- After infection, the parasite may migrate through the liver into the lungs *(T. cants* and *T cati),* within the wall of the gastrointestinal (GI) tract *(T. cants, T cati,* and *T. leonina),* or somatically within the tissues *(T. cants, T cati).* Puppies and kittens may begin to shed eggs within 2.5-3.5 weeks and generally continue to do so until age 4-6 months.
- Eggs are highly resistant and long-lived within the environment. They adhere easily to fomites. Eggs are most susceptible to heat. A 20% bleach solution will decrease the adherence of the eggs but will not kill them.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Roundworm eggs are easily detected in a simple fecal flotation procedure using zinc sulfate flotation media.

DIFFERENTIAL DIAGNOSIS

- Infections with *Ancylostoma caninum* (hookworms), *Trichuris vulpis* (whip-worms), *Giardia intestinalis,* and *Cystoisospora* (coccidia)
- *Campylobacter* enteritis
- Canine parvovirus
- Feline panleukopenia
- Intussusception or foreign body ingestion (if obstruction)

INITIAL DATABASE

Fecal examination should be routinely performed in all puppies and kittens up to 6 months of age.

TREATMENT

TREATMENT OVERVIEW

Owing to their zoonotic significance, these common helminth parasites must be removed from the gastrointestinal tract of both dogs and cats.

ACUTE GENERAL TREATMENT

- The Centers for Disease Control and Prevention (CDC) and Association of Veterinary Parasitologists recommend deworming all puppies beginning at 2 weeks, with additional treatments at 4, 6, and 8 weeks of age. Semimonthly deworming may be continued up to 12 weeks of age. These recommendations aim to reduce zoonotic risk by decreasing environmental parasite burden.
- Deworm kittens at 6 weeks of age and again at 8 and 10 weeks.
- Deworm puppies and kittens monthly after they reach 3 months of age.
- Deworm puppies and kittens even if fecal results are negative, to ensure removal of prepatent worms prior to shedding.
- Treat pregnant bitches to reduce further transplacental transmission: fenbendazole, 50 mg/kg q 24 h for 14 days.
- Treat lactating bitches and queens to prevent further transmammary transmission.
- Most deworming medications are effective against roundworms. Pyrantel pamoate (5-10 mg/kg PO; considered safe during pregnancy) is used most widely. Other anthelmintics (e.g., milbemycin oxime, moxidectin, selamectin) have antiascarid activity but are not used in a 2-week protocol as previously described. Ivermectin at parasiticidal doses may be effective *(T. canis* > *T. leonina),*but alternatives with a wider safety margin are preferred.
- Many products used for heartworm prevention are also effective against roundworms.

CHRONIC TREATMENT

Environmental decontamination should be considered in all animals, especially those with repeated infections or adult animals with infection.

DRUG INTERACTIONS

The parasiticidal dose of ivermectin (200 mcg/kg) should not be used in collies or other susceptible breeds/individuals (see pp. 625 and).

PROGNOSIS AND OUTCOME

Prognosis is excellent for appropriately treated animals.

PEARLS & CONSIDERATIONS

COMMENTS

- All puppies and kittens should be strategically dewormed to prevent environmental contamination and human exposure.
- The zoonotic risk associated with *Toxocara* spp. parasites outweighs their impact on dogs and cats.

PREVENTION

- Treatment of pregnant dogs and cats can decrease the level of transplacental and transmammary infection of puppies and kittens. Common treatment regimes described for dogs include fenbendazole, 50 mg/kg PO q 24 h, from day 40 of gestation to day 14 of lactation; or ivermectin, 200 mcg/kg, once a week from 3 weeks prior to whelping to 3 weeks after whelping.
- Pregnant cats may be treated with topical selamectin, 6 mg/kg, 6 weeks and 2 weeks before parturition and 2 weeks and 6 weeks after parturition.

TECHNICIAN TIPS

Warn all clients of the risks of exposure to *Toxocara,* especially those clients with young children or those who are immunosuppressed.

CLIENT EDUCATION

- Clients should be encouraged to commit to regular deworming of puppies and older dogs.
- Good hygiene is important in kennels and catteries; all feces should be properly removed from the area.

SUGGESTED READING

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Round Cell Tumors

BASIC INFORMATION

DEFINITION

- Round cell tumors are composed of a homogenous population of cells that have well-defined cytoplasmic margins, are round in shape, and have a round nucleus. Distinct cytologic characteristics of each type of round cell aid in definitive diagnosis.
- Tumor types include lymphoma, mast cell tumor (MCT), transmissible venereal tumor (TVT), histiocytoma, and plasma cell tumor/multiple myeloma. Malignant melanoma is highly variable in appearance and is often classified as a round cell tumor. Each of these is discussed in greater detail in individual chapters.
- Round cell tumors can be either malignant (e.g., lymphoma, grade II or III mast cell tumors) or benign (histiocytoma, grade I mast cell tumor). Most primarily affect the skin (mast cell tumor, histiocytoma, plasma cell tumor, transmissible venereal tumor) and may metastasize internally. Lymphoma primarily affects lymphoid organs and less commonly affects the skin and other organ systems.

SYNONYM

Discrete cell tumors

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dependent on tumor type

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Lymphoma (malignant lymphoma, lymphosarcoma) is seen in dogs and cats of all ages and can affect any organ system. In dogs, the most common form involves generalized lymph node infiltration; in cats, the gastrointestinal form prevails.
- Mast cell tumors (mastocytomas, mast cell sarcomas) are seen in dogs and cats; most common form is skin/subcutaneous mass. In cats, a splenic or visceral form can occur.
- Transmissible venereal tumors (TVT) are transplanted from dog to dog by direct contact. TVT is most commonly seen in intact dogs in the genital regions and oral and nasal cavities.
- Histiocytomas are most commonly seen in young dogs (<3 years age). They are usually small (<2 cm), red, raised, round, and alopecic. They usually spontaneously regress and may become ulcerated/inflamed as they regress.
- Plasma cell tumors (plasmacytomas) most commonly occur in dogs as skin and subcutaneous masses. The systemic form of plasma cell cancer is multiple myeloma. Plasma cell neoplasia is uncommon in cats.
- Melanomas are most commonly seen in the skin, oral cavity, and digits of dogs. They are rare in cats.

HISTORY, CHIEF COMPLAINT: Dependent on tumor type

PHYSICAL EXAM FINDINGS: Dependent on tumor type

ETIOLOGY AND PATHOPHYSIOLOGY

Dependent on tumor type

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Round cell tumors are one of three cellular categories of major tumor types: carcinomas (epithelial tumors), sarcomas (mesenchymal tumors), and round cell tumors. The diagnosis of round cell tumors is generally straightforward with cytologic examination; treatment, staging, and prognosis are dependent on tumor type.

DIFFERENTIAL DIAGNOSIS

Dependent on tumor type (see chapters on specific tumor types)

INITIAL DATABASE

- Cytologic evaluation will confirm the cell type (diagnosis) for many round cell tumors.
- The following cytologic characteristics are commonly seen in these specific cell types:
  - Lymphoma: high nuclear-to-cytoplasmic ratio; multiple nucleoli; thin rim of dark blue cytoplasm; chromatin is clumped; mitotic figures numerous; in large granular lymphocyte lymphoma (uncommon form of lymphoma seen most commonly in the gastrointestinal tract of cats): red to purple granules are present that are larger and less numerous than granules in MCT.
  - Mast cell tumor: low nuclear-to-cytoplasmic ratio; nuclear details obscured by pink to purple intracytoplasmic granules that are present in most MCT (in some poorly differentiated MCT, granules are absent); eosinophils are often present.
  - Transmissible venereal tumor: cytoplasmic vacuolation is common and distinctive; chromatin is coarse; nucleoli are prominent; mitotic figures may be seen; inflammatory cells such as lymphocytes and plasma cells may be seen.
  - Histiocytoma: low to intermediate nuclear-to-cytoplasmic ratio; anisocytosis and anisokaryosis common; the cytoplasm is pale and may contain fine granules; cytoplasmic vacuolation is sometimes seen; mitotic figures are occasionally seen; inflammatory cells are present when tumors are regressing (histiocytomas often spontaneously regress).
  - Plasma cell tumor: perinuclear clear zone adjacent to nucleus; eccentrically positioned nucleus; chromatin is clumped; large amount of dark blue cytoplasm; bi- and tri-nucleation can be seen but does not correlate with the degree of malignancy.
  - Melanoma: can have the appearance of an epithelial, mesenchymal, or round cell tumor; green, brown, or black intracytoplasmic granules often seen but not always present (absence = amelanotic melanoma).

ADVANCED OR CONFIRMATORY TESTING

- In some cases, the tumor type is not readily distinguished cytologically; a biopsy of the lesion should be submitted for histopathologic analysis. If the cell lineage is still not determined, immunohistochemistry or special stains may be performed.
  - Special stains such as toluidine blue or Giemsa can identify granules in MCT.
  - Immunohistochemistry involves the use of antibodies directed against specific cell antigens that are markers of individual cell types. Examples include CD3, CD4, CD8 (T lymphocytes); CD21, CD79a (B lymphocytes); Melan A or S-100 (melanocytes); CD-117 (c-kit) (mast cells).

TREATMENT 

TREATMENT OVERVIEW

Dependent on tumor type

ACUTE AND CHRONIC TREATMENT

Dependent on tumor type

PROGNOSIS AND OUTCOME 

Dependent on tumor type

SUGGESTED READING

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Powers B: Tumour pathology. BSAVA manual of canine and feline oncology, Haryana, India, 2003, Replika Press, pp –. 1017

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EDITOR: KENNETH M.RASSNICK

Root Signature (Nerve)

BASIC INFORMATION

DEFINITION

Non–weight-bearing lameness and pain resulting from disturbances in sensation within a nerve root or sensory nerve of the cervical or lumbosacral intumescence; common with nerve root compression in the cervical or lumbar intumescence

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dependent on underlying cause; dogs, older adults (neoplasia); cats, young adults (lymphoma)

GENETICS & BREED PREDISPOSITION: DOGS: dachshund, cocker spaniel, beagle, other chondrodystrophoid breeds (intervertebral disk disease [IVDD]); German shepherds (degenerative lumbosacral stenosis)

RISK FACTORS: CATS: multicat household (risk of feline leukemia virus [FeLV])

CONTAGION & ZOONOSIS: CATS: FeLV (cat-to-cat)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Acute (IVDD)
- Chronic, progressive (neoplasia)
- Intermittent (degenerative lumbosacral stenosis)

HISTORY, CHIEF COMPLAINT

- Thoracic limbs > pelvic limbs
- Non–weight-bearing lameness and pain
- Paravertebral pain
- Trauma
- Difficulty rising, reluctance to jump
- Lack of response to non steroidal antiinflammatory medications

PHYSICAL EXAM FINDINGS

- Non–weight-bearing lameness (limb typically held in flexion)
- Often ipsilateral caudal cervical muscle spasms with disk extrusions
- Focal hyperesthesia (pain), typically following the dermatomal distribution of the affected nerve. A hallmark of nerve root signature is pain.
- Paresis and occasionally hypotonia of the affected limb
- +/− Neurogenic muscle atrophy if chronic (>1 week)
- +/− Ipsilateral Horner's syndrome (T1-T3)
- +/− Ipsilateral cutaneous trunci deficit (C8, T1)
- Paraspinal pain, resistance to cervical manipulation
- Axillary or inguinal pain
- Palpable axillary mass (uncommon)
- Paraparesis, hemiparesis, or tetraparesis if involvement of the spinal cord
- Evidence of external trauma

ETIOLOGY AND PATHOPHYSIOLOGY

- Lateralized or foraminal intervertebral disk extrusion
- Neoplasia (peripheral nerve sheath tumors, lymphoma, primary neural tumors, metastatic)
- Trauma
- Degenerative lumbosacral stenosis
- Discospondylitis

- Summary: clinical signs result from a sensory disturbance within the dorsal root or spinal nerve, typically by compression.
- The spinal cord may be affected in all cases, causing long tract signs (e.g., gait deficit distal to the lesion).
- The dorsal longitudinal ligament of the vertebral column is thicker in the cervical region, predisposing animals to lateral disk extrusions at this site.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Nerve root signature is a clinical diagnosis made by distinguishing lameness due to neurogenic pain from orthopedic lameness. Paravertebral pain, muscle atrophy, and neurologic deficits and a normal orthopedic exam are all helpful in identifying nerve root signature.

DIFFERENTIAL DIAGNOSIS

- Orthopedic disorders
- Soft-tissue injury

INITIAL DATABASE

- Complete neurologic (see p. 1311) and orthopedic (see p. 1315) examinations
- Vertebral radiographs: rule out orthopedic causes, bony neoplasia, chronic diskospondylitis; may support a diagnosis of IVDD, degenerative lumbosacral stenosis, or nerve sheath neoplasm (enlarged intervertebral foramen).
- Many animals have orthopedic disease unrelated to the clinical signs.

ADVANCED OR CONFIRMATORY TESTING

- MRI is far superior to all other imaging modalities for ruling out nerve sheath neoplasia and neuritis.
- Myelography and epidurography: useful for IVDD, degenerative lumbosacral stenosis, nerve sheath neoplasm
- CT (see p. 1233) and MRI (see p. 1302): permit evaluation of the nerve roots, location of extruded disk material.
- Electromyography (EMG see online chapter: Electromyography and Nerve Conduction Velocity): changes are present 1 week following denervation of muscle.
- Cerebrospinal fluid (CSF) analysis (see p. 1228)
- Biopsy: allows definitive diagnosis of confirmed mass lesions; benefit must be weighed against risk of procedure.
- Surgical exploration

TREATMENT

TREATMENT OVERVIEW

- Removal of the source of nerve root or spinal nerve impingement
- Provision of the optimal environment for nerve recovery

ACUTE GENERAL TREATMENT

Dependent on underlying cause:

- Surgical decompression for IVDD, degenerative lumbosacral stenosis
- Tumor resection with or without limb amputation and laminectomy for peripheral nerve sheath neoplasm; surgical intervention should be considered early in these cases (reduce extension of tumor/spinal cord involvement).
- Conservative therapy: generally ineffective in relieving pain of cervical IVDD

CHRONIC TREATMENT

- Attempt conservative therapy (protection of the distal limb with a boot, physiotherapy) for traumatic injuries. Amputation should be delayed for 6 months if possible to allow for reinnervation.
- Radiation therapy: nerve sheath tumors
- Lifelong exercise modification: IVDD
- Physiotherapy: if trauma has compromised limb use

POSSIBLE COMPLICATIONS

- Persistent or progressive clinical signs
- Recurrence or acute progression of clinical signs (IVDD)
- Self-mutilation associated with dysesthesia
- Distal limb trauma associated with decreased sensation and normal activity
- Surgical complications

RECOMMENDED MONITORING

Follow-up exam and serial diagnostic studies as directed by the animal's clinical progression

PROGNOSIS AND OUTCOME 

Dependent on underlying cause:

- Good to excellent (according to clinical signs) with IVDD treated with decompression
- Fair to good (according to clinical signs) with degenerative lumbosacral stenosis
- Guarded to fair with traumatic injury
- Poor with nerve sheath neoplasia

PEARLS & CONSIDERATIONS 

COMMENTS

- It can be difficult to distinguish orthopedic from neurologic causes for clinical signs, and both may be present with traumatic injury. Careful examination with particular attention to muscle tone and sensory deficits is important.
- A ruptured cranial cruciate ligament is often mistaken for a lumbar nerve root signature and vice versa.
- Nerve sheath neoplasms are most common in the cervical intumescence (80%).

CLIENT EDUCATION

Monitor for recurrence of clinical signs

SUGGESTED READING

McDonnell J: Neurologic conditions causing lameness in companion animals. Vet Clin North Am Small Anim Pract31120011738

AUTHOR: GREGKILBURN

EDITOR: ETIENNECÔTÉ

Rocky Mountain Spotted Fever

BASIC INFORMATION

DEFINITION

An acute, potentially life-threatening tickborne rickettsial disease affecting dogs and people

EPIDEMIOLOGY

SPECIES, AGE, SEX

- **Species:** dogs and people are primarily affected. Seropositive cats are not clinically ill.
- **Age:** young dogs (<2 years) are at greater risk.

GENETICS & BREED PREDISPOSITION: Dogs: purebred dogs, especially German shepherds, may be predisposed.

RISK FACTORS: Tick exposure

CONTAGION & ZOONOSIS: Direct transmission does not occur from dogs to people. Dogs are short-term reservoirs and sentinels.

GEOGRAPHY AND SEASONALITY: Rocky Mountain spotted fever (RMSF) is found in North, Central, and South America. The majority of cases in the United States occur in the Southeast; disease occurrence is highest from March to October.

ASSOCIATED CONDITIONS & DISORDERS: Coinfection with other tickborne diseases such as ehrlichiosis can occur.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Clinical and subclinical illnesses have been reported.
- Clinical disease can be systemic or more localized to various systems (dermatologic, neurologic, ocular).

HISTORY, CHIEF COMPLAINT

- Incubation is 2-14 days after tick exposure. There is no carrier state.
- Initial signs are usually vague.
- Depression, anorexia, musculoskeletal pain, and vomiting are often noted.
- Varied presentations: epistaxis, head tilt, limb/scrotal edema, stiff gait

PHYSICAL EXAM FINDINGS

- Fever: commonly seen within 2-3 days of exposure
- Pain (arthralgia/myalgia, abdominal pain)
- Dyspnea/cough (interstitial pneumonitis)
- Cutaneous lesions: petechial/ecchymotic hemorrhages (especially on mucous membranes), edema, hyperemia, vesicles, and macules are all possible.
- Ocular (uveitis/chorioretinitis) and/or neurologic abnormalities (e.g., head tilt)
- Splenomegaly, lymphadenomegaly

ETIOLOGY AND PATHOPHYSIOLOGY

- *Rickettsia rickettsii* is an obligate intracellular parasite. Ticks become infected by horizontal transmission, transtadially, or by transovarial passage.
- Vectors: *Dermacentor variabilis* (American dog tick; eastern United States), *D. andersoni* (wood tick; western United States), *Rhipicephalus sanguineas* (brown dog tick; Arizona/California), and *Amblyomma americanum* (lone star tick; North Carolina).
- Transmission to the host requires at least 5-20 hours of tick attachment.
- Vasculitis, local necrosis, thrombosis, and plasma loss occur.
- Thrombocytopenia is due to consumption (vasculitis ± disseminated intravascular coagulation [DIC]), antiplatelet antibodies,

and/or whole blood loss.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Seasonal occurrence, clinicopathologic changes, and response to therapy suggest the diagnosis. Clinical suspicion justifies treatment while confirmation is pending, since a fulminant course may occur in some individuals. Serologic titers are confirmatory 1-3 weeks later.

DIFFERENTIAL DIAGNOSIS

- Acute ehrlichiosis/anaplasmosis (CBC, oculoneural signs, lameness, proteinuria)
- Babesiosis (CBC, neurologic signs, proteinuria)
- Borreliosis (lameness, proteinuria)
- Leptospirosis (CBC; gastrointestinal, renal, ocular, hepatic changes)
- Immune-mediated diseases (e.g., immune-mediated thrombocytopenia, polyarthropathy, glomerulonephritis)
- Canine distemper (ocular, neurologic, respiratory, GI signs)
- Bacterial diskospondylitis, intervertebral disc disease (stiff painful gait)
- Pneumonia (cough/dyspnea)
- Acute renal failure (acute glomerulonephritis and shock)
- Pancreatitis, enterocolitis (vomiting/diarrhea ± hemorrhage)
- Vestibular disease, acute meningoencephalitis (neurologic signs)

INITIAL DATABASE

- CBC: thrombocytopenia most common; leukopenia or leukocytosis (left shift possible, toxic changes); mild to severe anemia
- Serum biochemistry profile: hypoalbuminemia, azotemia, low Na/Cl/K/Ca, increased liver enzymes
- Fluid analysis (joint or cerebrospinal fluid if affected): mild increase in protein and cells, initially neutrophils, then monocytes
- Proteinuria due to vasculitis/glomerulonephritis

ADVANCED OR CONFIRMATORY TESTING

- IFA documentation of fourfold or greater increase between acute/convalescent titers or an acute titer of 1:1024 or greater is confirmatory.
- Latex agglutination (LA) titer of 1:32 is confirmatory.
- Cross-reactivity with nonpathogenic rickettsial organisms may occur. Some “nonpathogenic” rickettsiae may be pathogenic after all, but not all cross-react with RMSF.
- Direct FA testing for antigen (skin/tissue samples)
- PCR testing (blood/tissue) for RMSF and other rickettsiae

TREATMENT

TREATMENT OVERVIEW

Early recognition and prompt institution of appropriate antimicrobial therapy are associated with a good response to treatment and excellent prognosis. Delayed therapy is associated with complications including renal disease, neurologic disease, vasculitis, and coagulopathies and carries a more guarded prognosis.

ACUTE GENERAL TREATMENT

- Doxycycline, 5-10 mg/kg PO, IV q 12 h for 14-21 days; or tetracycline, 22 mg/kg PO, IV q 8 h for 14-21 days); *or*
- Enrofloxacin, 5-10 mg/kg PO, slow IV, IM q 12 h for 14 days; *or*
- Chloramphenicol, 15-30 mg/kg PO, SQ, IV, IM q 8 h for 14 days
- Prednisolone (1-4 mg/kg PO q 24 h) does not potentiate severity in experimental infections and may minimize immune-mediated complications.
- Fluid and supportive therapies to improve perfusion; caution to avoid exacerbating tissue edema

POSSIBLE COMPLICATIONS

Long-term sequelae may include chronic kidney disease due to loss of renal reserve, or scarring from thrombosis and aeral gangrenous necrosis of digits, nasal planum, and other sites.

RECOMMENDED MONITORING

- Cases are often seronegative acutely; repeated serologic testing at least 1 week after initial onset confirms seroconversion or fourfold rise in acute/convalescent titers. Early antibiotics may blunt rise.
- Monitor platelet and coagulation parameters for signs of severe coagulopathy, including DIC.
- Titers decrease after 4-5 months.

PROGNOSIS AND OUTCOME

- With early diagnosis, prognosis is usually excellent.
- Delayed diagnosis, fulminant disease, and the use of ineffective antibiotics (penicillins, cephalosporins, etc.) increase mortality.

PEARLS & CONSIDERATIONS

PREVENTION

- Owners should limit pet's outdoor roaming, especially in wooded areas.
- Adequate tick control is ideal.
- Lifelong immunity may follow treated disease.

CLIENT EDUCATION

- RMSF in dogs is a warning to owners that ticks in their area carry RMSF (dogs and people may be exposed).
- Ticks removed from pets must not be crushed by unprotected fingers, lest owners' cuticles be exposed to infective tick hemolymph/feces.

SUGGESTED READING

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EDITOR: DOUGLASS K.MACINTIRE

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Right Bundle Branch Block

BASIC INFORMATION

DEFINITION

An intracardiac conduction disturbance involving failure of normal (rapid) conduction from the bundle of His through the right bundle branch to the Purkinje fibers in the right ventricle. The result is a wide, bizarre-appearing QRS complex on the electrocardiogram (ECG). Right bundle branch block (RBBB) has no clinically meaningful hemodynamic effect on patients and is often a variant of normal. Its main clinical importance lies in the fact that it must not be misinterpreted as a ventricular arrhythmia.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs of any age and either sex; less common in cats

GENETICS & BREED PREDISPOSITION: Incomplete RBBB has been recognized in a family of beagles in association with congenital right ventricular structural disease.

ASSOCIATED CONDITIONS & DISORDERS: RBBB often occurs in normal animals; however, it may be associated with underlying structural heart diseases such as:

- Cardiomyopathy
- Congenital heart disease
- Heartworm disease

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

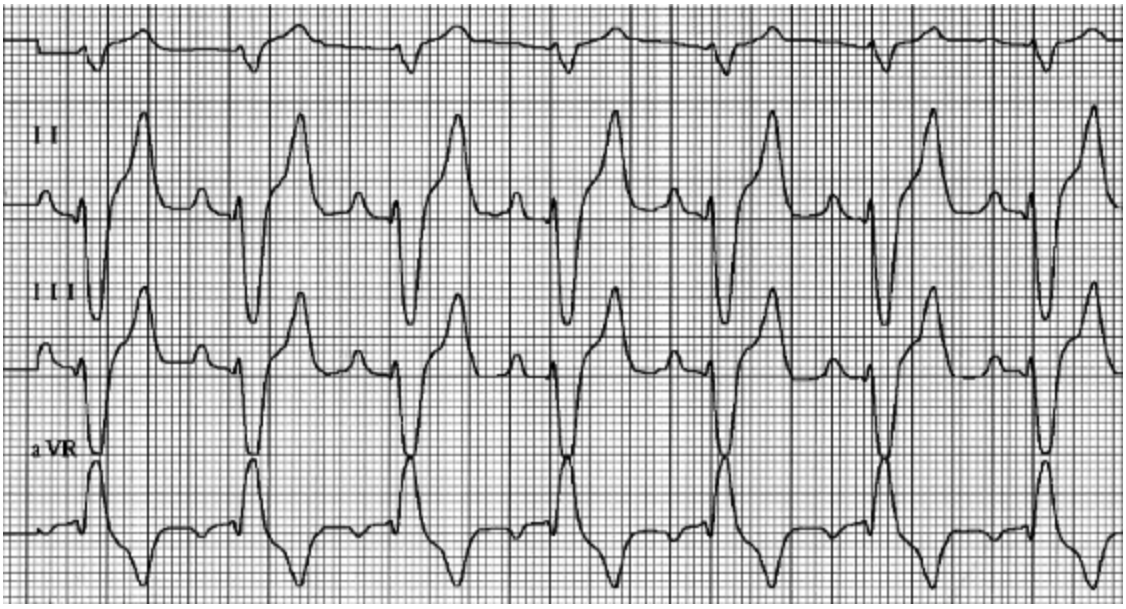
- Incomplete or complete RBBB depending on where the block occurs in the right bundle branch
- Intermittent bundle branch block (left bundle branch block [LBBB] or RBBB) may occur that is heart rate dependent.

HISTORY, CHIEF COMPLAINT: RBBB is an electrocardiogram (ECG) phenomenon only; no overt physical manifestations are expected from RBBB itself.

PHYSICAL EXAM FINDINGS: Typically RBBB is clinically silent, and no clinical signs are observed. However, in some individuals, split heart sounds may be present owing to prolonged right ventricular ejection time and delayed closure of the tricuspid (splitting of the first heart sound) and pulmonic (splitting of the second heart sound) valves. A split second heart sound is most common.

ETIOLOGY AND PATHOPHYSIOLOGY

- With RBBB, impulse formation in the sinoatrial node, atrial depolarization, and passage of the impulse through the AV node all can occur normally, but distribution of the impulse through the Purkinje fibers in the right ventricle is blocked.
- Conduction to the right ventricle still occurs but is very slow because it must travel from muscle cell to muscle cell.
- This results in a marked delay in conduction to the right ventricle, and the QRS complex becomes wide and bizarre on the ECG.
- Additionally, this slow conduction toward the right results in a right axis deviation on the surface ECG.



RIGHT BUNDLE BRANCH BLOCK Four-lead ECG (I, II, III, aVR) showing RBBB. Every QRS complex is preceded by a P wave at a repeatable interval, indicating normal conduction from the atria through the AV node to the ventricles. Rhythm is regular (R-R interval is constant), and heart rate is 150 beats/min. QRS complexes are wide and bizarre. ECG diagnosis is normal sinus rhythm with RBBB. (50 mm/sec, 1 cm = 1 mV.)

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is purely electrocardiographic: it is suspected when QRS duration is longer than normal, S waves are present in leads I, II, II, aVF, and the left precordial leads, and the rhythm appears to be supraventricular in origin.

DIFFERENTIAL DIAGNOSIS

- Right ventricular hypertrophy
- Ventricular ectopy
- Ventricular escape rhythm
- Motion artifact

INITIAL DATABASE

By definition, RBBB is an electrocardiographic diagnosis.

- Electrocardiogram characteristics of complete RBBB (see figure):
  - Prolonged QRS complex duration (canine: > 0.07 second; feline: > 0.06 second)
  - Wide and negative QRS complexes with an S wave in leads I, II, III, aVF, and left precordial leads (CV6LL [V2] and CV6LU [V4])
  - Positive QRS complexes in leads aVR, aVL, and CV5RL (V1 or rV2).
- Electrocardiogram characteristics of incomplete RBBB:
  - When the morphology of the QRS complex as described above is noted, but the QRS duration is normal or only slightly prolonged, incomplete RBBB is suspected. It can be very challenging to differentiate this finding from right ventricular hypertrophy, and assessment of the ventricle (e.g., echocardiographically) is usually required. If the ventricle is structurally normal, incomplete RBBB is diagnosed by exclusion.

ADVANCED OR CONFIRMATORY TESTING

- Thoracic radiographs to evaluate for right ventricular enlargement
- Echocardiogram to assess heart structure and function

TREATMENT

TREATMENT OVERVIEW

No specific treatment necessary for RBBB:

- RBBB does not result in clinical or hemodynamic sequelae by itself and therefore does not require treatment.
- The right bundle branch is anatomically vulnerable to injury, and therefore RBBB may be observed in otherwise normal dogs.

POSSIBLE COMPLICATIONS

- Misdiagnosis of RBBB as premature ventricular complexes (PVCs) or ventricular tachycardia can lead to treatment—and toxicosis—with antiarrhythmic drugs.
- Complete block of both the right and left bundle branches produces complete (third-degree) atrioventricular block (rare).

PROGNOSIS AND OUTCOME

RBBB is not a progressive or deleterious entity, so prognosis is good except when associated with structural heart disease, in which case prognosis is the same as that of the underlying disorder.

PEARLS & CONSIDERATIONS

COMMENTS

The bizarre QRS morphology seen with bundle branch block can be confused with ventricular ectopy:

- If P waves are present and the PR interval is consistent, the complex is likely coming from a supraventricular site (and the bizarre QRS morphology is due to BBB rather than ventricular ectopy). However, sometimes P waves are buried and not visible, although the rhythm is supraventricular in origin (particularly with tachycardias). Since most dogs have sinus arrhythmia and some degree of irregularity to the heart rhythm, the regularity of rhythm can be a helpful clue (see pp. 1024 and 1165).
- Supraventricular rhythms (such as sinus rhythm, sinus tachycardia, atrial fibrillation, etc.) respond to vagal maneuvers with slowing of the heart rate, even when RBBB is present. Ventricular arrhythmias do not.

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AUTHOR: MEGSLEEPER

EDITOR: ETIENNECÔTÉ

Rhinosporidiosis

BASIC INFORMATION

DEFINITION

A chronic granulomatous disease of humans and animals affecting mucosal surfaces, cutaneous and/or subcutaneous tissues; caused by infection with the microorganism *Rhinosporidium seeberi*. *Rhinosporidium* induces tumor-like growth of epithelial cells, manifesting as single or multiple rhinosporidial polyp-like masses (granulomas).

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Species: occurs sporadically in dogs, extremely rare in cats
- Sex: male dogs > female dogs; male predominance is also evident in humans.
- Age range in dogs: 1.5-13 years (mean 5 years)

GENETICS & BREED PREDISPOSITION: Large-breed dogs most commonly affected

RISK FACTORS

- Wet environment
- Contact with stagnant water
- Nasal mucosal trauma

CONTAGION & ZOONOSIS

- Not contagious; no animal-animal or animal-human transmission reported; humans and animals may become infected from a common environmental source.
- Rhinosporidiosis is primarily a human disease, but it has also been documented in dogs, cats, cattle, horses, mules, goats, buffalo, ducks, swans, and other waterfowl.

GEOGRAPHY AND SEASONALITY: Occurs sporadically in the United States (usually the Southeast) and in other countries (Europe, Africa, Canada); endemic in India and Sri Lanka (over 80% of human cases)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: In people, the disease usually involves nasal and pharyngeal (85% of cases) and/or conjunctival (9% of cases) mucosa, but rarely, cutaneous, subcutaneous, tracheal, genitourinary, and osseous involvement may occur. Disseminated disease with pulmonary involvement has been documented. In dogs and cats, only nasal disease has been reported.

HISTORY, CHIEF COMPLAINT: Presenting complaints are those of nasal disease, including stertor, sneezing, nasal discharge, or epistaxis.

PHYSICAL EXAM FINDINGS

- Nasal discharge
- Epistaxis common
- Nasal polyps are sometimes visible:
    - Fleshy mass evident in the nostril; often ulcerated
    - Rhinosporidial polyp or mass characteristically has miliary, white pinpoint granules (<0.5 mm diameter) visible on surface; these are sporangia (maturing bodies of the organism).

ETIOLOGY AND PATHOPHYSIOLOGY

- This organism was previously classified as a fungus but is presently classified in the protistan class, Mesomycetozoea, at the animal-fungal divergence in the phylogenetic tree.
- Transmission and pathogenesis of rhinosporidiosis largely unknown.

- Infection presumed to occur when spores reach traumatized nasal mucosa. Infection is often associated with contact with stagnant water, but the ocular form predominates in humans living in arid countries, potentially because dust serves as the fomite for inoculation of the organism.
- Once the spore reaches mucosal tissue (usually nose or conjunctiva), it proliferates in epithelial tissue to form sporangia, which can be seen grossly on the polyp surface.
- The organism triggers proliferation of epithelial tissue and a mixed (usually granulomatous) inflammatory response.
- Clinical signs result from obstruction by the proliferative tissue, associated inflammation, and increased nasal secretions and/or ulceration and bleeding from the mass.
- The infection remains localized to the site of inoculation except in rare human cases where dissemination occurs. Autoinoculation (transfer from an initial lesion to a new site by the fingers) is suspected to occur in people and result in multiple lesions.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Rhinosporidium is an uncommon to rare cause of obstructive nasal disease and epistaxis in dogs and cats. In animals with clinical signs, rhinosporidial masses may be characteristically evident at the nares, providing an obvious source of tissue for diagnostic testing.

DIFFERENTIAL DIAGNOSIS

- Nasal tumor
- Nasal foreign body/granuloma
- Nasopharyngeal polyp (cats)
- Other causes of chronic rhinitis: fungal (e.g., aspergillosis, cryptococcosis), lymphoplasmacytic, parasitic (*Pneumonyssoides, Cuterebra*), viral (cats)

INITIAL DATABASE

- Cytologic examination of nasal exudates or of impression smears or fine-needle aspirate samples from nasal masses
  - Granulomatous inflammation (lymphocytes, plasma cells, macrophages) and sporangia (round, thick-walled, 2-8 micron diameter)
  - Important cytologic differential is coccidioidomycosis (sporangium of *R. seeberi* is larger, has thicker walls and larger, more numerous endospores than spherules of *Coccidioides*)
- Nasal imaging: skull radiographs or CT

ADVANCED OR CONFIRMATORY TESTING

Rhinoscopy or rhinotomy

- Nasal biopsy: for definitive diagnosis if cytologic evaluation inconclusive:
  - Diagnosis confirmed by finding sporangia containing endospores; readily identified in affected tissues

TREATMENT

TREATMENT OVERVIEW

Treatment goals are to alleviate nasal obstruction and other clinical signs and to eliminate infective organisms. Most cases are treated by surgical excision alone.

ACUTE GENERAL TREATMENT

- Surgical excision of rhinosporidial masses, preferably by electrocautery, is the treatment of choice, but recurrence is common.
- Drug therapy postoperatively to prevent recurrence or for medical treatment if surgery is not an option is of questionable efficacy:
  - Dapsone is the only drug that has shown some antirhinosporidial effect:
    - Arrests maturation of sporangia, promotes stromal fibrosis
    - Has been used to prevent polyp recurrence after initial surgical excision
    - 1 mg/kg PO q 8 h for 2 weeks, then q 12 h for 4 months

        - Toxicity (see below) may limit use.
    - Ketoconazole; anecdotal efficacy as sole treatment or in preventing recurrence:
        - 8.7 mg/kg PO with food q 8 h for 21 days
- Topical antiseptics (10% povidone-iodine, 1% silver nitrate, 2% chlorhexidine) have been recommended for treatment of the base of the polyp or mass immediately following surgical excision and for disinfection of surgical equipment.
- Inability to establish experimental infection or to culture *Rhinosporidium* in vitro limits ability to study pathogenesis or test efficacy of antimicrobial and antiseptic agents.

CHRONIC TREATMENT

Repeated surgical excision or protracted/repeated medical treatment may be necessary.

DRUG INTERACTIONS

Dapsone and ketoconazole may alter metabolism of drugs that undergo hepatic biotransformation.

POSSIBLE COMPLICATIONS

- Recurrence of rhinosporidial masses (2-12 months after surgery) is the most common complication.
- Dapsone may cause aplastic anemia, agranulocytosis, cutaneous drug eruption, acute gastrointestinal (GI) signs, and hepatic necrosis.
- Ketoconazole may cause hepatic necrosis and GI signs.

RECOMMENDED MONITORING

- Monitor for recurrence of nasal signs.
- With medical treatment, a CBC and serum biochemistry profile (dapsone) or liver enzymes and bilirubin (ketoconazole) should be monitored every 2-4 weeks.

PROGNOSIS AND OUTCOME

Surgery may be curative, especially for a single polyp. However, recurrence is common, especially with broad-based masses or multiple polyps.

PEARLS & CONSIDERATIONS

COMMENTS

- Not contagious
- Most cases are treated by surgical excision alone; radical excision may be necessary.
- Medical management, while reported, is of questionable efficacy.

PREVENTION

No specific prevention is available.

SUGGESTED READING

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Rhinitis, Lymphoplasmacytic

BASIC INFORMATION

DEFINITION

Chronic, gradually progressive inflammatory nasal disease of unknown etiology characterized by infiltration of the nasal mucosa with lymphocytes and plasma cells. The disorder is recognized with increasing frequency in dogs.

SYNONYMS

Chronic idiopathic rhinitis/rhinosinusitis, chronic inflammatory rhinitis, immune-mediated rhinitis

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs: any age, although young adult to middle-aged dogs of either sex are considered at risk.
- Cats: young adult to middle-aged cats of either sex

GENETICS & BREED PREDISPOSITION: The disease is seen primarily in large-breed dogs, although dachshunds may be predisposed.

RISK FACTORS

- Diseases causing chronic inflammation with epithelial erosion, turbinate lysis, and remodeling, such as long-standing or recurrent infections (e.g., foreign body, aspergillosis), can provoke lymphoplasmacytic nasal infiltrates.
- The idiopathic disease is not associated with an identifiable underlying cause of inflammation.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: The disease is chronic, sometimes with very mild signs initially, followed by moderate to severe signs.

HISTORY, CHIEF COMPLAINT

- Nasal discharge
- Sneezing
- Stridor
- Reverse sneezing
- Ocular discharge and rubbing at the nose (occasionally)

PHYSICAL EXAM FINDINGS

- Unilateral or bilateral serous, mucoid, or bloody nasal discharge
- Decreased air passage through one or both nares
- Submandibular lymph node enlargement
- General condition is normal

ETIOLOGY AND PATHOPHYSIOLOGY

- Poorly defined, but hypothesized to be either a chronic inflammatory response to an inhaled irritant, pollutant, or allergen or an immune-mediated process
- The local tissue immune response mounted is clearly distinct from that of sinonasal aspergillosis, therefore the disease is not due to undiagnosed sinonasal aspergillosis.
- Chronic inflammation causes loss of epithelium and squamous metaplasia, reduced population of ciliated cells, hyperplasia of subepithelial glands, increased amount of viscid mucus, and impaired ciliary clearance.
- Retention of mucus plugs, inhaled bacteria, and irritable particles maintain and aggravate inflammation.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Lymphoplasmacytic infiltration of nasal mucosa can be observed as a sequela to many chronic nasal diseases, and must be differentiated from the "idiopathic" condition by exclusion of other causes of rhinitis.

DIFFERENTIAL DIAGNOSIS

Other causes of nasal discharge (see p. 746):

- Dogs:
  - Fungal rhinitis
  - Nasal neoplasia
  - Dental disease
  - Foreign bodies
  - Nasal mites
  - Ciliary dyskinesia
- Cats:
  - Chronic viral upper respiratory tract infection
  - Nasopharyngeal polyps
  - Nasopharyngeal stenosis
  - Others as for dogs

INITIAL DATABASE

- Plain radiographs of the nasal cavities, sinuses, and dental roots can help eliminate other structural disorders such as neoplasia, fungal rhinitis, and dental disease but cannot confirm the diagnosis.
- Bacterial cultures can be positive or negative; positive cultures rarely reflect a primary role of bacteria in pathogenesis.
- Results of CBC, biochemistry panel, and urinalysis are usually normal.

ADVANCED OR CONFIRMATORY TESTING

- CT (see p. 1233) and/or MRI (see p. 1302) of the nasal cavities and sinuses can help identify differentials, such as neoplasia, fungal rhinitis, and dental disease, with more accuracy than plain radiographs but cannot confirm the diagnosis.
- Rhinoscopy (see p. 1335) findings are variable and can include:
  - Copious thick mucus or mucopurulent discharge
  - Mucosal hyperemia
  - Proliferative or thickened nasal mucosa
  - Turbinate lysis or remodeling
  - Pseudopolypoid appearance of mucosa
  - Absence of other causes of nasal discharge (aspergillosis, foreign bodies, etc.)
- Histopathologic examination of nasal mucosal biopsies predominantly shows mild to severe lymphoplasmacytic infiltration.

TREATMENT

TREATMENT OVERVIEW

Treatment can be challenging, as there is no primary therapy that has proven consistently effective for all patients.

ACUTE GENERAL TREATMENT

- Antibiotics are of little benefit unless there is a secondary bacterial infection.
- Glucocorticoids at immunosuppressive dosages:
  - Prednisone 1-2 mg/kg PO q 12 h, then gradually tapered to lowest dose that controls clinical signs.
  - Topical (nasal spray, drops, or aerosols) administration of poorly absorbed glucocorticoids (such as fluticasone propionate) may be beneficial without provoking secondary effects of systemic glucocorticoid therapy.
  - Many dogs do not respond to glucocorticoid therapy.
- Other antiinflammatory agents such as piroxicam could potentially have some benefit, but efficacy has not been documented.
- In severe nonresponsive cases, consider additional oral immunosuppressive agents:

- Azathioprine (dogs: 1-2 mg/kg PO q 24 h for 10-14 days, then q 48 h), *or*
- Cyclosporine (3-5 mg/kg PO q 12 h; monitor serum concentrations)

- Mucolytic drugs:
  - *N*-acetylcysteine has a wide therapeutic range, with dosage usually 5-10 mg and up to 100 mg/kg PO q 12 h.
    - Intranasal or aerosol delivery of 5%-20% solution has also been described.
  - Bromhexine hydrochloride (0.5-1 mg/kg PO) or through aerosol delivery

CHRONIC TREATMENT

- Intranasal saline (drops or aerosol delivery)
- Mucolytics (as noted in previous paragraphs)
- Long-term oral glucocorticoids: give the lowest dose at the greatest interval needed to control clinical signs.

POSSIBLE COMPLICATIONS

- Secondary bacterial rhinitis
- Chronic sinusitis

RECOMMENDED MONITORING

Identify and treat episodes of secondary bacterial rhinitis accordingly.

PROGNOSIS AND OUTCOME

- Although clinical signs may appear distressing to owners, and some cases remain refractory to any treatment, the disease is rarely life threatening.
- In the worst cases, maintenance therapy is generally successful in keeping clinical signs mild.
- Treatment must be sustained, since relapses frequently occur.
  - A cure is uncommonly obtained; persistence of mild to moderate clinical signs despite treatment is common.
- Owners should prevent their pets' exposure to potential exacerbating factors (e.g., cigarette smoke, perfumes).

PEARLS & CONSIDERATIONS

COMMENTS

- Definitive diagnosis is established by elimination of other potential causes of chronic lymphoplasmacytic infiltration of the nasal mucosa, such as chronic aspergillosis, chronic or recurrent infection due to dental disease, primary ciliary dyskinesia, or intranasal neoplasia.
- The disease is chronic and progressive, and cure is rarely achieved.
- There is no therapeutic gold standard.

TECHNICIAN TIPS

While of low diagnostic yield, Cytologie examination of nasal exúdate can occasionally identify another underlying cause (e.g., cryptococcosis, rarely nasal neoplasia) of nasal cavity disease.

CLIENT EDUCATION

- Treatment must be sustained, since relapses are common.
- Complete cure is rare, but a normal quality of life is expected in most cases.
- Persistence of some degree of clinical signs is expected despite treatment.
- Potential exacerbating factors should be avoided.

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AUTHOR: CÉCILECLERCX

EDITOR: RANCE K.SELLON

Rhinitis, Bacterial

BASIC INFORMATION

DEFINITION

Inflammation of one or both nasal cavities associated with a bacterial infection that is often secondary to a primary nasal disease

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Rhinitis is possible in dogs and cats of all ages and breeds depending on underlying cause.
- Puppies may develop bacterial rhinitis as a result of congenital abnormalities or immune deficiencies.
- Viral upper respiratory tract infections can lead to rhinitis in cats.
- Kittens are at risk for viral upper airway diseases that predispose to bacterial rhinitis.

GENETICS & BREED PREDISPOSITION: Predisposition reflects susceptibility to primary disease processes:

- Toy breeds are more susceptible to rhinitis associated with dental root infections.
- Dolichocephalic breeds of dogs are at risk for acquiring nasal aspergillosis and neoplasia.

RISK FACTORS: Bacterial rhinitis is most often secondary to a primary nasal disease:

- In dogs, primary disorders include:
  - Foreign body (especially active hunting dogs; plant material as foreign body)
  - Dental root infection
  - Congenital/inherited abnormalities such as primary ciliary dyskinesia and soft palate defects, choanal atresia/stenosis
  - Lymphoplasmacytic rhinitis
  - Fungal rhinitis (aspergillosis)
  - Neoplasia
  - Fracture or osteomyelitis of conchae or facial bones from trauma
- In cats, primary diseases include:
  - Viral or *Mycoplasma* infection (most common)
  - Nasopharyngeal polyps
  - Choanal atresia/stenosis
  - Neoplasia (carcinomas, lymphosarcoma)
  - Fungal rhinitis (cryptococcosis, less commonly aspergillosis)

CONTAGION & ZOONOSIS: Kittens in multiple-cat environments have increased risk of viral infections.

ASSOCIATED CONDITIONS & DISORDERS: Epistaxis and stridor

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Acute or recurrent, depending on primary cause

HISTORY, CHIEF COMPLAINT

- Sneezing
- Nasal discharge
- Sometimes unilateral or bilateral epistaxis
- Head shaking, pawing the nose, snorting (nasal foreign body)
- Halitosis, inappetence (dental disease)

PHYSICAL EXAM FINDINGS

- Unilateral or bilateral mucopurulent nasal discharge
- Decreased (most commonly) or increased air passage through nares

- Enlarged submandibular lymph node(s)
- Evidence of systemic disease is uncommon
- Other signs are possible depending on primary disease

ETIOLOGY AND PATHOPHYSIOLOGY

Nasal turbinates (acting as powerful filters) and mucociliary clearance in the distal third of the nasal cavities are excellent defense mechanisms against infection. Secondary or recurrent bacterial infections develop when a primary nasal disease has impaired these defense mechanisms.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

There are many causes of mucopurulent nasal discharge (see Risk Factors above).

INITIAL DATABASE

- Oral and dental examinations (see p. 1295) to exclude dental disease, palatal and choanal defects
- Plain radiographs of the nasal cavities, sinuses, and dental roots (under general anesthesia) to identify an inciting cause
- Bacteriologic cultures are rarely useful, because the organisms identified are commonly present in normal individuals, and it is the predisposing nasal disease that must be identified and managed.
- Results of CBC, serum biochemistry profile, and urinalysis are often normal.

ADVANCED OR CONFIRMATORY TESTING

Advanced testing is recommended to rule out primary nasal cavity diseases:

- Rhinoscopy (direct and retrograde) (see p. 1335)
- Cytologic or histologic evaluation of nasal mucosal samples
- CT or MRI is superior to standard radiography for imaging the nasal cavity.
- Viral culture or PCR tests for viral infections of cats
- PCR tests for *Mycoplasma/bacterial* infections of cats
- Electron microscopy (primary ciliary dyskinesia)

TREATMENT

TREATMENT OVERVIEW

The key to long-term resolution of bacterial rhinitis in most patients is identification and treatment, whenever possible, of an underlying primary nasal disease.

ACUTE GENERAL TREATMENT

- Broad-spectrum antibiotics: per os, intranasal, or aerosol delivery as appropriate for the animal for short periods of time (1 week is sufficient in most cases). For example, administer amoxicillin, 20 mg/kg PO q 8 h; cefadroxil, 20 mg/kg PO q 8 h; or amoxicillin-clavulanate, 15 mg/kg PO q 12 h.
- Antibiotics need not be selected on the basis of Gram stain or culture and sensitivity (C&S) testing, except in recurrent cases.
- In cats with upper airway disease, amoxicillin, azithromycin, doxycycline, and quinolones have been shown effective.

CHRONIC TREATMENT

- Intranasal administration of sterile physiologic solution several times a day
- Mucolytics:
  - *N*-acetylcysteine has a wide therapeutic range, with dosage usually 5-10 mg/kg and up to 100 mg/kg PO q 12 h.
    - Intranasal or aerosol delivery of 5%-20% solution has also been described.
  - Bromhexine hydrochloride (0.5-1 mg/kg PO) or through aerosol delivery
- Contraindicated treatments: reduction of inflammation with short-acting corticosteroids and attempts to provide relief with decongestants are not indicated.

POSSIBLE COMPLICATIONS

Inflammation and injury to the ciliated nasal epithelium can decrease mucociliary clearance in the distal third of the nasal cavity and cause turbinate lysis or remodeling (especially in young kittens with severe viral infections or dogs with nasal aspergillosis). This will in turn cause mucus to accumulate and further promote bacterial infection.

RECOMMENDED MONITORING

Clinical signs of the condition

PROGNOSIS AND OUTCOME

Prognosis varies depending on the primary cause.

PEARLS & CONSIDERATIONS

COMMENTS

- Most animals with bacterial rhinitis have another primary nasal cavity disease; therefore, failure to achieve a prompt and sustained response to empirical therapy (or spontaneous resolution) should provoke recommendations for advanced testing.
- Obtaining a diagnosis and implementing specific treatment lessen the likelihood of chronic and irreversible epithelial and turbinate lesions that could otherwise predispose the animal to bacterial rhinitis.

TECHNICIAN TIPS

While usually of low diagnostic yield, cytologic examination of nasal exudate is inexpensive and in a few patients, will identify an underlying primary nasal cavity disease (e.g., cryptococcosis, occasionally nasal neoplasia).

CLIENT EDUCATION

Bacterial rhinitis secondary to a viral upper respiratory infection in cats can be difficult to control in the long term without daily medication administration for extended periods of time.

SUGGESTED READING

Hartmann AD, Helps CR, Lappin MR: Efficacy of pradofloxacin in cats with feline upper respiratory tract disease due to *Chlamydophila felts* or *Mycoplasma* infections. J Vet Intern Med2220084452

Meler E, Dunn M, Lecuyer M: A retrospective study of canine persistent nasal disease: 80 cases (1998-2003). Can Vet J4920087176

Ruch-Gallie RA, Veir JK, Spindel ME: Efficacy of amoxicillin and azithromycin for the empirical treatment of shelter cats with suspected bacterial upper respiratory infections. J Feline Med Surg102008542550

AUTHOR: CÉCILECLERCX

EDITOR: RANCE K.SELLON

Rheumatoid Arthritis

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

An uncommon, progressive, immune-mediated, inflammatory polyarthropathy characterized by erosion of articular cartilage

SYNONYMS

- Canine: immune-mediated erosive polyarthritis
- Greyhounds: erosive polyarthritis of greyhounds (PG)
- Feline: feline chronic progressive polyarthritis (FCPP)

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Rheumatoid arthritis (RA): variable: usually young to middle-aged animals
- PG: young greyhounds (3-30 months of age)
- FCPP: cats of any age can be affected: most are young adult males.

GENETICS & BREED PREDISPOSITION

- RA: small breeds commonly affected
- PG: breed specific
- FCPP: domestic short-haired cats, Persians, Siamese cats

ASSOCIATED CONDITIONS & DISORDERS: Dogs:

- Felty's syndrome: RA, splenomegaly, and neutropenia
- Sjögren's syndrome: nonerosive or erosive polyarthritis, keratoconjunctivitis sicca (KCS), xerostomia
- Occasional association of RA with amyloidosis

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Early:
  - Initially indistinguishable from idiopathic polyarthritis (see p. 894)
  - Acute single or multiple leg lameness with anorexia is possible.
  - PG and FCPP: onset often more insidious
- Later: chronic intermittent lameness: angular deformities secondary to ligamentous damage, mostly in the carpus, metacarpus, tarsus, and metatarsus

PHYSICAL EXAM FINDINGS

- Joint pain, soft-tissue swelling, reduced range of motion, joint crepitus; distal joints most severely affected
- Low-grade fever
- Mild generalized lymphadenopathy

ETIOLOGY AND PATHOPHYSIOLOGY

- Etiology unknown
- Synovitis arises from a type III (immune complex) hypersensitivity reaction. Synovial lymphocytes and plasma cells produce rheumatoid factors (RFs), immunoglobulin (Ig) M and IgA auto-antibodies directed against altered endogenous IgG.
- Immune complexes activate complement and attract neutrophils (accumulate in the joint fluid).
- Vascular granulation tissue (pannus) erodes the articular cartilage and destroys subchondral bone.
- Inflammation and damage to the joint capsule and collateral ligaments lead to joint instability and angular deformities.

- Electron microscopy has identified distemper viral particles in synovial macrophages.
- FCPP: unknown etiology; association with feline syncytium-forming virus.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A minimum database (CBC, serum biochemistry profile, urinalysis), radiographs of affected joints (erosive changes in all but the early stages), and synovial fluid sampling (cytologic analysis/culture) are indicated in all cases and help distinguish RA/PG/FCPP from other polyarthritides.

DIFFERENTIAL DIAGNOSIS

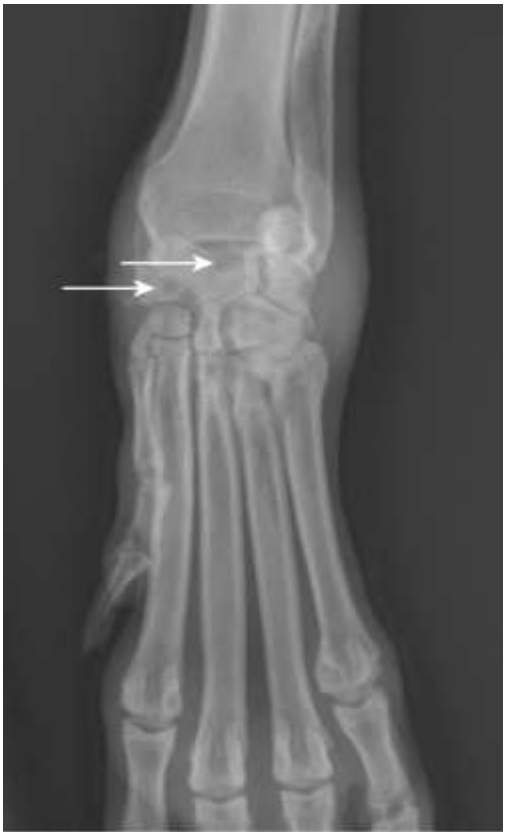
- Idiopathic nonerosive polyarthritis (see p. 894)
- Bacterial polyarthritis
- Systemic lupus erythematosus
- Reactive polyarthritis
- Neoplasia

INITIAL DATABASE

CBC, serum biochemistry profile, urinalysis: all typically normal; leukocytosis, neutrophilia, hyperglobulinemia, hyperfibrinogenemia, and proteinuria possible.

ADVANCED OR CONFIRMATORY TESTING

- Radiographs of affected joints indicated in all cases. Findings vary with duration of illness.
- Early stage: periarticular swelling; minimal bony changes
- Later: periarticular osteoporosis, subchondral lucencies (“erosive” changes), joint swelling
- Late stage: extensive bone destruction, joint space collapse, subluxations and luxations
- FCPP: marked periosteal new bone; focal erosions, especially hocks and carpi
- Arthrocentesis, synovial fluid analysis indicated in all cases: thin (nonviscous), cloudy, hypercellular (neutrophils predominate); culture negative; mucin clot test negative
- Rheumatoid factor (RF): lacks sensitivity/specificity; positive in 20%-70% of RA dogs; false positives with other inflammatory diseases; IgA RF more specific and more prevalent with severe erosive disease
- Synovial biopsy: proliferative synovitis with lymphocytes, plasma cells, and macrophages



RHEUMATOID ARTHRITIS Radiographic evidence of subchondral bony lysis of the carpal bones *(arrows)* in this dog with rheumatoid arthritis.

(Courtesy LeeAnn Pack, Atlantic Veterinary College, University of Prince Edward Island, Canada.)

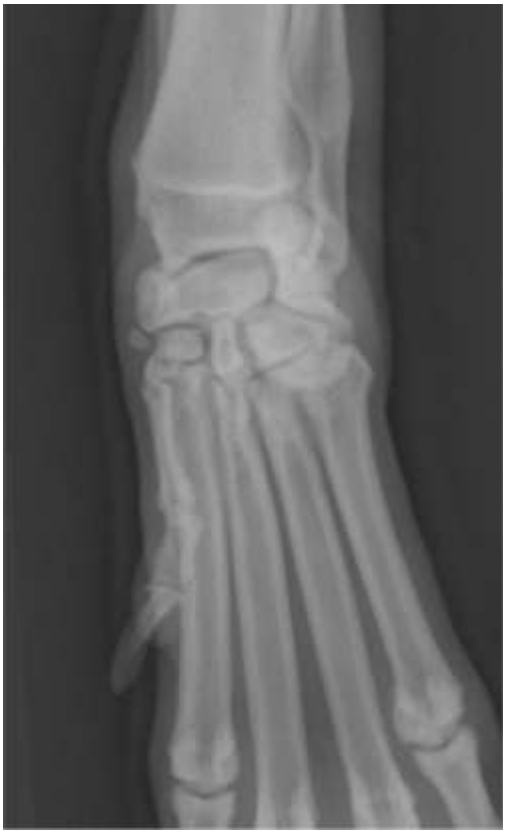
TREATMENT

TREATMENT OVERVIEW

A cure is not possible; clinical remission is the goal. Immunosuppressive drugs are the mainstay of treatment.

ACUTE GENERAL TREATMENT

- Nonsteroidal antiinflammatory drugs (NSAIDs) have not proven to be successful. The high doses required for human RA have intolerable gastrointestinal (GI) side effects in dogs.
- Glucocorticoids, in combination with azathioprine, cyclophosphamide, or gold salts, are preferable and often required for remission.
- Prednisone/prednisolone: 1-2 mg/kg PO q 12 h for 2-3 weeks. If lameness and synovial fluid inflammation subside, the dose is reduced gradually over 3-4 months to lowest dose that maintains remission.
- Azathioprine: 2 mg/kg PO q 48 h (dogs)
- Cyclophosphamide: 2 mg/kg PO q 24 h, 4 consecutive days weekly
- Chrysotherapy (gold salts): requires concurrent use of glucocorticoids; two options:
    - Sodium aurothiomalate:
        - 1 mg/kg IM once weekly for 10 weeks or until clinical remission
        - Give a small test dose first.
        - To maintain remission: 1 mg/kg IM q 30 days
    - Auranofin:
        - 0.05-2 mg/kg PO q 12 h (maximum 9 mg/d)
        - Diarrhea common
- FCPP: combination of glucocorticoids and cyclophosphamide may be of benefit in early stages. Gold salts are highly toxic in cats. Combination methotrexate and leflunomide shows promise and requires further study.
- PG: treatment with NSAIDs, glucocorticoids, or cytotoxic drugs has been unrewarding.



NORMAL CARPUS Normal carpus in a healthy dog for comparison.

(Courtesy LeeAnn Pack, Atlantic Veterinary College, University of Prince Edward Island, Canada.)

CHRONIC TREATMENT

- Taper prednisone/prednisolone to lowest dosage that maintains clinical remission (e.g., 1 mg/kg, q 48 h or lower). Continue cytotoxic drug barring adverse effects (e.g., myelosuppression).
- Evaluate the patient's synovial fluid monthly to guide dose reduction.
- Monitor CBC and platelet counts frequently to detect myelosuppression from cytotoxic drugs.

BEHAVIOR/EXERCISE

- Judicious exercise restriction, weight control

POSSIBLE COMPLICATIONS

- Long-term glucocorticoids: hyperadrenocorticism
- Cyclophosphamide: bone marrow suppression, cystitis
- Azathioprine: bone marrow suppression. Occasionally hepatotoxicity, pancreatitis. Avoid use in cats.
- Gold salts: fever, thrombocytopenia, leukopenia, dermatitis, glomerulonephritis, stomatitis
- Avoid administering cytotoxic drugs if the animal has concurrent infections.

RECOMMENDED MONITORING

- Physical exam and joint fluid analysis to assess remission
- CBCs to assess myelosuppression
- Liver panel to assess for hepatotoxicity (azathioprine)

PROGNOSIS AND OUTCOME

- Poor long-term prognosis
- Even with appropriate therapy, the condition of most patients deteriorates over time.

- Joint pain and instability may necessitate arthrodesis (questionable benefits in joints other than carpus).

PEARLS & CONSIDERATIONS

COMMENTS

- RF blood testing is not reliably accurate (positive in only 20%-70% of affected dogs; other factors can cause false-positive results); an accurate diagnosis of RA is multifactorial, involving physical exam, radiographs of affected joints, and arthrocentesis.
- RA may initially resemble idiopathic polyarthritis, but eventually joint destruction becomes apparent.

TECHNICIAN TIPS

- To increase odds of a positive culture (confirming bacterial synovitis rather than RA), it has been suggested to submit cultures in blood culture media.
- Pain associated with arthritis should not be mistaken for reluctance or other behavioral traits; these patients may be too painful to walk, may be more prone to aggression if handled, or both, and should be handled as gently as possible until clinical signs have improved.

CLIENT EDUCATION

Poor prognosis for cure; progressive disease that requires frequent rechecks

SUGGESTED READING

Hanna FY: Disease modifying treatment for feline rheumatoid arthritis. Vet Comp Orthop Traumatol1820059499

AUTHOR: LILIANCORNEJO

EDITOR: SUSAN M.COTTER

Rhabdomyosarcoma

BASIC INFORMATION

DEFINITION

A rare primary neoplasm of striated muscle

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Rare in dogs. When affected, dogs often are less than 18 months old, but some cases have been reported in older dogs.
- Rare in cats. There is one report of a rhabdomyosarcoma at an injection site in a cat.

GENETICS & BREED PREDISPOSITION: The young age at diagnosis and occasional presence of more than one tumor suggest a hereditary basis for the disease. However, the low incidence of these tumors makes it difficult to determine genetic or breed predispositions.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Botryoid rhabdomyosarcoma is a rare tumor usually found in the bladder of young, large-breed dogs.
- Other locations reported for rhabdomyosarcoma include the mouth or oropharynx, the tongue, larynx, heart (very rare), and peripheral skeletal muscle.

HISTORY, CHIEF COMPLAINT

- Presenting clinical signs depend on the location of the tumor.
- Dogs with oral and tongue tumors present for evaluation of signs related to an oral mass (halitosis, oral bleeding, discharge, visible mass).
- Dogs with laryngeal tumors may present for evaluation of dysphonia, dysphagia, inspiratory dyspnea, or respiratory distress.
- Tumors in the bladder cause signs attributable to a bladder mass (hematuria, pollakiuria, dysuria).

PHYSICAL EXAM FINDINGS: Physical exam findings vary depending on the location of the primary tumor and are reflected in the presenting complaints.

ETIOLOGY AND PATHOPHYSIOLOGY

- The cell of origin of these tumors is a myocyte in striated muscle.
- Lesions caused by rhabdomyosarcomas depend on the location of the primary tumor and the invasion into and destruction of surrounding normal structures.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Definitive diagnosis can only be confirmed via histopathologic examination. Identification of the primary tumor and subsequent biopsy may be challenging owing to the internal location of many rhabdomyosarcomas (heart, bladder, etc.). Diagnostic imaging can be helpful to identify the extent of the local tumor.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis depends on the location of the primary tumor:

- Bladder: transitional cell carcinoma, other bladder tumors

- Heart: hemangiosarcoma, aortic body tumors, other cardiac tumors
- Oral cavity: melanoma, squamous cell carcinoma, fibrosarcoma

INITIAL DATABASE

- Fine-needle aspirate Cytologie analysis may help identify the tumor type prior to other diagnostics.
- Three-view thoracic radiographs to rule out pulmonary metastases
- Abdominal ultrasound:
  - To rule out abdominal metastases
  - Abdominal ultrasonography and echocardiography generally are the diagnostic tests of choice for identifying masses in the bladder or heart, respectively

ADVANCED OR CONFIRMATORY TESTING

- CT or MRI may be necessary to delineate the local extent of the tumor in some locations (e.g., oropharynx, larynx) and to plan for surgery or radiation therapy.
- Diagnosis is based on histopathologic evaluation of biopsy samples. Special immunohistochemical stains may be necessary to differentiate rhabdomyosarcoma from other soft-tissue sarcomas, especially poorly differentiated tumors.
  - Bladder tumors often require cystotomy to obtain a suitable biopsy and attempt surgical excision. Botryoid ("resembling a cluster of grapes") rhabdomyosarcoma often has a gross appearance that is characteristically multilobulated.

TREATMENT

TREATMENT OVERVIEW

Definitive treatment is based on complete eradication of the primary tumor whenever possible. Palliative treatment options, such as palliative radiation, may help control pain or discomfort in patients with advanced tumors or in patients where definitive treatment cannot be tolerated.

ACUTE AND CHRONIC TREATMENT

- Treatment of the primary tumor usually involves aggressive surgical resection.
- Radiation therapy has not been extensively investigated for treatment of rhabdomyosarcoma. It may be indicated for tumors that cannot be removed with surgery alone. However, the response to radiation is not known.
- Chemotherapy may be indicated for rhabdomyosarcomas. Many cases develop metastases, and chemotherapy may be beneficial, although the response to chemotherapy is not known.
- Peripheral rhabdomyosarcomas arising from skeletal muscle should be approached like other peripheral soft-tissue sarcomas (see p. 1034).

POSSIBLE COMPLICATIONS

Complications of treatment for rhabdomyosarcomas depend on the types of treatments and the location of the primary tumor (see p. 1034).

RECOMMENDED MONITORING

Rhabdomyosarcomas may require more frequent monitoring for metastases (thoracic radiographs, abdominal ultrasound typically q 2-3 months) because of possible high metastatic rates.

PROGNOSIS AND OUTCOME

- Prognosis is guarded to grave for dogs with rhabdomyosarcoma of the bladder, heart, or oral cavity. Many dogs have masses that are not resectable, and metastases are common after treatment of the primary tumor.
- Surgical resection has been reported to result in a fair prognosis in a few cases. These include a dog with a perianal tumor treated with surgery, radiation, and chemotherapy that developed metastasis at 252 days and two dogs treated with laryngectomy and tracheostomy that lived 18 and 22 months after surgery; all three of these dogs developed metastasis.
- Prognosis for rhabdomyosarcoma arising from skeletal muscle is not known.

PEARLS & CONSIDERATIONS

COMMENTS

Young animals that are treated for tumors may be more likely to develop late complications of chemotherapy and radiation (second malignancies, bone necrosis, central nervous system necrosis, radiation-induced tumors). This should be taken into consideration when deciding about treatment for rhabdomyosarcoma in young dogs. However, the poor prognosis for many of these tumors makes late side effects less of a concern.

CLIENT EDUCATION

Clients should be educated to monitor their pets for masses or signs of tumor development, even in young dogs. Early detection may allow for more successful treatment of these tumors.

SUGGESTED READING

Liptak JM, Forrest LJ: Soft tissue sarcomas. Small animal clinical oncology, Philadelphia, 2007, WB Saunders, pp –. 425454

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Reverse Sneezing

BASIC INFORMATION

DEFINITION

A paroxysmal and noisy inspiratory effort localized to the nasopharynx, during which the owner commonly thinks the animal is suffocating; commonly encountered in dogs

SYNONYM

Mechanosensitive aspiration reflex

EPIDEMIOLOGY

SPECIES, AGE, SEX: Clinically, reverse sneezing is more commonly seen in dogs of any sex or age, depending on the underlying cause. Reverse sneezing can be experimentally induced in cats.

GENETICS & BREED PREDISPOSITION

- Idiopathic form: any breed of dog can be affected.
- Secondary to nasal mites: primarily large-breed dogs, potentially all types of dogs
- Secondary to nasal neoplasia: primarily dolichocephalic dogs

CONTAGION & ZOONOSIS: Nasal mite *(Pneumonyssoides caninum):* mode of transmission is not well established.

GEOGRAPHY AND SEASONALITY: Nasal mite: exists worldwide but is especially prevalent in the United States and northern European countries (Norway, Sweden, Finland).

ASSOCIATED CONDITIONS & DISORDERS: Reverse sneezing can be a normal occurrence in many dogs but can also be associated with nasal or nasopharyngeal disease (material coming from the nasal cavities, inflammation, abscess, foreign body, tumor, choanal atresia) and nasal mites.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Incidental episodes that do not require any treatment
- Repeated frequent episodes that are associated with other causes of nasal or nasopharyngeal disease

HISTORY, CHIEF COMPLAINT

- Incidental episodes of reverse sneezing are typically short in duration (a few seconds to 1 minute) and are generally self-limiting. Between episodes, the animal is generally normal.
- Frequent episodes of reverse sneezing may be a reflection of underlying disease and thus associated with signs of nasal/nasopharyngeal disease such as sneezing, nasal discharge, epistaxis, stertor, or others according to the etiology.

PHYSICAL EXAM FINDINGS: Incidental episodes of reverse sneezing: normal physical examination. Reverse sneezing associated with:

- Nasal/nasopharyngeal inflammation and bacterial infection of various origins:
  - Unilateral or bilateral serous to bloody discharge
  - Sneezing
  - Stertor
  - Decreased or sometimes increased nasal air passage
  - Systemic signs are rare.
- Nasal tumor:
  - Decreased nasal air passage (unilateral or bilateral)
  - Unilateral or bilateral serous, mucopurulent, or bloody discharge
  - Sneezing

    - Stertor
    - Facial or hard palate deformity (occasionally)
- Nasal aspergillosis:
    - Sneezing
    - Unilateral serous, mucopurulent, or bloody discharge
    - Depigmentation of nasal planum
    - Pain with palpation of facial bones
    - Increased nasal air passage
    - Decreased appetite and poor body condition are possible.
- Nasal mite:
    - Sneezing
    - Reverse sneezing, which may be the only abnormality in some dogs
    - Nasal discharge
    - Facial pruritus and hyposmia

ETIOLOGY AND PATHOPHYSIOLOGY

- Incidental reverse sneezing can be a normal occurrence.
- Receptors and myelinated trigeminal nerve endings situated in the lateral aspects of the nasopharynx respond to local stimulation, implying a reflex pathway. Any local stimulation can activate the reflex, which causes a strong inspiration of material from the nasopharynx to the oropharynx through a decreased nasopharyngeal opening.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is based almost exclusively on history: recognition of the characteristically loud, stertorous inspiratory episode that is sudden in onset and termination and occurs in an animal that is usually otherwise well.

DIFFERENTIAL DIAGNOSIS

When reverse sneezing occurs frequently (daily or several times a day) and/or is accompanied by other clinical signs, nasal or nasopharyngeal disease is possible:

- Nasal or nasopharyngeal tumor
- Cyst
- Foreign body
- Abscess
- Mycotic infection
- Chronic lymphoplasmacytic rhinitis, sinusitis
- Nasopharyngitis
- Nasal mites

INITIAL DATABASE

- Results of CBC, biochemistry panel, and urinalysis are usually unremarkable.
    - Eosinophilia may be present in some cases of nasal mites.
    - Anemia and hypoproteinemia may be present in animals with nasal or nasopharyngeal disorders that cause heavy and/or repeated bloody discharge.
- Nasal radiographs can be useful for the diagnosis of underlying diseases.

ADVANCED OR CONFIRMATORY TESTING

- If the episodes only occur at home (not in the veterinary hospital), and it is unclear whether they are consistent with reverse sneezing, clinicians can make the diagnosis by instructing the owner to videotape the episodes when they occur.
- Direct rhinoscopy and results of culture and cytologic and histopathologic evaluation of nasal samples are useful for the diagnosis of primary nasal diseases, whereas posterior rhinoscopy is needed for the diagnosis of nasopharyngeal diseases.
- CT scans and/or MRIs are useful in the diagnosis of some underlying conditions, such as neoplasia and aspergillosis.

TREATMENT

TREATMENT OVERVIEW

Reduce nasopharyngeal irritation by treating the underlying disorder when possible.

ACUTE GENERAL TREATMENT

Acute episodes of reverse sneezing associated with perceived severe discomfort of the animal can be shortened by opening the dog's mouth and gently pulling on the tongue or giving the animal something to lick or drink.

CHRONIC TREATMENT

- Incidental episodes need no treatment.
- Increased frequency of episodes without any other sign of nasal or nasopharyngeal disease:
    - A short period of nonsteroidal antiinflammatory drug (NSAID) administration (e.g., ketoprofen, 1 mg/kg PO q 24 h) may limit repeated reflex induced by local inflammation.
    - Treatment against the nasal mite if present (ivermectin, 0.1-0.4 mg/kg [100-400 mcg/kg] PO or SQ once every 3 weeks for 3 treatments; or milbemycin oxime, 0.5-1 mg/kg PO once weekly for 3 consecutive weeks)
- Related to nasal or nasopharyngeal disorders: treatment dictated by the underlying condition

PROGNOSIS AND OUTCOME

- Excellent for incidental episodes and when the underlying cause is nasal mite infestation
- Otherwise variable depending on the underlying etiology

PEARLS & CONSIDERATIONS

COMMENTS

The presence of clinical signs that suggest nasal or nasopharyngeal disease in conjunction with reverse sneezing should prompt diagnostic testing to detect underlying diseases.

TECHNICIAN TIPS

Nasal lavage, accomplished either by direct or retrograde methods, in conjunction with examination of nasal lavage fluid, can be helpful to clean the area when occluded as well as provide material for culture, cytologic, and histopathologic examinations.

CLIENT EDUCATION

Clients should learn not to worry during acute episodes of reverse sneezing, since there is in fact no real danger of suffocation.

SUGGESTED READING

Doust R, Sullivan M: Nasal discharge, sneezing, and reverse sneezing. Textbook of respiratory diseases in dogs and cats, St Louis, 2004, Saunders Elsevier, pp –. 1920

AUTHOR: CÉCILECLERCX

EDITOR: RANCE K.SELLON

Retinal Detachment

BASIC INFORMATION

DEFINITION

Separation of the neural retina (inner nine layers) from the underlying retinal pigment epithelium (RPE) as a result of primary inherited retinal disease or secondary to other intraocular disease (acquired); may be focal, multifocal, or complete; extent of retinal involvement determines degree of vision impairment

EPIDEMIOLOGY

SPECIES, AGE, SEX: Affects dogs and cats; age of onset and sex predisposition vary with underlying cause.

- Inherited (dogs):
  - Severe retinal dysplasia: congenital
  - Multifocal retinopathy: nonprogressive multifocal serous retinal detachments that manifest between 3 and 4 months of age
  - Collie eye anomaly (CEA): retinal detachments occur in up to 10% of CEA affected dogs; commonly young pups; may also develop later in life.
- Acquired:
  - Secondary to vitreous degeneration (liquefaction of the vitreous); usually older dogs
  - Systemic hypertension; typically older animals

GENETICS & BREED PREDISPOSITION: Dogs:

- Retinal dysplasia: presumed autosomal recessive in many predisposed breeds, including English springer spaniels, Bedlington terriers, American cocker spaniels, and miniature schnauzers; presumed an incomplete dominant inheritance in breeds with associated skeletal deformities, including Labrador retrievers and Samoyeds
- Multifocal retinopathy: autosomal recessive condition in Cotons de Tulear
- CEA: predisposed breeds include collies, Shetland sheepdogs, border collies, and Australian shepherds.
- Shih tzus are predisposed to vitreous degeneration and rhegmatogenous (retina is torn) retinal detachments.

RISK FACTORS: Acquired:

- Ocular trauma (see p. 249)
- Uveitis (see p. 1151)
- Glaucoma (see p. 448)
- Cataracts (see p. 181)
- Intraocular neoplasia (see p. 620)
- Lens luxation (see p. 644)
- Bleeding disorder (e.g., coagulopathy due to anticoagulant rodenticide intoxication; see p. 493)
- Surgical lens removal (lensectomy)
- Systemic hypertension (see p. 1068)
- Old age

ASSOCIATED CONDITIONS & DISORDERS

- Cataracts
- Hyphema (see p. 571)
- Retinal degeneration (see p. 983)
- Systemic diseases causing uveitis (see p. 1151)
- Diseases causing systemic hypertension (see p. 1068)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Bilateral or unilateral

- Inherited versus acquired
- Rhegmatogenous (retinal tear) versus nonrhegmatogenous
- Focal, multifocal, complete
- Bullous versus flat
- Exudative versus nonexudative
- Tractional

HISTORY, CHIEF COMPLAINT: Similar to retinal degeneration (see p. 983) ± bleeding inside eye

PHYSICAL EXAM FINDINGS: May produce no clinical signs if detachment is focal or multifocal, but typical findings in complete detachment are:

- Pupil(s) dilated or fixed and dilated
- Pupillary light reflex (PLR) decreased (i.e., sluggish and incomplete) or absent
- ± Anisocoria (asymmetric pupil size, especially if unilateral lesion; only pupil of affected eye is dilated).
- Blindness (variable vision impairment if incomplete)
- Gray to white membrane (retina) with blood vessels and/or hemorrhage often visible through pupil behind lens
- With or without signs of:
  - Uveitis (see p. 1151)
  - Hyphema (see p. 571)
  - Glaucoma (see p. 448)
  - Cataracts (see p. 181)
  - Systemic disease (acquired)

ETIOLOGY AND PATHOPHYSIOLOGY

- A potential space exists between the neural retina and the RPE (subretinal space).
- Exudative/nonexudative:
  - Breakdown of the blood-retinal barrier, allowing the following into the subretinal space:
    - Serous fluid ± hemorrhage (e.g., hypertension; hyperviscosity; vasculitis)
    - Exudative fluid (e.g., posterior uveitis due to systemic bacterial or mycotic infection)
- Rhegmatogenous:
  - Tear in retina allows vitreous to enter the subretinal space (e.g., hypermature cataracts, after lensectomy, CEA, old age or breed predisposition to vitreous degeneration/liquefaction, retinal degeneration).
- Tractional:
  - Fibrous or fibrocellular tissue pulling on the retina, with separation of the neural retina from RPE (e.g., ocular trauma resulting in vitreous hemorrhage, posterior uveitis and hyalitis [inflammation of the vitreous])
- Causes: see Risk Factors above.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis rests on examination of the fundus, typically through a complete ophthalmic exam (ocular ultrasound if the ocular medium is opaque [e.g., hyphema or cataract]). Examination of the posterior segment of the eye can be difficult, and making a diagnosis of retinal detachment can be challenging. Prompt referral to a veterinary ophthalmologist is advisable for all cases of vision impairment or blindness of undetermined cause.

DIFFERENTIAL DIAGNOSIS

Other causes of blindness (see p. 141)

INITIAL DATABASE

Complete ophthalmic examination (see p. 1313), including:

- Direct or indirect ophthalmoscopy to assess the posterior segment of the eye, including:
  - Optic nerve (optic disk hidden under membrane of detached retina with complete rhegmatogenous/ “morning glory” form)
  - Tapetum (dorsal reflective mirror; hyporeflective/grayish, dull discoloration ± hemorrhage with most forms of retinal detachment; hyper-reflective/brighter with complete rhegmatogenous form, because retina remains attached at/hangs off optic disk and no longer covers underlying tapetum).
  - Nontapetal fundus (typically pigmented and located ventrally; whitish/gray discoloration ± hemorrhage with retinal

detachment)
- Retinal vasculature: well-focused, small arteries and larger veins normally come from the optic disk and course peripherally. With retinal detachment, blood vessels change their course and become out of focus. With certain forms of retinal detachment, blood vessels may be visualized in the pupil behind the lens.

ADVANCED OR CONFIRMATORY TESTING

- Ocular ultrasound if ocular media opaque, preventing evaluation of deeper ocular structures
- Histopathologic evaluation of eye when eye is blind and painful and enucleation advised
- Referral is advisable for all cases of blindness of undetermined cause for additional workup (see p. 141).

TREATMENT

TREATMENT OVERVIEW

Treat underlying cause and restore vision or preserve remaining vision when possible.

ACUTE GENERAL TREATMENT

- Variable depending on underlying cause, duration, extent, and type of retinal detachment.
- Treat underlying cause, when possible, to prevent progressive retinal detachment.
- Promptly refer animals with acute blindness of undetermined cause to a veterinary ophthalmologist for early diagnosis and treatment (medical and/or surgical).

POSSIBLE COMPLICATIONS

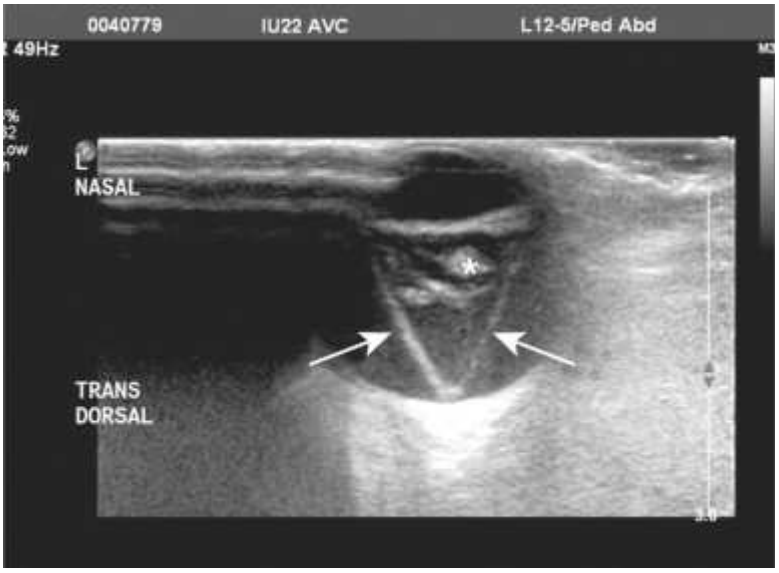
- Permanent blindness
- Cataracts
- Retinal degeneration (see p. 983)
- Hyphema (see p. 571)
- Uveitis ± secondary glaucoma
- Corneal/scleral trauma due to vision impairment (see p. 249)

RECOMMENDED MONITORING

- Variable depending on underlying cause
- Monitor for secondary cataracts and uveitis ± glaucoma

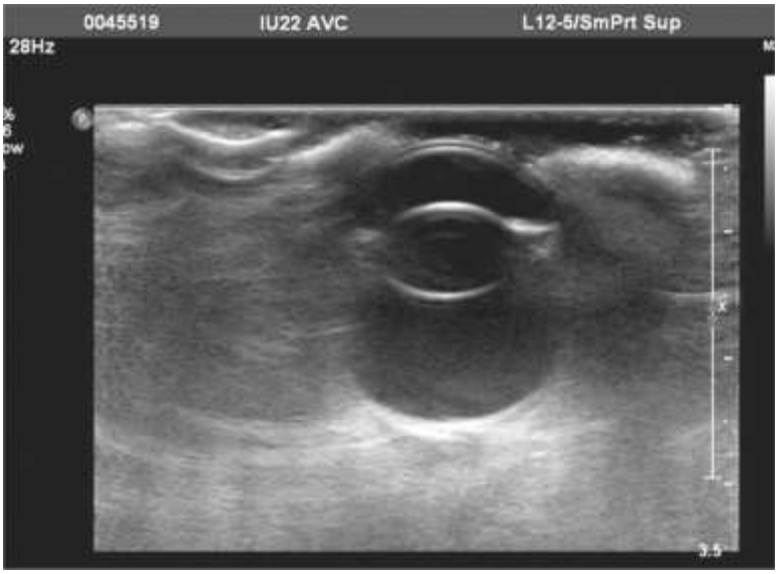
PROGNOSIS AND OUTCOME

- Variable depending on underlying cause, duration, extent, and type of retinal detachment
- Prognosis for vision with focal or multifocal forms is typically good, especially if underlying cause addressed and does not recur.
- Prognosis for vision with complete retinal detachment is typically guarded.



RETINAL DETACHMENT Ultrasound image of an eye (anterior/rostral is at top of image) showing retinal detachment *(arrows).* Note also the globoid hyperechogenicity consistent with vitreous hemorrhage and/or degeneration *(asterisk)* posterior to the misshapen hyperechoic lens compatible with a hypermature cataract.

(Courtesy Dr. Lee Ann Pack, Atlantic Veterinary College, UPEI, Canada.)



RETINAL DETACHMENT Ultrasound image of a normal eye for comparison. Separated, linear echogenicity (retina) seen in the other figure is not apparent in a normal eye.

(Courtesy Dr. Lee Ann Pack, Atlantic Veterinary College, UPEI, Canada.)

PEARLS & CONSIDERATIONS

COMMENTS

Irreversible retinal degeneration occurs quickly following retinal detachment; therefore, prompt diagnosis and treatment of underlying cause (when possible) are crucial.

PREVENTION

Ophthalmic screening of animals used for breeding by a board-certified veterinary ophthalmologist and registration through the Canine Eye Registration Foundation (www.vmdb.org/cerf.html) will help remove animals with inherited forms of retinal detachment from the breeding population.

CLIENT EDUCATION

- Retinal detachment may indicate systemic disease and may or may not be reversible, depending on cause; therefore, diagnostic testing is advised.
- Animals often adjust well to blindness.

SUGGESTED READING

Grahn BH: Chronic retinal detachment and giant retinal tears in 34 dogs: outcome comparison of no treatment, topical medical therapy, and retinal reattachment after vitrectomy. Can Vet J 48:1031, 2007

AUTHOR & EDITOR: CHERYL L.CULLEN

Retinal Degeneration

BASIC INFORMATION

DEFINITION

Deterioration of the retina due to primary inherited retinal disorders or secondary to other intraocular disease (acquired); may be focal, multifocal, or generalized. Extent of retinal involvement determines degree of vision impairment.

SYNONYM

Retinal atrophy

EPIDEMIOLOGY

SPECIES, AGE, SEX: Affects dogs and cats; age of onset and sex predisposition vary with underlying cause:

- Inherited:
  - Progressive retinal atrophy (PRA): early onset (i.e., dysplasia; 12 weeks of age) and late onset (i.e., degeneration; typically detected by 2 to 5 years of age) in dogs and cats
  - Retinal pigment epithelial dystrophy (RPED); young dogs; uncommon
- Acquired:
  - Sudden acquired retinal degeneration (SARD) typically affects middle-aged to older dogs; females are predisposed.

GENETICS & BREED PREDISPOSITION

- Dogs:
  - PRA: autosomal recessive in most predisposed breeds, including poodles, cocker spaniels, Irish setters, and collies
  - RPED: high frequency in briards
- Cats: PRA is seen in Abyssinians as autosomal dominant (dysplasia) and autosomal recessive (degeneration).

RISK FACTORS

- See Uveitis, p. 1151.
- See Retinal Detachment, p. 985.
- See Glaucoma, p. 448.
- See Intraocular Neoplasia, p. 620.
- Nutritional deficiency (e.g., taurine in cats; vitamin A or E in dogs and cats)
- Toxicosis (e.g., idiosyncratic reaction to enrofloxacin, typically at high doses [>5 mg/kg per day], or griseofulvin in cats)
- Metabolic (e.g., mucopolysaccharidosis, dogs and cats; see p. 1054).

ASSOCIATED CONDITIONS & DISORDERS

- Cataracts
- Retinal detachment
- Systemic diseases causing uveitis (see p. 1151)
- See Hyperadrenocorticism, p. 548, regarding SARD.
- See Taurine Deficiency, p. 1075, regarding taurine deficiency in cats.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Bilateral or unilateral
- Inherited versus acquired
- Acute onset versus progressive
- Focal, multifocal, generalized

HISTORY, CHIEF COMPLAINT: Variable depending on underlying cause; owner may report any or all of the following:

- Acute or progressive vision impairment or blindness
- Red eye and/or other signs of glaucoma (see p. 448) or uveitis (see p. 1151)
- Greenish reflection to eye (tapetal reflection in dilated pupil)
- "Enlarged eye" (illusional due to dilated pupil or caused by buphthalmos; see p. 778)

PHYSICAL EXAM FINDINGS

- May show no clinical signs if focal
- Generalized:
  - Often bilateral
  - Dilated pupils and sluggish to absent pupillary light reflexes (PLRs)
  - Vision disturbances: ranging from impaired night vision (nyctalopia) and/or day vision (hemeralopia) (e.g., PRA) to complete blindness (e.g., SARD; end-stage PRA)
  - With/without signs of:
    - Uveitis (see p. 1151)
    - Glaucoma (see p. 448)
    - Cataracts (see p. 181)
    - Systemic disease (acquired)

ETIOLOGY AND PATHOPHYSIOLOGY

- Inherited:
  - Breed-specific genetic abnormality in photoreceptor metabolism, termed ***PRA:***
    - PRA: always bilateral; variable rate of progression; leads to blindness when both rods and cones affected:
      - Early onset: photoreceptors fail to develop normally (i.e., dysplasia).
      - Late onset: photoreceptors develop normally but degenerate:
        - Typically, rods affected first, causing nyctalopia
        - Eventually cones also affected, resulting in hemeralopia and blindness
  - RPED is a genetic abnormality affecting the RPE layer, with secondary effects on the neural retina (nine inner retinal layers); uncommon.
- Acquired:
  - SARD is idiopathic, always bilateral, dogs only:
    - Sudden blindness within days or 1-2 weeks
    - Normal fundic examination acutely; when disease is end-stage, generalized retinal degeneration is present that is indistinguishable from PRA.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Examination of the posterior segment of the eye (i.e., fundic examination) is the cornerstone of diagnosis but can be difficult, so making a diagnosis of retinal degeneration can be challenging. Prompt referral to a veterinary ophthalmologist is advisable for all cases of vision impairment or blindness of undetermined cause.

DIFFERENTIAL DIAGNOSIS

- Acute, nonred, quiet-eye blindness (e.g., SARD):
  - Optic neuritis
  - Optic chiasmal lesion
  - Postchiasmal/cortical blindness (pupil size and PLRs usually normal)
- Progressive blindness (e.g., PRA):
  - Slowly progressive cataracts
  - Progressive corneal discoloration
- "Red eye" blindness (e.g., glaucoma):
  - Uveitis
  - Cataracts
  - Lens luxation
  - Complex corneal ulceration
- See Blindness, p. 141.

INITIAL DATABASE

Complete ophthalmic examination (see p. 1313); fundic abnormalities may include:

- Optic nerve (pale and small with end-stage retinal degeneration)
- Tapetum (dorsal reflective mirror; hyperreflective/brighter with retinal degeneration)
- Nontapetal fundus (typically pigmented and located ventrally; whitish/gray depigmentation and/or mottled hyperpigmentation with retinal degeneration)
- Retinal vasculature (small arteries and larger veins normally come from the optic disk and course peripherally; with retinal degeneration, the retinal vessels become narrowed and eventually diminish in number; no retinal vessels are discernable with end-stage retinal degeneration).

ADVANCED OR CONFIRMATORY TESTING

- Histopathologic evaluation of eye (when eye blind and painful, enucleation is advised).
- Genetic screening of blood sample for various inherited ocular diseases, including PRA (available for certain breeds).
- ACTH stimulation testing to evaluate cortisol and sex hormones, blood pressure screening (see p. 1209), and urinalysis in cases diagnosed with SARD (see pp. 548 and 6)
- Referral is advisable for all cases of blindness of undetermined cause for additional evaluation:
    - Electroretinography (ERG; see p. 1255) to assess retinal function:
        - Flatline response (i.e., no retinal function) in SARD
        - Variable to flatline response in PRA, depending on stage of disease
        - See Blindness, p. 141.

TREATMENT

TREATMENT OVERVIEW

No treatment exists to regenerate the retina, and the presentation of these patients for vision loss often means the disease process has affected the retina extensively. Therefore, treatment of retinal degeneration consists of controlling or reversing an underlying cause when one can be identified.

ACUTE GENERAL TREATMENT

- Treat underlying cause (e.g., glaucoma, uveitis) when possible, to prevent progression of acquired retinal degeneration.
- Investigational treatments under evaluation include gene therapy and retinal allograft transplantation.

POSSIBLE COMPLICATIONS

- Cataracts
- Retinal detachment ± hyphema
- Uveitis ± secondary glaucoma
- Corneal/scleral trauma (see p. 249) due to vision impairment

RECOMMENDED MONITORING

- Variable depending on underlying
- Clinicians should monitor the animal for secondary cataracts and lens-induced uveitis (see p. 181).
- If SARD is suspected but cannot be confirmed with ERG, repeated fundic examinations at 3, 6, and 12 months are indicated for clinical signs of progressive retinal degeneration.

PROGNOSIS AND OUTCOME

- Permanent blindness with SARD and PRA
- Prognosis is typically good with focal retinal degeneration caused by scarring from previous posterior uveitis and/or retinal detachment, assuming disease process does not recur.

PEARLS & CONSIDERATIONS

COMMENTS

- There is no available treatment to regenerate the retina.
- Avoid enrofloxacin doses greater than 5 mg/kg/d in cats.

PREVENTION

- Ophthalmic screening by a veterinary ophthalmologist of animals used for breeding, and registration through the Canine Eye Registration Foundation (www.vmdb.org/cerf.html), will help remove PRA- and RPED-affected animals from the breeding population.
- Genetic testing of blood samples for breed-specific inherited ocular diseases will help detect carrier and affected animals.

CLIENT EDUCATION

- Retinal degeneration alone does not cause ocular pain.
- Animals often adjust well to blindness.

SUGGESTED READING

Carter RT: Elevations in sex hormones in dogs with sudden acquired retinal degeneration syndrome (SARDS). J Am Anim Hosp Assoc 45:207,2009

Genetic testing for various inherited ocular diseases. www.optigen.com/opt9_test.html

Montgomery KW: Acute blindness in dogs: sudden acquired retinal degeneration syndrome versus neurological disease (140 cases, 2000-2006). Vet Ophthalmo 11:314, 2008

AUTHOR & EDITOR: CHERYL L. CULLEN

Restrictive/Unclassified Cardiomyopathy, Feline

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

- Restrictive cardiomyopathy (RCM): relatively uncommon primary disorder of the myocardium; characterized by severe left or biatrial enlargement with normal to slightly thickened ventricular myocardium, normal to slightly reduced ventricular volume, and normal to slightly reduced systolic function. On a two-dimensional echocardiogram, the presence of right and left ventricles of normal dimensions together with moderate to marked biatrial enlargement in the absence of any valvular, shunting, or stenotic lesions are hallmarks of RCM.
- Restrictive physiology (secondary RCM): common physiologic consequence of changes to the myocardium (usually fibrosis); results in a restrictive filling pattern. Commonly develops secondary to cardiac diseases such as DCM, chronic valvular insufficiencies or end-stage hypertropic cardiomyopathy (HCM).
- Unclassified cardiomyopathy (UCM): relatively common disorder of the myocardium; characterized by severe left or biatrial enlargement with mixed ventricular myocardial changes, including areas of thickening mixed with areas of thinning, mild to severe ventricular dilation, and mild to severe systolic dysfunction (decreased ventricular contractility), which could be global or regional.

SYNONYMS

- Intermediate-form cardiomyopathy: ICM (UCM)
- Restrictive filling or physiology: ventricular filling is similar to restrictive cardiomyopathy (RCM) but echocardiographic findings reveal abnormal ventricular myocardium

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Feline, middle-aged to older; no apparent sex predilection, although a female predominance has been reported.
- Accurate prevalence is difficult to determine owing to overlapping diagnostic criteria in the past. However, RCM/UCM appears to be the second most common myocardial disease in the cat after hypertrophic cardiomyopathy.

GENETICS & BREED PREDISPOSITION: No definitive breed predilection but may be seen more commonly in certain breeds (Persian, Birman, Balinese, Siamese, Burmese)

ASSOCIATED CONDITIONS & DISORDERS

- Congestive heart failure (CHF) is commonly seen: left-sided (pulmonary edema) or biventricular (pulmonary edema, pleural effusion, ascites).
- Cardiogenic embolism (systemic arterial thromboembolism) may be more commonly associated with this form of myocardial disease compared to hypertrophic cardiomyopathy.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Primary RCM: idiopathic disorder involving ventricular stiffness and in which ventricular dimensions are normal.
- Secondary RCM: myocardial disorders involving ventricular stiffness and in which ventricular dimensions are abnormal (see pp. 565 and 309). The information presented below will focus on primary RCM.
- Clinical presentation is variable but similar with both types of cardiomyopathy (RCM/UCM).

HISTORY, CHIEF COMPLAINT

- Dyspnea and tachypnea (from pulmonary edema) are most common. Some cats will have ascites and dyspnea from pleural effusion.
- Some cats will present for cardiogenic embolism, with or without concomitant CHF. Some cats will have a history of episodic lameness not associated with trauma.

PHYSICAL EXAM FINDINGS: Can be quite variable but could include:

- Soft systolic murmur (seemingly less common than in hypertrophic cardiomyopathy, presumably because left ventricular outflow tract obstruction and systolic anterior motion of the mitral valve occur less frequently with RCM/UCM).
- Gallop heart sound is often noted, especially if CHF is present.
- Muffled heart/lung sounds when pleural effusion is present
- Pulmonary crackles possible with pulmonary edema
- Ascites as a manifestation of biventricular CHF
- Absent femoral arterial pulses, cyanosis of nailbeds, cool paws, and firm, painful gastrocnemius muscles if aortic thromboembolism is present
- Pulse deficits from arrhythmias may be noted.

ETIOLOGY AND PATHOPHYSIOLOGY

- Primary RCM: idiopathic
- Secondary, noninfiltrative restrictive physiology:
  - Dilated cardiomyopathy
  - Hypertrophic cardiomyopathy
  - Diffuse myocardial fibrosis
- Secondary, infiltrative restrictive physiology:
  - Myocarditis
- Secondary RCM endomyocardial form:
  - Endomyocardial fibrosis (idiopathic)
- UCM:
  - Regional or diffuse areas of fibrosis
  - Regional or diffuse intramural myocardial ischemia (unproven)
- RCM/UCM: similar pathophysiologic effects resulting from excessive ventricular stiffness and, therefore, limitation in ventricular diastolic filling
  - Severely impaired (restricted) filling of ventricles induces diastolic dysfunction/failure, which results in elevated atrial pressures, pulmonary or systemic venous pressures, and congestion (pulmonary edema and/or ascites, respectively).
  - Systolic function is variable depending upon the underlying cause of the myocardial disease.
  - Dilated atria can allow blood stasis as well as having areas of endocardial fibrosis; both factors can result in mural thrombus formation.
- Emboli originating from a cardiac thrombus can infarct the terminal aorta, thoracic limbs, kidneys, bowel, or brain.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Restrictive cardiomyopathy and UCM commonly result in acute onset of dyspnea with or without cardiogenic embolism (saddle thrombi), often in cats with no known history of heart disease. While thoracic radiographs can confirm congestive heart failure, echocardiography is required to make a definitive diagnosis of the underlying cardiac disease.

DIFFERENTIAL DIAGNOSIS

- Physical:
  - Tachypnea/dyspnea:
    - Pulmonary disease
    - Pleural disease
    - CHF from other causes
  - Muffled heart/lung sounds:
    - Pleural disease
    - Obesity
    - Pneumothorax
  - Pulmonary crackles:
    - Pulmonary disease
    - Ascites:
      - Abdominal disease (generally more common than CHF as a cause of ascites in cats)
      - Effusive disease (e.g., feline infectious peritonitis, neoplasia, others)
      - CHF from other causes
    - Heart murmur:
      - Other cardiac disease
      - Physiologic murmur (i.e., anemia, hyperthyroidism)

        - Caudal paresis/paralysis:
            - Neurologic disease
            - Trauma
    - Electrocardiogram (ECG):
        - Arrhythmias:
            - Other cardiac disease
            - Systemic disease
            - Trauma
    - Thoracic radiographs:
        - Cardiomegaly
        - Other cardiac disease
        - Pericardial disease
    - Pulmonary infiltrates:
        - Pulmonary disease
        - Noncardiogenic pulmonary edema
    - Pleural effusion:
        - Pleural disease
        - Neoplastic disease
        - Effusive disease

INITIAL DATABASE

- ECG:
    - Arrhythmias are commonly seen.
        - Atrial premature complexes (APCs), ventricular premature complexes (VPCs), atrial fibrillation
    - Evidence of left ventricular and/or atrial enlargement may be seen.
- Thoracic radiographs:
    - Cardiomegaly:
        - Variable: usually left ± right atrial enlargement
        - Possible left ventricular enlargement
    - Pulmonary venous congestion/edema:
        - Often present
    - Pleural effusion:
        - Can be seen
- Echocardiogram:
    - Severe left atrial or biatrial dilation
    - Relatively normal-appearing ventricles (primary idiopathic RCM or secondary infiltrative restrictive physiology)
    - Hypertrophic segments interspersed with thin segments of the ventricular myocardium, with variable systolic function and ventricular dilation (secondary, noninfiltrative restrictive physiology, and UCM)
    - Left atrial thrombi may be seen.
    - Pericardial effusion may be present.
    - By definition, regurgitant valvular lesions, cardiac shunts, and stenotic lesions are absent or insignificant with primary RCM but can be seen with secondary RCM (restrictive physiology).

ADVANCED OR CONFIRMATORY TESTING

- Spectral Doppler echocardiogram (ventricular inflow):
    - Increased E wave amplitude
    - Shortened E wave deceleration time
    - Reduced A wave amplitude
    - Increased E/A wave ratio
    - Preserved respiratory variability on transtricuspid inflow profile
- Tissue Doppler imaging:
    - Reduced Ea and Aa velocities

TREATMENT

TREATMENT OVERVIEW

The vast majority of cats with RCM/UCM present in CHF and/or for cardiogenic embolism. Most of these cats will require acute treatment for these complications and then require lifelong chronic therapy to delay recurrence of CHF or cardiogenic embolism.

ACUTE GENERAL TREATMENT

- See Heart Failure, Acute/Decompensated, p. 468.
- See Aortic Thromboembolism, p. 88.
- There is no known treatment for slowing the progression or reversing idiopathic RCM or UCM.

CHRONIC TREATMENT

- Prevent recurrent fluid retention (lifelong treatment):
  - Furosemide: 1-2 mg/kg PO q 12-24 h (use lowest dose possible to maintain congestive-free state)
  - ACE inhibitors (either one is acceptable):
    - Enalapril: 0.25-0.5 mg/kg PO q 12-24 h
    - Benazepril: 0.25-0.5 mg/kg PO q 12-24 h
- Improve cardiac function:
  - Digoxin (if systolic dysfunction [decreased left ventricular contractility] is present): 0.03125 mg PO q 24-48 h
  - Pimobendan (if systolic dysfunction [decreased left ventricular contractility] is present): 0.625-1.25 mg PO q 12 h (not clinically studied or approved at this time). Monitor for anxiety/hyperesthesia, tachycardia as possible adverse effects.
  - β-Blockers (especially if ventricular arrhythmias are present):
    - Atenolol: 6.25-12.5 mg PO q 12-24 h
- Prevent cardiogenic embolism (arterial thromboembolism); lifelong treatments. Options can include any one of the following:
  - Antiplatelet agents:
    - Clopidogrel: 18.75 mg PO q 24 h (usually well tolerated, but if vomiting is seen, give with food); *or*
    - Aspirin: 25 mg/kg PO q 48-72 h (usually well tolerated but rarely can result in GI ulceration); *or*
    - Combination clopidogrel and aspirin (usually well tolerated but increased risk for bleeding)
  - Anticoagulants:
    - Low-molecular-weight heparins:
      - Dalteparin: 100 IU/kg SQ q 12-24 h; or
      - Enoxaparin: 1-1.5 mg/kg SQ q 12-24 h (has been shown to have an antithrombotic effect without measurable anti-Xa levels)
    - Synthetic Xa-inhibitors:
      - Fondaparinux: 0.06 mg/kg SQ q 12 h
  - Combination therapy:
    - Clopidogrel + dalteparin *or* enoxaparin *or* fondaparinux

BEHAVIOR/EXERCISE

Cats receiving antithrombotics have an increased risk for bleeding. Avoiding moderate or greater trauma should be avoided, so uncontrolled access to the outdoors should be avoided.

DRUG INTERACTIONS

- Aggressive diuretic administration together with ACE inhibitor therapy can result in acute, reversible renal failure.
- Combined antithrombotics theoretically can confer an increased risk of bleeding, although this has not been seen clinically.

POSSIBLE COMPLICATIONS

- Recurrent, intractable congestive heart failure is most common cause of death.
- Cardiogenic embolism can result in acute decompensation, reduced quality of life, or sudden death.

RECOMMENDED MONITORING

- Owners should watch for onset of dyspnea and possible embolic events.
- Repeated evaluation of thoracic radiographs and echocardiogram to evaluate for progression and alterations to medical therapy.

PROGNOSIS AND OUTCOME

- Guarded to good for treatment of acute CHF
- Guarded for treatment of acute cardiogenic embolism
- Poor to guarded for long-term survival (months to 1 year)

PEARLS & CONSIDERATIONS

COMMENTS

- RCM and UCM are irreversible diseases, and the cat is likely to have recurrent CHF episodes even with effective therapy.
- While cardiogenic embolism is a negative prognostic indicator and likely to occur again, many of these cats can do quite well with appropriate therapy and time; owners should at least consider treating such cats.

TECHNICIAN TIPS

- Intravascular volume overload can happen quickly, so excessive flushing of IV catheters with heparinized saline should be avoided.
- Development of reperfusion injury/hyperkalemia can happen very quickly in cats with cardiogenic embolism; monitor heart rate, serum electrolyte, and acid-base status closely.

CLIENT EDUCATION

Owners should watch for onset of dyspnea and possible signs of embolie events.

SUGGESTED READING

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Hogan DF: Prevention and management of thromboembolism. Consultations in feline internal medicine, ed 5, St Louis, 2006, Elsevier Saunders, pp. 331–345

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EDITOR: ETIENNE COTÉ

Renomegaly

BASIC INFORMATION

DEFINITION

Unilateral or bilateral enlargement of the kidneys. See table for normal anatomic parameters.

SYNONYMS

Kidney enlargement, nephromegaly

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dependent on underlying cause

GENETICS & BREED PREDISPOSITION: Persians and other longhaired cats are more commonly affected by polycystic kidney disease, which is inherited in an autosomal-dominant fashion in Persian cats.

Modified from Christie BA: Anatomy of the urinary system. In Slatter D, editor: Textbook of small animal surgery, ed 3, Philadelphia, 2003, Saunders, p 1562.

Characteristic Features of the Kidneys

Feature	Dog	Cat
Type	Unipyramidal (fused pyramids)	Unipyramidal (single pyramids)
Kidney mass as a percentage of body weight	0.6	0.6-1.0
Total nephrons per kidney	415,000	190,000
Kidney length in proportion to length of lumbar vertebra (L2)	2.9	2.7
Kidney width in proportion to length of lumbar vertebra (L2)	1.6	1.7
Ventral displacement in proportion to length of lumbar vertebra (L2)	L: 0.7	L: 0.7
	R: 0.3	R: 0.7
Diffusely hyperechoic renal cortex on ultrasound exam	Pathologic	Normal or pathologic

RISK FACTORS: Presence of certain infectious diseases (i.e., feline leukemia virus [FeLV], feline infectious peritonitis [FIP], leptospirosis) or disorders that may lead to urinary obstruction (i.e., urolithiasis, neoplasia)

CONTAGION & ZOONOSIS: Cat-to-cat transmission of FeLV and FIP can occur. Leptospirosis can be transmitted to other animals as well as to humans.

ASSOCIATED CONDITIONS & DISORDERS: Acute renal failure or chronic kidney disease (CKD)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Unilateral or bilateral renal enlargement
- May be an incidental finding

HISTORY, CHIEF COMPLAINT

- Lethargy, depression

- Anorexia
- Polyuria and polydipsia (PU/PD)
- Vomiting

PHYSICAL EXAM FINDINGS

- Depression
- Fever
- Palpably enlarged kidneys (unilateral or bilateral)
- Renal or abdominal pain
- Abdominal enlargement
- Pale mucous membranes
- Oral ulcers or erosions
- Halitosis

ETIOLOGY AND PATHOPHYSIOLOGY

- Neoplasia:
  - Several primary renal and metastatic tumors can cause unilateral or bilateral renomegaly.
  - Examples include lymphoma (historically most common in cats and may be related to FeLV; renomegaly is usually bilateral), renal carcinoma (most common in dogs), nephroblastoma, and cystadenocarcinoma (can occur in German shepherds and is associated with dermatofibrosis).
- Inflammation/swelling:
  - Infectious causes include FIP (granulomatous inflammation), leptospirosis, and renal abscesses (abscesses usually unilateral).
  - Ethylene glycol intoxication can cause acute bilateral renal swelling and pain.
- Hydronephrosis:
  - Unilateral or bilateral ureteral obstruction due to strictures, uroliths, or neoplasia (ureteral or in the bladder trigone)
  - Ectopic ureters
- Other:
  - Polycystic kidney disease: most common in Persian and domestic longhaired cats
  - Compensatory hypertrophy: unilateral enlargement of remaining kidney following removal of or severe damage to the other
  - Hematoma: usually unilateral enlargement and following trauma (rare)
  - Portosystemic shunt (increased glomerular filtration rate is often concurrent; both can be reversible with shunt ligation).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Renomegaly is apparent on physical exam; whether one or both kidneys is/are enlarged is an important feature that helps narrow the differential diagnosis. Typically, abdominal ultrasound is used for characterizing the enlargement and making a definitive diagnosis in some cases. Basic laboratory tests help identify the impact on renal function and further pinpoint the specific disorder as needed.

DIFFERENTIAL DIAGNOSIS

- Other causes of abdominal masses or enlargement
- Specific causes (e.g., neoplasia, hydronephrosis, polycystic kidney disease, etc.)

INITIAL DATABASE

- CBC: inflammatory leukogram and/or nonregenerative anemia may accompany infectious or neoplastic diseases. Thrombocytopenia may be present with leptospirosis. Polycythemia and/or extreme leukocytosis can occur (although rarely) with some renal neoplasms.
- Serum biochemical profile: abnormalities are consistent with acute renal failure (ARF) or CKD: azotemia, hyperphosphatemia, hyperkalemia, or hypokalemia; urine specific gravity <1.030 (dogs) or 1.035 (cats). Hyperglobulinemia is present in some chronic inflammatory disorders (e.g., FIP).
- Urinalysis: proteinuria and hematuria with some neoplastic and inflammatory disorders. Calcium oxalate monohydrate and dihydrate crystals may be observed with ethylene glycol toxicity.
- Abdominal ultrasound (see table): very effective at differentiating major causes and detecting presence of uroliths
- Abdominal radiographs (see table): effective at ruling out other causes of abdominal enlargement/masses and identifying

radiopaque uroliths

ADVANCED OR CONFIRMATORY TESTING

- Urine culture and sensitivity (C&S)
- Serologic evaluation or other diagnostic tests for infectious disease (leptospirosis, FeLV, FIP)
- Thoracic radiographs to rule out metastatic disease
- Serum or urine ethylene glycol assay
- Aspirate cytologic examination of renal masses
- Excretory urography/intravenous pyelography.
- Renal biopsy (although contraindicated if a bleeding disorder, hydronephrosis, abscess, cyst or if only one kidney is present)
- Exploratory laparotomy

TREATMENT

TREATMENT OVERVIEW

- Resolve underlying cause of renomegaly if possible.
- Treat associated disorders (e.g., ARF or CKD).

ACUTE GENERAL TREATMENT

Treat ARF if present, and address any related toxicity (i.e., ethylene glycol) or infection (i.e., leptospirosis).

CHRONIC TREATMENT

- Neoplasia: may involve nephrectomy if disease is unilateral with no sign of metastatic disease, or chemotherapy if tumor is potentially responsive to drug therapy (e.g., lymphoma).
- Hydronephrosis: correct cause of obstruction or ectopic ureter.

PROGNOSIS AND OUTCOME

Depends on the underlying cause and concurrent disorders (e.g., renal failure)

SUGGESTED READING

Cuypers MD, Grooters AM, Willams J: Renomegaly in dogs and cats. Part I. Differential diagnosis. Compend Contin Educ Pract Vet19199710191032

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EDITOR: ETIENNECÔTÉ

Renal Tubular Acidosis

BASIC INFORMATION

DEFINITION

Renal tubular acidosis (RTA) is an uncommon group of renal tubular disorders that result in hyperchloremic metabolic acidosis with a normal glomerular filtration rate.

- The tubular defect may result in decreased tubular resorption of $Hco3^-$ (proximal RTA) or defective acid secretion (distal RTA).
- Proximal RTA may be recognized along with proximal tubular resorption defects of glucose, phosphate, sodium, potassium, uric acid, and amino acids as part of Fanconi syndrome (see p. 377).

SYNONYMS

- Classic or type I: distal RTA
- Type II: proximal RTA
- Type IV: hypoaldosteronism or aldosterone resistance causing distal RTA (see p. 573); hyperkalemic RTA

EPIDEMIOLOGY

SPECIES, AGE, SEX: RTA is rare in both dogs and cats. Age of onset is dependent upon etiology (inherited, 3 to 4 years of age; acquired, any age).

GENETICS & BREED PREDISPOSITION: Dogs: basenjis, border terriers, Norwegian elkhounds (Fanconi syndrome)

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Some or all may be present:

- Polyuria/polydipsia +/−
- Anorexia +/−
- Lethargy +/−
- Weakness +/−
- Signs consistent with urolithiasis (distal RTA) +/−
- Animals with proximal RTA often lack any signs of illness.

PHYSICAL EXAM FINDINGS

- Renomegaly +/−
- Dehydration +/−
- Poor haircoat +/−
- Muscular weakness +/−
- Weight loss +/−
- Nephrolithiasis/urolithiasis (distal RTA) +/−
- Bone demineralization (distal RTA) +/−

ETIOLOGY AND PATHOPHYSIOLOGY

Etiology:

- Inherited: dogs, Fanconi syndrome (see p. 377)
- Acquired:
  - Any substance that can cause renal tubular toxicosis; toxins (e.g., heavy metals, ethylene glycol, 4-pentenoate, maleic acid), drugs (gentamicin, cephalosporins, outdated tetracycline, cisplatin, salicylate, streptozotocin). Tubular toxicosis reported after feeding jerky treats.
  - Copper storage disease (dogs):
  - Neoplasia (multiple myeloma)

- Hypoparathyroidism with concurrent hypovitaminosis D
- *Escherichia coli* pyelonephritis (cats)
- Ischemia-induced renal failure
- Hypoaldosteronism or aldosterone resistance (e.g., spironolactone)

Pathophysiology:

- Proximal RTA:
  - Dysfunction of the proximal tubule, leading to decreased bicarbonate resorption
  - Distal tubular bicarbonate resorption mechanisms are intact.
  - Acidosis is less severe than in distal RTA, since the distal tubule is able to partially compensate.
- Distal RTA:
  - Impaired hydrogen ion secretion in the collecting ducts
  - Urinary acid secretion is decreased, little change in bicarbonate resorption.
  - Nephrocalcinosis, urolithiasis (typically calcium phosphate), bone demineralization, and potassium wasting are possible features.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

RTA should be considered in animals with hyperchloremic metabolic acidosis if recognized on serum chemistry profile and confirmed by blood gas analysis. Specific findings on diagnostics tests differ depending on the form of RTA (distal, proximal, hyperkalemic).

DIFFERENTIAL DIAGNOSIS

- Hyperchloremic metabolic acidosis: diarrhea, Fanconi syndrome, posthypocapnic metabolic acidosis, dilutional acidosis, hypoadrenocorticism, medications (carbonic anhydrase inhibitors, spironolactone, ammonium chloride)
- Alkaline urine: urinary tract infection with urease-producing bacteria (e.g., *Proteus, Staphylococcus, Klebsiella* spp.), postprandial, dietary

INITIAL DATABASE

- CBC: typically unremarkable
- Serum biochemistry profile: hypokalemia, hyperchloremia, normal anion gap, decreased Tco2
  - Hyperkalemia and hyponatremia may be seen with aldosterone deficiency or resistance (type IV RTA).
- Blood gas analysis: hyperchloremic metabolic acidosis is expected.
- Urinalysis: proximal RTA = pH < 6, distal RTA = pH > 6. Glucosuria common in proximal RTA only.
- Urine culture: urinary tract infection with urease-producing bacteria must be ruled out.
- Abdominal radiographs or ultrasound: rule out nephrolithiasis or urolithiasis (distal RTA only).

ADVANCED OR CONFIRMATORY TESTING

- Glomerular filtration rate: normal, but measurement not routinely required.
- Differentiation of proximal and distal RTA (important for therapeutic management):
  - Urinary fractional excretion of $Hco3^{-}$:
    - Urine fractional excretion of $Hco3^{-}$ is measured after normalization of plasma $Hco3^{-}$ with alkali administration.
      - Normal (<5%) with distal RTA
      - Markedly increased (>15%) with proximal RTA
  - Ammonium chloride tolerance test:
    - Administer 110 mg/kg ammonium chloride PO. Monitor urine pH before and q 1 h for 6 hours after administration:
      - In healthy dogs and cats, urine pH should decrease to a minimum of 5.0 and 5.5, respectively, after ammonium chloride administration.
      - Failure to acidify urine is consistent with distal RTA.

TREATMENT

TREATMENT OVERVIEW

Treatment goals are resolution of acidemia (Tco2 or $Hco3^-$ > 12 mEq/L) and correction of hypokalemia (if present).

ACUTE AND CHRONIC TREATMENT

- Administration of a mixture of potassium and sodium citrate (1 mEq/kg to >10 mEq/kg q 24 h):
  - The dose and ratio of potassium to sodium citrate should be titrated to maintain plasma potassium and bicarbonate within the respective reference ranges.
  - Generally, proximal RTA requires higher alkali dosages than distal RTA.
- Bicarbonate can be used as an alternative alkali (1-10 mEq/kg/d PO, titrated to effect). An 8-oz (227-gram) box of baking soda can be added to 3 qts (2.88 L) of distilled water to create a 1-mEq/mL solution of bicarbonate which can be kept refrigerated up to 2 months.
- Sodium bicarbonate can aggravate potassium wasting, necessitating potassium supplementation. Potassium gluconate should be used instead of potassium chloride.
- Type IV: therapy for hypoaldosteronism or discontinuation of aldosterone inhibitors.

NUTRITION/DIET

Although RTA is usually associated with a normal glomerular filtration rate, animals with progressive tubular disease and associated azotemia should receive a protein- and phosphorus-restricted renal diet.

POSSIBLE COMPLICATIONS

- Inadequate or overzealous administration of alkali or electrolytes can result in metabolic disturbances.
- Urolithiasis and osteomalacia are potential complications of distal RTA.

RECOMMENDED MONITORING

Blood gas analysis, urine pH, and serum potassium concentrations should be monitored regularly, with frequency of monitoring tailored according to severity of metabolic disturbance.

PROGNOSIS AND OUTCOME

- Prognosis is variable and dependent upon inciting cause and response to therapy.
- Animals with acquired RTA (especially toxin induced) may have spontaneous resolution. Others may develop progressive chronic kidney disease within a few months of diagnosis.
- Animals with complex tubular disorders (i.e., Fanconi syndrome) that have progressed to the point of showing overt clinical signs generally have a poorer prognosis.

PEARLS & CONSIDERATIONS

COMMENTS

- Renal tubular acidosis is a rare condition in small animals (with the exception of basenji dogs).
- Prior to diagnosis of RTA, other more common causes of metabolic acidosis should be definitively ruled out.

SUGGESTED READING

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Rose BD, Post TW: Clinical physiology of acid-base and electrolyte disorders, ed 5, New York, 2001, McGraw-Hill, pp –. 612635

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Renal Secondary Hyperparathyroidism

BASIC INFORMATION

DEFINITION

Renal secondary hyperparathyroidism (RSHP) results from the effects of excessive production of parathyroid hormone (PTH) in animals with chronic kidney disease (CKD)/renal failure.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Any animal with CKD

RISK FACTORS: CKD: IRIS (International Renal Interest Society) stages 3 and 4 most commonly, with some in stage 2; rare for those in stage 1

ASSOCIATED CONDITIONS & DISORDERS: Hyperphosphatemia, hypocalcemia, and CKD

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: History of CKD; chief complaint is usually associated with exacerbation of signs of CKD (see pp. 205 and 207).

PHYSICAL EXAM FINDINGS: Variable combinations of signs of CKD (see History, Chief Complaint and relevant cross-references [above]). Skull and jaw lesions ("rubber jaw") occasionally occur in growing dogs with RSHP.

ETIOLOGY AND PATHOPHYSIOLOGY

- Declining kidney function increases phosphorus retention, which leads to increased PTH:
  - Increased circulating phosphorus inhibits renal synthesis of calcitriol, the active form of vitamin D, removing calcitriol-mediated inhibition of PTH synthesis.
- Increased secretion of PTH stimulates calcitriol synthesis; however, maintenance of normal calcitriol concentrations will be at the cost of continued elevation of PTH.
- Progressive decline in calcitriol synthetic capacity and circulating concentrations reduces calcium (Ca) entry into the circulation from bone and intestine, decreasing serum ionized calcium (Ca^i) concentrations. Excessive PTH rarely results in hypercalcemia (tertiary hyperparathyroidism).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis should be suspected in patients with CKD.

DIFFERENTIAL DIAGNOSIS

- Primary and tertiary hyperparathyroidism
- Hypovitaminosis D; nutritional secondary hyperparathyroidism

INITIAL DATABASE

- Laboratory assessment of CKD
- Total serum Ca: usually normal to low, occasionally slightly high; serum Ca^i is more reliable and often does not parallel serum total Ca.

ADVANCED OR CONFIRMATORY TESTING

- Measure serum PTH concentration using a two-site method for intact PTH; contact a veterinary laboratory for sample collection, preparation, and submission instructions (can degrade during transport if not chilled). Increased PTH can occur

within reference range (usually upper half) in early phases of CKD.
- Measure Cai with PTH to determine appropriateness of the response.
- Measure 25-hydroxy-vitamin D; many patients with renal secondary hyperparathyroidism also have a component of nutritional secondary hyperparathyroidism.
- Radiography may reveal diffuse bone demineralization. Pathologic fractures are rare. The earliest lesion in facial bones of young growing animals is lamina dura dentes demineralization, seen using high-definition dental technique (see p. 1246).
- High-frequency ultrasonography of the neck will reveal parathyroid gland enlargement of multiple glands.

TREATMENT

TREATMENT OVERVIEW

The goals of treatment are to decrease PTH levels and reduce the rate of CKD progression by reducing dietary phosphorus intake, increasing endogenous synthesis of calcitriol and, as indicated, by further reducing intestinal phosphate absorption (binders) and providing exogenous calcitriol.

ACUTE GENERAL TREATMENT

Reduce the animal's phosphorus intake by providing a phosphorus-restricted diet, which ranges in content from 0.4-1.6 mg P/kcal.

CHRONIC TREATMENT

- If restriction of phosphorus intake is inadequate or if phosphorus-restricted diets are refused, provide intestinal phosphorus binders with food, starting at the lowest dose and increasing the dose as necessary to control serum phosphorus to a target of approximately 4 mg/dL (lower half of reference range). Intestinal phosphorus-binding effects are greatest when the binder is given with food (increases fecal phosphorus excretion). Options include:
  - Aluminum hydroxide (30-90 mg/kg per day in food)
  - Calcium carbonate (90-150 mg/kg per day in food)
  - Calcium acetate (60-90 mg/kg per day in food)
  - Chitosan (1 g/10 lb twice daily with food)
  - Lanthanum carbonate (35-50 mg/kg per day in food)
- Aluminum- and calcium-containing binders can be used in combination to reduce the dose of each, which minimizes the risk of hypercalcemia and aluminium accumulation.
- Prescribe calcitriol (2.5-3.5 ng/kg PO q 24 h) after serum P < 6 mg/dL.
- Recommend therapy for animals with CKD as appropriate (see p. 207).

DRUG INTERACTIONS

Calcitriol can accentuate soft-tissue mineralization in animals with increased serum Cai or phosphorus.

POSSIBLE COMPLICATIONS

- Ionized hypercalcemia (>6 mg/dL in dogs; 5.5 mg/dL in cats): increased total serum Ca occurs in 10%-20% of dogs and cats with CKD before treatment; Cai may be increased, normal, or low. Hypercalcemia is dangerous only when Cai is increased. When Ca is increased:
  - Change calcitriol supplementation from once daily administration to giving twice the dose every other day, or decrease the daily dose by 50% to decrease Ca absorption from the intestine.
  - If serum phosphorus is too low with phosphate restricted diets, increase the animal's dietary phosphorus intake.
  - Change to a class of non-calcium containing intestinal phosphate binder if hypercalcemia develops while the animal is receiving calcium salt phosphate binders, or decrease the daily dose by 50%.

RECOMMENDED MONITORING

- Measure PTH and Cai (from the same sample) after 1, 3, and 6 months of therapy to determine initial and subsequent adequacy of RSHP control and twice yearly thereafter for stable animals.
- Modify extent of dietary phosphorus restriction, dosage, and types of intestinal phosphorus binders and changes in calcitriol dose on PTH and Cai results.
- Measure serum phosphorus to ensure control of hyperphosphatemia.
- Refer animals with persistently increased Cai for evaluation of primary or tertiary hyperparathyroidism.
- Monitor the animal's CKD as needed.

PROGNOSIS AND OUTCOME

- Days to weeks of survival if CKD is severe and renal secondary hyperparathyroidism cannot be controlled
- Months to years of survival is possible but guarded to poor for animals with CKD and uncontrolled RSHP. Long-term survival in cats with treatment of CKD is far more common than in dogs.
- Worse for animals with uncontrollable hyperphosphatemia
- Survival increases with appropriate PTH-lowering therapy.

PEARLS & CONSIDERATIONS

COMMENTS

- Nearly impossible to lower PTH if serum P > 6 mg/dL
- Reference ranges for serum phosphorus levels often include results from growing animals, which are much higher than for adult animals.
- The goal for serum phosphorus during CKD is 4 mg/dL (midrange to lower half of reference range) versus the upper limit of many reference ranges for adults (<6 mg/dL).

PREVENTION

- Appropriate phosphorus restriction can control or prevent development of RSHP in early CKD.
- Calcitriol can prevent development of parathyroid gland hyperplasia in RSHP.
- Calcitriol treatment is necessary to control RSHP in more advanced CKD.

CLIENT EDUCATION

Medical progress visits will be necessary to monitor CKD and determine adequacy of RSHP control.

SUGGESTED READING

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EDITOR: KATHRYN E. MICHEL

Renal Neoplasia

BASIC INFORMATION

DEFINITION

Neoplasms arising in the kidney parenchyma of epithelial (carcinoma), mesothelial (sarcoma), or mixed embryonal (nephroblastoma) origin

SYNONYMS

Wilms' tumor (nephroblastoma), kidney tumors

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs: older adults. Nephroblastomas reported in young dogs. Cats: Older adults, but young cats may develop feline leukemia virus (FeLV)-related lymphoma.

GENETICS & BREED PREDISPOSITION: Nodular dermatofibrosis genetically associated with multiple, bilateral renal cystadenocarcinomas in German shepherds

RISK FACTORS: Dogs: no sex predominance, except possibly sarcomas in females. Cats: FeLV infection associated with renal lymphoma.

CONTAGION & ZOONOSIS: Cats: FeLV-related lymphoma (cat-to-cat)

ASSOCIATED CONDITIONS & DISORDERS: Paraneoplastic polycythemia; nodular dermatofibrosis with renal cystadenocarcinoma

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Primary renal tumors are associated with minimal clinical signs until advanced stage
- Renal lymphoma in cats may disseminate to the central nervous system (CNS)

HISTORY, CHIEF COMPLAINT

- Hematuria
- Lethargy
- Inappetence
- Abdominal mass
- Weight loss
- Vomiting
- Polyuria/polydipsia (PU/PD)
- Flank pain
- Behavior changes
- Acute collapse

PHYSICAL EXAM FINDINGS

- Renomegaly
- Abdominal mass
- Pale mucous membranes
- Abdominal distension +/– fluid wave
- Shock (if actively bleeding)

ETIOLOGY AND PATHOPHYSIOLOGY

- Lymphoma: may occur spontaneously (dogs and cats) or associated with FeLV (cats)
- Carcinoma: renal cell carcinoma, transitional cell carcinoma, or adenocarcinoma with tubular or papillary differentiation:

    - Mass in renal parenchyma leads to hematuria and proteinuria.
    - Pyuria common; may be secondary to inflammation from tumor or bacterial infection
    - Anemia secondary to blood loss (with hypoalbuminemia) or diminished renal erythropoietin production
    - Polycythemia (rare) due to erythropoietin or erythropoietin-like secretion
    - Metastasis common (16%-48% at diagnosis, 61% at death)
    - Unilateral or (rarely) bilateral
- Sarcoma: hemangiosarcoma, renal sarcoma, leiomyosarcoma, fibrosarcoma, malignant fibrous histiocytoma, and spindle-cell sarcomas reported
    - May be metastatic from other site
    - Hematuria common
    - Hypoalbuminemia less common
    - Polycythemia (rare)
    - Flank pain more common than in carcinomas
    - Metastasis common
- Nephroblastoma:
    - Anemia
    - Associated with young, but reported in older dogs
    - Metastasis common
- Benign tumors:
    - Hemangioma most common (dogs)
    - Renal adenomas and leiomyomas most common (cats)

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A renal tumor should be suspected in cases of persistent hematuria, flank pain, polycythemia, or retroperitoneal mass. Confirmation of the diagnosis requires imaging including radiography, ultrasonography, or advanced planar imaging.

DIFFERENTIAL DIAGNOSIS

- Physical exam:
    - Abdominal mass +/− pain +/− ascites:
        - Urinary tract infection, urolithiasis, bladder tumor
        - Mass in spleen, mesenteric lymph node, or retroperitoneal space
        - Ruptured splenic or hepatic mass with hemoperitoneum
        - Abdominal trauma or coagulopathy with peritoneal or retroperitoneal bleeding
        - Renal cysts
        - Hydronephrosis
    - Abdominal pain without mass:
        - Pyelonephritis
        - Ethylene glycol ingestion
- Radiographic:
    - Mass in spleen, mesenteric lymph node, or retroperitoneal space
    - Ruptured splenic or hepatic mass with hemoperitoneum
    - Retroperitoneal fluid: blood or urine
    - Renal cyst or hydronephrosis
- Ultrasonographic:
    - Renal abscess or granuloma
    - Metastatic neoplasia
- Urinalysis:
    - Urinary tract infection
    - Urolithiasis
    - Ureter or bladder tumor
    - Idiopathic renal hematuria

INITIAL DATABASE

- CBC, chemistry profile, urinalysis: anemia or polycythemia possible, thrombocytopenia occasionally, azotemia (prerenal and renal), hypoalbuminemia, proteinuria, and hematuria
- Abdominal radiographs: mass, possibly peritoneal or retroperitoneal fluid
- Thoracic radiographs: metastasis (16%-48% at diagnosis)
- Abdominal ultrasound: renal mass and possibly metastasis to any abdominal organ, including adrenal gland and vena cava

- Prothrombin time and partial thromboplastin time if suspect disseminated intravascular coagulation

ADVANCED OR CONFIRMATORY TESTING

- Cytology or biopsy necessary for diagnosis
- Renal scintigraphy or excretory urogram to assess functional renal mass prior to nephrectomy
- Veterinary bladder tumor antigen test (V-BTA [Alidex Inc, Redmond, Wash.]) may detect renal pelvic transitional cell carcinoma.
- Echocardiogram if hemangiosarcoma, to rule out cardiac mass
- Cerebrospinal fluid (CSF) tap and bone marrow aspirate cytologic analysis if lymphoma (to stage disease)

TREATMENT

TREATMENT OVERVIEW

The goal of treatment is to remove the source of bleeding, pain, or polycythemia. Surgery is the primary treatment modality with demonstrated benefit for tumors other than lymphoma. Complete resection is ideal.

ACUTE GENERAL TREATMENT

- Stabilize with crystalloids, colloids, and oxygen-carrying capacity.
- Address renal insufficiency with fluid diuresis.
- Surgically remove bleeding mass.
- Begin chemotherapy with caution in lymphoma:
  - L-Asparaginase, 10,000 U/m^2 IM once on day 1
  - Cytosine arabinoside, 50 mg/m^2 subcutaneously q 12 h × 3 days for first week starting day 1
  - Vincristine, 0.5 mg/m^2 IV q 7 days starting day 1
  - Cyclophosphamide, 50 mg/m^2 PO once daily for 4 days each week starting day 1 if no evidence of cystitis
- Alleviate pain with opioids.

CHRONIC TREATMENT

- Lymphoma: if remission achieved with COAP protocol (see pp. 669 and 675), after 6 weeks administer doxorubicin IV at 30 mg/m^2 for dogs >30 kg or 1 mg/kg for dogs <30 kg and cats, q 3 weeks.
- Others:
  - No prospective clinical trials exist
  - Most literature reports based on doxorubicin or actinomycin-D
  - Anecdotal reports of response to carboplatin for carcinomas
  - Carcinomas may express cyclooxygenase 2 (COX-2), so 0.3 mg/kg piroxicam PO once daily recommended if azotemia absent.

BEHAVIOR/EXERCISE

Postoperative physical restriction as usual for a laparotomy

DRUG INTERACTIONS

Avoid combining drugs with similar toxicity profiles, such as cisplatin and piroxicam.

POSSIBLE COMPLICATIONS

Neutropenia, thrombocytopenia, sepsis, and renal injury secondary to chemotherapy

RECOMMENDED MONITORING

- Monitor CBC prior to every chemotherapy treatment and 7-10 days later.
- Monitor BUN, creatinine, and urine specific gravity for renal function.

PROGNOSIS AND OUTCOME

- Benign: good
- Lymphoma: guarded to poor
  - 60% remission rate; median duration 4 months (cats)
  - For solid tumors, survival is dependent on therapy.
  - 16-month median with surgery
  - < 1-month median without surgery
  - Chemotherapy not demonstrated to make a difference
- Carcinomas: guarded to poor
  - Rare survivals >1 year
- Sarcomas: guarded to poor
  - Reportedly more aggressive than carcinomas
- Nephroblastomas: guarded to poor
  - Rare reports of long survivals
- Metastatic potential of all tumors is high.
  - Lymphoma metastasis to CNS is lower with cytosine arabinoside in chemotherapy protocol.
  - Chemotherapy effect on metastasis of carcinomas, sarcomas, nephroblastomas unevaluated

PEARLS & CONSIDERATIONS

COMMENTS

- Hematuria in the absence of other clinical signs may suggest renal neoplasia.
- Early detection is critical for successful treatment.
- Definitive diagnosis is necessary for prognosis and therapeutic decisions.
- Complete resection offers best chances for long survival.
- Polycythemia usually resolves with nephrectomy.

TECHNICIAN TIPS

- Polycythemia (PCV > 55%-65%, depending on breed) may be a sign of renal tumor.
- Careful handling of all excreta from dogs receiving chemotherapy is important to prevent exposure to active metabolites.

CLIENT EDUCATION

Signs are subtle and nonspecific, so advanced diagnostic tests and imaging are most useful early. Nephrectomy may be palliative and maximize quality of remaining life.

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Klein MK, et al: Canine primary renal neoplasms: a retrospective review of 54 cases. J Am Anim Hosp Assoc 24:443–452, 1987.

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UROLOGY: LEAH A. COHN

Renal Dysplasia

BASIC INFORMATION

DEFINITION

Disorganized renal development resulting from arrested or anomalous cellular processes; occurs uncommonly in dogs and rarely in cats.

SYNONYMS

Familial renal disease, progressive juvenile nephropathy

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs (rarely cats) of either gender; onset of signs ranges from weeks to years of age, with most animals developing signs prior to 2 years.

GENETICS & BREED PREDISPOSITION: Familial; reported in a number of common breeds (e.g., golden retriever, boxer, cocker spaniel, Lhasa apso, shih tzu) and less common breeds (e.g., Dutch kooiker, Finnish harrier, soft-coated wheaten terrier).

RISK FACTORS: In utero viral infection (e.g., canine herpesvirus, feline panleukopenia)

ASSOCIATED CONDITIONS & DISORDERS

- Chronic kidney disease (CKD; staged as I to IV; see p. 205)
- Stunted growth
- Renal (fibrous) osteodystrophy
- Systemic hypertension

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Familial
- Nonfamilial

HISTORY, CHIEF COMPLAINT: Clinical signs may be absent. When present, abnormalities may include:

- Anestrus +/−
- Anorexia/wasting (if stage III to IV CKD present)
- Bone pain (if osteodystrophy present)
- Depression/lethargy (if stage III to IV CKD present)
- Hematuria +/−
- Polyuria and polydipsia (PU/PD) common
- Poor wound healing (if stage III to IV CKD present)
- Stunted growth +/−
- Vomiting/diarrhea (if stage III to IV CKD present)

PHYSICAL EXAM FINDINGS: Physical examination may be unremarkable, but abnormalities can include:

- Calcinosis circumscripta uncommon
- Dehydration (if stage III to IV CKD present)
- Enlarged mandible/maxillae (if osteodystrophy present)
- Muscular twitching (if osteodystrophy present)
- Oral ulceration/halitosis (if uremia present)
- Pallor (if stage III to IV CKD present)
- Pathologic fracture (if osteodystrophy present)
- Pliable mandible (“rubber jaw”) (if osteodystrophy present)
- Poor haircoat +/−

- Small kidneys on abdominal palpation common but inconsistent finding
- Small stature/poor body condition common but inconsistent finding

ETIOLOGY AND PATHOPHYSIOLOGY

- The microscopic appearance of kidneys should be mature by 70 days of age (some development and histologic change normally continues during the first 2 months of life). Disorganized parenchymal development with immature or anomalous structures characterizes renal dysplasia with histologic features inappropriate for the animal's age.
- Poorly developed kidneys result in renal failure and eventual death.
- Diminished renal conversion of vitamin D to the active form, calcitriol, contributes to secondary hyperparathyroidism and subsequent renal osteodystrophy. This complication is more pronounced in juvenile renal disease.

DIAGNOSIS 

DIFFERENTIAL DIAGNOSIS

Azotemia:

- Prerenal (e.g., dehydration, gastrointestinal bleeding)
- Renal (e.g., acute renal failure or CKD of any cause)
- Postrenal (e.g., urinary obstruction, urinary tract rupture)

INITIAL DATABASE

- Blood pressure (BP; see pp. 1068 and 1209):
  - CBC: nonregenerative anemia
- Serum biochemical profile: abnormalities become more likely and more severe as stage of CKD progresses. Common findings include:
  - Azotemia
  - Hyperphosphatemia
  - Hypokalemia
  - Hypercalcemia/hypocalcemia
  - Metabolic acidosis
  - Hypercholesterolemia
  - Hypoalbuminemia
- Urinalysis: isosthenuric or minimally concentrated urine characteristic, variable hematuria, proteinuria, glucosuria
- Urine culture and sensitivity (C&S) to rule out secondary infection
- Abdominal radiography:
  - Small kidneys
  - Poor abdominal detail (young age, poor body condition)
  - Soft-tissue mineralization
- Ultrasonography:
  - Small, irregularly shaped kidneys
  - Thin renal cortex
  - Hyperechoic renal parenchyma
  - Poor corticomedullary distinction
  - Soft-tissue mineralization

ADVANCED OR CONFIRMATORY TESTING

- Serum parathyroid hormone (PTH) concentration: initially normal, then rises. Intention is to delay/prevent this rise using calcitriol therapy.
- Serum ionized calcium: to confirm biologically significant hypercalcemia; may be normal initially and then may increase as PTH concentration rises.
- Assessment of glomerular filtration rate: may have a role in evaluating nonazotemic animals suspected of having renal dysplasia.
- Renal histopathologic examination: required to confirm diagnosis:
  - Asynchronous nephron development
  - Immature glomeruli and/or tubules
  - Persistent fetal mesenchyme
  - Persistent metanephric ducts
  - Atypical tubular epithelium

- Dysontogenetic metaplasia

TREATMENT

TREATMENT OVERVIEW

Renal dysplasia cannot be reversed or cured; the goal of therapy is to delay progression of kidney disease, maintain hydration, address signs of uremia, and address complications of overt CKD such as anemia and acid-base and electrolyte disorders.

ACUTE GENERAL TREATMENT

Acute treatment will address uremia, dehydration, electrolyte, and acid-base disorders (see pp. 207 and 205).

CHRONIC TREATMENT

- See Chronic Kidney Disease, Occult ("Asymptomatic"), p. 205; Chronic Kidney Disease, Overt ("Symptomatic"), ; Protein-Losing Nephropathy, ; Renal Secondary Hyperparathyroidism, p. 976. Besides those described below, other treatments to consider address hyperphosphatemia, systemic hypertension, GI ulceration, anorexia, anemia, hypokalemia, and acidosis.
- Vomiting: address promptly, as dehydration may lead to rapid deterioration of renal function. Commonly used antiemetics include maropitant (dogs 2 mg/kg PO q 24 h for 5 days), metoclopramide (0.2-0.5 mg/kg SQ or IM q 8 h), or ondansetron (0.1-0.2 mg/kg IV q 12 h). Provide crystalloid fluid therapy as needed to replace losses.
- Bone pain (renal osteodystrophy): opioids (e.g., full mu agonists [e.g., oxymorphone, 0.03-0.2 mg/kg SQ, IM, or IV; fentanyl patch] or buprenorphine, 0.01-0.02 mg/kg SQ, IM, or IV q 6-8 h). Avoid administering nonsteroidal antiinflammatory drugs (NSAIDs), which have potentially negative renal effects.
- Early calcitriol therapy may delay or prevent bone changes and should be considered before hyperphosphatemia occurs:
  - Initial dose 1.65-3.63 ng/kg (= 0.00165-0.00363 mcg/kg) PO q 24 h (dogs and cats); dose is adjusted based primarily on serum calcium and phosphorus concentrations (± PTH concentrations).
  - Maintain Ca (mg/dL) × P (mg/dl) product of <70; avoid hypercalcemia; if total calcium elevated, confirm with ionized calcium.
  - Ideally, PTH should be within reference range during treatment. If low, dose is decreased; if high, dose is increased.
  - Calcitriol loses efficacy when phosphorus >8 mg/dL. Typically, calcitriol is used in conjunction with a phosphorus-reducing diet and noncalcium-containing phosphate binders.

NUTRITION/DIET

Renal diets with optimal protein and phosphorus content are indicated (see p. 207).

DRUG INTERACTIONS

- Vascular calcium channel blockers (amlodipine) and angiotensin-converting enzyme (ACE) inhibitors used concurrently may produce hypotension.
- Phosphate binders can interfere with absorption of orally administered medications.
- Concurrent use of calcitriol and calcium-containing phosphate binders, thiazide diuretics, corticosteroids, and barbiturates should be avoided.
- Nephrotoxic drugs (e.g., aminoglycosides) or drug combinations (e.g., NSAIDs plus ACE inhibitors) should be avoided whenever possible.
- Drugs which undergo renal elimination may need adjustment in dose strength or frequency in animals with CKD.

POSSIBLE COMPLICATIONS

- Hypotension may result from use of a calcium channel blocker and/or ACE inhibitors.
- Calcitriol may lead to hypercalcemia and/or ectopic mineralization of tissues.
- Complications of CKD include uremia, systemic hypertension, GI ulceration, anemia, electrolyte disorders, acidosis renal osteodystrophy.

RECOMMENDED MONITORING

- Monitor calcium and phosphorus levels 2 weeks after beginning calcitriol therapy and at least monthly thereafter for adjusting dosages. Ideally, measure PTH levels prior to and 1-2 months after therapy has started.
- The clinician is advised to monitor the animal as he/she would other animals with CKD (see p. 207); monitoring includes complete physical examination; measurement of BP; serum biochemistry profiles and blood gas determinations to assess azotemia, electrolyte, and acid-base status; and monitoring for clinical signs suggesting urinary tract infection.

PROGNOSIS AND OUTCOME

- Depends on degree of dysplasia, age at onset of signs, severity of dysfunction at diagnosis, and subsequent treatment.
- It is an irreversible condition; long-term prognosis is generally poor.

PEARLS & CONSIDERATIONS

COMMENTS

- Renal dysplasia can occur in any breed of dog or cat.
- There is no specific therapy, but animals are managed as for CKD and its complications.

PREVENTION

- Do not breed affected animals.
- Inform owners of appropriate vaccination of cats against panleukopenia.

CLIENT EDUCATION

Owners should research breed-associated diseases prior to considering adoption or purchase.

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AUTHORS: ADAM MORDECAI,RANCE K. SELLON

EDITOR: LEAH A. COHN

Regurgitation

BASIC INFORMATION

DEFINITION

The passive, retrograde expulsion of food and/or fluid from the esophagus or pharynx into the oral and/or nasal cavities

EPIDEMIOLOGY

SPECIES, AGE, SEX: Congenital causes may produce clinical signs as early as weaning; acquired forms usually in young to middle-aged animals. Idiopathic megaesophagus occurs spontaneously in adult dogs between 7 and 15 years of age, without sex or breed predisposition.

GENETICS & BREED PREDISPOSITION

- Dogs:
  - Wire-haired fox terriers and miniature Schnauzers: hereditary megaesophagus
  - German shepherd, Newfoundland, Great Dane, Irish setter, and sharper familial megaesophagus
  - German shepherd and Irish setter: vascular ring anomalies
  - German shepherd: gastroesophageal intussusception
  - German shepherd, Jack Russell terrier, springer spaniel, Labrador retriever, and Scottish terrier: myasthenia gravis
  - Shar-pei: hiatal hernia
  - Medium- to large-breed dogs: hypothyroidism; link to megaesophagus remains anecdotal.
  - Great Dane, rottweiler, standard poodle, and West Highland white terrier (hypoadrenocorticism)
- Cats: Siamese (familial megaesophagus); longhaired breeds (hairballs)

ASSOCIATED CONDITIONS & DISORDERS: Aspiration pneumonia (most common and serious complication of megaesophagus), rhinitis, esophageal strictures

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Esophageal
- Pharyngeal

HISTORY, CHIEF COMPLAINT

- “Vomiting” is commonly reported by owners of animals that are regurgitating; accordingly, clinicians should question owners about what the animal does when food is ejected from the mouth (more details in Differential Diagnosis below).
- Coughing
- Dyspnea
- Weakness
- Weight loss

PHYSICAL EXAM FINDINGS: Findings are variable:

- Emaciation
- Weakness
- Esophageal bulge (pressure on abdomen, close nostrils)
- Fever
- Respiratory signs
- Abnormal neurologic examination

ETIOLOGY AND PATHOPHYSIOLOGY

- Regurgitation indicates esophageal or pharyngeal dysfunction due to mechanical obstructive disease or functional (motility) abnormalities such as megaesophagus.

- Esophageal disease:
  - Megaesophagus: primary (idiopathic) or secondary
  - Esophagitis
  - Esophageal obstruction/foreign body
  - Esophageal mass (e.g., *Spirocerca lupi)*
  - Esophageal diverticulum
  - Esophageal stricture/stenosis
  - Vascular ring anomaly
  - Other motility disorder
  - Thoracic neoplasia (e.g., thymoma)
- Pharyngeal disease:
  - Pharyngeal obstruction
- Other alimentary tract disease:
  - Gastroesophageal intussusception
  - Pyloric outflow obstruction
  - Hiatal hernia
- Neuromuscular disease:
  - Myasthenia gravis
  - Botulism
  - Tetanus
  - Anticholinesterase activity (e.g., organophosphate toxicity)
  - Dysautonomia
  - Polyradiculoneuritis
- Immune-mediated:
  - Systemic lupus erythematosus
  - Polymyositis
- Intoxications:
  - Lead
  - Thallium
  - Organophosphate
- Endocrine:
  - Hypothyroidism (speculative)
  - Hypoadrenocorticism

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The essential first step is to clarify whether regurgitation, dysphagia, or vomiting is present. Some patients may exhibit more than one, or the owner may not be sure, but in most cases it is possible to identify regurgitation specifically from the history. The next step consists of obtaining thoracic radiographs for confirmation and to assess the lung parenchyma for evidence of aspiration. An extensive diagnostic workup is generally involved with megaesophagus, because many primary disorders may cause it.

DIFFERENTIAL DIAGNOSIS

- It is essential to distinguish regurgitation from vomition and dysphagia, since the underlying causes, treatment approaches, and outcomes are generally very different.
- Regurgitation: passive (usually); undigested food (covered by mucus or saliva); sausage shaped; neutral pH; immediately postprandial or delayed (hours). Forceful abdominal compressions leading to ejection of food from the mouth suggest vomiting rather than regurgitation (see pp. 1173 and 1175).

INITIAL DATABASE

- Usually normal
- CBC: Aspiration pneumonia may occasionally cause leukocytosis.
- Serum chemistry: some metabolic diseases can result in esophageal dysfunction (e.g., electrolyte imbalance with hypoadrenocorticism).
- Thoracic, pharyngeal, and cervical radiographs: megaesophagus, vascular ring anomaly, foreign bodies, and other such findings
- Contrast radiography/esophagram

ADVANCED OR CONFIRMATORY TESTING

- Fluoroscopy (see p. 1205)
- Esophagoscopy
- Esophageal manometry
- Radiographic scintigraphy to measure transit time
- Thyroid-stimulating hormone (TSH) and free T4 tests: hypothyroidism
- ACTH stimulation test: hypoadrenocorticism
- Antinuclear antibody test: immune-mediated causes
- Acetylcholine (ACh) receptor antibody test: myasthenia gravis
- Bioassay techniques: botulism and tetanus
- Toxin analysis: lead, thallium, and organophosphates

TREATMENT

TREATMENT OVERVIEW

Successful treatment requires elimination of the underlying cause whenever possible; temporary or lifelong supportive care helps minimize the risk of complications.

ACUTE GENERAL TREATMENT

- Aspiration pneumonia: appropriate antibiotic therapy and supportive care
- For esophageal disease other than idiopathic megaesophagus: treat and correct disease (e.g., surgery for removal of foreign bodies or vascular anomalies).
- For systemic causes of regurgitation: treat underlying disease.

CHRONIC TREATMENT

- Megaesophagus (see p. 1408)
- Bypass the esophagus with a gastrostomy tube (see pp. 1270, 1273) if necessary.
- Motility-modifying drugs are controversial in treating megaesophagus, because their efficacy is unproven; increasing lower esophageal tone could hinder the transit of food from esophagus to stomach:
    - Metoclopramide (0.2-0.5 mg/kg PO q 8 h or q 12 h) increases the lower-esophageal sphincter pressure and gastric emptying and reduces gastroesophageal reflux.
    - Cisapride (0.5 mg/kg q 8 h or q 12 h) increases lower esophageal peristalsis and sphincter pressure (cats > dogs) and accelerates gastric emptying. This drug can be difficult to obtain.

POSSIBLE COMPLICATIONS

- Aspiration pneumonia
- Esophageal rupture due to foreign bodies
- Esophageal stricture formation
- Esophageal reflux

RECOMMENDED MONITORING

- Check for resolution of clinical signs for animals whose causes were systemic.
- Regularly check thoracic radiographs for signs of aspiration pneumonia.

PROGNOSIS AND OUTCOME

Depend greatly on the cause of the regurgitation and presence or absence of complications

PEARLS & CONSIDERATIONS

COMMENTS

- Clinicians should make sure the animal is regurgitating and not vomiting.
- Aspiration pneumonia often does not increase the white blood cell (WBC) count, even if extensive.

CLIENT EDUCATION

The owner should be aware of the clinical signs of aspiration pneumonia and seek immediate veterinary attention if they occur.

SUGGESTED READING

Woolley CS: Dysphagia and regurgitation. In Ettinger SJ, editor: Textbook of veterinary internal medicine, Philadelphia, 2010, WB Saunders, pp 191–195.

AUTHOR: NINETTE KELLER

EDITOR: ETIENNE CÔTÉ

Reflex Dyssynergia

BASIC INFORMATION

DEFINITION

Upper motor neuron (UMN) dysfunction preventing coordinated urinary bladder contraction and urethral sphincter relaxation during micturition. Sacral spinal cord lesions, diseases associated with the urethra, and an idiopathic condition can each mimic reflex dyssynergia.

SYNONYMS

Detrusor-sphincter dyssynergia, detrusor-sphincter incoordination, functional urethral obstruction, UMN bladder

EPIDEMIOLOGY

SPECIES, AGE, SEX: Affects dogs and cats of any age, depending on causation. More often observed in male dogs; an idiopathic dyssynergia-like condition affects predominantly large-breed male dogs.

RISK FACTORS

- Thoracolumbar spinal cord injury/disease
- Dyssynergia-like condition:
  - Following relief of urethral obstruction
  - Sacral spinal cord injury/disease

ASSOCIATED CONDITIONS & DISORDERS

- Bladder atony/hypotonia
- Urinary tract infection

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- True reflex dyssynergia: neurogenic suprasacral lesions
- Dyssynergia-like conditions: neurogenic and non-neurogenic disorders

HISTORY, CHIEF COMPLAINT

- Frequent attempts at voiding with inability to empty bladder completely are characteristic.
- Normal initiation of voiding with interruption of urine stream; short spurts of urine followed by cessation of urine flow.
- Animal may strain with no urine produced.

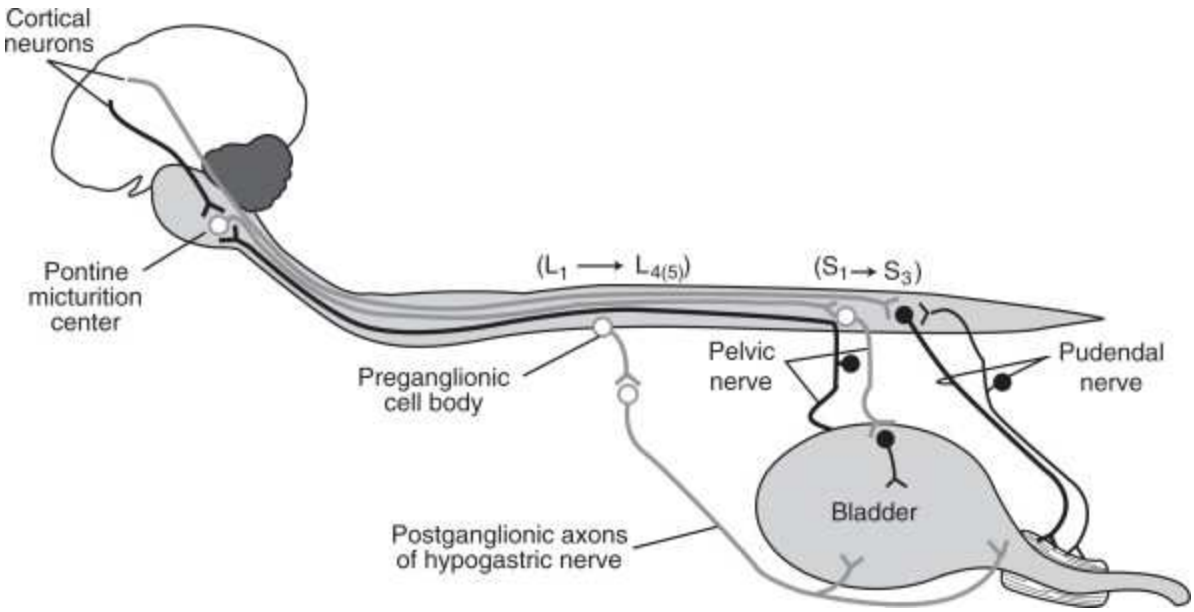
PHYSICAL EXAM FINDINGS

- Manual bladder expression difficult
- Clinicians should palpate the bladder before and after voiding: turgid, incomplete emptying of bladder, increased residual urine volume are expected.
- Perineal reflex is present or exaggerated.
- Neurologic dysfunction unrelated to urination may be present.
- Rectal and vaginal examinations are indicated to assess structural causes (e.g., sacral vertebral lesion) versus other causes of dysuria (e.g., urethral lith or mass). Anal tone is normal/good.
- Observation of urination: thin, interrupted urine stream

ETIOLOGY AND PATHOPHYSIOLOGY

- Disordered urinary retention resulting from central nervous system (CNS) lesion located between the pontine micturition center and the sacral spinal cord (suprasacral spinal cord: L7 to brainstem)

- UMN lesion causes a loss of inhibitory pathways:
  - To sympathetic innervation of the internal urethral sphincter (smooth muscle)
  - To somatic innervation (pudendal nerve) of the external urethral sphincter (striated muscle)
- Additional factors include increased sensory input (sacral nerves), increased sympathetic output, and bladder neck hypertrophy.
- Neurogenic dyssynergia-like conditions occur when pelvic nerve damage results in weakened detrusor contraction that cannot override urethral sphincter tone.
- In animals with non-neurogenic dyssynergia-like conditions, there is a similar failure of simultaneous relaxation of the internal or external urethral sphincter with detrusor contraction. This may be idiopathic or may follow irritation/disease of the urethra.



REFLEX DYSSYNERGIA Neurologic pathways to and from the urinary bladder.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A diagnosis of primary reflex dyssynergia is made by exclusion of other conditions that mimic signs. The diagnostic plan should include eliminating conditions that cause mechanical (anatomic) obstruction of the urethra. The physical and neurologic examinations can define an anatomic or neurologic differential.

DIFFERENTIAL DIAGNOSIS

- Anatomic urethral obstruction:
  - Intraluminal (e.g., urethral plug/lith, transitional cell carcinoma, urethritis)
  - Extraluminal (e.g., prostatomegaly, pelvic granuloma)
- Functional urethral obstruction (dyssynergia-like conditions):
  - Neurogenic:
    - Sacral spinal cord disease
    - Pelvic plexus injury
    - Cauda equina disease
  - Non-neurogenic:
    - Idiopathic
    - Following relief of urethral obstruction
    - Secondary urinary tract infection
    - Bladder neck obstruction
    - a-Adrenergic agonist administration (e.g., phenylpropanolamine, pseudoephedrine)
    - Myopathic disease
- Bladder wall atony (see p. 104)

INITIAL DATABASE

- Urethral catheterization: unobstructed. Residual urine volume increased (normal, 0.2-0.4 mL/kg in dogs; or <10 mL in dogs and <2 mL in cats).
- Rectal examination: good anal tone, no pelvic/urethral mass
- Neurologic examination (see p. 1311), including perineal and bulbocavernosus reflexes:
  - Neuroanatomic lesion localization: spinal cord, usually T3-L3
- Clinical pathologic examination:
  - CBC and serum biochemistry: unremarkable
  - Urinalysis and urine culture: secondary urinary tract infection common
- Caudal abdominal and pelvic radiographs, abdominal ultrasound: no urethral obstruction or mass, possible vertebral injury/disease

ADVANCED OR CONFIRMATORY TESTING

- Contrast urethrography: rule out urethral obstruction if necessary.
- Cystoscopy and urethroscopy: identify masses, obtain biopsies, remove small calculi.
- Neurodiagnostic procedures: confirm lesion localization, extent of lesion, and suspected cause:
  - Myelography to evaluate for intramedullary or extramedullary compressive disease
  - Electromyography of the anal sphincter muscle to assess pudendal nerve
  - Somatosensory-evoked response testing to evaluate ascending sensory pathways
  - Advanced imaging:
    - MRI
    - CT
- Urodynamic procedures:
  - Cystometry to assess bladder function
  - Urethral pressure profile to assess urethral tone, which is the only means to confirm idiopathic dyssynergia-like condition
  - Leak point pressure measurement to assess urethral resistance

TREATMENT

TREATMENT OVERVIEW

It is important to treat the underlying cause. Supportive therapies include bladder emptying and pharmacologic management. Bladder emptying prevents secondary bladder atony (see p. 104) and urine retention that predispose to urinary tract infection. Pharmacologic therapy is often empirical; starting at lower end of the dosage range, response to therapy is noted and dose adjusted.

ACUTE GENERAL TREATMENT

- Urinary bladder catheterization:
  - Indwelling urinary catheter (closed-collection system)
  - Intermittent catheterization has a lower risk of inducing UTI
- Urethral sphincter relaxation (see p. 104):
  - Smooth muscle relaxation (a-antagonists):
    - Phenoxybenzamine: dogs, 0.25 mg/kg PO q 8-12 h; cats, 1.25-5 mg/cat PO q 12 h. Onset of action is delayed up to 4 days. Possible side effects: hypotension, tachycardia, and increased intraocular pressure. Contraindications: cardiovascular disease, glaucoma, and renal failure. (Commercially prepared product, Dibenzyline 10-mg capsules [Wellspring Pharmaceutical Corp.], has become cost-prohibitive; USP-grade powder for compounding is more cost-effective.)
    - Prazosin: dogs, 1 mg/15 kg PO q 8-12 h; cats, 0.25-0.5 mg/cat PO q 12-24 h. Possible side effects are hypotension and mild sedation; contraindications same as phenoxybenzamine, above.
  - Striated muscle relaxation (skeletal muscle relaxants):
    - Diazepam: dogs, 2-10 mg/dog PO q 8 h; cats, 2-5 mg/cat PO q 8 h, or 0.2-0.5 mg/kg IV as needed. A centrally acting muscle relaxant. Possible side effects: sedation, excitation, and idiosyncratic acute hepatocellular necrosis in cats.
    - Methocarbamol: dogs, 15-20 mg/kg PO q 8 h; cats, initial dose 33 mg/kg PO q 8 h, then 20 mg/kg PO q 8 h. A centrally acting muscle relaxant. Possible side effects: weakness, sedation, lethargy and vomiting.
- May add drugs to stimulate detrusor muscle contraction (see p. 104):
  - Bethanechol (parasympathomimetic): dogs, 5-25 mg PO q 8 h; cats, 1.25-5 mg PO q 8 h. Possible side effects: ptyalism, vomiting, diarrhea, and bronchoconstriction; contraindications are urinary or gastrointestinal (GI) obstruction.
  - Cisapride (prokinetic; enhances acetylcholine release): dogs, 0.5 mg/kg PO q 8 h; cats, 1.25-5 mg/cat PO q 8-12 h. Possible side effects: diarrhea and abdominal pain.

CHRONIC TREATMENT

- Resolution of underlying disorder
- Intermittent bladder catheterization or manual bladder expression
    - Complete emptying with manual expression may take several attempts; allow the animal to relax between attempts.
- Long-term drug therapy
- Address secondary urinary tract infection (see p. 276).

DRUG INTERACTIONS

Start treatment with an α-antagonist (e.g., prazosin) prior to bethanechol. Bethanechol may enhance urethral sphincter tone (has nonspecific cholinergic effects on the caudal mesenteric ganglia, causing further stimulation to the hypogastric nerve).

RECOMMENDED MONITORING

- Observe voiding activity daily.
- Monitor residual urine volume.
- Perform a periodic urine culture/urinalysis after removal of indwelling catheter and at least every 3 months until condition has resolved.

PROGNOSIS AND OUTCOME

- Good prognosis with resolution of underlying disease but may require weeks to resolve
- Good prognosis for resolution of dyssynergia-like conditions when underlying cause eliminated (e.g., urethral inflammation)
- Fair prognosis for medical control of idiopathic dyssynergia-like condition

PEARLS & CONSIDERATIONS

COMMENTS

- Reflex dyssynergia is a common sequela of severe spinal cord injury.
- If prolonged recovery from the spinal cord injury is expected, initiate an α-antagonist early (3-5 days from initial onset of action).

PREVENTION

Successful management depends on identification and treatment of underlying disorder.

TECHNICIAN TIPS

- Aseptic protocols (cleanse external catheter and genital areas; change collection bag) to reduce risks for urinary tract infection should be instituted in patients requiring urinary catheterization.
- Secondary urine overflow also will increase risks for urine scald and decubitus ulceration. The patient should be kept clean and dry on a padded surface with frequent (q 4 h) rotation if recumbent.

CLIENT EDUCATION

- Manual bladder expression or intermittent catheterization may be required.
- Watch for signs of urinary tract infection (e.g., change in color or odor).

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Refeeding Syndrome

BASIC INFORMATION

DEFINITION

Potentially fatal shifts in fluid and electrolytes associated with either enteral or parenteral feeding of previously malnourished animals or those with little or no food intake for 10 or more days. True incidence is unknown in veterinary medicine, but given the fact that this is a preventable idiogenic problem, clinicians should be familiar with this syndrome.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Can occur in any malnourished animal; aged and critically ill animals may be at increased risk.

RISK FACTORS: Malnutrition, prolonged starvation, emaciated, animals receiving supplemental nutritional support, overly aggressive nutritional support of malnourished animals, animals that have neurologic problems and dysphagias, reportedly diabetic ketoacidosis (dogs), and hepatic lipidosis (cats)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: This is a secondary syndrome. Variable combinations of fluid retention, hypokalemia, hypophosphatemia, and hypomagnesemia may occur within the first 4 days of refeeding by any route. However, these abnormalities maybe noted in as little as 24 hours after the start of refeeding. Overt clinical signs tend to become apparent when serum phosphorus < 1.5 mg/dL (0.5 mmol/L). Thiamin (vitamin B1) deficiency has been reported in humans but not in animals with refeeding syndrome.

HISTORY, CHIEF COMPLAINT

- Animals generally are malnourished or have had prolonged starvation and/or are undergoing treatment for an illness that requires nutritional support. Therefore, signs of the primary illness may initially overshadow the chief complaint of refeeding syndrome.
- Chief complaint depends on the exact pattern of abnormalities secondary to the fluid shifts and serum electrolytes in each animal.

PHYSICAL EXAM FINDINGS

- Weakness, weight loss, reduced muscle mass, and signs resulting from primary disease process are all possible physical exam findings. Signs of individual abnormalities vary with severity and presence of concurrent illness. Many animals do not show clinical signs until the abnormality is severe; these tend to be primarily related to fluid and electrolyte abnormalities.
- Fluid shifts resulting in fluid overload or retention: rapid weight gain ± serous nasal discharge, chemosis, restlessness, shivering, tachycardia, tachypnea, dyspnea, pulmonary crackles, vomiting, and diarrhea. These clinical signs may occur even when on recommended or conservative fluid rates.
    - Hypokalemia: (serum K^+ < 3.5 mEq/L), severe muscle weakness, arrhythmia, ileus, and decreased urinary concentrating ability
    - Hypophosphatemia: (serum $PO4^{2-}$ < 1.5 mg/dL or 0.5 mmol/L), hemolytic anemia, muscle weakness, rhabdomyolysis, renal tubular defects, cardiac dysfunction, fluid intolerance and arrhythmias
    - Hypomagnesemia: (serum Mg^{2+} < 1 mEq/L), cardiac arrhythmia, tremors, weakness, tetany, and secondary hypokalemia and hypocalcemia

ETIOLOGY AND PATHOPHYSIOLOGY

- Disease and malnutrition result in decreased serum levels of glucose. Catecholamines, glucagon, and glucocorticoid hormones increase to maintain serum glucose levels via gluconeogenesis by utilizing triacylglycerides and protein as precursors.
- The body has adapted to the decreased caloric intake (starvation metabolism) or increased caloric utilization (stress metabolism if concurrent disease process is present) with resulting depletion of lean body mass and intracellular electrolytes. These alterations may occur early in the clinical course.
- Refeeding allows use of carbohydrates (glucose) as the primary fuel source once more.
- Carbohydrate intake results in increased insulin secretion. This stimulates cellular uptake of phosphorus for manufacture of

adenosine triphosphate (ATP) and protein synthesis, which can lead to profound hypophosphatemia and subsequent hemolysis.
- Feeding can also drive other molecules and electrolytes into the cells, resulting in acute extracellular deficiencies (hypoglycemia, hypomagnesemia, and hypokalemia) and fluid balance abnormalities.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

This syndrome should be suspected in any animal with a significant alteration (a change of 20% or greater) in the serum concentrations of potassium, phosphorous, or magnesium after the onset of any type of nutritional support. These electrolyte abnormalities may occur in as brief a time period as 24 hours and up to 5 days after the onset of nutritional support.

DIFFERENTIAL DIAGNOSIS

- Any disease with prolonged anorexia or malnutrition
- Exacerbation of the primary disease

INITIAL DATABASE

- Body weight
- Serum glucose, albumin
- Venous blood gas and serum biochemical profile, including electrolyte determinations: hypokalemia, hypophosphatemia, hypomagnesemia are common.
- CBC: generally unremarkable
- Urinalysis

TREATMENT

TREATMENT OVERVIEW

Therapy consists of normalization of serum electrolytes via intravenous supplementation and close monitoring, maintaining fluid balances, and a gradual reintroduction of calories to the patient. The amount of time it takes to achieve resting energy expenditure (REE) calories depends upon the severity of the underlying cause and the length of time the patient was without adequate caloric intake. A general rule of thumb is to go slow and take between 4 and 7 days to achieve REE. Frequently these patients require 24-hour monitoring, central sampling lines, blood transfusions, multiple constant rate infusions, point-of-cage laboratory testing, and intensive nursing care.

ACUTE GENERAL TREATMENT

- When the signs of refeeding syndrome first become apparent: reduce the rate of feeding by 50%–75%.
- Red blood cell transfusions if severe anemia.
- Address electrolyte deficits according to the following table: *Caution with use in renal failure patients. *Do not exceed 0.5 mEq/kg/h. †Do not exceed 60 mEq/L concentration being infused through a peripheral vein. ‡Administered as a CRI, never as a bolus.*To convert to mg/dL, multiply the mmol/L value by 3.1.†Both the CRI and bolus methods should be used with caution in renal failure. Renal failure patients, decrease dose by 30%-50%.

Recommendations for Intravenous Electrolyte Supplementation in Refeeding Syndrome

Phosphate (Potassium Phosphate = 4.4 mEq K^+ and 3 mmol $PO4^{2-}$)				
Serum Concentrations mmol/L*	**Dose†**	**Monitor Serum Levels**		
0.7-1	0.03 mmol/kg/h	Every 8-12 hours		
0.5-0.7	0.03-0.09 mmol/kg/h	Every 6-8 hours		
<0.5	0.09-0.12 mmol/kg/h	Every 4-6 hours		
Magnesium (Magnesium Sulfate or Chloride)				
	Dose (mEq/kg/d)	**Dose (mEq/kg/h)**	**Dose (mg/kg/d)**	**Dose (mg/kg/h)**
Continuous rate infusion (CRI)	0.75-1 mEq/kg/d	0.02-0.04 mEq/kg/d	125 mg/kg/d	3.7-5.2 mg/kg/h
Bolus	0.16-0.24 mEq/kg		20-30 mg/kg	
Potassium Chloride (2 mEq/mL)				
Serum Concentrations (mEq/L)	**mEq/L KCl to Add to 1 L Fluid**	**Maximal Fluid Infusion Rate (mL/kg/h)**		
3.6-5.0	20	25		
3.1-3.5	28	18		
2.6-3.0	40	12		
2.1-2.5	60	8		
<2.0	80	6		

- The trends of change are more important than the absolute lab values.
- Continue to provide some caloric input as electrolyte abnormalities are being addressed, and closely monitor fluid ins and outs.

CHRONIC TREATMENT

- Slow increase in the caloric amounts until normal intake returns
- The more severe the abnormalities, the slower the increase in caloric support should be.
- The length of time from introduction of calories to REE may be 4-7 days' time.

NUTRITION/DIET

No specific diet can prevent this syndrome. The amount and rate of caloric input result in electrolyte and fluid shifts in susceptible patients.

POSSIBLE COMPLICATIONS

- Repair of hypokalemia and hypocalcemia in hypomagnesemic animals may depend on magnesium replacement.
- Phosphorus supplementation must be gradual (i.e., slow CRI over hours to days) to reduce the risk of renal failure and hypocalcemia.
- Must closely monitor changes in serum electrolyte concentrations and cardiovascular system (ECG and blood pressure) during therapy

RECOMMENDED MONITORING

- Body weight taken daily
- Glucose and electrolyte concentrations q 4-6 h until normalized, then daily during enteral or parenteral feeding
- Hematocrit if hypophosphatemia is present
- Venous blood gases every 6-12 hours until cardiovascular stability is achieved
- Renal parameters and urine output
- ECG and blood pressure until electrolyte concentrations have normalized

PROGNOSIS AND OUTCOME

Guarded to good depending on underlying problem, familiarity with the syndrome, level of patient care, and severity of refeeding syndrome.

PEARLS & CONSIDERATIONS

COMMENTS

Although not common in veterinary animals, a high index of suspicion for the syndrome should be maintained in any depleted animal during the initial period (24 hours to 5 days) of refeeding. This is a potentially fatal syndrome which is exacerbated by our therapeutic intervention of providing nutritional support.

PREVENTION

- Correctly identify fluid and electrolyte abnormalities, and start to correct prior to instituting nutritional support.
- Identify at-risk patients.
- Use caution in return to feeding (e.g., start with 25%-50% of basal energy requirements or 5–10 Kcal/kg/d).
- Monitor electrolytes, blood gas, and renal parameters daily.
- Recognize that some replacement-fluid recommendations assume normal food intake; ill and hospitalized animals often are anorexic and may require less fluid supplementation.

TECHNICIAN TIPS

- Daily physical examinations by the technical staff
- Encouragement to the veterinarians in the use of central lines and frequent monitoring
- Discouragement of the use of forced syringe feedings
- General excellent nursing care such as grooming and ensuring patient comfort

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Red Eye

BASIC INFORMATION

DEFINITION

- Conjunctival, episcleral/scleral, or palpebrai hyperemia
- The term *red eye* does not traditionally apply to redness within the anterior chamber (i.e., hyphema).

SYNONYMS

Conjunctival hyperemia, conjunctival injection, episcleral/scleral hyperemia or injection

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs and cats, no age or gender predisposition

RISK FACTORS

- Trauma
- Systemic infectious or inflammatory diseases
- Coagulopathy
- Current therapy with potentially irritating topical ophthalmic medications (e.g., pilocarpine, neomycin, prostaglandin analogs, aminoglycosides)

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Variable but may include any or all of the following:

- “Red” eye, by definition (layperson's description: ”bloodshot” eye)
- Blepharospasm
- Ocular discharge
- Cloudiness of eye
- Loss of vision

PHYSICAL EXAM FINDINGS

- Conjunctival vessel hyperemia: diffuse conjunctival redness:
  - Usually indicates ocular surface (i.e., superficial) disease, including:
    - Conjunctivitis
    - Superficial keratitis (see and 825)
  - Vessels appear to originate in conjunctival fornix and branch as they approach limbus.
- Episcleral/scleral hyperemia: discrete engorgement and tortuosity of episcleral vessels:
  - Usually indicates intraocular disease (see pp. 1151 and 448), deep corneal disease (see p. 250), or episcleritis/scleritis (see p. 356)
  - Vessels originate near limbus and follow a deep, straight course toward the conjunctival fornix.
- Both conjunctival and episcleral/scleral vessel injection can occur in the same eye. Ocular discharge and blepharospasm are nonspecific signs; other signs depend on the underlying cause of red eye:
  - Blepharitis; hyperemic, swollen eyelids:
    - ± Mucopurulent ocular discharge
    - Normal intraocular examination
  - Conjunctivitis (see pp. 237 and); hyperemic conjunctiva:
    - Chemosis (conjunctival swelling)
    - Ocular discharge
    - Normal intraocular examination
  - Keratitis (see and 825):
    - Corneal opacities (see p. 245)
    - Corneal vascularization (see p. 254)
    - Corneal vessels that cross the limbus and branch suggest superficial corneal disease.

        - Vessels that start at the limbus and form a dense, straight pattern on cornea suggest deep corneal disease and/or intraocular disease.
        - ± Fluorescein dye retention
    - Uveitis (see p. 1151); any or all of the following:
        - Aqueous cells or flare
        - Constricted pupil
        - Abnormal appearance to iris (see p. 624)
        - Hyphema (see p. 571)
        - Fibrin clot in anterior chamber
        - Hypopyon (see p. 583)
        - Low intraocular pressure.
    - Glaucoma (see p. 448):
        - Dilated pupil
        - Diffuse corneal edema
        - ± Buphthalmos (see p. 778)
        - Fundic exam: optic disk cupping
        - Lens luxation (see p. 644): consistent with primary or secondary glaucoma

ETIOLOGY AND PATHOPHYSIOLOGY

Dilation of conjunctival and/or episcleral/scleral vessels:

- Typically inflammatory response to superficial and/or deep ocular disease
- May be caused by passive congestion (e.g., large, space-occupying orbital lesion; see p. 790)

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Initial suspicion comes from history and/or physical examination. Diagnosis of the cause of red eye is achieved with a comprehensive ophthalmic examination.

DIFFERENTIAL DIAGNOSIS

- See Etiology, above.
- A "red" eye may also involve more than one ocular disease (e.g., corneal ulceration with secondary uveitis).

INITIAL DATABASE

Complete ophthalmic examination (see p. 1313), including:

- Schirmer tear test; a low result (<5-10 mm/min) indicates keratocon-junctivitis sicca (KCS).
- Fluorescein stain application; a positive result (stain retention) indicates corneal ulceration.
- Intraocular pressure measurement; elevated level (>30 mm Hg) is diagnostic of glaucoma; level is typically low (<10-15 mm Hg) with uveitis.

ADVANCED OR CONFIRMATORY TESTING

- Variable depending on results of initial examination and testing (i.e., suspected cause)
- Corneal or conjunctival swabs for cytologic examination, ± culture and sensitivity (C&S), for conjunctivitis, corneal ulcers, keratitis, or blepharitis
- CBC, serum chemistry panel, titers for infectious disease, radiography, ultrasonography for certain causes of uveitis (see p. 1151)
- Biopsy of lesion and histopathologic exam for refractory or complex blepharitis or episcleritis/scleritis

TREATMENT

TREATMENT OVERVIEW

Treatment goals are to control/resolve underlying cause, decrease inflammation, eliminate infection if present, achieve appropriate

intraocular pressure if abnormal, eliminate ocular pain, and maintain vision.

ACUTE AND CHRONIC TREATMENT

- Loss of vision is an emergency that requires immediate determination and treatment of underlying cause (see p. 141). Glaucoma, severe uveitis, and severe keratitis should be considered in acute or progressive vision loss concurrent with red eye(s).
- Blepharitis:
  - Determine underlying cause.
  - Patient often needs systemic antibiotic and/or antiinflammatory therapy.
  - See Demodicosis, p. 289; Juvenile Cellulitis, ; Pemphigus Complex, p. 850.
- See Keratoconjunctivitis Sicca, .
- See Conjunctivitis, Cats, p. 237; Conjunctivitis, Dogs, .
- See Corneal Ulceration, p. 250.
- See Uveitis, .
- See Glaucoma, p. 448.
- See Episcleritis/Scleritis, .
- See Orbital Disease, p. 790.

POSSIBLE COMPLICATIONS

Variable depending on underlying condition and cause; may include:

- Loss of eye
- Loss of vision
- Worsening of systemic disease

PROGNOSIS AND OUTCOME

- Variable depending on underlying cause
- Lack of vision at presentation is often a poor prognostic indicator (return of vision uncommon).

PEARLS & CONSIDERATIONS

COMMENTS

Avoid:

- Topical corticosteroids in any eye with positive fluorescein dye retention (or unknown fluorescein status).
- Systemic corticosteroids until preliminary diagnostic tests are performed or a diagnosis is reached, because these drugs are generally contraindicated for treating infectious systemic disease.

CLIENT EDUCATION

Seek veterinary attention promptly at first sign of red eye, because many causes of red eye are globe and/or vision threatening.

SUGGESTED READING

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Recurrent Flank Alopecia, Canine

BASIC INFORMATION

DEFINITION

Skin disorder of unknown etiology characterized by episodes of truncal hair loss with spontaneous regrowth that often occurs on a recurrent basis

SYNONYMS

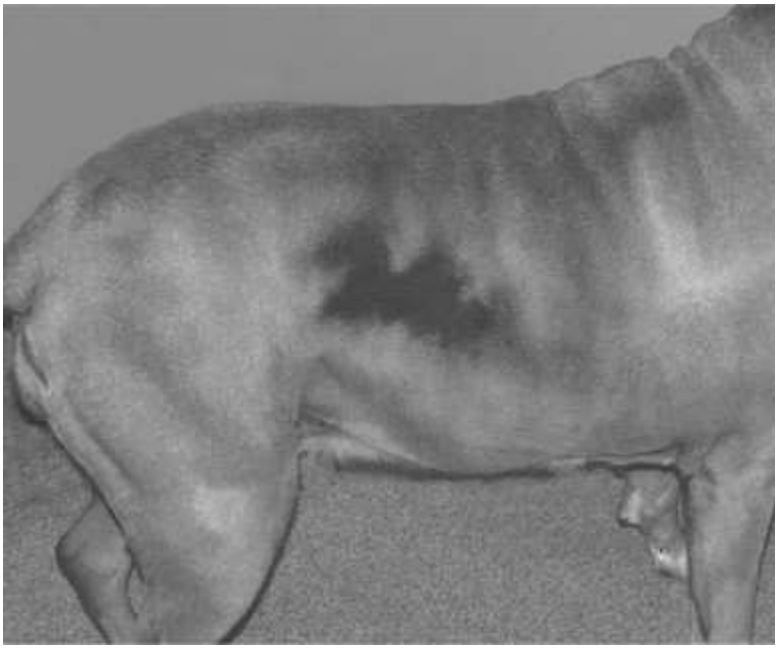
Canine recurrent flank alopecia (CRFA), canine idiopathic cyclic flank alopecia, cyclic follicular dysplasia, seasonal flank alopecia

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs of either sex and any reproductive status can be affected.
- Mean age at onset of first episode is 4 years (range 8 months to 11 years).
- Most dogs have an onset of alopecia between November and March (Northern Hemisphere).

GENETICS & BREED PREDISPOSITION: Boxers may account for approximately half of all cases, but other breeds at high risk include English bulldog, Airedale terrier, and schnauzer (miniature, standard, and giant). Although CRFA seems to affect virtually any breed, this condition appears to be rare to absent in the plush-coat Nordic breeds, German shepherds, and cocker spaniels.



RECURRENT FLANK ALOPECIA, CANINE Recurrent flank alopecia in a boxer. Note characteristic distribution of alopecia and hyperpigmentation.

(Copyright Dr. Manon Paradis.)

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Fairly abrupt onset of bilateral alopecia affecting the thoracolumbar region

PHYSICAL EXAM FINDINGS

- Nonscarring alopecia, usually bilaterally symmetrical, with well-demarcated borders
- Marked hyperpigmentation of the alopecic skin is common.
- The alopecia is usually confined to the thoracolumbar region, but on rare occasions, this condition is seen in association with

alopecia on the dorsum of the nose, base of the ears, base of tail, and perineum.
- Spontaneous regrowth of a normal coat occurs in 3-8 months (range: 1-14 months) in most dogs.
- Most dogs develop recurrent alopecic episodes every year; however, some dogs have an occasional year when the alopecia does not recur.
- The degree of alopecia is variable, with some dogs developing a virtually identical hair loss (size and duration) year after year, and other dogs developing larger areas and/or longer episodes of hair loss as years go by.
- In a few cases, hair regrowth may become less complete after several episodes; it may even progress to an end-stage permanent flank alopecia and marked hyperpigmentation.
- Occasionally a dog may have only one isolated episode of alopecia during its lifetime.

ETIOLOGY AND PATHOPHYSIOLOGY

- The high incidence in some breeds and the familial character of CRFA suggest a genetic influence.
- The seasonal nature and annual recurrence suggest that photoperiod may be involved. The higher incidence of CRFA at higher latitude (around or north of the 45th parallel in the Northern Hemisphere) supports the implication of light exposure in this disorder.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is based on history, clinical findings, and ruling out other differentials (e.g., exclusion of hypothyroidism in dogs >2 years of age). The rapid onset of well-demarcated truncal alopecia with spontaneous hair regrowth in predisposed breeds and the absence of inflammation and pruritus make it quite distinctive.

DIFFERENTIAL DIAGNOSIS

- Endocrinopathies (hypothyroidism, hyperadrenocorticism, hyperestrogenism)
- Other follicular dysplasias
- Telogen defluxion

INITIAL DATABASE

- Thyroid testing for adult dogs
- Other endocrine testing if indicated by history and physical exam findings

ADVANCED OR CONFIRMATORY TESTING

Skin biopsies for dermatohistopathologic examination:

- Nonspecific changes suggestive of endocrinopathies may be observed. In addition, truncated, keratin-filled atrophic primary and secondary hair follicles (“witch's feet”) are suggestive of, but not pathognomonic for, CRFA.
- Biopsies may further support the diagnosis but are sometimes not performed by dermatologists who are confident in the diagnosis based on characteristic lesions and seasonal recurrence.

TREATMENT

TREATMENT OVERVIEW

The goal is to reduce or prevent hair loss.

ACUTE AND CHRONIC TREATMENT

- Oral melatonin, administered at the rate of 3-6 mg/dog PO q 8-12 h for 1-2 months, may be beneficial in up to 50%-75% of cases (whether initiated before or shortly after the onset of alopecia).
- To prevent hair loss, administer melatonin 1-2 months prior to the expected episode of alopecia.
- To shorten the duration of an existing alopecic episode, start melatonin administration as soon as possible after the onset of alopecia.

PROGNOSIS AND OUTCOME

Dogs affected with CRFA are healthy otherwise, and benign neglect is a valuable therapeutic approach.

PEARLS & CONSIDERATIONS

COMMENTS

The unpredictable course of CRFA and the spontaneous regrowth of hair render the evaluation of any therapeutic agent difficult, whether used for preventing the condition or to shorten an existing episode of alopecia.

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Rectoanal Stricture

BASIC INFORMATION

DEFINITION

Uncommon disorder involving narrowing of anal or rectal lumen diameter

SYNONYM

Anorectal stricture

EPIDEMIOLOGY

SPECIES, AGE, SEX: While atresia ani is a congenital failure to form a normal anal opening and is seen in young puppies and kittens, stricture formation is generally a sequela to disease processes that occur in middle-aged to older animals. RISK FACTORS: Anal trauma or surgery

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Tenesmus, diarrhea, hematochezia, and ribbon-like stools
- Animals with advanced or metastatic malignancy may present with weight loss, anorexia, and lethargy.

PHYSICAL EXAM FINDINGS: Stricture is usually palpable on digital rectal examination.

ETIOLOGY AND PATHOPHYSIOLOGY

- Stricture may be related to a primary infiltrative process such as inflammatory, infectious, or neoplastic disease.
- Stricture formation may also be seen secondary to surgery, penetrating trauma, radiation, or enema administration.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is suspected based on presenting history and physical/rectal examination findings. Confirmation of the cause of the stricture may require endoscopy and biopsy.

DIFFERENTIAL DIAGNOSIS

Possible causes of rectoanal stricture:

- Neoplasia:
  - The most common malignant tumor of the rectum is adenocarcinoma (see p. 37).
  - Other tumor types include lymphoma, leiomyosarcoma, and hemangiosarcoma.
  - Benign neoplasia may include adenoma, fibroma, or leiomyoma.
- Inflammatory disease such as colitis
- Infectious disease: histoplasmosis has been reported to cause rectal stricture in one dog.
- Trauma: direct or from bone ingestion
- Scar formation secondary to surgery (e.g., anal sacculectomy, perianal fistula repair, mass excision), enema, or radiation therapy

INITIAL DATABASE

- Gentle digital rectal palpation
- Assessment of location (identifying possible organ of origin), symmetry (circumferential versus focal), pain, and evidence of metastasis (palpation of sublumbar lymph nodes)

- CBC, serum chemistry analysis, and urinalysis: usually within normal limits
- Abdominal radiographs:
  - Potential for visualizing area of stenosis as well as megacolon cranial to stricture
  - Evidence of underlying cause of stricture, metastatic disease (± thoracic radiographs)

ADVANCED OR CONFIRMATORY TESTING

- Contrast radiography may help localize stricture (see p. 1204).
- Abdominal ultrasound can help assess for diffuse metastatic disease.
- Colonoscopy should be used for visualizing extent of stricture formation and to acquire biopsy samples.

TREATMENT

TREATMENT OVERVIEW

Treatment is aimed at increasing luminal size through the strictured area and preventing recurrence by treating the underlying cause.

ACUTE GENERAL TREATMENT

- With the animal under general anesthesia, mild strictures can be dilated using gentle digital or balloon bougienage.
- Treatment with balloon dilation and local triamcinolone injections has been reported to improve clinical signs in dogs with non-neoplastic strictures.
- Surgical intervention, if possible, is indicated to resect stricture or cause of stricture and obtain a definitive biopsy sample:
  - Use a rectal pull-through or dorsal rectal approach.
  - Colostomy has been reported in dogs as an option for rectal obstruction or perforation.

POSSIBLE COMPLICATIONS

Surgical complications include incontinence, dehiscence, infection, and recurrence of stricture or neoplasia.

PROGNOSIS AND OUTCOME

- Prognosis is related to histopathologic findings. Approximately 50% of rectal neoplasms are malignant. Reported outcome for adenocarcinoma is poor.
- Regardless of the underlying etiology, there is a high likelihood for stricture reformation. Multiple balloon or surgical procedures may be required to correct the problem, and this likelihood should be discussed with the owner prior to initiating treatment.

PEARLS & CONSIDERATIONS

COMMENTS

- It is common to cause iatrogenic tears of the rectum or anus during stricture treatment, so care is warranted when performing digital or balloon bougienage.
- If resection of stricture is performed, avoid enema administration for 24 hours prior to surgery to reduce intraoperative fecal contamination (fecal spillage from the anus during surgery).

TECHNICIAN TIPS

- Close observation of the patient's ability to defecate will be required in postoperative/posttreatment period. Adjustments in diet (type and consistency) plus the addition of stool softeners (Metamucil) may be necessary.
- Temporary postoperative/posttreatment fecal incontinence will necessitate good perineal hygiene.

SUGGESTED READING

Webb C, et al: Rectal strictures in 19 dogs: 1997-2005. J Am Anim Hosp Assoc 43:332–336, 2007.

AUTHOR: JANET KOVAK MCCLARAN

EDITOR: RICHARD WALSHAW

Rectal Prolapse

BASIC INFORMATION

DEFINITION

Rectal prolapse is eversion of the anal mucosa or full-thickness rectal wall through the anal opening.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Can occur at any age, but young dogs and cats are most frequently affected.

GENETICS & BREED PREDISPOSITION: Manx cats may be predisposed. RISK FACTORS: Recent perineal surgery ASSOCIATED CONDITIONS & DISORDERS: Any condition that causes tenesmus may be associated with rectal prolapse: gastrointestinal (GI) parasitism; neoplasia of the colon, rectum, or anus; rectal foreign bodies; colitis; perineal hernia; prostatic disease; urinary disease; dystocia.

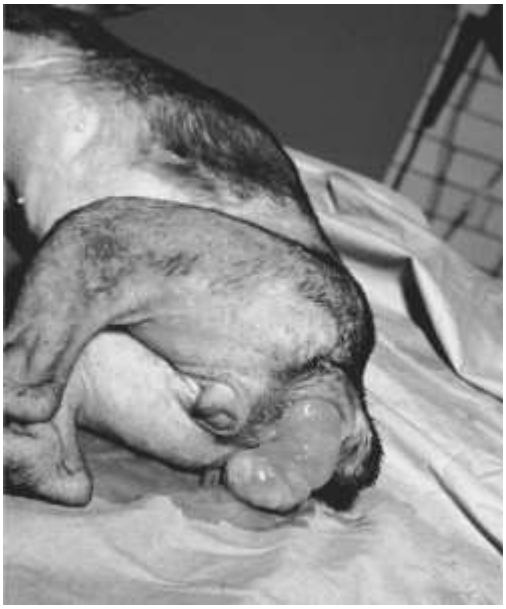
CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Partial prolapse (mucosa only)
- Complete prolapse (all layers of the rectal wall)

HISTORY, CHIEF COMPLAINT

- Visualization of red tissue protruding from anus
- Straining to defecate or urinate (tenesmus)
- Diarrhea



RECTAL PROLAPSE Clinical image of rectal prolapse in a dog.

(Courtesy Dr. Richard Walshaw.)

PHYSICAL EXAM FINDINGS

- Partial prolapse: a few millimeters of red, swollen mucosa protruding through anus
- Complete prolapse: cylindrical mass protruding from anus; tissue may be red, ulcerated, or necrotic.
- Other findings consistent with underlying cause for straining (i.e., enlarged prostate, palpable neoplastic mass, etc.)

ETIOLOGY AND PATHOPHYSIOLOGY

- Animal affected by underlying disease that causes straining
- Repetitively increased intraabdominal pressure from straining causes weakness of perirectal and perianal connective tissue or muscles, resulting in prolapse.
- Inflammation or edema of mucosa may result in more straining and can exacerbate prolapse.
- Prolapsed tissue may become traumatized or desiccate, resulting in ulceration and necrosis.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

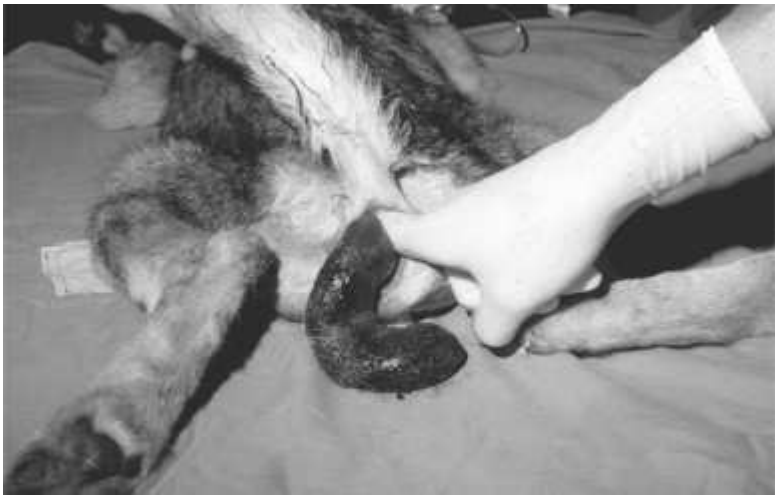
The diagnosis is made by visual inspection and rectal palpation.

DIFFERENTIAL DIAGNOSIS

- Prolapsed intussusception. Therapeutic importance of differentiating from rectal prolapse: prolapsed intussusception generally requires laparotomy, whereas rectal prolapse does not.
- Neoplastic mass protruding from anus

INITIAL DATABASE

- Rectal examination: insert a blunt probe between prolapsed tissue and rectal wall. The probe cannot be passed cranially with rectal prolapse but will pass at least a few centimeters into a fornix created by everted colon in cases of prolapsed intussusception.
- CBC, serum chemistry profile, urinalysis, and urine culture may identify underlying cause of straining and indicate an animal's metabolic status.
- Abdominal radiographs may demonstrate conditions associated with rectal prolapse (i.e., neoplastic masses, prostatomegaly, urinary calculi).
- Fecal analysis for intestinal parasitism



RECTAL PROLAPSE Clinical image of colonic intussusception, an important differential diagnosis for rectal prolapse. In this condition, a digit may be passed into the rectum, as shown in this anesthetized animal. With rectal prolapse, bowel is everted at the anus, not within the colon, and rectal palpation is not possible.

(Courtesy Dr. Richard Walshaw.)

ADVANCED OR CONFIRMATORY TESTING

- Abdominal ultrasonography to identify associated conditions
- Proctoscopy and biopsy to rule out potential underlying causes (colitis, neoplasia); may be indicated in older animals, but is rarely needed in young animals.

TREATMENT

TREATMENT OVERVIEW

Treatment consists of correction of the prolapse by manual reduction (if viable) or surgical resection (if necrotic), and prevention of recurrence by treating the underlying cause of the problem.

ACUTE GENERAL TREATMENT

- Acute treatment with patient under general anesthesia to prevent tenesmus during prolapse reduction.
- Lavage prolapsed tissue with saline and inspect viability.
- Apply lubricant and manually reduce (gentle digital pressure) if tissue is viable.
    - Apply dextrose (50%) to tissue to decrease edema and aid in reduction.
- Place purse-string suture around rectum at mucocutaneous junction to maintain reduction. The purse-string suture should be tight enough to prevent prolapse but should still allow for passage of soft stools. Tightening the suture over a syringe case (3 mL in most small animals is adequate) may prevent overtightening.
- Resection and anastomosis of diseased tissue if tissue is not viable

CHRONIC TREATMENT

- Maintain purse-string suture for 3-5 days, and begin treatment of underlying cause of straining.
- If the patient undergoes resection and anastomosis, he/she should receive a low-residue diet and stool softeners to reduce postoperative straining.
- Perform a colopexy if prolapse repeatedly recurs after appropriate acute treatment.

POSSIBLE COMPLICATIONS

- Continued tenesmus
- Dyschezia, hematochezia
- Recurrent prolapse
- Leakage, dehiscence, and stricture if resection performed

PROGNOSIS AND OUTCOME

Good prognosis if surgically treated and underlying cause reversible

PEARLS & CONSIDERATIONS

COMMENTS

- Place a lubricated finger or small syringe case in rectum while tightening purse-string suture to prevent overtightening.
- Apply a local anesthetic to the rectal tissue after removal of the purse-string suture, which may help prevent recurrence.
- Empirically treat all young animals with rectal prolapse for intestinal parasitism, even if fecal flotation result is negative.

TECHNICIAN TIPS

Important points regarding postreduction/postoperative care:

- Maintain appropriate level of analgesia/sedation:
    - Pain control
    - Prevention of tenesmus (to prevent recurrence)
- Perianal/perineal hygiene:
    - Especially after defecation
    - Warm-pack the area to decrease swelling and ease discomfort.
- Diet:
    - Prevent tenesmus, constipation, and diarrhea.
    - GI diet (e.g., Iams Low Residue) to promote formed but soft stool
    - Stool softener (Metamucil R) to promote pain-free defecation and no tenesmus

SUGGESTED READING

Aronson L: Rectum and anus. In Slatter D, editor: Textbook of small animal surgery, Philadelphia, 2002, WB Saunders, pp 682–708.

Popovitch CA, et al: Colopexy as a treatment for rectal prolapse in dogs and cats: a retrospective study of 14 cases. Vet Surg 23:115, 1994.

AUTHOR: JANET KOVAK MCCLARAN

EDITOR: RICHARD WALSHAW

Radiation Therapy: Adverse Reactions

BASIC INFORMATION

DEFINITION

Radiation reactions are considered acute (or early) if they occur during or shortly after radiation and subside after radiation completion. Reactions with clinical signs that persist over a longer period of time or occur months to years after treatment are considered chronic (or late).

SYNONYM

Radiation complications

EPIDEMIOLOGY

SPECIES, AGE, SEX: Any patient treated with radiation will be at risk for development of radiation reactions.

RISK FACTORS

- Radiation dose, fraction size, radiation energy, overall treatment time, field size, previous surgery, concurrent administration of chemotherapy, and necrotic or unhealthy tissues may influence a patient's risk for the development of adverse radiation reactions. Cats are less likely to have radiation side effects than dogs.
- Site-specific risk factors include:
  - Skin: presence of skin folds, tangential radiation fields, poor nutrition, individual differences, use of bolus, use of electron therapy, coincident infection
  - Head/neck: periodontal disease, coincident infection, concurrent xerostomia
  - Heart: doxorubicin treatment

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Acute effects: depend on total dose, dose per fraction, and overall treatment time
- Chronic effects: depend highly on dose per fraction

HISTORY, CHIEF COMPLAINT: Owners are most likely to report history or complaints in form of physical exam findings listed below.

PHYSICAL EXAM FINDINGS: All physical exam findings are directly related to tissues present within radiation therapy field and usually confined to limits of the radiation treatment field.

- Skin effects:
  - Acute: hyperemia, dry desquamation, moist desquamation, ulceration, necrosis, hair loss, lymphedema, pain
  - Chronic: telangiectasia, fibrosis, necrosis, lymphedema, hyperpigmentation or hypopigmentation, leukotrichia, loss of pliability/flexibility/range of motion, pain, dry desquamation, chronic wound
- Head/neck effects:
  - Acute: stomatitis, mucositis, pharyngitis, esophagitis (erythema, edema, confluent or patchy white/yellow membrane formation), xerostomia, dry/cracked lips, ulceration, pain, difficulty swallowing, secondary infection with bacteria or fungi (soft, curdlike white patches), swelling of parotid/submandibular salivary glands, keratitis, keratoconjunctivitis sicca, blepharospasm, periocular crusting, corneal edema
  - Chronic: osteonecrosis (bone pain, swelling, evidence of infection, exposed bone, nonhealing gingival ulcers), xerostomia, regurgitation, dental caries, keratoconjunctivitis sicca, cataract formation, retinitis, blindness
- Bone effects (chronic): clinical/radiographic evidence of fracture, necrosis, infection, or secondary tumor
- Heart effects (acute/chronic): signs relative to pericarditis, chronic constrictive pericarditis, or restrictive cardiomyopathy due to myocardial fibrosis, such as fever, tachycardia, presence of pericardial effusion, cardiac tamponade, pleural effusion, dyspnea, conduction abnormalities, exercise intolerance, subclinical valvular defects
- Bladder effects (acute/chronic): pain on palpation, clinicopathologic evidence of cystitis (pollakiuria, nocturia, dysuria, hematuria)
- Lung effects (acute/chronic): clinical and radiograph signs compatible with acute pneumonitis and chronic fibrosis (fever, dyspnea, cough, production of sputum, signs of right heart failure if pulmonary hypertension exists). Fibrosis usually, not

always, preceded by pneumonitis.
- Colon/rectal effects (acute/chronic): diarrhea secondary to acute enteritis, hematochezia, sense of urgency, chronic diarrhea, proctitis, stricture, fistula formation secondary to chronic colorectal/anorectal injury
- Central nervous system effects (acute/chronic): signs compatible with location of irradiation field (neurologic deficits, seizures, ataxia, blindness, dementia, somnolence, endocrinopathies)

ETIOLOGY AND PATHOPHYSIOLOGY

- Radiation lesions induced in normal tissues are attributed primarily to loss of specific target cells or clonogenic cells. Hence, acute effects develop in rapidly renewing tissues such as skin, gastrointestinal (GI) tract, or bone marrow.
- This target cell theory also applies to vascular damage as the predominant lesion in chronic effects, as endothelial cells are slowly lost to mitotic death.
- In addition, cytokines induced immediately after irradiation have been shown to contribute to the progression of chronic effects.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Few differentials exist for radiation therapy site-specific side effects short of progression or recurrence of tumor.

INITIAL DATABASE

- Minimum database to rule out metabolic contribution to complications
- Diagnostic imaging (radiographs, CT, MRI) where applicable to determine extent/nature of disease
- Biopsies where necessary to differentiate tumor recurrence from radiation reaction
- Clinician-based assessment: Veterinary Radiation Therapy Oncology Group (VRTOG) Acute/Chronic Radiation Scoring Scheme (see reference)

ADVANCED OR CONFIRMATORY TESTING

Generally not necessary. In people:

- Chronic skin fibrosis measured by tissue compliance meter, ultrasound measurement, or BTC-2000 suction device in humans
- Xerostomia measured by functional radioisotope imaging, salivary flow output, and patient assessment in humans
- Pulmonary function tests for confirmation of decreased lung capacity

TREATMENT

TREATMENT OVERVIEW

- Improving patient quality of life by minimizing pain, establishing return to function, and ruling out tumor recurrence
- Amelioration of acute side effects may decrease risk of chronic side effects for some tissue types.

ACUTE TREATMENT

- Skin effects:
  - Protect irradiated skin from heat, cold, sunlight, friction, and other sources of irritation.
  - Avoid use of tape.
  - Avoid swimming.
  - Clean moist desquamation with aluminum subacetate (Domeboro) soaks, 1/3 strength hydrogen peroxide (1%), or diluted chlorhexidine solution.
  - Use of skin care products anecdotal but include: Aquaphor, Collasate, vitamin A/E ointment, aloe vera gel, Theracare, 1% hydrocortisone ointment, silver sulfadiazine, Miaderm, Biafine, Radioplex.
  - Keep site free of crusts to encourage reepithelialization.
  - Use of ointments preferable to creams or lotions
  - Bandages promote moist environment and are not advised when possible. If necessary, use moisture vapor–permeable dressings (Tegaderm, Mepilex).
  - Antibiotic therapy to control infection, and antiinflammatory therapy to decrease inflammation
  - Pain management and breaks in radiation therapy where necessary

- Head/neck effects:
  - Stomatitis/mucositis/esophagitis:
    - Maintain good oral hygiene.
    - Use of soft, bland diet with decreased amount, increased frequency, and room temperature. Avoidance of salty, acidic foods.
    - Mouthwashes to cleanse and lubricate the oral cavity (saline, sodium bicarbonate solutions, dilute tea, dilute hydrogen peroxide, “magic mouthwash”; avoid alcohol preparations).
    - Topical anesthetics and coating agents such as viscous lidocaine (Xylocaine), sucralfate suspensions, Acemannan-containing gel all proven to ameliorate mucositis. NOTE: viscous lidocaine may burn initially prior to taking effect.
    - Omega-3 fatty acid, arginine, glutamine, and oral zinc supplementation all proven in humans to ameliorate pathologic or clinical evidence of mucositis
    - Antibiotics (aerobic gram-negative bacteria most likely) and/or antifungals topically (chlorhexidine rinse with topical suspension of nystatin) or systemically for secondary infections
    - Narcotic analgesics and nutritional support for severe effects
  - Xerostomia (dry mouth):
    - Increase fluid intake.
    - Maintain good oral hygiene.
    - Use of salivary substitutes (short-lived) or pilocarpine (Salagen) (may have unacceptable side effects), acupuncture, olive oil rinse, subcutaneous amifostine, and autotransplantation of salivary gland tissue to site outside radiation field all reported to ameliorate signs in humans.
  - Acute ocular effects: topical antibiotics and steroids if no corneal ulceration present; topical antibiotics and anesthetics if corneal ulceration present; supplementary eye lubrication
- Acute heart effects: pericarditis managed primarily by prevention. Rest, nonsteroidal antiinflammatory drugs, and mild diuretics often all that is needed during self-limiting, subclinical resolution. Subtotal parietal pericardiectomy if clinical signs do not resolve. Coenzyme Q10 used for prevention in humans.
- Acute bladder effects: maintain patient hydration; increase fluid intake to dilute urine (less irritating). Treat underlying urinary infections, treat bladder spasms (phenazopyridine hydrochloride, Urimax, flavoxate hydrochloride agents, oxybutynin used in human oncology), rule out recurrent tumor.
- Acute lung effects: glucocorticosteroids provide much clinical utility despite lack of published evidence. Rest, oxygen therapy, antibiotics as needed. Supportive care with expectorants and bronchodilators.
- Acute bowel effects: see chronic bowel effects below.
- Acute central nervous system side effects: edema and temporary demyelination usually responsive to antiinflammatory doses of steroids. Anticonvulsants as necessary.

CHRONIC TREATMENT

- Skin effects:
  - Fibrosis: physical therapy, impedance-controlled microcurrent treatment, hyperbaric oxygen, pain management, glucocorticosteroids in the initial setting (limited usefulness for established fibrosis), pentoxifylline ± vitamin E, and superoxide dismutase all are methods to delay or reduce fibrosis in human oncology. Investigational treatments include decorin (inhibitor of transforming growth factor beta [TGF-b]), angiotensin-converting enzyme (ACE) inhibitors, and interferons.
  - Lymphedema: Manual Lymphatic Drainage (specialized massage with specific stroke duration, orientation, pressure, sequence) combined with compression bandages, exercise, skin care, pressure gradient sleeves, and/or pneumatic pumps method to ameliorate lymphedema in human oncology. Diuretics to cause acute reduction in the initial setting (limited usefulness for long-term owing to removal of lymph fluid but not proteinaceous debris from interstitial space). Benzopyrones (coumarin), autologous lymphocyte injection, and selenium proven methods to improve resolution in humans. Of interest but less usefulness, glucocorticosteroids, weight management, hyperbaric oxygen, antibiotic therapy, flavonoids, surgical intervention.
- Chronic head/neck effects:
  - Osteonecrosis (a.k.a., osteoradionecrosis): antibiotics, surgical débridement
  - Esophageal stricture (see p. 365): dilatations and semisolid diet, feeding tubes, hydrocortisone injection at the stricture site
  - Xerostomia: see Acute Treatment above.
  - Cataract formation can be treated with surgical removal.
- Chronic bone effects: surgical intervention, antibiotics. Secondary tumor management as needed.
- Chronic heart effects: antipyretics for fever, centesis for tamponade, pericardiectomy if severe. Medical management by veterinary cardiologist.
- Chronic bladder cystitis/fibrosis: see Acute Treatment above. Surgical intervention for fistula formation.
- Pulmonary fibrosis ameliorated by captopril in human oncology. Oxygen and glucocorticosteroids as needed.
- Chronic bowel effects: initial management with increased dietary fiber and diphenoxylate (Lomotil) or loperamide. Addition of opioid analgesics titrated to effect. Topical viscous lidocaine for anorectal irritation. Glucocorticosteroid-containing suppositories (ProctoFoam, Canasa) for acute inflammation. Sucralfate or short-chain fatty acid (butyrate) enemas for bleeding. Topical formalin, topical amifostine, coagulation with electrocautery, laser therapy, argon plasma beam coagulation,

and hyperbaric oxygen for refractory bleeding in human oncology.
- Late central nervous system side effects: glucocorticosteroids (dexamethasone) ideal in early onset radiation necrosis. May consider surgical resection if area of necrosis is localized.

DRUG INTERACTIONS

- Concurrent use of some chemotherapeutics may exacerbate radiation side effects.
- Concurrent use of antioxidants may interfere with radiation cell kill.

POSSIBLE COMPLICATIONS

- Skin effects: progression of moist desquamation to full-thickness necrosis and secondary infection, necessitating surgical débridement. Unrelenting fibrosis or lymphedema, necessitating surgical intervention.
- Oral cavity effects: *Candida albicans* yeast infection can increase severity of stomatitis/mucositis. Rare reports of trismus (contractions of muscles of mastication) with reduced capacity to open mouth.

RECOMMENDED MONITORING

Advise recheck of patient at 1, 2, 3, 5, 7, 9, and 12 months and every 3-6 months post radiation therapy completion.

PROGNOSIS AND OUTCOME

Prognosis for most acute radiation reactions is excellent if managed efficiently and in a timely manner. Prognosis for most late radiation reactions is guarded to poor for complete recovery. Prevention of late radiation reactions is of great concern during radiation therapy planning.

PEARLS & CONSIDERATIONS

COMMENTS

- Use VRTOG Toxicity Criteria Scale to document reactions.
- This review is not all inclusive. Consult with veterinary radiation oncologist as need arises.

PREVENTION

- Use of intensity-modulated radiation therapy/image-guided radiation therapy/conformal radiation therapy techniques, to allow increased dose to tumor while also increasing normal tissue sparing
- Acute skin effects: reduce skin folds, remove bolus where necessary, avoid topical agents immediately prior to radiation therapy, use higher-energy radiation, and ensure surgical wounds have healed prior to initiation of radiation therapy.
- Chronic skin effects: early detection and treatment
- Head/neck effects: preradiation therapy dental prophylaxis and removal of unhealthy teeth to decrease severity of mucositis and risk of osteonecrosis. Amifostine as a radiation protector routinely used to prevent development of xerostomia (dry mouth) in humans. Ocular: tape eyelids open for anterior megavoltage beam fields to the eye to decrease dose to cornea and conjunctiva (otherwise, the eyelids will serve as a site of radiation dose buildup, increasing the radiation dose delivered to the cornea).

CLIENT EDUCATION

- Teach family members when to expect and how to manage acute effects. Promote role of radiation therapist in client education and side-effect management.
- Prepare notebook with photographs of radiation side effects as a tool for client education. Use serial photographs to display effects as they heal with time.
- Use handouts describing potential effects and management to encourage client information recall.

SUGGESTED READING

Bruner DW, Haas ML, et al: Manual for radiation oncology nursing practice and education, ed 3, Pittsburgh, 2005, Oncology Nursing Society.

Cox JD, Ang KK: Radiation oncology: rationale, technique, results, ed 8, St Louis, 2003, Mosby.

Dow KD, Bucholtz JD, Iwamoto R, et al: Nursing care in radiation oncology, ed 2, Philadelphia, 1997, WB Saunders.

LaDue T, Klein MK: Toxicity criteria of the veterinary radiation therapy oncology group. Vet Radiol Ultrasound 42:475– 476, 2001.

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Rabies

BASIC INFORMATION

DEFINITION

Fatal polioencephalitis of warm-blooded animals and humans caused by a *Lyssavirus* sp. and generally transmitted by the bite of an infected mammal

SYNONYMS

Hydrophobia, rage

EPIDEMIOLOGY

SPECIES, AGE, SEX: Warm-blooded animals of all ages are susceptible:

- Foxes, coyotes, wolves, and some rodents are highly susceptible.
- Moderately susceptible species include dogs, cats, horses, sheep, goats, and humans.
- In the United States, cats are the domestic species most frequently reported rabid, with −200−300 cases/year.
- Birds and opossums have a low susceptibility.
- Rabies has been reported in ferrets, rabbits, and one guinea pig.
- Often endemic in wild animals, with periodic outbreaks (epizootics)
- In the United States, the most important species-adapted strains are in the fox, raccoon, skunk, and bat.
- Salivary gland infections occur in vampire bats without producing clinical signs in the bats, resulting in prolonged viremia. Insectivorous bats may also be infected.

RISK FACTORS

- Contact with wildlife, especially raccoons, skunks, bats, and foxes
- Lack of vaccination against rabies
- Exposure to aerosols in bat caves
- Modified live-virus rabies vaccines used in immunocompromised animals

CONTAGION & ZOONOSIS

- Highly zoonotic disease
- Transmission is most commonly by bite.
    - The risk of human infection is far greater through a rabid animal's bite (5%-80%) than a scratch (0.1%-1%).

GEOGRAPHY AND SEASONALITY

- Worldwide
- Rabies-free regions include New Zealand, some Caribbean islands, the British Isles, parts of Scandinavia, Japan, and Hawaii.
- Rabies is a disease of wildlife in the United States:
    - Raccoons: mainly eastern part of the United States but now spreading west
    - Skunks: mainly in California and the north central and south central states
    - Bats: 48 contiguous United States and responsible for most human cases in the last 20 years
    - Foxes: Arctic fox in Alaska, red and gray fox in southeast United States
- The dog is the primary species involved in transmission of rabies in the Southern Hemisphere.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Clinical signs can be variable but predominantly arise from central nervous system (CNS) dysfunction.

- Prodromal form:
    - Characterized by a change in behavior, which may include anxiety, solitude, and apprehension

    - Fever may be present.
    - Pruritus may be present at the site of exposure.
    - Lasts 2-3 days
- Paralytic (dumb) form (majority of canine cases, minority of feline cases): o Characterized by lethargy, difficulty swallowing, ptyalism, voice or bark change, dropped jaw, and lower motor neuron paralysis, often first in the wounded limb
    - Lasts 1-7 days, from onset of overt signs to death
- Furious form (majority of feline cases, minority of canine cases):
    - Characterized by aggression, biting, altered voice, paralysis, seizures, and ataxia
    - Hyperesthesia and hyperresponsiveness to auditory and visual stimuli are possible
    - Lasts 2-4 days, from onset of overt signs to death

HISTORY, CHIEF COMPLAINT

- History of wound may or may not be present:
    - Given the pathophysiology of rabies, neurologic clinical signs beginning within 1 week of the occurrence of a wound are extremely unlikely to be related to rabies infection via the wound.
- Behavioral changes are very common and can be varied:
    - Aggression, viciousness, irritability, excitability, nervousness, apprehension, and anxiety
    - Abnormal or erratic behaviors, such as licking, biting, wandering, disorientation, ataxia, seizures, or paralysis
- Ptyalism and change in bark
- No clinical signs; exposure is suspected but not confirmed.

PHYSICAL EXAM FINDINGS: Onset of clinical signs is variable in timing: signs occur 2 weeks to several months after exposure. Signs include fever, dropped jaw, ptyalism, inability to swallow, and mandibular and laryngeal paralysis. Lower motor neuron limb signs, ataxia, and cranial nerve deficits may be present.

ETIOLOGY AND PATHOPHYSIOLOGY

- Single-stranded RNA virus of the genus *Lyssavirus,* family Rhabdoviridae
- Transmission:
    - Virus within saliva is transmitted via a wound or mucous membranes.
    - Inhalation of aerosolized virus may occur with exposure to bats.
    - Ingestion of infected tissues is also possible but rare.
    - Transmission has also occurred in humans through organ transplantation.
- Virus replicates in local tissues, where it enters neuromuscular junctions and neurotendinous spindles.
    - Virus is vulnerable to immune-mediated destruction (e.g., vaccine-induced) in local tissues but becomes protected once it reaches peripheral nerves or the CNS.
- Spreads by intraaxonal flow through peripheral nerves to the spinal cord and brain. Replicates within the CNS and then moves outward through peripheral, sensory, motor, and cranial nerves.
- Large amount of virus present in salivary glands, where it is shed. Salivary virus excretion begins up to 2 weeks before the onset of neurologic signs.
- The incubation period varies and depends on the innervation at the bite site, distance of the bite site to the CNS, and virus variant and amount of virus in the exposure; can range from 2 weeks to as long as 6 months or more.
- Once clinical signs are apparent, death ensues within 10 days.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is suspected in any animal with an unknown or incomplete rabies vaccination history that develops acute neurologic signs. Confirmation requires direct IFA of brain or nervous tissue.

DIFFERENTIAL DIAGNOSIS

- Encephalitis: viral (canine distemper, feline leukemia virus, feline immunodeficiency virus, feline infectious peritonitis); immune-mediated (e.g., granulomatous meningoencephalitis); rarely, protozoal, rickettsial, bacterial, fungal
- Pseudorabies
- Toxicity (e.g., lead)
- Cerebral cysticercosis caused by larval *Taenia solium* mimics rabies in dogs.
- Portosystemic shunt
- Hypoglycemia
- Neoplasia

- Trauma
- Causes of ptyalism (see p. 930)

INITIAL DATABASE

- The clinical suspicion of rabies is based on history and physical examination.
- CBC, serum chemistry panel, and urinalysis are unhelpful.

ADVANCED OR CONFIRMATORY TESTING

- Cerebrospinal fluid (CSF) analysis may show nonspecific increases in protein and leukocytes.
- Direct IFA test of nervous tissue is the confirmatory test of choice:
  - Chill—do not freeze—the body or brain of any dead/euthanized rabies suspect.
  - Immediately submit the brain to a state-approved laboratory for rabies IFA testing.
  - Use extreme caution in obtaining samples and shipping specimens; zoonosis can occur if rabies virus is aerosolized (e.g., when an electric saw is used for opening the skull and proper protection is not used) or is inadvertently inoculated.
- A new reverse transcriptase PCR is useful with small samples such as saliva and spinal fluid and has been shown to be as rapid as the IFA test.
- Direct IFA testing of dermis: skin biopsy of sensory vibrissae of the maxillary area should not be used (false-negative results).

TREATMENT

TREATMENT OVERVIEW

- Invariably fatal; recovery is extraordinarily rare.
- Suspects must be confined and quarantined.
- The first reported survival of a human who did not receive rabies pre- or postexposure prophylaxis was recently described. The case has prompted further exploration of the treatment she received, termed the “Wisconsin Protocol.” Rifampin, amantadine, and the induction of a ketamine/mid-azolam coma were the mainstays of treatment.

RECOMMENDED MONITORING

- Management of rabies suspects varies with immunization status and local laws. The attending veterinarian should contact the local state veterinarian.
- Most public health laws require a 10-day confined observation period after human exposure from a suspected dog or cat:
  - Virus shedding in saliva before the onset of neurologic signs in infected animals is usually 1-5 days but may be up to 13 days.
- All rabies suspects must be securely confined and monitored for behavioral changes and/or neurologic signs suggestive of rabies.
- A healthy dog or cat that bites or scratches an individual should be confined and monitored for 10 days:
  - If clinical signs do not develop within 10 days of bite/scratch, there has been no exposure to rabies virus.
  - If clinical signs consistent with rabies develop during the 10-day quarantine period, the animal must be euthanized and its brain submitted immediately for examination. If infection is confirmed within 24-48 hours, there is adequate time to begin human postexposure prophylaxis.
- Unvaccinated dogs or cats that are exposed to a known rabid animal or to any bat or wild, carnivorous mammal:
  - Typically the animals are placed in quarantine for up to 6 months.
  - The animals must be monitored for the onset of clinical signs (with vaccination 1 month prior to release) or euthanized immediately at presentation or at the time of onset of clinical signs consistent with rabies.
- Vaccinated dogs or cats that are exposed to a known rabid animal or to any bat or wild, carnivorous mammal:
  - Immediate revaccination for rabies is indicated.
  - A period of monitoring must follow, typically for 45 days. When a dog or cat with an expired rabies vaccination status is exposed to a rabid animal, individual factors will determine the recommended course. Clinicians should contact the state veterinarian.

PROGNOSIS AND OUTCOME

- Fatal
- Cats and dogs will typically succumb within 7-10 days after onset of clinical signs.
- Rare cases of recovery in dogs, cats, and humans

- Experimental treatment with nanoviri-cides has shown a 30% survival rate compared to standard treatment (0% survival); currently being investigated by the Centers for Disease Control and Prevention.

PEARLS & CONSIDERATIONS 

COMMENTS

- If clients are concerned regarding possible or known human exposure to rabies, they must see their physician immediately.
- Clinicians should notify the local public health official.
- Signs take weeks to months to develop after exposure, but once signs are present, death ensues quickly (<2 weeks).
- Travel to rabies-free areas has been facilitated by a vaccinate-microchip-and-blood test protocol that shows adequate neutralizing antibody levels (e.g., >0.5 IU/mL) and no clinical signs of rabies typically over a 6-month period prior to departure. This reduces the burden of travel on the pet (previously a 6-month quarantine in the destination country/state). The specific jurisdiction can provide detailed requirements (e.g., for the United Kingdom: http://www.defra.gov.uk/wildlife-pets/pets/travel/pets/index.htm).
- A new Rabies Rapid Screen Saliva test is being marketed by Dyne Immune but has not undergone sensitivity and specificity testing at this time and cannot be recommended until more data are published.

PREVENTION

- All dogs and cats should be vaccinated for rabies after 12 weeks of age, again at 12 months of age, and then every 3 years or yearly depending on state regulations.
- An immediate booster vaccination in immunized dogs and cats exposed to rabies is advised.
- Cats should only receive inactivated vaccines; do not use modified live virus (MLV) vaccines in cats.
- Disinfect contaminated cages, food dishes, and instruments with a diluted solution of 1 part bleach to 32 parts tap water.

TECHNICIAN TIPS

- Gloves should be worn during examination of all unknown or unvaccinated animals and during examination of bite wounds of unknown origin as a protection against rabies.
- The classic vicious, “foaming at the mouth” image is only true in some 10% of rabid dogs. A majority of dogs with rabies are lethargic and poorly responsive but highly infectious. Therefore, strict precautions to avoid being bitten are wananted around animals with these signs.

CLIENT EDUCATION

- Keep pets from roaming (“leash laws”).
- Inform clients of state and local policies.
- Advise the client to bring animal to a veterinarian immediately if exposure is suspected. With human exposure, individuals should immediately contact a physician.

SUGGESTED READING

Centers for Disease Control and Prevention: http://www.cdc.gov/ncidod/dvrd/rabies/

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Systemic Lupus Erythematosus

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

A multisystemic autoimmune disease affecting at least two different organ systems

EPIDEMIOLOGY

SPECIES, AGE, SEX: More commonly reported in dogs than cats; young to middle-aged animals are predisposed.

GENETICS & BREED PREDISPOSITION

- Systemic lupus erythematosus (SLE) is clearly heritable in dogs.
- German shepherds may be overrepresented.

GEOGRAPHY AND SEASONALITY: Exposure to UV light may trigger cutaneous lesions.

ASSOCIATED CONDITIONS & DISORDERS: When additional clinical signs occur, it is often difficult to determine if a concurrent disease is present or instead represents an additional manifestation or complication of SLE or its treatment.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: The diagnosis of SLE is made when any three of the following occur concurrently or over any period of time:

- Cutaneous lesions, especially skin exposed to sunlight and/or at mucocutaneous junctions
- Oral mucosal ulcers
- Nonseptic, nonerosive polyarthritis
- Glomerulonephritis
- Hemolytic anemia and/or thrombocytopenia
- Leukopenia
- Polymyositis or myocarditis
- Serositis (nonseptic inflammatory effusion in the abdominal, pleural, or pericardial cavity)
- Neurologic disorder (seizures, psychosis, or polyneuritis)
- Significant serum antinuclear antibody (ANA) titer

HISTORY, CHIEF COMPLAINT

- Lameness is the most common primary complaint in dogs.
- Nonspecific lethargy and poor appetite
- Skin lesions
- Signs may wax and wane, confusing response to treatment.

PHYSICAL EXAM FINDINGS

- Lameness with swollen, painful joints. The carpi, tarsi, elbows, and stifles are most frequently involved.
- Fever
- Lymphadenopathy and/or splenomegaly
- Cutaneous lesions: erythema, scaling, crusting, depigmentation, and alopecia. Lesions may develop on the skin, mucocutaneous junctions, and oral cavity.

ETIOLOGY AND PATHOPHYSIOLOGY

- SLE occurs when a stimulus triggers the appropriate susceptibility genes in a patient.
- Triggering factors may include vaccination, drug administration, stress, infection, or exposure to UV radiation.
- SLE patients produce antibodies directed against a broad range of nuclear, cytoplasmic, and cell-membrane molecules. Antibodies against the patient's own DNA are measured with the ANA test.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis of SLE is not based on a single test but on the constellation of clinical signs (see Disease Forms/Subtypes, above) and exclusion of other possible etiologies.

DIFFERENTIAL DIAGNOSIS

- Tickborne disease
- Neoplasia and paraneoplastic syndromes
- Bacterial, fungal, or viral infection
- Other immune-mediated diseases

INITIAL DATABASE

- CBC, including manual differential: may show anemia, leukocytosis, or leukopenia
- Platelet count: may be normal or low
- Serum biochemical profile: abnormalities reflect the site of inflammation (e.g., azotemia and hypoalbuminemia with glomerular involvement)
- Urinalysis: proteinuria is possible
- Urine protein/creatinine ratio
- Urine culture and sensitivity (C&S)
- Skin biopsies: may reveal inflammatory infiltrates at the dermoepidermal junction and vacuolar change in the basal columnar cells
- Radiographs of affected joints: may reveal nonerosive joint swelling
- Arthrocentesis of multiple joints: may reveal sterile neutrophilic inflammation
- Serum ANA titer:
    - Serum ANA commonly stated as a requirement for the diagnosis of SLE, but sensitivity and specificity of this test are not known in the dog and cat.
    - Normal ranges are determined by individual laboratories.
    - False-positive results can occur with various medications (nonsteroidal antiinflammatory drugs [NSAIDs], antibiotics, others).
    - False-positive or false-negative results can occur as a result of variable laboratory standardization, variable quality control, and other factors.
- Lupus erythematosus (LE) cell test: rarely useful
- Thoracic radiographs: may reveal pleural or pericardial effusion (usually subtle)
- Abdominal ultrasonography: usually normal
- Tickborne disease titers to rule out diseases that can mimic SLE (glomerulonephritis, polyarthritis, hematologic changes, etc.)
- Cats: feline leukemia virus (FeLV) and feline immunodeficiency virus (FIV) serologic tests

ADVANCED OR CONFIRMATORY TESTING

- see Disease Forms/Subtypes, above
- Coombs' test: usually negative
- Platelet autoantibodies: rarely useful
- Rheumatoid factor: usually negative
- Immunohistologic evaluation of skin biopsies (immunoperoxidase and immunofluorescent staining): may demonstrate immunoglobulin and complement deposits at the epidermal basement membrane, which are specific for immune-mediated dermatopathies.

TREATMENT

TREATMENT OVERVIEW

At least three aspects of treatment should be considered:

- Resolve clinical signs.
- Prevent renal failure.
- Realize that because of the natural waxing and waning of the disease, aggressive therapy may not be indicated for all cases.

ACUTE GENERAL TREATMENT

- Prednisone/prednisolone, 1 mg/kg PO q 12-24 h initially
- With severe disease, the addition of azathioprine, 2.2 mg/kg PO q 24 h, should be considered.
- Proteinuria may be lessened with enalapril, 0.5 mg/kg PO q 12 h, along with dietary protein optimization/restriction; omega-3 fatty acid supplementation and low-dose aspirin, 0.5 mg/kg q 12 h, may also be added.
- Closely monitor for gastrointestinal (GI) ulcers if NSAIDs and corticosteroids must be used together.

CHRONIC TREATMENT

- Treat the patient until all clinical and laboratory abnormalities have resolved, then attempt to taper drugs.
- In general, decrease doses by half every 2-4 weeks while monitoring clinical and laboratory abnormalities.
- The minimum duration of immunosuppressive therapy should be 4-6 months.
- If signs recur during drug taper, increase level to the previous dose, and attempt to taper more slowly.

BEHAVIOR/EXERCISE

Avoid outdoor activity and/or use topical sunscreen for patients showing cutaneous or mucocutaneous lesions.

DRUG INTERACTIONS

- Concurrent NSAIDs and corticosteroid administration should be avoided owing to the potential for GI ulceration.
- Prolonged administration of azathioprine may cause bone marrow suppression. To reduce the risk, administration q 48 h is recommended once clinical signs and laboratory abnormalities have resolved.

POSSIBLE COMPLICATIONS

- Progressive renal insufficiency
- Infections (such as urinary tract infection) from long-term immunosuppression

RECOMMENDED MONITORING

- If prednisone is administered, monitor body weight closely and avoid obesity.
- If azathioprine is administered, monitor CBC every 2 weeks while azathioprine is being administered daily. Bone marrow suppression is unusual when azathioprine is tapered to 2.2 mg/kg q 48 h; in this case, monitor CBC every 2-3 months.
- If immunosuppressive medications are needed chronically, a urine culture is indicated every 3 months even in the absence of clinical signs of infection.
- Monitor CBC, serum biochemistry profile, and urinalysis every 3 months once in remission.
- Serum ANA may be useful to detect relapse.

PROGNOSIS AND OUTCOME

- Not well-known; many cases wax and wane
- Good for most cases
- Progressive renal disease indicates guarded prognosis

PEARLS & CONSIDERATIONS

COMMENTS

- The diagnosis of SLE is not based on a single test but on the constellation of clinical signs and exclusion of other possible etiologies.
- Treatment with doxycycline is useful to exclude infectious causes of polyarthropathy.
- Arthrocentesis: perform arthrocentesis on at least three joints, even if not swollen or painful.
- Biopsy of skin lesions must include intact epithelium. Ulcerated lesions are inherently nondiagnostic. Erythematous areas adjacent to ulcers yield the most conclusive results.
- Many animals are euthanized not from progressive disease but due to adverse effects of corticosteroids. Avoid obesity, and routinely monitor for infection of the skin and urinary tract.
- Combination immunosuppressive therapy with azathioprine is often more effective and has fewer adverse effects than prednisone/prednisolone alone.

TECHNICIAN TIPS

Many of the effects of SLE, notably polyarthritis, may be painful. Patients showing clinical signs that are known or suspected to be caused by SLE should be handled and walked as gently as possible, with an awareness that pain may cause them to be uncooperative or aggressive even with handling that would be normal for a healthy animal.

PREVENTION

- Although a link has not been proven, future vaccinations should be limited to those considered absolutely essential.
- Stressful circumstances should be avoided if possible to minimize risk of recurrence.

CLIENT EDUCATION

- Routine monitoring should be scheduled to detect relapse of disease and adverse effects of immunosuppressive medications.
- Many dogs live normal lives after the diagnosis.

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Systemic Inflammatory Response Syndrome

BASIC INFORMATION

DEFINITION

- A systemic dysregulated inflammatory process which leads to disorders of microcirculation, organ perfusion, and finally to organ dysfunction. Untreated, systemic inflammatory response syndrome (SIRS) leads to multiple organ dysfunction syndrome (MODS; see 732) and death.
- SIRS is defined clinically as the presence of two or more of the following conditions in dogs and cats:
  - Dogs: body temperature > 40°C or < 38°C; heart rate > 120 bpm in a calm, resting dog; hyperventilation or PaCO2 < 30 mm Hg; and white blood cell (WBC) count > 18,000/mm^3 or < 5000/mm^3 or > 5% immature (band) forms.
  - Cats: body temperature > 40°C or < 38°C; heart rate > 140 bpm in a calm, resting cat; respiratory rate >20 breaths per minute or PaCO2 < 28 mm Hg; and WBC count > 18,000/mm^3 or < 5000/mm^3 or > 5% immature (band) forms.
  - SIRS may or may not be associated with infection.

EPIDEMIOLOGY

SPECIES, AGE, SEX: There are no species, age, or sex predilections.

HISTORY, CHIEF COMPLAINT: May include vague complaints such as lethargy, anorexia, vomiting, or diarrhea or may include a specific event (i.e., trauma, burn injury, heat stroke).

PHYSICAL EXAM FINDINGS

- Often varied and may include generalized depression, fever, tachycardia, or tachypnea.
- By definition, findings associated with an underlying inflammatory condition (i.e., pancreatitis, severe polytrauma) and two or more of the four criteria already listed are expected in animals with SIRS.
- Specific physical exam findings depend on the underlying cause of the SIRS.

ETIOLOGY AND PATHOPHYSIOLOGY

- SIRS can arise from a number of causes which commonly include sepsis, pancreatitis, burns, massive trauma (e.g., hit by car, fall from high elevation, attack by other animal), hypovolemic shock, immune reactions (autoimmune disease), heat stroke, and tissue ischemia of various causes.
- Inflammation is a response to infection, antigen challenge, or tissue injury that is designed to eradicate microbes or irritants and potentiate tissue repair; however, excessive inflammation may lead, via SIRS, to physiologic decompensation, organ dysfunction, and death.
- A balance normally exists among proinflammatory cytokines and antiinflammatory cytokines; however, for cases in which the proinflammatory response predominates, severe systemic inflammation may ensue as typified by SIRS.
- In addition to high circulating cytokine levels, systemic inflammation is also associated with activation of the clotting cascade and release of vasoactive mediators such as nitric oxide (NO).
  - High systemic cytokine levels may result in myocardial dysfunction, altered intracellular oxygen utilization, and direct inflammatory injury.
  - Activation of the clotting cascade can cause microvascular thrombosis and tissue hypoperfusion.
  - Increased production of NO and metabolites can lead to peripheral vasodilation, decreased peripheral vascular resistance, and hypotension.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis of SIRS is based upon having two or more of the following criteria: the presence of tachycardia (or bradycardia in cats), fever or hypothermia, tachypnea, and a leukocytosis/leukopenia with or without a left shift in a patient who has a condition known to incite the systemic release of inflammatory mediators.

DIFFERENTIAL DIAGNOSIS

SIRS is a catch-all phrase for systemic inflammation, multiple causes are possible.

INITIAL DATABASE

Main goal is to determine the source of the systemic inflammatory response:

- CBC: by definition, will show either a WBC count >18,000 or <5000/mcL or will show the presence of >5% band forms (immature neutrophils). Thrombocytopenia and evidence of hemoconcentration may be present.
- Serum biochemistry panel: commonly shows electrolyte abnormalities, hypoalbuminemia, hyperglycemia or hypoglycemia, hyperbilirubinemia, elevated blood urea nitrogen (BUN)/creatinine (azotemia), and/or elevated liver enzymes, depending on the source of the inciting problem and extent of inflammatory response's effects on visceral organs (progression towards MODS).
- Urinalysis: isosthenuria (normal free water excretion versus renal compromise if azotemia is present simultaneously), concentrated urine (if dehydration/hypovolemia and normal renal function), glucosuria (stress, diabetes mellitus), proteinuria (systemic inflammation, urinary tract inflammation, glomerulopathy), and cellular casts (tubular damage) may be seen.
- Urine culture and sensitivity (C&S) is indicated in animals with SIRS, even in the absence of an active urine sediment.
- Blood cultures should be considered.

ADVANCED OR CONFIRMATORY TESTING

Not specific, depends on disease/injury

TREATMENT

TREATMENT OVERVIEW

- In managing an animal with SIRS, there are three essential treatment principles:
  - Hemodynamic stability and support of acute life-threatening organ dysfunction
  - Prolonged support of vital organ function using interventions that minimize iatrogenic injury
  - Modulation of the host-based inflammatory response with interventions that target its specific mediators
- The specific therapeutic goals for treating the systemic inflammatory response syndrome depend on the underlying cause.

ACUTE GENERAL TREATMENT

- IV fluids (crystalloids and colloids) are used for treating hypovolemia and electrolyte abnormalities. During treatment, monitor and maintain electrolytes, BP, and central venous pressure (i.e., mean arterial pressure should be maintained above 60 mm Hg, and central venous pressure should be maintained above 5 mm Hg). Dextrose-containing solutions may need to be added to the treatment regimen if the patient is hypoglycemic; however, hyperglycemia should probably be avoided because an increase in mortality has been associated with hyperglycemia in humans with critical illness. Blood products (plasma, whole blood, and/or packed red blood cells [RBCs]) may need to be used if continued blood loss is documented (see 1347).
- Crystalloid fluids: initial shock dose of 90 mL/kg (dog), 70 mL/kg (cat). Administer this dose IV as a bolus of one-third of the total amount. Then reassess the patient (i.e., measure BP, heart rate), and administer the remainder of the shock dose if the measured parameters have not normalized or substantially improved.
- Colloid fluids: colloids are useful when hypoperfusion and/or hypotension persist and when the shock dose of fluids has already been given as crystalloids. Administer Hetastarch (or other colloid) IV either as a bolus or as a constant rate infusion. A dose for initial bolus is 10-20 mL/kg in dogs and 10-15 mL/kg in cats (should be given over 10-15 minutes in a cat, because it has been associated with nausea). Administer a constant rate infusion of 20 mL/kg per day after the initial bolus if the patient's disease process and cardiovascular status require continued colloid therapy. In humans, coagulopathies have been associated with the use of hetastarch. Therefore, colloids should be used with caution in patients with known coagulopathies.
- Fresh frozen plasma transfusion: 10 mL/kg
- Whole blood transfusion: 20 mL/kg should be given over 4 hours and can be given faster if the patient requires it because of active bleeding; monitor for transfusion reactions (fever, tachypnea, vomiting; see pp. 1347 and 1111).
- Packed RBC transfusion: dose of 10 mL/kg, at a rate of over 3-4 hours; can be given faster if patient requires the transfusion because of active bleeding or hemolysis; monitor for transfusion reactions (fever, tachypnea, vomiting; see pp. 1347 and 1111).
- Antimicrobial therapy may be necessary if bacterial translocation or subsequent infections are suspected as possible complications (e.g., transition towards sepsis). Type and dosage of antibiotic depends on suspected source of infection. For example, bacterial translocation from the gastrointestinal (GI) tract, as can occur after prolonged hypotension or a primary GI insult (e.g., parvoviral enteritis), should be treated with a combination of ampicillin, 22 mg/kg IV q 8 h, and either enrofloxacin, 5 mg diluted 1:1 in sterile water and given slowly IV q 12-24 h (q 24 h maximum in cats, owing to retinal toxicity risk; with caution in patients < 6 months old); or gentamicin, 5-6 mg/kg IV q 24 h (only if renal function is adequate and patient is fully hydrated).

- Corticosteroids are generally contraindicated for patients with SIRS unless relative adrenal insufficiency is suspected.

PROGNOSIS AND OUTCOME

The prognosis and outcome for SIRS depend on the underlying cause and its severity.

PEARLS & CONSIDERATIONS

COMMENTS

SIRS caused by a noninfectious etiology may nevertheless progress to sepsis due to development of a nosocomial infection.

SUGGESTED READING

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Systemic Hypertension

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

A sustained elevation in the arterial blood pressure (BP). In dogs and cats, systemic hypertension is suspected if sustained systolic BP > 160 mm Hg, diastolic BP > 95 mm Hg, or both.

SYNONYM

Arterial hypertension

EPIDEMIOLOGY

SPECIES, AGE, SEX: Systemic hypertension occurs in both dogs and cats, and there is no significant age or sex predisposition in either species. However, some systemic diseases commonly associated with systemic hypertension (e.g., chronic kidney disease, hyperthyroidism) are more common in older animals.

GENETICS & BREED PREDISPOSITION: There is no breed predisposition in cats. Sighthounds (e.g., deerhounds, Irish wolfhounds) have higher normal BP ranges than other breeds. Although essential hypertension has been diagnosed in one family of dogs, systemic hypertension usually occurs secondary to other diseases and as such is not inherited.

ASSOCIATED CONDITIONS & DISORDERS

- Although essential (cause unknown) hypertension is diagnosed in veterinary patients, most cases of systemic hypertension occur as a complication of another systemic disease. In cats, the most common diseases associated with systemic hypertension are chronic kidney disease and hyperthyroidism. Many cats with hyperthyroidism have subclinical kidney disease; in these animals, it is unclear whether kidney disease, hyperthyroidism, or both are responsible for the hypertension. The prevalence of hypertension in cats with diabetes mellitus is still unclear.
- In dogs, the diseases most commonly associated with systemic hypertension are chronic kidney disease (especially proteinuric renal disease), hyperadrenocorticism, diabetes mellitus, and pheochromocytoma. Less typical causes of systemic hypertension in either species include hyperaldosteronism, acromegaly, and use of hypertensive medications (e.g., phenylpropanolamine, excessive thyroxine supplementation).

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Systemic hypertension can be diagnosed based on clinical signs (clinical systemic hypertension) or as part of a diagnostic evaluation of a systemic disease, with the animal showing no overt clinical signs (subclinical systemic hypertension).

HISTORY, CHIEF COMPLAINT

- Signs associated with the underlying disease
- Lethargy, changes in activity or appetite, or mentation changes:
  - Owner may interpret the signs as “signs of aging.”
- Acute blindness, intraocular hemorrhage
- Intracranial neurologic signs:
  - Generalized seizures
  - Focal facial seizures

PHYSICAL EXAM FINDINGS

- Signs of underlying systemic disease (e.g., signs of kidney disease or hyperthyroidism)
- Ocular: vitreal or retinal hemorrhage, retinal detachment, hyphema, vascular tortuosity
- Nervous system: signs of intracranial disease, changes in mentation (usually decreased but may include heightened anxiety), seizures (generalized or focal facial)
- Cardiovascular system: new murmur (typically a murmur of mitral insufficiency), arrhythmia, gallop sound, left ventricular hypertrophy on echocardiographic examination
- Other: epistaxis, photophobia

ETIOLOGY AND PATHOPHYSIOLOGY

- Likely to be multifactorial; individual mechanisms may predominate in some diseases:
  - Abnormalities in renal sodium handling
  - Inappropriate activation of the reninangiotensin-aldosterone system
  - Inappropriate activation of the sympathetic nervous system
  - Hypersensitivity to the effects of cortisol
  - Blood volume expansion secondary to underlying disease states
- Better understanding of mechanisms in individual diseases is likely to lead to more effective tailoring of therapy.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected in one of two clinical contexts: either a patient is evaluated for clinical signs consistent with hypertensive decompensation (e.g., acute vision loss), or systemic hypertension is identified in a compensated patient (e.g., as part of evaluating a patient that has chronic kidney disease). BP measurement is a simple confirmatory test, but technical confounders, notably patient anxiety (the white coat effect) and incorrect cuff size or placement, must be avoided to achieve an accurate reading.

DIFFERENTIAL DIAGNOSIS

- Ocular signs: coagulopathies; uveitis; inflammatory, infectious, or neoplastic diseases; trauma
- Neurologic signs: intracranial lesions
- Cardiovascular signs: primary cardiac disease, other secondary cardiac diseases
- Epistaxis: coagulopathies, trauma, neoplasia, fungal rhinitis

INITIAL DATABASE

- Initial diagnostic testing as guided by underlying disease if known
- BP measurement (see p. 1209)
- If systemic hypertension is diagnosed in a patient without known predisposing disease:
  - Dogs: CBC, serum chemistry profile, urinalysis with urine protein analysis if proteinuria is present, complete funduscopic examination
  - Cats: CBC, serum chemistry profile, urinalysis, serum thyroxine if patient is ≥10 years old, complete funduscopic examination
  - Both species: consider thoracic radiographs or abdominal ultrasound.

ADVANCED OR CONFIRMATORY TESTING

Repeated BP measurements over the course of several hours may be needed if animal is excited or very anxious during the first measurement period.

TREATMENT

TREATMENT OVERVIEW

- Systemic hypertension with clinical signs present:
  - First priority: prompt reduction of systolic BP to <160-180 mm Hg
  - Second priority: initiating clinical evaluation for causative disease
- Systemic hypertension found in conjunction with causative underlying disease but no clinical signs of hypertension are present:
  - Institute optimal therapy of causative condition.
  - Confirm elevated BP values on more than 1 occasion to lessen the chance of anxiety- or excitement-related elevations of BP.
  - If systolic BP > 180 mm Hg on more than one measurement occasion, begin antihypertensive therapy.
  - Systolic BP is 160-180 mm Hg on more than one measurement occasion:
    - If underlying disease can be controlled (e.g., hyperthyroidism or hyperadrenocorticism) or cured (e.g., hyperthyroidism if surgery/ radioiodine therapy is available), monitor BP during therapy of underlying disease, and treat if systolic BP continues to exceed 160 mm Hg after optimal therapy of underlying disease.
    - If underlying disease is unknown or unlikely to be cured (e.g., chronic kidney disease), begin antihypertensive

therapy.

ACUTE GENERAL TREATMENT

- Discontinue any hypertensive medications.
- Emergency antihypertensive therapy for animals with acute ocular or neurologic signs:
  - Dogs, either oral or IV therapy (start at low end of dose and titrate to effect):
    - Nitroprusside: 0.5-5 mcg/kg/min as continuous rate infusion IV; *or*
    - Hydralazine (oral): 0.5-2 mg/kg PO q 12 h
  - Cats:
    - Amlodipine: 0.625 mg PO q 24 h if cat =5 kg; 1.25 mg PO q 24 h if cat >5 kg; *or*
    - Hydralazine: 0.5-2 mg/kg PO q 12 h

CHRONIC TREATMENT

Dogs: medications from different groups may be added if original medication is not adequate to control hypertension:

- Angiotensin-converting enzyme inhibitors:
  - Enalapril: 0.5 mg/kg PO q 12-24 h; *or*
  - Benazepril: 0.25-0.5 mg/kg PO q 24 h
- Calcium (Ca) channel blockers:
  - Amlodipine: 0.01-0.2 mg/kg PO q 12-24 h

Cats:

- Ca channel blockers (preferred first line therapy):
  - Amlodipine: 0.625 mg PO q 24 h if cat ≤5 kg; 1.25 mg PO q 24 h if cat >5kg
- Angiotensin-converting enzyme inhibitors:
  - Usually inadequate as monotherapy but may have additive effects when given with other medications
  - Enalapril: 0.5 mg/kg PO q 12-24 h
  - Benazepril: 0.25-0.5 mg/kg PO q 12-24 h
- Beta-antagonists (beta-blockers):
  - May be useful to control heart rate if hyperthyroidism is present
  - Atenolol: 6.25 mg PO q 24 h if cat ≤5 kg; 12.5 mg PO q 24 h if cat >5kg

DRUG INTERACTIONS

- BP-lowering sedatives (e.g., acepromazine) should be used with caution in animals receiving any antihypertensive medication.
- Two medications from the same drug group should not be used together (e.g., benazepril and enalapril).

POSSIBLE COMPLICATIONS

- Hypotension:
  - Resuscitate as needed.
  - Reduce dose of BP medication.
  - Reevaluate need for antihypertensive medication.
- Uncontrolled hypertension despite drug therapy:
  - Review medications and administration information with caregiver.
  - Add medications from other classes if needed.
  - Consult a specialist for further additions/modifications if hypertension is not controlled with two antihypertensive medications at upper end of dosing ranges.
- Previously controlled hypertension now out of desired target range:
  - Dogs: hypertension may worsen over time, or underlying disease may be inadequately controlled:
    - Ensure optimal therapy of underlying disease.
    - Screen for hypertensive medications and check postpill serum thyroxine concentration in animals receiving thyroid supplementation.
    - Add additional antihypertensive medications or increase doses of present medications to high end of dosage range if tolerated.
  - Cats: hypertension control is usually stable once achieved. If BP continues to increase over time, treat as recommended in dogs, above.

RECOMMENDED MONITORING

- Once the condition is controlled, check BP in hypertensive patients every 3 months.
- If doses/medications change, recheck BP in 3-5 days after change to ensure efficacy.

PROGNOSIS AND OUTCOME

- If retinal detachment (see p. 985) has occurred, the retina may reattach with good control of blood pressure, but prognosis for return of vision is variable.
- Prognosis for resolution of other clinical signs of hypertension (e.g., focal facial seizures, changes in mentation, hyphema) is favorable if BP can be controlled with medication and underlying diseases can be controlled as well.
- Prognosis of systemic hypertension may be affected by prognosis of causative disease.

PEARLS & CONSIDERATIONS

COMMENTS

- Owners may interpret clinical signs of hypertension as “signs of aging,” and vigilance regarding monitoring of BP in animals at risk will detect subclinical cases.
- Any dog or cat with a systemic disease known to cause hypertension should have its BP monitored periodically regardless of clinical signs.
- High BP detected in young animals with no risk factors is often spurious.

CLIENT EDUCATION

For optimal patient management, inform clients that:

- Hypertension is usually a complication of another disease rather than primary disease in itself.
- Control of hypertension is necessary to avoid catastrophic ocular or neurologic damage and to minimize ongoing damage to susceptible organs (e.g., kidneys).
- If the underlying disease is not curable, therapy for systemic hypertension is likely to be lifelong.
- Many patients will require more than 1 medication to adequately control hypertension, and the need for medication may increase over time.

SUGGESTED READING

Brown S, et al: Guidelines for the identification, evaluation, and management of systemic hypertension in dogs and cats. J Vet Intern Med 21:542, 2007.

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Synovial Cell Sarcoma

BASIC INFORMATION

DEFINITION

A malignant tumor in the tissue lining the capsule of a joint

SYNONYM(S)

SCS, synovial sarcoma

EPIDEMIOLOGY

SPECIES, AGE, SEX: The median reported age is 8.5 years. Rare in cats.

GENETICS & BREED PREDISPOSITION: Golden retrievers and flat-coated retrievers seem to be overrepresented.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Histopathologically, there are two cell types: epithelioid (synovioblastic) and spindle (fibrosarcomatous) cell types.

HISTORY, CHIEF COMPLAINT: Most animals present with a slow-growing mass over a joint and concurrent lameness.

PHYSICAL EXAM FINDINGS: The clinical signs are directly related to the site of involvement and local invasiveness. Physical examination abnormalities include lameness and the presence of a mass near the affected joint. Other lameness-related findings could include stiffness of gait, reduced range of motion, crepitus, joint swelling, and pain. Depending on the duration of disease, joint instability may be present (ligament tear, subluxation). Other nonspecific clinical signs include lethargy, anorexia, and hemiparesis.

ETIOLOGY AND PATHOPHYSIOLOGY

- Synovial cell sarcoma (SCS) is a locally invasive tumor, and underlying bone destruction is common.
- Metastasis to regional lymph nodes, lungs, and other sites occurs in up to 25% of cases.
- In dogs, SCS most frequently involves the stifle and elbow, although other sites have been reported.
- No known etiologic factors

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A diagnosis of SCS is suspected based on the clinical presentation of chronic progressive lameness if the neoplasm is involving an appendicular joint, typically in an older dog.

DIFFERENTIAL DIAGNOSIS

- Degenerative joint disease, immune-mediated, or infectious arthritis
- Histiocytic sarcomas also occur in the periarticular tissue of large appendicular joints (see 535). This is the main tumor to distinguish SCS from, since the biological behavior and therapy is distinct.
- Other joint tumors reported in dogs include fibrosarcoma, rhabdomyosarcoma, osteosarcoma, malignant fibrous histiocytoma, liposarcoma, hemangiosarcoma, myxoma, malignant giant cell tumor of soft tissue, lymphoma, hemangioma, and undifferentiated sarcoma.
- Histologically, it may be challenging to differentiate SCS from histiocytic sarcoma, other mesenchymal tumors, and epithelial malignancies. Special immunohistochemical stains are almost always necessary to confirm a diagnosis of SCS.

INITIAL DATABASE

- Regional radiographs of the affected joint are recommended to help rule out other causes of musculoskeletal lameness.

  - Regional radiographic abnormalities include soft-tissue swelling; in advanced cases, cortical destruction and periosteal reaction are evident.
  - Radiographic evidence of lysis involving the proximal and distal bones of a joint is suggestive of SCS; however, other soft-tissue sarcomas can cross the joint space and should be ruled out.
- Fine-needle aspirate (FNA) and cytologic examination of the mass or the affected joint are useful in identifying and differentiating other causes of lameness.
- After a diagnosis of malignancy has been confirmed, the minimum database should include laboratory evaluation of CBC, serum biochemical analysis, urinalysis, three-view thoracic radiographs, cytologic or histologic examination of the draining lymph node, and abdominal ultrasound to rule out any abdominal visceral metastasis.

ADVANCED OR CONFIRMATORY TESTING

- If necessary, a CT scan or an MRI can be performed to evaluate the local extension of the causative lesions.
- An immunohistochemistry test is necessary to confirm a histologic diagnosis and differentiate SCS from histiocytic sarcoma and other malignancies; however, reliability of current immunohistochemistry stains may be equivocal, owing to marked variation in proportions and differentiation of the cellular elements involved with the mesenchymal tissue adjacent to the synovial membrane.
- In cases of SCS, positive histochemical staining for cytokeratin (epithelial marker) and histologic grade may predict outcome and prognosis.

TREATMENT

TREATMENT OVERVIEW

Limb amputation is the mainstay of the treatment. If an en bloc excision or limb amputation is not an option, external beam radiation therapy can be considered with a curative or palliative intent.

ACUTE GENERAL TREATMENT

- Analgesic and nonsteroidal antiinflammatory drugs (NSAIDs) are often indicated for pain palliation.
- Limb amputation
- Local resection followed by radiotherapy to the tumor bed can be attempted if the animal is not a candidate for limb amputation. Efficacy of radiotherapy is not known.

CHRONIC TREATMENT

Efficacy of chemotherapy has not been determined for canine SCS. For dogs with high-grade tumors or dogs that present with overt metastasis, adjuvant chemotherapy with drugs such as doxorubicin, platinum agents, and ifosfamide may prove beneficial. Consultation with a medical oncologist is recommended.

RECOMMENDED MONITORING

Periodic evaluation for distant metastasis and local recurrence

PROGNOSIS AND OUTCOME

- Clinical outcome is excellent after limb amputation in cases with no gross detectable metastatic disease. A median survival of 28-36 months has been reported in dogs treated by means of limb amputation alone, with or without adjuvant chemotherapy.
- It may be possible to better determine the prognosis of dogs with SCS based on certain prognostic factors. Prognostic factors for survival of dogs with SCS treated with amputation include clinical stage (no metastases: >48 months; metastases: 3 months), histologic grade (grade I or II: 36 months; grade III: 7 months), and cytokeratin staining (negative: >48 months; positive: 4 months).

PEARLS & CONSIDERATIONS

COMMENTS

- Histopathologically, the majority of cases exhibit a biphasic pattern resembling both mesenchymal and epithelioid origins. Because of these features, pathologists may have to differentiate between a poorly differentiated carcinoma, histiocytic

sarcoma, and SCS.
- SCS is rarely diagnosed in cats. Among the nine reported cases of feline SCS, there have been six reports of malignant SCS and three reports of benign synovioma.

SUGGESTED READING

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Syndrome of Inappropriate Antidiuretic Hormone Secretion

BASIC INFORMATION

DEFINITION

Disorder caused by release of antidiuretic hormone (ADH) in the absence of normal osmotic or nonosmotic stimuli

SYNONYMS

Secretion of inappropriate antidiuretic hormone; SIADH. Antidiuretic hormone: vasopressin

EPIDEMIOLOGY

SPECIES, AGE, SEX: Rare disease of the dog; no gender or age predilection

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Lethargy
- Inappetence
- Neurologic signs

PHYSICAL EXAM FINDINGS

- Weakness
- Tremors
- Seizures
- No evidence of peripheral edema or ascites

ETIOLOGY AND PATHOPHYSIOLOGY

- In this syndrome, ADH release occurs independent of normal stimuli secondary to central nervous system (CNS) disease or as an idiopathic occurrence.
- In dogs, the syndrome of inappropriate antidiuretic hormone secretion (SIADH) has been reported as an idiopathic phenomenon in two cases, secondary to a CNS disease in two cases (hypothalamic tumor, amebic meningoencephalitis), in a dog with heartworm disease, and in a dog with an undifferentiated carcinoma.
- In people, SIADH has been associated with pulmonary disease, cranial disease, malignant neoplasms, and drugs.
- Inappropriate ADH release results in increased water resorption at the renal collecting ducts, which leads to volume expansion and hyponatremia.
- Volume expansion leads to reduced proximal tubular sodium resorption and enhanced natriuresis.
- Neurologic signs secondary to cerebral edema occur as a consequence of volume expansion and hyponatremia.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

SIADH is rarely diagnosed but should be considered in patients with hyponatremia for which other differentials have been excluded via complete database (CBC/biochemistry profile/urinalysis), ACTH stimulation testing, thyroid testing, and clinical signs. Paired urine and plasma osmolality and urine and plasma sodium measurements are required for confirmation of diagnosis.

DIFFERENTIAL DIAGNOSIS

- Hyponatremia (see 1402):
  - Hypoadrenocorticism
  - Diabetes mellitus
  - Gastrointestinal (GI) sodium loss (vomiting, diarrhea)
  - Chronic congestive heart failure

- Psychogenic polydipsia
- Artifact (hyperlipidemia)
- Acute renal failure
- Severe liver disease
- Nephrotic syndrome
- Severe hypothyroidism with myxedema

INITIAL DATABASE

- CBC, serum biochemical profile, urinalysis: hyponatremia, normal renal parameters
- Thoracic radiographs: possible underlying pulmonary disease, such as primary or metastatic neoplasia
- Adrenocorticotropic hormone (ACTH) stimulation test: normal response
- Total thyroxine level (T4): normal or low. Further testing to exclude primary hypothyroidism may be required (see 1403).

ADVANCED OR CONFIRMATORY TESTING

- Plasma osmolality: decreased (<280-310 mOsm/kg)
- Urine osmolality: inappropriately increased (>100 mOsm/kg) in the face of plasma hypoosmolality and hyponatremia
- Urine sodium concentration: increased despite hyponatremia

TREATMENT

TREATMENT OVERVIEW

Therapy for SIADH centers on correction of hyponatremia and therapy of the underlying disease if identified.

ACUTE GENERAL TREATMENT

- Severe hyponatremia (<120 mEq/L; see 1402) should be corrected with IV fluid therapy using conventional crystalloid solutions (0.9% saline, lactated Ringer's solution) to raise serum sodium levels at a rate of less than 8-12 mEq/L/day.
- Hypertonic saline (3%-5%) should be used with caution, as it may raise the serum sodium concentrations too rapidly in cases of chronic hyponatremia.
- Administration of furosemide in conjunction with fluid therapy reduces the risk of extracellular fluid (ECF) volume expansion in already overhydrated patients.
- Once serum sodium concentrations have been corrected to >125 mEq/L, water intake may be restricted to a volume less than urine output to promote free water loss and restore normal body fluid volume.

CHRONIC TREATMENT

- Chronic management of SIADH is directed at treating the underlying cause.
- A selective ADH receptor antagonist, OPC-31260 (Otsuka Pharmaceutical, Tokyo), has been reported to palliate signs in a dog with SIADH over a 3-year treatment period (3 mg/kg PO q 12 h).
- Other antidiuretic hormone receptor antagonists (e.g., tolvaptan, conivaptan) are available for human patients, but their use in dogs with clinical hyponatremia remains poorly described (novel treatment).

POSSIBLE COMPLICATIONS

- Rapid correction of chronic hyponatremia can result in osmotic demyelination syndrome due to brain dehydration as free water moves out of the brain and into the relatively hypertonic serum (see 1402).
- Clinical signs of osmotic demyelination syndrome occur 3-4 days after rapid correction of hyponatremia, are neurologic in nature (lethargy, ataxia, hypermetria, paresis), and may be fatal.

RECOMMENDED MONITORING

Serial (q 4 h) monitoring of serum sodium concentration during acute correction phase and periodic monitoring during chronic management

PROGNOSIS AND OUTCOME

Prognosis is dependent on the underlying cause of SIADH.

PEARLS & CONSIDERATIONS

COMMENTS

- ADH release may be stimulated by various drugs used during anesthesia (barbiturates, narcotics) and can result in impaired free water excretion and hyponatremia in the postoperative period, similar to what is seen in animals with SIADH. Restriction of water intake is generally sufficient to restore normal water balance in these animals.
- During treatment, never increase serum sodium concentration by more than 0.5 mEq/L/h (risk of osmotic demyelination syndrome and life-threatening cerebral complications).

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Syncope

BASIC INFORMATION

DEFINITION

A sudden and transient loss of consciousness resulting in collapse, followed by spontaneous recovery. The cause is a transient cerebral deficiency of oxygen.

SYNONYMS

Faint, collapse

Neurocardiogenic syncope: vasovagal syncope

Tussive syncope: “cough-drop” phenomenon

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dependent on underlying cause: cardiac versus noncardiac causes. Acquired heart disease: middle-aged to older animals; congenital heart disease: young animals.

GENETICS & BREED PREDISPOSITION

- Tussive syncope (older small-breed dogs with pulmonary disease)
- Neurocardiogenic syncope (boxer, golden retrievers, brachycephalic breeds?)
- According to underlying heart disease (many breed predilections)

RISK FACTORS

- Autonomic dysfunction (neurocardiogenic syncope)
- Drugs: -blockers, diuretics, vasodilators (hypotensive syncope)

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Acute collapse, with altered or loss of consciousness
- Either no clinical signs or staggering or ataxia prior to the event
- Exercise, excitement, or coughing may precipitate the event.
- ± Clonic movements
- ± Involuntary urination or defecation
- No postictal phase
- Duration: seconds (and virtually always < 1 minute; otherwise, likely to be fatal)
- Recovery: complete and rapid

PHYSICAL EXAM FINDINGS: Dependent on underlying disorder(s):

- Cardiac:
  - ± Murmur
  - ± Arrhythmia
  - ± Altered arterial pulse quality
  - ± Pulse deficits
  - ± Cyanotic mucous membranes
  - ± Pulmonary rales or crackles
- Neurologic exam (see p. 1311):
  - ± Cranial nerve abnormalities
  - ± Altered reflexes
  - ± Proprioceptive deficits
  - ± Altered mentation
- Upper airway exam:

- ± Brachycephalic syndrome (i.e., stenotic nares, hypoplastic trachea, everted laryngeal saccules, elongated soft palate)

ETIOLOGY AND PATHOPHYSIOLOGY

- Cardiac:
  - *Bradyarrhythmias:* syncope can result when there is a >6-8 second pause in electrical activity (i.e., failure of subsidiary pacemaker in third-degree atrioventricular [AV] block, sinus arrest associated with sick sinus syndrome [SSS]).
  - *Tachyarrhythmias:* rates > 300 bpm for >6 seconds (i.e., supraventricular tachycardia [SVT] or ventricular tachycardia) in dogs; cats uncommonly experience syncope with tachyanhythmias but more so with bradycardias. Heart rate and time necessary for syncope may vary depending on underlying cardiac structure (i.e., a slower heart rate for a shorter duration may cause syncope in an animal with underlying myocardial or valvular heart disease). Various outcomes: nonsustained tachyarrhythmia results in a return to sinus rhythm; overdrive suppression leads to sinus arrest or possibly ventricular fibrillation.
  - *Outflow obstruction* (i.e., pulmonic stenosis, subaortic stenosis, cor pulmonale due to heartworm disease with secondary pulmonary hypertension):
    - Classic theory: exercise results in vasodilation of systemic arterioles. Fixed obstruction to flow results in inadequate increase in cardiac output, leading to hypotension and syncope.
    - Alternate theory: contractility, cardiac output, and flow increase through stenosis during exercise. Increased left ventricular systolic pressure causes overstimulation of left ventricular mechanoreceptors. Reflex activation of cardiac afferent vagal fibers results in increased parasympathetic tone to heart and systemic blood vessels, resulting in bradycardia, vasodilation, and subsequent syncope.
  - *Cyanotic heart disease:* (i.e., right-to-left patent ductus arteriosus, tetralogy of Fallot): syncope is due to hypoxemia and/or hyperviscosity of blood from polycythemia, or else is from arrhythmias.
  - *Masses obstructing inflow or outflow of blood (rare):* intracardiac mass lesions reduce cardiac output by restricting blood flow through atrioventricular valves or obstructing a ventricular outflow tract. Pericardial disease compromises cardiac output by interfering with systemic venous return (i.e., cardiac tamponade).
  - *Congestive heart failure:* syncope mechanism presumed to be similar to autonomic dysfunction (see below).
- Noncardiac:
  - *Neurologic syncope:* increased intracranial pressure with resultant decrease in cerebral perfusion (i.e., cerebral edema, brain tumors, meningitis, encephalitis, cerebral vascular obstructions, acute bleed). Syncope occurs very rarely, in contrast to seizures, with these diseases.
  - *Metabolic syncope:* abrupt decrease in oxygen or nutrient delivery (i.e., glucose) to the brain (oxygen concentration is affected by blood flow, hemoglobin concentration, and oxygen tension). Seizures > syncope.
  - *Tussive syncope:* proposed mechanisms:
    - Increased intrathoracic pressure transiently increases intracranial pressure and diminishes cardiac venous return and resultant cardiac output; cerebral blood flow is decreased during paroxysms of coughing.
    - Coughing stimulates vagal afferent transmission to the vasomotor center in the medulla, with subsequent stimulation of vagal efferente to the heart and blood vessels (bradycardia, hypotension).
  - *Autonomic dysfunction:* excessive baroreflex resulting in cardiac inhibition and/or peripheral vasodilation (i.e., neurocardiogenic syncope, carotid sinus sensitivity, carotid body tumor).
  - *Peripheral vasomotor dysfunction:* abnormality of peripheral vasoconstriction, muscle tone, heart rate, and/or respiration, resulting in syncope (postural hypotension).
  - *Undetermined:* ~40% of human syncope cases despite extensive testing; likely similar percentage in veterinary medicine

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

Diagnosis is largely based on patient signalment; historical events prior to, during, and after the episode; and complete cardiovascular and neurologic exams. Since the episode often is not witnessed directly by the veterinarian (to confirm or refute syncope), a simple test is video recording by the owner when an event occurs at home. Confirmatory testing may involve ambulatory electrocardiogram (ECG) monitoring and/or central nervous system (CNS) imaging depending on the suspected cause. Consider consultation with and/or referral to a veterinary cardiologist +/− veterinary neurologist.

DIFFERENTIAL DIAGNOSIS

- Primary cardiac disease (see above)
- Hypotension (inadequate cardiac output, poor vascular tone)
- Hypoxemia (pulmonary thromboembolism, pulmonary disease, right-to-left shunt)

- Abnormal blood or metabolic constituents (hypoglycemia, hypokalemia, anemia)
- Neoplasia (splenic hemangiosarcoma)
- Neurologic and neuromuscular disorders (epilepsy, structural central nervous system disorders, narcolepsy, myasthenia gravis)

INITIAL DATABASE

- CBC: ± anemia, thrombocytopenia
- Serum biochemistry panel: ± electrolyte abnormalities, ± metabolic derangements
- Urinalysis: ± proteinuria with AT III loss and subsequent hypercoagulable state (thromboembolism)
- Blood pressure: normal result does not rule out transient hypotension
- ± Heartworm antigen test
- ± Heartworm microfilaria test
- Thoracic radiographs: ± evidence of structural heart disease, ± pulmonary parenchymal abnormalities (i.e., pulmonary artery abnormalities with heartworm disease, cardiogenic pulmonary edema)
- Echocardiogram: ± congenital or acquired heart disease
- Resting ECG: ± rhythm abnormalities
- Neurologic exam (see p. 1311): ± neurologic deficits

ADVANCED OR CONFIRMATORY TESTING

- Videotaping: episodes that are not convincingly syncopal based on history alone (a common problem) and do not occur in the veterinary facility may be evaluated objectively by having the owner videotape them at home.
- Holter monitor (see p. 1287): 24-hour ECG; helpful in establishing a diagnosis 42% of the time
- Cardiac event recorder: digital loop recorder that is patient or owner activated, programmed to capture the heart rate and rhythm prior to and after the syncopal episode(s); diagnostic yield 85%
- Abdominal ultrasound: may be helpful in identification of mass(es)
- CT/MRI/cerebrospinal fluid tap: neurologic disease. see pp. 1233, 1302, and 1228.

TREATMENT

TREATMENT OVERVIEW

Treatment involves addressing the primary etiology in order to alleviate syncopal episodes and prevent sudden death.

ACUTE GENERAL TREATMENT

Acute treatment is aimed at the underlying cause or at stabilization procedures:

- Blood loss: fluids, blood products, etc.
- Pericardial effusion with cardiac tamponade: pericardiocentesis
- Continuous ECG
- *Bradyarrhythmias*
  - SSS, third-degree AV block: medical management may be effective if arrhythmia is due to excessive vagal tone and atropine responsive (i.e., anticholinergics [propantheline] and -agonists [terbutaline]; see individual diseases for specific treatment recommendations). Temporary pacemaker if bradyarrhythmia is refractory to medical management and animal is showing persistent clinical signs.
- *Tachyarrhythmias:*
  - Ventricular tachycardia: oral or intravenous medical management depending on malignancy of the arrhythmia (i.e., oral options: mexiletine, sotalol, amiodarone, atenolol; intravenous options: lidocaine, procainamide, esmolol); see p. 1165. Cautious use of or avoid -blockers in cases with systolic dysfunction/dilated cardiomyopathy.

CHRONIC TREATMENT

- Treatment of underlying cause if systemic disorder
- Bradyarrhythmias:
  - Medically refractory SSS, high-grade second-degree AV block, third-degree AV block: permanent pacemaker
- Tachyarrhythmias: see p. 1165
- Severe outflow obstructions:
  - Limit exertion in all cases.
  - Subaortic stenosis (SAS; see p. 1057): -blockers if severe
  - Pulmonic stenosis (see p. 941): -blockers if severe

    - Hypertrophic obstructive cardiomyopathy (see p. 565): β-blocker, calcium channel blocker
    - Heartworm disease with secondary pulmonary hypertension (see pp. 474 and)
- Cyanotic heart disease-induced polycythemia: phlebotomy, or hydroxyurea 50 mg/kg PO q 48-72 h, adjusted based on response
- Congestive heart failure (see p. 470)
- Neurologic syncope: treatment of underlying cause
- Metabolic syncope: treatment of underlying cause
- Tussive syncope: cough suppressant (e.g., butorphanol, 0.1-0.5 mg/kg PO q 8-12 h), bronchodilator (aminophylline, 10 mg/kg PO q 8 h), treatment with diuretics (e.g., furosemide, 2 mg/ kg IV, SQ) if pulmonary edema is present
- Autonomic dysfunction: anticholinergics (e.g., propantheline bromide, 0.5-1 mg/kg PO q 8 h if bradycardia related), -blocker (e.g., atenolol, 0.25-1 mg/kg PO q 12 h if tachycardia related). Treatment modalities are aimed at maintaining heart rate and/or preventing sympathetic surge. Medical management fails to address hypotensive component of reflex arc, and animals may continue to faint, potentially requiring a pacemaker.

BEHAVIOR/EXERCISE

- Limit exertion/excitement in severe outflow obstructions, cyanotic heart disease, impending/decompensated left congestive heart failure, ventricular arrhythmias, and neurocardiogenic syncope.

DRUG INTERACTIONS

β-Blockers, diuretics, and vasodilators can exacerbate hypotension.

POSSIBLE COMPLICATIONS

Sudden death

RECOMMENDED MONITORING

Serial evaluations as needed to acquire initial database and confirmatory testing

PROGNOSIS AND OUTCOME

- Highly dependent on underlying etiology
- Excellent for bradyarrhythmias treated with pacemaker implantation
- Fair to good with supraventricular tachycardia responsive to medical therapy
- Guarded with ventricular tachycardia treated medically; poor if systolic dysfunction/dilated cardiomyopathy present
- Variable prognosis with outflow obstructions (i.e., severe SAS has a poor long-term prognosis).
- Good with tussive syncope treated medically if cough responds well to therapy
- Good prognosis with autonomic dysfunction. Treatment is usually unrewarding. Fortunately, sudden death is not common.
- Poor prognosis: neoplasia

PEARLS & CONSIDERATIONS

COMMENTS

- Syncopal episodes may be difficult to differentiate from seizures. Video-recording and ECG event monitoring (see p. 1287) are simple, noninvasive tests that greatly help differentiate between the two.
- Syncope, while uncommon in cats, occasionally occurs with hypertrophic obstructive cardiomyopathy and with bradyarrhythmias (e.g., third-degree AV block).
- In SSS, bradyarrhythmias (e.g., sinus arrest) typically cause syncopal episodes warranting pacemaker therapy prior to addressing tachyarrhythmias (e.g., SVT; see p. 111).
- In 40% of human cases, an etiology is never identified; similar percentages are suspected in veterinary medicine.

PREVENTION

- Tussive syncope: cough suppressant, bronchodilator, treatment with diuretics if pulmonary edema is present
- Autonomic dysfunction: anticholinergics, β-blocker

TECHNICIAN TIPS

- In-house ECG telemetry is useful for identifying bradyarrhythmias and tachyarrhythmias.
- “Seizure bells” can be placed on hospitalized patients presenting for syncope to help alert the staff when an animal has an episode.

CLIENT EDUCATION

- Treatment and prognosis are dependent on the underlying etiology.
- Sudden death is possible but is dependent on the underlying etiology.

SUGGESTED READING

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Supraspinatus/Infraspinatus Tendon Disorders

BASIC INFORMATION

DEFINITION

Disorders of the extraarticular tendons in the shoulder area of dogs, often representing degenerative changes bilaterally

SYNONYMS

- Supraspinatus mineralization: calcification of supraspinatus tendon
- Supraspinatus tendinosis: nonmineralized tendinopathy, chronic tendinopathy, chronic tendon injury, chronic tendinitis, biceps tendon impingement, tendon enlargement

EPIDEMIOLOGY

SPECIES, AGE, SEX: Medium to large-breed adult dogs of both genders

GENETICS & BREED PREDISPOSITION: Supraspinatus tendon disorders have been associated with Labrador retrievers and rottweilers. Infraspinatus contracture is classically seen in hunting or working dogs. Ossification of infraspinatus tendon-bursa has only been described in Labrador retrievers.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Supraspinatus mineralization and tendinosis represent degenerative disorders and are likely related. Infraspinatus muscle contracture may be of traumatic origin. Ossification of the infraspinatus tendon-bursa is a recently described disorder of unknown origin.

HISTORY, CHIEF COMPLAINT: Supraspinatus mineralization and tendinosis, and infraspinatus tendon-bursa ossification lead to intermittent or waxing-waning weight-bearing unilateral front limb lameness with gradual onset. Infraspinatus contracture is associated with acute onset of lameness, resolving initially but leading to a subsequent chronic lameness, with characteristic stance and gait abnormalities.

PHYSICAL EXAM FINDINGS

- All disorders may be associated with disuse atrophy of spinatus muscles.
- Dogs with supraspinatus mineralization or tendinosis tend to show signs of pain on shoulder flexion. They may or may not show signs of pain on digital palpation of the supraspinatus tendon. Signs of pain are elicited by palpation of the bicipital tendon in some cases.
- Dogs with infraspinatus contracture, in the acute stage, may show tenderness/pain during muscle palpation. In the chronic stage, this disorder leads to a stance with the elbow adducted and the foot abducted. During the stride, the distal limb circumducts in a lateral arc. There is atrophy of the infraspinatus muscle, and the limb is permanently supinated. In lateral recumbency with the affected side up, the dog may be unable to rest the distal limb on the floor/table. Pain is usually not evident in the chronic stage.
- Infraspinatus tendon-bursa ossification is associated with pain on direct digital pressure over the tendon insertion in half of affected individuals.

ETIOLOGY AND PATHOPHYSIOLOGY

- Supraspinatus mineralization and tendinosis are probably overuse syndromes and are localized in the avascular zone of the tendon, an area predisposed to poor healing. These two conditions have very similar histopathologic features and may both represent chronic tendon injury.
- Supraspinatus disorders lead to swelling and increased mass of the tendon insertion, which may cause pressure and impingement/displacement of the underlying bicipital tendon.
- Infraspinatus contracture may be a result of traumatic incomplete rupture of the muscle, which becomes replaced with fibrotic tissue.
- Ossification of the infraspinatus tendon of insertion may coincide with ossification (osteochondromatosis) of the bursa, or each condition can occur alone. A degenerative cause is suspected.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

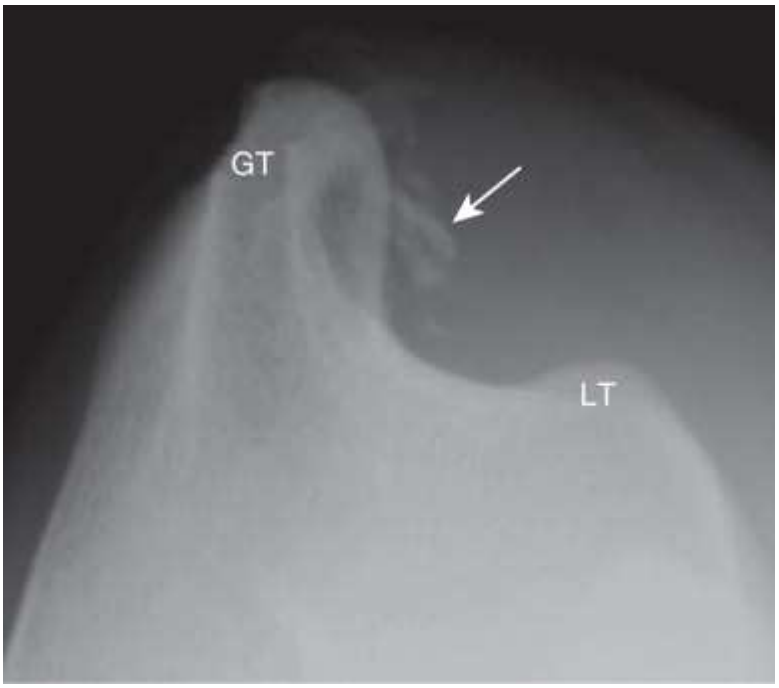
Infraspinatus contracture in the chronic stage may be diagnosed with physical examination. Supraspinatus mineralization and ossification of infraspinatus tendon-bursa require radiographic examination. Supraspinatus tendinosis is not evident on radiographic examination and requires advanced imaging. Supraspinatus mineralization and ossification of the infraspinatus tendon-bursa may be coincidental, and other reasons for lameness must be ruled out before pursuing treatment.

DIFFERENTIAL DIAGNOSIS

- Bicipital tenosynovitis, with or without tendon mineralization
- Osteoarthritis of the glenohumeral joint
- Shoulder instability/luxation
- Elbow dysplasia
- Osteosarcoma of the proximal humerus
- Nerve sheath tumor (especially prior to onset of neurologic dysfunction)

INITIAL DATABASE

- Orthopedic and neurologic evaluations
- Radiography of the scapulohumeral joint; lateral, craniocaudal, and cranioproximal-craniodistal views—the latter for supraspinatus/biceps tendon imaging. Supraspinatus mineralization is located craniomedial to the greater tubercle but not centered within the intertubercular groove.
- CBC, serum biochemistry panel, urinalysis: in older dogs



SUPRASPINATUS/INFRASPINATUS TENDON DISORDERS Radiographic skyline view. Supraspinatus mineralization is evident medial to the greater tubercle *(arrow). GT,* Greater tubercle; *LT,* lesser tubercle.

ADVANCED OR CONFIRMATORY TESTING

- Localization of pain involves applying digital pressure to the insertion of the supraspinatus tendon (craniomedial greater tubercle of humerus), the bicipital tendon (intertubercular groove), and infraspinatus tendon of insertion (lateral and distal to greater tubercle). Note that these disorders inconsistently result in pain on direct palpation of the structures.
- MRI of the shoulder joint is an excellent imaging modality in these disorders and many of their differential diagnoses.
- Ultrasonographic examination of the cranial shoulder area may identify the increased tendon mass of supraspinatus, tendinosis, mineralization/ossification of supra- or infraspinatus tendons, and may identify differential or coinciding diagnoses such as bicipital tenosynovitis.
- Arthroscopic examination of the shoulder joint further identifies differential or coinciding disorders.

TREATMENT

TREATMENT OVERVIEW

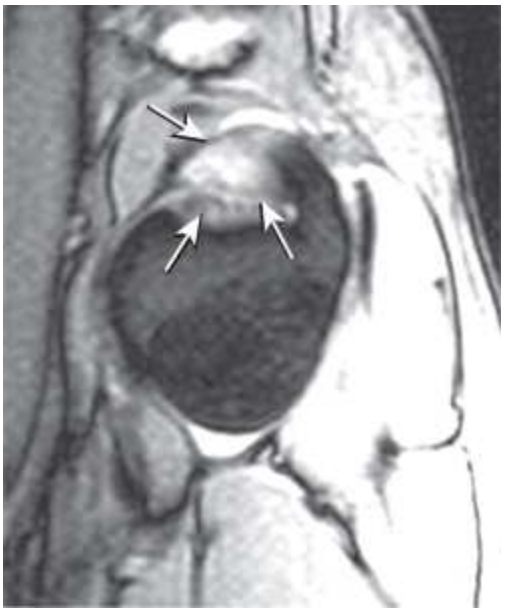
Surgical treatment is usually indicated if lameness is refractory to rest and antiinflammatory medication. With infraspinatus contracture, the goal is return to full function of the affected limb.

ACUTE GENERAL TREATMENT

- Supraspinatus tendinopathies usually do not respond to nonsteroidal antiinflammatory drug (NSAID) treatment, and corticosteroid injections are likely contraindicated.
- Extracorporeal shockwave therapy has led to improvement in a few dogs with supraspinatus mineralization.
- If acute infraspinatus trauma is suspected, early fasciotomy may be indicated to decompress the muscle and avoid compartment syndrome. However, the acute phase is often not identified, owing to the spontaneous recovery of the initial lameness.
- Seven of 13 dogs with ossification of the infraspinatus tendon-bursa improved after injection of long-acting corticosteroid (methylprednisolone acetate, 20 mg/mL, 1-2 mL IA once or twice, 3 weeks apart) into the glenohumeral joint, or NSAID treatment. One case improved after 4 months of restricted activity only. Medical management should be attempted prior to considering surgery.

CHRONIC TREATMENT

- Surgery for supraspinatus mineralization entails longitudinal tendon incisions to evacuate the mineralized deposits. Surgery for supraspinatus tendinosis has only been reported in a few cases, but good to excellent results have been achieved by resection of the mass in the tendon insertion and thus decompression of the bicipital tendon. Arthroscopic examination of the shoulder joint in the same session is usually indicated to rule out other intraarticular coinciding or differential disorders.
- Degenerative tendon disorders in people may be treated with rest alone for 6 months or more, and some human studies show similar outcomes of long-term rest as in surgically treated cases.
- Infraspinatus contracture treatment consists of tenotomy and excision of the tendon insertion. Immediate ability to pronate the limb is achieved. Leash walks are performed immediately postoperatively, and normal activity is resumed 10-14 days after infraspinatus tenotomy.
- Ossification of infraspinatus tendon-bursa in cases refractory to medical management have been treated by excision of ossified masses, leading to improvement in 4/6 cases.



SUPRASPINATUS/INFRASPINATUS TENDON DISORDERS Transverse magnetic resonance mage (MRI) through proximal humerus in a dog with supraspinatus tendinosis. An increased mass of high signal intensity is located within the insertion of the supraspinatus tendon, craniomedially on the greater tubercle *(arrowheads).* Biceps tendon is visible medially in intertubercular groove *(arrow).*

NUTRITION/DIET

Dietary management to prevent or treat obesity is likely beneficial for long-term management.

BEHAVIOR/EXERCISE

- Exercise is restricted for 2-4 weeks after supraspinatus surgery. Physical therapy with passive range-of-motion exercises and walking are recommended as soon as possible after surgery. However, swimming may not be indicated, as it has been suggested to put increased strain on the supraspinatus tendon. Swimming or other vigorous exercise should be avoided until 8-12 weeks after supraspinatus surgery.
- Supraspinatus disorders may be caused by overuse. Excessive high-impact activities may have to be discontinued. Jumping and digging have been proposed to result in increased supraspinatus strain.
- After supraspinatus healing is complete, consistent daily low-impact physical activity (walking, swimming, running on soft surfaces) is recommended.
- Surgical treatment for infraspinatus contracture usually returns the dog to full function.

POSSIBLE COMPLICATIONS

- Seroma
- Infection
- Unresolving lameness, reflecting a degenerative process such as mineralization, may be an incidental finding.

PROGNOSIS AND OUTCOME

- Dogs with supraspinatus mineralization have shown good to excellent outcome (mild intermittent lameness to normal function) in 80%–90% of operated cases and in all of 3 cases treated conservatively (rest and NSAIDs). Extracorporeal Shockwave therapy resolved lameness in 2 dogs reexamined at 20 and 49 days, respectively.
- Surgical treatment of supraspinatus tendinosis has shown good to excellent outcome in 7/8 cases.
- Surgical treatment of infraspinatus contracture usually leads to en excellent outcome.
- Though 12/13 dogs with ossification of infraspinatus tendon-bursa improved with medical and/or surgical treatment, the majority continued to show a mild lameness.

PEARLS & CONSIDERATIONS

COMMENTS

- Supraspinatus mineralization and tendinosis may lead to increased pressure on the bicipital tendon and have been associated with bicipital tenosynovitis.
- Deeply positioned supraspinatus mineralizations may be more prone to cause clinical signs than superficial ones because of increased interference with the biceps tendon.
- None of the tendon disorders have an inflammatory background, and antiinflammatory treatment with corticosteroids is dubious and potentially harmful. However, clinical response has been noted with glenohumeral joint injection of corticosteroids in ossification of infraspinatus tendon-bursa.
- Never inject corticosteroids into a joint if the synovial fluid is discolored, cloudy, or has decreased viscosity. Do not inject corticosteroids into a tendon, because it severely impairs tendon healing.
- Long-term rest alone (>6 months) and other physical therapy modalities such as eccentric loading may be effective treatments for degenerative tendinopathy but have not been evaluated in veterinary medicine.

SUGGESTED READING

Fransson BA: Treatment of supraspinatus tendon disorders in dogs. In Bonagura JD, Twedt DC, editors: Kirk's current veterinary therapy, ed 14, St Louis, 2009, Saunders Elsevier, pp 1117–1120.

AUTHOR: BOEL A. FRANSSON

EDITOR: JOSEPH HARARI

Superficial Necrolytic Dermatitis

BASIC INFORMATION

DEFINITION

A progressively debilitating skin disease associated with a severe internal disease process

SYNONYMS

Hepatocutaneous syndrome, glucagonoma syndrome, metabolic epidermal necrosis, necrolytic migratory erythema, diabetic dermatopathy

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Uncommon in dogs, rare in cats
- Middle-aged to geriatric patients; no sex predilection

GENETICS & BREED PREDISPOSITION: Cocker spaniel, Shetland sheepdog, West Highland white terrier, and Scottish temer

RISK FACTORS: Administration of phenobarbital. Ingestion of mycotoxin.

ASSOCIATED CONDITIONS & DISORDERS: Most cases have been associated with hepatopathy, which explains the former name, *hepatocutaneous syndrome.* A few cases have been associated with a functional pancreatic α-cell glucagon secreting tumor (also known as glucagonoma syndrome). Other associated conditions in dogs include cirrhosing or fibrosing hepatopathy (see p. 212), idiopathic vacuolar hepatopathy (see p. 1153), diabetes mellitus (see p. 1547), extrapancreatic glucagonoma (liver, spleen, adrenal glands and mesenteric lymph nodes), copper storage disease, hyperglucagonemia. Associated diseases in cats include pancreatic carcinoma, hepatopathies, and thymic amyloidosis.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Owners usually observe footpad lesions first, as dermatologie changes may precede onset of clinical signs of internal disease. Lethargy, anorexia, weight loss, lameness, reluctance to walk/signs of pedal pain, and pruritus are frequently reported. Other chief complaints may include polyuria and polydipsia. Dermatitis may wax and wane.

PHYSICAL EXAM FINDINGS: Dermatologie lesions are characterized by thickening, Assuring, and crusting of footpads, and interdigital erythema. Crusts, erosions, and ulcers can affect pinnae, mucocutaneous junctions (oral cavity, eyes, anus and genitalia), elbows and other pressure points, ventral abdominal and inguinal regions. Regional lymphadenopathy and hyperthermia are possible.

ETIOLOGY AND PATHOPHYSIOLOGY

A proposed mechanism: glucagonemia-induced glycogenesis from amino acids or increased hepatic catabolism of amino acids results in low plasma amino acid concentration and epidermal cellular starvation (i.e., keratinocyte degeneration, necrosis, and epidermal edema). Deficiencies of essential fatty acids, zinc, and biotin and hypoalbuminemia may also be involved.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis of SND is initially suspected on physical exam of the skin (especially footpads), hepatic ultrasonographic findings, or a combination of both. No single test result is pathognomonic for SND; a conclusive clinical diagnosis is reached with histopathologic analysis of skin biopsies and hepatic ultrasonographic findings, and is further solidified if a commonly associated disorder (see above) is present. If serum levels of liver enzymes/bile acids are normal, and the liver does not show the typical ultrasonographic pattern but typical dermatohistopathologic findings are present, consider glucagonoma as the primary cause.

DIFFERENTIAL DIAGNOSIS

- Autoimmune/immune mediated causes: pemphigus foliaceus, drug-induced pemphigus, systemic lupus erythematosus, paraneoplastic pemphigus, cutaneous vasculitis, erythema multiforme, toxic epidermal necrolysis
- Infectious causes: bacterial (pyoderma), fungal (dermatophytosis, *Malassezia* dermatitis), protozoal (leishmaniasis)
- Parasitic causes: demodicosis
- Nutritional causes: zinc-responsive dermatosis
- Neoplastic causes: epitheliotropic lymphoma
- Idiopathic: nasodigital hyperkeratosis

INITIAL DATABASE

- The minimal dermatologic database includes deep skin scrapings (typically negative, although secondary demodicosis may occur), cytologic evaluation of the skin (patients often have a bacterial or *Malassezia* overgrowth) +/− dermatophyte culture (typically negative).
- The minimal clinicopathologic database includes a CBC (nonregenerative anemia, leukocytosis are possible), serum biochemistry profile (elevated alkaline phosphatase, alanine aminotransferase, serum glucose and fructosamine levels; hypoalbuminemia; decreased blood urea nitrogen) and urinalysis (glucosuria).

ADVANCED OR CONFIRMATORY TESTING

- Abdominal ultrasonography:
  - Ultrasonographic hepatic findings are characterized by hypoechoic nodules with a hyperechoic trabecular network throughout the liver, resulting in a “honeycomb” or “Swiss cheese” pattern of the hepatic parenchyma. Occasionally hepatic metastases are detected. Ultrasonographic detection of pancreatic and extrapancreatic glucagonomas can be difficult.
- Histopathology and immunohistochemistry:
  - Skin biopsy: epidermis has a “French or Dutch flag” (i.e., red-white-blue layers) appearance:
    - Upper layer (stratum corneum): parakeratotic hyperkeratosis staining red (eosinophilic); crusts
    - Middle layer (stratum spinosum): intracellular edema, vacuolation, and necrosis of the keratinocytes staining white (pallor)
    - Deep layer (stratum basale): hyperplasia staining blue (basophilic)
- Ultrasound-guided hepatic biopsy (first perform platelet count, arterial blood pressure, and coagulation panel to assess bleeding risk). Hepatic neoplasia or idiopathic vacuolar hepatopathy (characterized by nodular hyperplasia and hepatocyte vacuolar degeneration adjacent to areas of parenchymal collapse). Immunohistochemistry can demonstrate antiglucagon antibody-positive neoplastic cells on samples obtained from pancreas, liver, spleen, adrenal glands, and mesenteric lymph nodes by ultrasound-guided biopsy, exploratory laparotomy, or postmortem.
- Other assays:
  - Fasting and postprandial bile acid values are frequently elevated (nonspecific).
  - Complete plasma amino acids (hypoaminoacidemia supportive of diagnosis of SND) testing is available at Amino Acid Analysis Laboratory Service (University of California, Davis). Contact laboratory for sample handling and cost (www.vetmed.ucdavis.edu/vmb/aal/aal.html).
  - Because of their lack of specificity, usefulness of plasma glucagon (hyperglucagonemia) and serum insulin (hyperinsulinemia) testing is limited.

TREATMENT

TREATMENT OVERVIEW

Treatment consists of a threefold approach: supportive therapy for the dermatologic manifestations, management of internal disease process (which may require hospitalization), and surgical removal of neoplasm whenever possible.

ACUTE GENERAL TREATMENT

- Pain management
- Treat secondary bacterial and fungal infections with appropriate therapy (avoid systemic azole antifungal therapy because of potential hepatotoxicosis).
- Gentle shampoo therapy

CHRONIC TREATMENT

- Slow intravenous amino acid infusions: 25 mL/kg over 6-8 hours. Repeat every 7-14 days based on response. Some dermatologists recommend 3 treatments the first week, followed by once or twice weekly thereafter. Most patients will demonstrate clinical improvement within 5-10 days.

    - 10% crystalline amino acid crystalline solution (Aminosyn [Abbott Laboratories]) is product of choice. Because of the high osmolality of this solution, a central (jugular) venous catheter is recommended to reduce risk of thrombophlebitis.
    - 3% amino-acid and electrolyte solution (ProcalAmine [B. Braun]) is an alternative product. Lower cost and lesser hypertonicity (can therefore be injected in peripheral veins).
- Insulin therapy if indicated
- Somatostatin analog, octreotide (inhibits glucagon release), 2 mcg/kg SQ q 12 h, can improve skin lesions and systemic signs in patients with nonresectable or relapsing glucagonoma-associated disease. Anorexia is a likely side effect.

NUTRITION/DIET

- High-quality, high-protein diet. Adding 3-6 entire hard-boiled eggs or egg whites per day to the diet may be beneficial.
- Vitamin E supplementation, 400 IU q 12 h PO
- Oral essential fatty acid and zinc methionine supplementation (Zinpro), 1.5 mg/kg q 24 h PO
- Oral nutraceutical *S*-adenosylmethionine, 18-22 mg/kg PO q 24 h (SAMe, Denosyl SD-4, Zentonil, S-Adenosyl) can attenuate liver damage.

DRUG INTERACTIONS

Using antiinflammatory doses of oral glucocorticosteroids is controversial. It may give temporary relief, but diabetes and deterioration of the liver are possible complications.

POSSIBLE COMPLICATIONS

- Discomfort experienced while walking may become sufficiently severe to constitute a reason for euthanasia.
- Monitor for signs of encephalopathy (slow down infusion rate if indicated) when using intravenous amino acid infusions.
- Postsurgical pancreatitis and biliary obstruction may occur.

PROGNOSIS AND OUTCOME

- SND in dogs: guarded to poor, even in dogs with a history of phenobarbital administration, and despite drug discontinuation.
- Glucagonoma syndrome in dogs: good. Surgical excision of pancreatic tumor may result in remission.
- SND in cats: poor

PEARLS & CONSIDERATIONS

TECHNICIAN TIP

The pododermatitis associated with SND may be extremely painful. Use care and a gentle approach when walking dogs suspected or confirmed of having SND (may be reluctant to walk owing to intense foot pain; do not misinterpret this as “stubbornness”).

SUGGESTED READING

Byrne KP: Metabolic epidermal necrosis: hepatocutaneous syndrome. Vet Clin North Am Small Anim Pract 29:1337, 1999.

March PA, et al: Superficial necrolytic dermatitis in 11 dogs with a history of phenobarbital administration (1995-2002). J Vet Intern Med 18:65, 2004.

AUTHOR: VINCENT DEFALQUE

EDITOR: MANON PARADIS

Subinvolution of Placental Sites

Additional Images Available on Website

BASIC INFORMATION

DEFINITION

Delay of the normal uterine involution process in the bitch beyond 12 weeks after whelping, manifesting as persistent bloody vaginal/vulvar discharge in a dog that is otherwise well

SYNONYMS

SIPS, metrorrhagia (uterine bleeding) postpartum, placentitis postpartum

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Not often observed clinically; however, histopathologic prevalence is 8%–21%.
- Young bitches < 3 years old; no effect of litter size

RISK FACTORS: Low parity (especially in first pregnancy/litter)

ASSOCIATED CONDITIONS & DISORDERS: Anemia, postpartum metritis, and uterine rupture could occur as a result of subinvolution of placental sites but are very rare sequelae.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- History of recent whelping
- Likely primiparous bitch (first litter)
- Hemorrhagic vaginal/vulvar discharge persistent even after pups are weaned
- Persistent postparturient serosanguineous vaginal/vulvar discharge
- Bitch is otherwise in good health.

PHYSICAL EXAM FINDINGS

- Discharge is red rather than normal brown lochia.
- Slight pallor of mucous membranes if discharge is copious
- Abdominal palpation: discrete uterine swellings of various sizes often felt on palpation
- Physical exam generally reveals an otherwise healthy animal.

ETIOLOGY AND PATHOPHYSIOLOGY

- Normally, expulsion of the fetal membranes and lochia takes place in the immediate postpartum period, and a mild serosanguineous discharge may last 3-5 weeks after parturition.
- With SIPS, the endometrium and myometrium are invaded by placental cells (trophoblasts).
- Failure of these cells to regress prevents normal involution, which then results in chronic hemorrhagic vaginal/vulvar discharge in a bitch that usually has no other clinical signs. Severe metrorrhagia is rare in absence of coagulopathy or uterine laceration.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is often presumptive (history and physical exam). Typically primiparous younger bitches with a range of hemorrhagic vaginal discharge: from a few drops of blood passing from the vulva for several weeks postpartum that usually subside without therapy, to acute life-threatening metrorrhagia requiring transfusion.

DIFFERENTIAL DIAGNOSIS

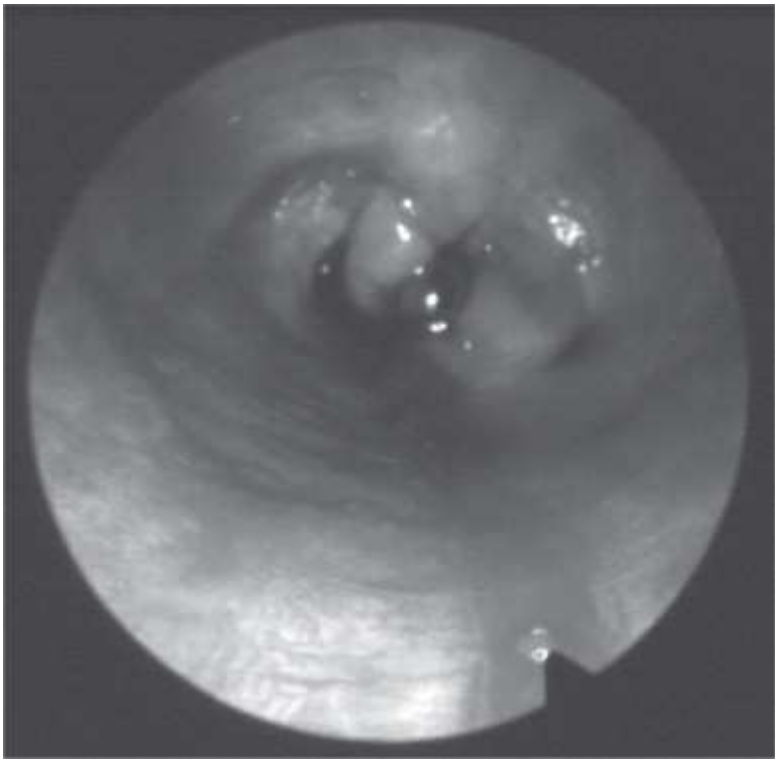
- Proestrus
- Metritis
- Cystic endometrial hyperplasia/pyometra
- Vaginitis
- Vulvar, vaginal, or uterine tumor
- Urinary tract hemorrhage (e.g., bacterial cystitis, calculi)
- Coagulopathy
- Brucellosis
- Trauma

INITIAL DATABASE

- CBC: unremarkable. Note: mild normocytic, normochromic anemia is normal in postpartum bitches.
- Serum biochemistry profile: unremarkable
- Vaginal cytologic examination showing trophoblasts

ADVANCED OR CONFIRMATORY TESTING

- Definitive diagnosis: histologic examination based on biopsy specimen of placental sites (rarely done)
- Vaginoscopy (see p. 1361): to distinguish vaginal bleeding from blood derived from the uterus
- Abdominal ultrasound: focal thickenings of the uterine wall and a fluid-distended lumen; color Doppler velocity measurements of blood flow differentiates SIPS from normally involuting uteruses.
- Abdominal radiographs: focal areas of uterine irregularity



SUBINVOLUTION OF PLACENTAL SITES Vaginoscopic view of the cranial vagina from a bitch with subinvolution of placental sites (SIPS), showing bloody discharge originating from the uterus.

(Courtesy Auke C. Schaefers-Okkens.)

TREATMENT

TREATMENT OVERVIEW

Often, spontaneous remission occurs without the need for medical or surgical intervention. Ovariohysterectomy (OHE) is required in

acute cases with severe metrorrhagia.

ACUTE GENERAL TREATMENT

- Observation (benign neglect):
  - Erosion through the uterine wall resulting in peritonitis is possible but rare.
  - In most cases, SIPS resolves spontaneously.
- OHE indicated if:
  - Bitch is not intended for future breeding.
  - Hemorrhage is severe.
- Acute life-threatening uterine bleeding may require blood transfusion (see p. 1347)
- Systemic and intrauterine antibiotics may be indicated when metritis or peritonitis is present.
- Megestrol acetate (not earlier than 6 weeks after parturition): first week of treatment, 0.1 mg/kg once daily PO; second week of treatment, 0.05 mg/kg once daily PO

POSSIBLE COMPLICATIONS

- Infection: bloody vaginal discharge in bitches > 6 weeks after parturition with no signs of endometritis (this is a period in which endometritis is normally not seen):
  - By not treating the discharge, can continue until next proestrus/estrus
- Endocrine adverse effects of megestrol acetate

RECOMMENDED MONITORING

Recheck animals showing any signs of systemic illness.

PROGNOSIS AND OUTCOME

- With spontaneous remission, future reproductive success is not compromised.
- Affected bitches are not predisposed to SIPS in subsequent pregnancies.

PEARLS & CONSIDERATIONS

COMMENTS

SIPS is the most common cause for persistent postparturient serosanguineous vaginal/vulvar discharge in an otherwise healthy bitch.

PREVENTION

Ovariohysterectomy or not breeding an intact female dog will prevent this problem from occurring.

CLIENT EDUCATION

Careful monitoring for complications such as vaginitis (foul smelling) that may lead to metritis and systemic illness.

SUGGESTED READING

Dickie MB, et al: Diagnosis and therapy of the subinvolution of placental sites in the bitch. J Reprod Fertil Suppl 47:471, 1993.

AUTHOR: CARLOS GRADIL

EDITOR: MICHELLE KUTZLER

Subcutaneous Emphysema

BASIC INFORMATION

DEFINITION

Accumulation of air in subcutaneous tissues

EPIDEMIOLOGY

SPECIES, AGE, SEX: More often seen in cats than in dogs (cats have a thin dorsal tracheal membrane compared to dogs).

RISK FACTORS

- Endotracheal intubation, especially in cats
- Jugular venipuncture
- Trauma to airways
- Bite wounds (anaerobic infection of subcutis; disruption of the pulmonary system by penetrating wounds)
- Surgery of the airways, especially upper airway surgery

ASSOCIATED CONDITIONS & DISORDERS

- Pneumomediastinum
- Pneumoretroperitoneum
- Pneumopericardium
- Pneumothorax

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- History of recent anesthesia with intubation, trauma, or surgery
- History of recent jugular venipuncture, transtracheal aspiration, or other penetrating medical procedure of the neck
- Dyspnea, discomfort
- Rapid onset of swelling of the body, initially around the neck but may progress to total body

PHYSICAL EXAM FINDINGS: Animal may manifest respiratory discomfort. Characteristic crackling sensation (crepitus) on palpation of the skin overlying the trapped air is pathognomonic.

- Initially focal (especially around the neck) and progressing rapidly to affect the whole body: suggests airway perforation/rupture as source; dyspnea, discomfort may or may not be present.
- Focal in an animal showing signs of severe illness; may suggest infection-related subcutaneous emphysema. A meticulous search for penetrating wounds is indicated.

ETIOLOGY AND PATHOPHYSIOLOGY

- A break in the integrity of the airway at any point between the pharynx and terminal bronchioles
- An independent source of gas formation (bacteria) in the subcutis
- With any of the following three mechanisms, air may remain trapped in the subcutaneous tissues by unidirectional valve action of the airway trauma:
    - Rupture of dorsal tracheal membrane (cats > dogs)
    - Rupture of dorsolateral or ventrolateral tracheal annular ligament
    - Penetrating wound in cervical area

Specific etiologies:

- Related to anesthetic administration of intubation:
    - Overinflation of endotracheal cuff
    - Use of a stiff stylet to guide the endotracheal tube through the larynx causes punctures in trachea

- Manipulation of the head without disconnecting the endotracheal tube
- Surgical
- Traumatic:
  - Bite wounds
  - Lacerations or penetrating foreign objects, including jugular venipuncture and transtracheal aspirates
- Infectious:
  - Inoculation of gas-forming bacteria (e.g., anaerobes) during penetrating injuries such as bite wounds anywhere on the body can produce infection of the subcutis.
- Idiopathic

SUBCUTANEOUS EMPHYSEMA External appearance of a domestic long-haired cat with marked subcutaneous emphysema. Note severe distention of the subcutaneous space, manifesting as a diffusely bloated appearance over the torso but not the head.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A history of recent intubation or tracheal trauma with or without acute onset of increased body size is suggestive. The characteristic "bubble wrap"–like feeling on palpation and/or the presence of subcutaneous air on radiographs confirms the diagnosis.

DIFFERENTIAL DIAGNOSIS

Tracheal avulsion/rupture; radiographs reveal physical separation of the trachea; surgery is required.

INITIAL DATABASE

- CBC and serum biochemical profile: generally unremarkable for cases of airway trauma; may show evidence of infection (neutrophilia, left shift, toxic changes) if subcutaneous emphysema is due to anaerobic infection of the subcutis.
- Radiographs of neck and thorax show presence of air trapped under the skin.

ADVANCED OR CONFIRMATORY TESTING

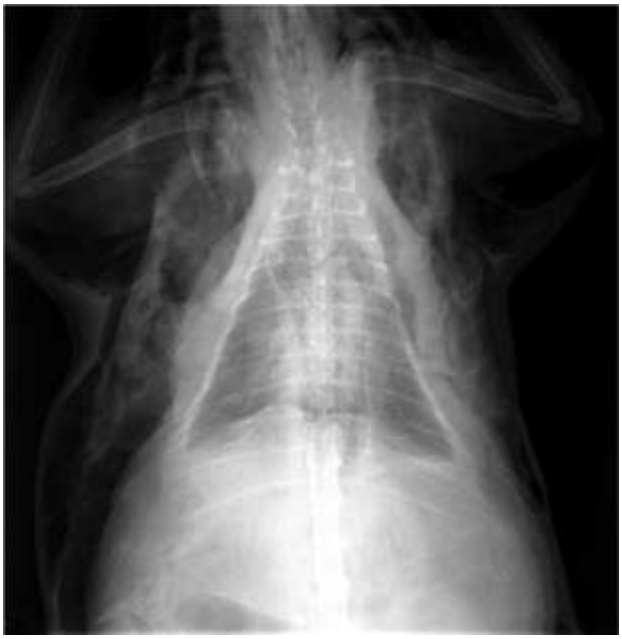
Tracheoscopy:

- Lesions may be difficult to visualize.
- Negative finding does not rule out tracheal trauma as cause for subcutaneous emphysema.
- CT scan of trachea may be required to detect presence and/or extent of tracheal rupture.
- Surgical exploration if severe

TREATMENT

TREATMENT OVERVIEW

Most patients will heal spontaneously in 1-2 weeks. More severe trauma requires surgical repair.



SUBCUTANEOUS EMPHYSEMA Radiograph showing severe subcutaneous emphysema, apparent as gas lucencies throughout the subcutis.

ACUTE GENERAL TREATMENT

- In animals without respiratory discomfort:
  - Supportive care while awaiting spontaneous absorption of the air
  - Cage rest
- In animals with mild discomfort:
  - Consider light sedation
  - Removal of air via an 18-G or 16-G needle. Air may be gently massaged toward the needle for evacuation. Needle suction alone may not able to remove the trapped air. Air removal via skin stab incisions is not advised.
  - Repeat this procedure to keep the animal comfortable as needed.
  - Penrose drains can be placed into the subcutis (similar to treating a subcutaneous abscess) to allow for continuous drainage of air. Generally less labor intensive and more effective than repeated centesis.
  - Analgesia (e.g., with butorphanol, 0.1-0.3 mg/kg IV q 4-6 h)
- In animals with recurrent/refractory subcutaneous emphysema and progressive respiratory distress:
  - If dyspnea is due to compression of the airways by trapped air in the subcutis or mediastinum, trapped air should be allowed to drain, leading to improved respiratory effort.
  - Surgical repair of the trachea if conservative measures are inadequate or if radiography suggests tracheal avulsion/rupture
  - Analgesia (e.g., with butorphanol, 0.1-0.3 mg/kg IV q 6-8 h)

DRUG INTERACTIONS

Avoid subcutaneous drug administration until normalized.

POSSIBLE COMPLICATIONS

Depending on the etiology of the subcutaneous emphysema: tracheal rupture, pneumothorax, and pneumoretroperitoneum are possible, as is sepsis (if bacterial infection of the subcutis).

RECOMMENDED MONITORING

Evaluate rate and depth of respiration as an indicator for the level of comfort in the animal and consider the need for surgical

treatment.

PROGNOSIS AND OUTCOME

In animals that do not develop respiratory distress, the prognosis is good, and spontaneous recovery will occur between 3 and 15 days.

PEARLS & CONSIDERATIONS

COMMENTS

- Most animals will recover with supportive care and will not require surgery.
- Sloughing of the skin is not a recognized complication of subcutaneous emphysema.
- Some animals show discomfort and pain during the presence of subcutaneous emphysema. Analgesic treatment should be initiated.
- Avoid subcutaneous drug administration in patients with subcutaneous emphysema (variable absorption).

TECHNICIAN TIPS

- Prevent overinflation of endotracheal cuffs.
- Perform cautious, appropriate jugular venipuncture, especially in cats.
- Disconnect endotracheal tubes prior to repositioning of the animal's head.

SUGGESTED READING

Bhandal J, Kuzma A: Tracheal rupture in a cat: diagnosis by computed tomography, Can Vet J 49:595–597, 2008.

Hardie EM, et al: Tracheal rupture in cats: 16 cases (1983-1998), J Am Vet Med Assoc 214(4):508–512, 1999.

AUTHOR: HANS GELENS

EDITOR: ELIZABETH ROZANSKI

Subaortic Stenosis

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

- Common congenital malformation of the canine heart; uncommon in kittens.
- Hallmark: a narrowing of the outflow tract of the left ventricle (LVOT)
- May be fixed (fibrous nodule, band, annulus, fibromuscular tunnel) or dynamic (systolic anterior motion of the mitral valve or SAM, asymmetric septal hypertrophy)

SYNONYMS

Subvalvular aortic stenosis, SAS

EPIDEMIOLOGY

SPECIES, AGE, SEX

- First noted in puppies < 12 months old (usually after 6 to 8 weeks of age)
- The lesion has never been documented during fetal life in any species.
- The severity of narrowing often is progressive during a puppy's growth, and the true severity of narrowing cannot be determined until the dog is fully grown (at least 1 year old).
- Depending on the study, subaortic stenosis (SAS) is either the most common congenital heart defect of dogs or is second to patent ductus arteriosus.
- In cats, hypertrophic cardiomyopathy (see p. 565) affecting the interventricular septum or associated with SAM may produce the same effect of left ventricular outflow obstruction as SAS.

GENETICS & BREED PREDISPOSITION

- Large-breed dogs (Newfoundland, golden retriever, rottweiler, boxer, German shepherd, Bouvier des Flandres, Bernese mountain dogs and Dogues de Bordeaux)
- Hereditary transmission (autosomal dominant with a polygenic pattern) has been demonstrated in the Newfoundland dog and is suspected in the golden retriever (autosomal recessive)
- Cannot be attributed specifically to sire or dam in any breed (no apparent sex linkage)
- Recognized risk of mildly affected dogs to produce more severely affected offspring

ASSOCIATED CONDITIONS & DISORDERS

- Mild/moderate aortic valvular regurgitation/insufficiency: very commonly observed echocardiographically in dogs with SAS; often inaudible on auscultation.
- Mitral dysplasia, patent ductus arteriosus, and a variety of aortic arch abnormalities have also been associated with some SAS cases.
- Dogs with SAS are predisposed to bacterial endocarditis of the aortic valve.
- A decreased aortoseptal angle is often seen with SAS and possibly represents a predisposing anatomic factor.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Many distinct malformations are grouped under the heading of SAS.

- Fixed obstruction:
  - Grade 1: small raised nodules of thickened endocardium
  - Grade 2: narrow ridge of thickened endocardium that partially encircles the left ventricular outflow tract
  - Grade 3: fibrous band, ridge, or collar completely encircles the left ventricular outflow tract.
  - This grading system is only for gross pathologic findings. It is unrelated to murmur intensity or clinical signs.
- Dynamic obstruction:
  - Systolic anterior motion of the mitral valve:
    - Narrowing of the left ventricular outflow tract and papillary muscle distortion caused by left ventricular hypertrophy slightly distort the mitral valve such that a small amount of mitral regurgitation occurs.

- Septal hypertrophy or malalignment:
  - The left ventricular hypertrophy induced by SAS may itself further contribute to left ventricular outflow obstruction because of hypertrophy of the interventricular septum.
  - The aortic arch may be congenitally malaligned in its attachment to the left ventricular outflow tract, resulting in SAS due to protrusion of the interventricular septum into the subvalvular area.

HISTORY, CHIEF COMPLAINT: In most cases, the condition causes a heart murmur in a dog not showing any overt clinical signs. However, severe cases may show:

- Exertional fatigue or syncope
- Congestive heart failure (CHF) (rare)
- Sudden death
- Some moderate cases show exaggerated or long-lasting panting after exercise as their only clinical sign

PHYSICAL EXAM FINDINGS: Often unremarkable except for a systolic, ejection-type (crescendo-decrescendo) heart murmur, heard loudest in the left cranial thorax (between the third and fifth intercostal spaces) or at the thoracic inlet (immediately lateral to the trachea). Intensity of the heart murmur grossly correlates with severity of disease:

Grades 1 to 3/6 = mildly to moderately affected dogs

Grades 4 to *6/6* = severely affected dogs

- Murmur may radiate cranially through the carotid arteries to the neck and head or to the right hemithorax
- Weak and slow rising femoral pulse (*pulsus parvus et tardus*) in severe cases
- A diastolic heart murmur is sometimes heard with aortic valve insufficiency
- Premature beats and pulse deficits (due to ventricular arrhythmias) may be detected, in severe cases

ETIOLOGY AND PATHOPHYSIOLOGY

- The etiology is multifactorial and may be caused by the combination of persistence of embryonal endocardial tissue that retains potential capacity for chondrocytes proliferation and predisposing anatomic characteristics of the LVOT such as increased mitral-aortic separation, decreased aortoseptal angle and a small aortic annulus which increase the shear stress and stimulate cellular proliferation
- The consequence of SAS, regardless of its subtype is an elevated left ventricular pressure overload that results in:
  - An increase in left ventricular systolic pressure and a pressure gradient across the subaortic lesion.
  - An increased blood flow velocity through the left ventricular outflow tract.
  - Compensatory left ventricular concentric hypertrophy (diffuse, symmetrical thickening of the left ventricle).
- This process may lead to left-sided CHF in some cases.
- With worsening SAS over time, left ventricular thickening may exceed intra-myocardial (coronary) blood supply, which does not grow along with the hypertrophied myocardial cells:
- The result is relative underperfusion of left ventricular tissue and ventricular arrhythmias or, less commonly, myocardial infarction.
- Either process may be responsible for sudden death (common in severe SAS).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is first suspected on auscultation of a systolic heart murmur loudest at the left or right heart base or cranial sternal region. Electrocardiography, thoracic radiographs, and blood tests may help raise or lower the likelihood of SAS, but a definitive diagnosis requires Doppler echocardiography.

DIFFERENTIAL DIAGNOSIS

- Other systolic heart murmur heard between the left second and fourth intercostal spaces:
  - Pulmonic stenosis
  - Tetralogy of Fallot
  - Atrial septal defect
  - Incompletely ausculted patent ductus arteriosus
- High output states:
  - Hyperthyroidism
  - Anemia
  - Fever

- Exercise (rare); note that physical activity increases the heart rate, which may make apparent a murmur of SAS that was not audible at rest. The distinction between this phenomenon and a benign, exercise-induced heart murmur requires echocardiography.

- Juvenile "innocent" heart murmur:
  - Puppies and kittens < 6 months old
  - Soft heart murmur, grades 1 to 3/6, short (early to midsystolic)
  - Often disappears with a change in body position or exercise/increase in heart rate
  - Electrocardiogram (ECG), thoracic radiographs, and echocardiogram are normal

INITIAL DATABASE

- ECG:
  - May be normal in mild to moderate cases
  - Left ventricular hypertrophy pattern often present (R wave > 3 mV in lead II) but not striking even in some moderate to severe cases; unreliable as a screening tool
  - ST segment may be slurred, depressed, or elevated in severe cases (myocardial hypoxia)
  - Ventricular arrhythmias in severe or long-standing cases
- Thoracic radiographs:
  - Often normal; unreliable as a screening tool for SAS
  - Helpful mostly to rule out congestive heart failure
  - Variable left-sided cardiomegaly (left ventricular and atrial enlargement), usually only with moderate to severe cases
  - Poststenotic dilatation of the aortic root may be visible in severe cases
- Echocardiogram: (definitive diagnosis):
  - Two-dimensional (2-D):
    - Often normal in mildly affected dogs
    - Subvalvular obstruction lesion or narrowed left ventricular outflow tract
    - Left ventricular concentric hypertrophy (diffuse, symmetrical left ventricular thickening)
    - Variable dilatation of the left atrium
    - Dilated ascending aorta
  - M-Mode:
    - Normal to increased left ventricular fractional shortening (poorly sensitive)
    - SAM sometimes observed
  - Doppler study:
    - Turbulent, high-velocity systolic signal in the left ventricular outflow tract and aortic root. Normal range (controversial) = up to 2 m/s; "gray zone" = 2-2.3 m/s; >2.3 m/s = highly suggestive of SAS when corresponding murmur and breed are also present; exception in the boxer breed and possibly others, where such elevated velocities may be normal (requiring two-dimensional aortic measurements for further evaluation)
    - Determination of the peak pressure gradient in combination with the indexed effective orifice area (IEOA) estimates the severity of disease; peak pressure gradient = 4 × (Doppler-derived LVOT velocity in m/s)^2
      - 16-40 mmHg = mild SAS
      - 40-100 mmHg = moderate SAS
      - >100 mmHg = severe SAS
      - IEOA < 0.6 cm^2/m^2 = severe SAS
    - Diastolic signal of aortic regurgitation is present in most cases of SAS

ADVANCED OR CONFIRMATORY TESTING

Cardiac catheterization and angiography: virtually never used for diagnosis. The procedure is invasive, requires general anesthesia, and provides little additional information over echocardiography.

TREATMENT

TREATMENT OVERVIEW

- No definitive treatment exists for curing SAS
- Only severe cases need therapy. True moderate and mild cases are asymptomatic and do not need therapy. Rarely, some moderate cases will have ventricular arrhythmias which will be addressed through medical treatment.
- Excision of the stenotic tissue via open-heart surgery or dilatation of the stenosis via non-invasive balloon valvuloplasty have not yet been shown to provide an outcome that is superior to conservative, medical management.
- Recurrence of the stenotic lesion is often observed after balloon dilation or surgery possibly as a result of anatomic characteristics of the LVOT that were left unaltered after surgery (e.g., abnormal aortoseptal angle).

ACUTE GENERAL TREATMENT

see Ventricular Arrhythmias, p. 1165; Heart Failure, Acute/Decompensated, p. 468.

CHRONIC TREATMENT

- Mild SAS: no treatment
- Moderate SAS: mild exercise restriction (only avoid vigorous activity) and ß-adrenergic blocking agent to prevent or control ventricular arrhythmias when present:
  - Atenolol, 0.25-1 mg/kg PO q 12-24 h; begin at low dose and increase titration over 2-4 weeks until upper end of dose range or signs of intolerance (lethargy, inappetence) warranting dosage reduction; *or*
  - Sotalol, 0.5-2 mg/kg PO q 12 h, up titration as per atenolol. Sotalol might be more effective in certain breeds (e.g., boxers).
- Severe SAS:
  - Open resection of the obstructing lesion is possible.
  - Balloon dilation of the stenosis; survival not longer than with medical management
  - β-Adrenergic blocking agent to prevent or control ventricular arrhythmias:
    - Atenolol or sotalol (see above); exercise restriction
- SAS with CHF: see p. 468

DRUG INTERACTIONS

- Concurrent use of antacids can alter the bioavailability of atenolol.
- Calcium channel blockers may cause hypotension and bradycardia when administered together with atenolol.
- Effects of theophylline can be blocked by β-adrenergic blocking agents like propranolol.

POSSIBLE COMPLICATIONS

- Ventricular arrhythmias/ventricular tachycardia
- Exertional syncope or sudden death
- Left-sided heart failure
- Aortic valve endocarditis

RECOMMENDED MONITORING

- Control ventricular arrhythmias when present (ambulatory ECG recordings [see] recommended if syncope is noted and for monitoring efficacy of antiarrhythmic treatment if possible).
- SAS is a progressive disease when a dog is growing; therefore, the final cardiac evaluation should be done at 12 months of age or older to stage the severity of disease.

PROGNOSIS AND OUTCOME

- Favorable: mild to moderate SAS
  - Normal quality of life and longevity, especially when follow-up visit shows no progression of SAS
- Poor: severe SAS
  - Median survival time is 19 months when untreated.
  - Most dogs die suddenly, usually within the first 3 years of life.
  - Medical management might increase median survival to 4.5 years.

PEARLS & CONSIDERATIONS

COMMENTS

- The combination of a =grade 4/6 ejection heart murmur that radiates cranially to the thoracic inlet and over the carotid arteries along with a weak femoral pulse in a puppy is highly suggestive of severe SAS.
- The severity of ventricular arrhythmias detected by extended (24-hour) ambulatory ECG recordings correlates with the severity of disease.
- Dogs with peak pressure gradients > 125 mm Hg are very likely to develop serious complications or sudden death.
- Because of the progressive nature of SAS during growth, the lesion/heart murmur may be clinically silent in very young puppies but becomes increasingly prominent at >2-3 months of age.

- Overtly healthy boxer dogs may have systolic murmurs without obvious SAS. This phenomenon is potentially caused by a relatively smaller outflow tract in that breed, predisposing them to increased ejection velocity and development of murmurs.
  - Grades I-III/VI murmur
  - No SAS lesion on echocardiography
  - Differentiation between SAS and the normal state in these dogs is challenging and requires echocardiography (left ventricular thickening, left atrial enlargement, and aortic insufficiency suggest SAS), ECG (ventricular arrhythmia of left ventricular origin suggests SAS), and follow-up exams (progression of these abnormalities and of Doppler-derived pressure gradient suggest SAS).
- Identification of the most mildly affected animals (clinically silent "carrier") such as dogs with a soft systolic murmur only apparent at higher heart rates, and a structurally normal heart on two-dimensional echocardiography, remains extremely challenging. Diagnosis in these cases involves a combination of physical examination, Doppler echocardiography, and tightly controlled follow-up exams (both the animal in question and its siblings and/or offspring).

PREVENTION

- Vigilance regarding the possible need for antibiotics is important in all SAS cases during periods of anticipated bacteremia (dental procedures, surgery, severe skin disease, other concurrent bacterial disease); avoiding overuse of antibacterials is also important.
- Use breeding dogs that have been screened for SAS.

CLIENT EDUCATION

- In cases of severe SAS, avoid prolonged, vigorous exercise.
- Contact breeders to notify them of SAS cases.

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AUTHOR: MARIE C. BÉLANGER

EDITOR: ETIENNE CÔTÉ

Stunted Growth

BASIC INFORMATION

DEFINITION

Slowed or retarded growth rate; failure to attain expected body size/stature; uncommon disorder

SYNONYMS

Cretinism (congenital hypothyroidism [rare]); delayed growth, dwarf, runt, poor-doer, unthrifty; pituitary dwarfism (growth hormone deficiency, hyposomatotropism [rare])

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs and cats, age and sex vary with cause
- Failure to grow is usually recognized by 1 year of age (most noted prior to 2 years).
- First 3 months: growth hormone deficiency, congenital hypothyroidism, cleft palate, congenital megaesophagus, persistent right aortic arch (PRAA), other vascular ring anomaly, parasitism, juvenile hyperparathyroidism
- Under 1 year: juvenile diabetes, portosystemic shunt, exocrine pancreatic insufficiency, cardiac abnormalities, renal disease, osteochondrodystrophies, ciliary dyskinesia
- Under 2 years: most noted prior to 2 years. Nutritional deficiencies in giant breed dogs might manifest later. Renal diseases, hepatopathies.

GENETICS & BREED PREDISPOSITION

- Pituitary dwarfism: German shepherd, Karelian bear dog, spitz, toy pinscher
- Congenital hypothyroidism: fox terrier, boxer, giant schnauzer, Abyssinian cat
- Osteochondrodysplasia: various, including Labrador retriever, Irish setter
- Cleft palate: shih tzu, English bulldogs, pointers, Swiss sheepdog, Brittany spaniel
- Congenital megaesophagus: Irish setter, German shepherd, Labrador retriever, miniature schnauzer
- Vascular ring anomaly: German shepherd, Irish setter
- Pancreatic acinar atrophy: German shepherd
- Portosystemic shunt: Havanese, Yorkshire terrier, Maltese, Dandy Dinmont terrier, pug, miniature schnauzer
- Polycystic kidney disease: Cairn terrier, West Highland white terrier, Persian, Himalayan
- Hereditary nephritis: English cocker spaniel, Samoyed
- Renal dysplasia: Malamute, chow chow

RISK FACTORS

- Varies with disease
- Most risk factors are not identified except genetic diseases.
- Malnutrition: poor-quality feed
- Hypothyroidism: maternal exposure to iodine-131 (^{131}I)

CONTAGION & ZOONOSIS: Some intestinal parasites present risks of visceral larval migrans to humans.

ASSOCIATED CONDITIONS & DISORDERS

- Juvenile diabetes mellitus: pancreatic acinar atrophy and exocrine pancreatic insufficiency
- Pituitary dwarfism: hypoadrenocorticism
- Portosystemic shunt: urate urolithiasis, microvascular dysplasia
- Megaesophagus: myasthenia gravis, vascular ring anomaly
- Cleft palate: middle ear abnormalities

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Nutritional:
  - Poor feed or insufficient supply
  - Mechanical problems: cleft palate, megaesophagus, PRAA
  - Maldigestion/malabsorption: parasites, intestinal infections (salmonella, histoplasmosis), pancreatic acinar atrophy
- Endocrine:
  - Congenital hyposomatotropism, congenital hypothyroidism, juvenile hyperparathyroidism, diabetes mellitus
- Cardiac diseases:
  - Patent ductus arteriosus, others
- Metabolic:
  - Portosystemic shunt, microvascular dysplasia
  - Renal dysplasia, other nephritis
- Chondrodysplastic

HISTORY, CHIEF COMPLAINT

- May be unnoticed by owner
- Pet lags behind littermates in growth.
- Diet history, deworming history, onset and progression of signs are important.
- Medication exposure
- Signs of mental dullness
- Polyuria/polydipsia

PHYSICAL EXAM FINDINGS

- Varies with disease. Important distinctions are good versus poor body condition and proportionate versus disproportionate dwarfism:
  - Hyposomatotropism and chondrodysplastic animals are in good body condition, whereas other disorders lead to poor body condition.
  - Congenitally hypothyroid patients and chondrodysplastic patients are disproportionate dwarfs (limbs are exceptionally short). This is in contrast to proportional dwarfism (e.g., toy poodle) in which the limbs, trunk, and head are of appropriate relative sizes.
- Examine patient for:
  - Mental dullness or disorientation
  - Dwarfism
  - Cleft palate
  - Cough, respiratory distress
  - Heart murmur
  - Bloated abdomen
  - Signs of diarrhea staining coat

ETIOLOGY AND PATHOPHYSIOLOGY

Specific pathophysiologic mechanism varies with disease:

- Inability to ingest, absorb, or utilize nutrients
- Inability to properly execute growth

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Stunted growth may be obvious on the physical exam or subtle. Evaluation for inciting factors begins with history (errors in management or basic care) and physical examination (signs of concurrent or contributory disorders) and proceeds to basic laboratory tests and diagnostic imaging as needed. Unusual endocrinopathies may be considered diagnoses of exclusion.

DIFFERENTIAL DIAGNOSIS

see Disease Forms/Subtypes, above.

INITIAL DATABASE

- Fecal flotation
- CBC:
  - Microcytic anemia: portosystemic shunt, polycythemia
  - Eosinophilia: hypoadrenocorticism, parasitism
  - Lymphocytosis/neutropenia: hypoadrenocorticism
- Serum biochemistry panel:
  - Low albumin: exocrine pancreatic insufficiency, portosystemic shunt, infiltrative bowel disease
  - Hyperglycemia: diabetes mellitus
  - Hypoglycemia: hypoadrenocorticism
  - High calcium with normal or low phosphorus: hypoparathyroidism
  - High blood urea nitrogen: renal disease versus prerenal azotemia
- Urinalysis:
  - Urine specific gravity < 1.035: kidney disease, hypothyroidism; may be normal in nonazotemic patient (elimination of free water)
  - Glucose: diabetes mellitus
  - Protein: nephritis, glomerulopathies
  - Casts, infection: nephritis
  - Urate uroliths: portosystemic shunt, microvascular dysplasia
- T4: congenital hypothyroidism

ADVANCED OR CONFIRMATORY TESTING

- Trypsinlike immunoreactivity: pancreatic acinar atrophy/exocrine pancreatic insufficiency
- Urine bacterial culture and sensitivity
- ACTH stimulation test: hypoadrenocorticism
- Abdominal ultrasound: kidney disease, portosystemic shunt
- Scintigraphy: portosystemic shunt, ciliary dyskinesia
- Xylazine stimulation, serum level of insulin-like growth factor: hyposomatotropism

TREATMENT

TREATMENT OVERVIEW

Correct diseases that are reversible.

ACUTE GENERAL TREATMENT

Generally not acute presentations

CHRONIC TREATMENT

- Varies with disease
- Examples, depending on disorder: close portosystemic shunt, treat parasitism, improve diet, provide thyroxine, insulin, pancreatic enzyme replacement.

POSSIBLE COMPLICATIONS

- Death: patent ductus arteriosus, portosystemic shunt, extreme malnutrition
- Diabetic ketoacidosis: congenital diabetes mellitus
- Aspiration pneumonia: megaesophagus, PRAA

RECOMMENDED MONITORING

Frequent physical exams

PROGNOSIS AND OUTCOME

- Guarded; most of the diseases are serious and irreversible.
- With surgical reversal, improved longevity of portosystemic shunt patients and patent ductus arteriosus patients may be achieved as long as underlying microvascular dysplasia and irreversible cardiac changes, respectively, are not present.

- Osteochondrodysplastic dogs can fare well, but the disorder is irreversible.

PEARLS & CONSIDERATIONS

COMMENTS

- Key to diagnosis is distinction between good and poor thrift and proportionate and disproportionate dwarfism.
- Adequate nutrition and effective deworming should be assured prior to more expensive diagnostics.

PREVENTION

Careful attention to genetic lines in purebred dogs

CLIENT EDUCATION

The prognosis varies with the disease.

SUGGESTED READING

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AUTHOR: DENNIS SPANN

EDITOR: ETIENNE CÔTÉ

Strychnine Toxicosis

BASIC INFORMATION

DEFINITION

A rapid-onset (30 minutes to 2 hours after ingestion), potentially fatal toxicosis characterized by neurologic dysfunction. Now rare, mainly of historical interest.

SYNONYM

Strychnine: *Nux vomica*

EPIDEMIOLOGY

SPECIES, AGE, SEX

- All animals are susceptible; dogs are more commonly involved than cats.
- Male dogs are more commonly involved.

GENETICS & BREED PREDISPOSITION: Younger dogs and large-breed dogs, such as German shepherds, are overrepresented.

GEOGRAPHY AND SEASONALITY

- Year-round
- Rural and urban dogs equally affected
- Most cases are reported in the western part of the United States and in the Midwest.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Availability or presence of strychnine-containing bait in pet's environment; evidence of exposure
- Rapid onset of apprehension (30 minutes to 2 hours), nervousness, chewing movements, muscular rigidity, tonic-clonic convulsions

PHYSICAL EXAM FINDINGS

- Hyperesthesia, apprehension, nervousness initially
- Severe muscle stiffness, rigidity
- Hyperthermia (>104°F[>40°C]), caused by muscle activity and not febrile in origin
- Sawhorse stance
- Eventually, tetanic seizures (marked by violent, stiff limb movements):
  - Occur spontaneously or may be initiated by external stimuli (touch, sound, sudden bright light)
- Opisthotonos, mydriasis, exophthalmos, and cyanosis may be present before death.
- Vomiting and hypersalivation (uncommon)

ETIOLOGY AND PATHOPHYSIOLOGY

Source:

- Strychnine is a bitter indole alkaloid from the seeds of the vinelike Southeast Asian or Australian trees, *Strychnos nux-vomica* and *Strychnos ignatii*.
- Since 1978 in the United States, strychnine has been a restricted-use pesticide and rodenticide (licensed exterminators only) or has been forbidden in certain U.S. states. Over-the-counter preparations contain <0.5% strychnine; preparations used by licensed exterminators may contain up to 5% strychnine.
- Malicious or accidental strychnine toxicosis occurs when nontarget animals ingest strychnine-containing baits.

Mechanism of Toxicosis:

- Strychnine competitively and reversibly inhibits the inhibitory neurotransmitter glycine at postsynaptic neuronal sites in the spinal cord and medulla. This results in unchecked reflex stimulation of motor neurons affecting all the striated muscles, resulting in generalized rigidity and tonic-clonic seizures caused by these direct central nervous system (CNS) effects.
- Death usually results from respiratory arrest and exhaustion from prolonged seizuring.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Strychnine toxicosis should be suspected based on history of exposure if available and rapid onset of neurologic signs (muscular rigidity, seizures). Diagnosis can be confirmed by identifying strychnine alkaloid in vomitus or urine, but submission and turnaround time makes this confirmation clinically impractical. Given the rapid course of progression of this disorder, treatment is initiated when strychnine intoxication is confirmed (e.g., container with label is available) or reasonably suspected.

DIFFERENTIAL DIAGNOSIS

- Other intoxications causing seizures: metaldehyde, tremorgenic mycotoxins/garbage toxicosis, organochlorine, organophosphorus or carbamate pesticides, zinc phosphide, nicotine
- Tetanus
- Hypocalcemic tetany
- Hepatic encephalopathy

INITIAL DATABASE

Because of the rapid onset of clinical signs, no specific changes are expected on CBC, serum biochemistry profile, or urinalysis at presentation, other than elevated creatine kinase (CK); metabolic acidosis and myoglobinuria possible.

ADVANCED OR CONFIRMATORY TESTING

- On postmortem examination, no characteristic lesions are seen. In cases that have prolonged convulsions before death, agonal hemorrhages of the heart and lungs and cyanotic congestion due to anoxia may be seen.
- Occasionally, poisoned animals may have undigested red or green strychnine-laced grain seeds (wheat, milo, barley) in their stomach.
- Presence of strychnine alkaloid in the vomitus, stomach contents, liver, kidney, or urine is considered diagnostic. In living animals, submit stomach contents (vomitus or stomach washings) or urine early (within the first several hours of exposure). Urine may not contain detectable amounts of strychnine if samples are collected late (1-2 days after the exposure). Seal samples (stomach contents, liver, or kidney) in a plastic bag, freeze them, and then submit them to a veterinary diagnostic laboratory for strychnine analysis.

TREATMENT

TREATMENT OVERVIEW

Because of rapid progression, strychnine toxicosis is a medical emergency. Patients presented early (prior to onset of clinical signs) should be decontaminated via induction of vomiting and administration of activated charcoal. In patients already showing clinical signs, treatment is targeted to reducing or abolishing those signs (controlling seizures, maintaining respirations, and general supportive care). Because CNS effects cause seizures and respiratory depression, many patients will require anesthesia for 24-48 hours.

ACUTE GENERAL TREATMENT

- Control seizures and prevent asphyxia. Do not attempt to decontaminate patients that are already showing neurologic effects. Control seizures and stabilize the patient first.
    - Anticonvulsants:
        - Diazepam, 0.5-2 mg/kg IV, has been used with variable success.
        - If unsuccessful, pentobarbital sodium, 3-15 mg/kg IV to effect; repeated as needed
        - Short-lasting alternative requiring constant rate infusion (easier to titrate, more costly) is propofol, 3-6 mg/kg IV to effect, then 0.2-0.6 mg/kg/min infusion to effect (maintain anesthesia).
        - Isoflurane gas anesthesia: used if seizures are not controlled with the preceding treatment measures
    - Muscle relaxants:
        - Methocarbamol, 100-200 mg/kg IV; repeat as needed; maximum dose of 330 mg/kg per day; *or*

        - Glyceryl guaiacolate (5% solution, 50 mg/mL), 110 mg/kg IV to effect
    - Intubate and provide positive pressure ventilation for severely affected animals (see p. 1362).
- Decontamination of patient:
    - Induction of vomiting (see p. 1364): useful within 30 minutes and only in patients showing no clinical signs
    - Gastric lavage (see p. 1281): used if emesis cannot be induced or when suspected lethal doses have been ingested; intubate the patient with a cuffed endotracheal tube to reduce aspiration risk if the patient is unconscious.
    - Enterogastric lavage: also called *through-and-through lavage*; induce general anesthesia (unless patient is already unconscious). Begin with gastric lavage followed by an enema/colonic irrigation under low pressure and at body temperature. Continue until fluids exit via the gastric tube; used if known ingestion of potentially lethal dose. Premedication: atropine, 0.04 mg/kg IV (to decrease enteric muscle tone, helping fluid flow).
    - Activated charcoal, 2-4 g/kg, with a cathartic such as sorbitol (5-10 mL/kg, 3% solution) PO or via stomach tube
- Supportive care:
    - IV fluid diuresis (24-48 hours or longer)
    - Treat hyperthermia if present (see p. 1281).
    - Confine the patient in a dark, quiet room.
    - Acidification of urine: ammonium chloride, 100 mg/kg PO q 12 h, may help increase urinary excretion of strychnine.

POSSIBLE COMPLICATIONS

- Myoglobinuria and associated renal failure
- Disseminated intravascular coagulation from hyperthermia

RECOMMENDED MONITORING

- Body temperature
- Respiratory rate and character
- Acid-base status

PROGNOSIS AND OUTCOME

- Poor prognosis if status epilepticus uncontrolled by medications listed above; consider euthanasia.
- Good prognosis if seizures are controlled early

PEARLS & CONSIDERATIONS

COMMENTS

- Sporadic strychnine poisoning of animals still occurs.
- Strychnine is ionized in an acidic pH; therefore, it is mainly absorbed from the small intestine, emphasizing the importance of rapid intervention before the onset of signs. Strychnine and its metabolites are mainly excreted in the urine. A toxic dose is eliminated within 24-48 hours following exposure.
- Oral lethal dose in dogs is 0.75 mg/kg; for cats, the dose is 2 mg/kg.
- Ingestion of 1.7 g (1/4 tsp) of 0.5% strychnine bait in a 25-lb (11.3-kg) dog can be lethal.

PREVENTION

Do not use strychnine-containing baits in any pet's environment.

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Stridor and Stertor, Respiratory

BASIC INFORMATION

DEFINITION

Stridor: a harsh, high-pitched sound occurring during inspiration as a result of partial upper airway obstruction Stertor: inspiratory noise occurring specifically during sleeping, e.g., snoring

EPIDEMIOLOGY

SPECIES, AGE, SEX: No predilection, given the broad spectrum of possible underlying diseases

GENETICS & BREED PREDISPOSITION: Brachycephalic breeds are predisposed to partial upper airway obstruction and stridor.

RISK FACTORS

- Nasal/nasopharyngeal disorders, either through primary obstruction (mass, foreign body, mucosal edema) or secondarily due to obstruction by discharge
- Pharyngeal, laryngeal, and tracheal disorders

ASSOCIATED CONDITIONS & DISORDERS: Powerful, sustained inspirations against an obstructed upper airway are associated with the development of noncardiogenic pulmonary edema.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Owners may report stridor individually as a chief complaint or concurrently with other signs suggesting respiratory disease (coughing, nasal discharge, sneezing, dyspnea, epistaxis), pharyngeal disease (gagging, dysphagia), or intermittent complete respiratory obstruction (decreased exercise tolerance, syncope). Clinical signs often may be exacerbated by excitement. Many animals show no clinical signs at rest. Owner may report voice change with laryngeal involvement.

PHYSICAL EXAM FINDINGS

- Stridor of nasal cavity origin: nasal discharge, occlusion of air flow from one or both nostrils, stenotic nares in brachycephalic breeds, stridor disappears with open-mouth breathing, periodontal disease with evidence of tooth root abscessation or tooth loss
- Stridor of pharyngeal, laryngeal, or tracheal origin: coughing, gagging, dyspnea, hyperthermia, open-mouth gasping, unilateral discharge from the ear (sometimes seen in cats with nasopharyngeal polyps)

ETIOLOGY AND PATHOPHYSIOLOGY

- During inspiration, air pressure in the upper airway is low, allowing air to flow in through the nares or mouth and fill the lungs.
- Obstruction narrows airway diameter, causing turbulence proximal to the obstruction during inspiration. The turbulence is audible as stridor.
- Any obstructions of the upper airway can be drawn into the lumen during inspiration (dynamic obstruction), exacerbating the obstruction and causing further airflow turbulence and stridor.
- Stridor may be absent on expiration if the pressure of exhaled air opens the airway (e.g., laryngeal paralysis, other dynamic obstructions).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Physical examination and radiographs of the trachea and lungs help localize the lesion causing respiratory stridor. Rhinoscopy, laryngoscopy, tracheoscopy, and/or CT scans are often necessary to determine the exact etiology of the airway obstruction.

DIFFERENTIAL DIAGNOSIS

- Stridor of nasal cavity origin:
  - Brachycephalic syndrome (stenotic nares)
  - Foreign body (nasal)
  - Neoplasia (nasal)
  - Nasopharyngeal polyp
  - Rhinitis (fungal, bacterial, viral, parasitic, tooth root abscess, chronic vomiting or regurgitation)
  - Trauma
  - Coagulopathy
- Stridor of pharyngeal, laryngeal, or tracheal origin:
  - Brachycephalic syndrome (elongated soft palate; everted laryngeal saccules; hypoplastic trachea)
  - Laryngeal paralysis
  - Foreign body (pharyngeal, laryngeal, or tracheal)
  - Neoplasia (pharyngeal, laryngeal, or tracheal)
  - Nasopharyngeal polyp
  - Trauma
  - Coagulopathy
  - Laryngeal or tracheal collapse
  - Tracheal stenosis
  - Extraluminal compression of the trachea (neoplasia, granuloma, cervical lymphadenopathy)

INITIAL DATABASE

- CBC, serum biochemistry profile, and urinalysis to rule out underlying systemic diseases
- Nasal cavity stridor:
  - Assessing airflow through both nostrils, using a wisp of cotton ball or a cold glass slide (warm, moist, expired air fogging the glass if the nasal passage is patent)
- Pharyngeal, laryngeal, and tracheal stridor:
  - Cervical radiographs to rule out laryngeal and tracheal masses and foreign bodies:
    - The normal larynx (especially if mineralized and/or radiographed obliquely) should not be misinterpreted as a foreign body.
  - Thoracic radiographs:
    - Intrathoracic trachea
    - Lungs (noncardiogenic pulmonary edema; underlying abnormalities, e.g., infection, pulmonary hemorrhage [coagulopathy])

ADVANCED OR CONFIRMATORY TESTING

- Coagulation profile to rule out coagulopathies
- Nasal cavity stridor:
  - Rhinoscopy (see p. 1335) with biopsies, cytologic examination, and bacterial culture and sensitivity (aerobic) if discharge is present
  - CT (see p. 1233) scan of nasal cavity and pharynx
  - Dental radiographs (see p. 1246; tooth root abscesses)
- Pharyngeal, laryngeal, and tracheal stridor:
  - Laryngoscopy (see p. 1295) under light general anesthesia to evaluate laryngeal and oral anatomy and rule out laryngeal paralysis
  - If severe open-mouth inspiratory dyspnea: may be possible to visualize caudal pharynx and larynx with patient awake (laryngeal paralysis, pharyngeal foreign body, laryngeal/pharyngeal mass), using only a bright light source
  - Pharyngoscopy and tracheoscopy with biopsies, cytologic examination, and bronchoalveolar lavage

TREATMENT

TREATMENT OVERVIEW

Remove or decrease obstruction of the upper airway. In moderate cases, oxygen supplementation and sedation may be required. In severe cases, tracheotomy may be necessary to restore air flow to the lungs.

ACUTE GENERAL TREATMENT

- Nasal stridor: rarely associated with dyspneic crisis, as dogs and cats will open-mouth breathe to circumvent nasal obstruction.
- Pharyngeal, laryngeal, and tracheal stridor: if associated with severe obstruction, may cause (in increasing order of severity)

severe upper airway dyspnea, cyanosis, collapse, and respiratory arrest

- Patients with marked respiratory stridor associated with exaggerated, severe inspiratory efforts require immediate attention.
  - Calm environment
  - Oxygen supplementation if tolerated (see p. 1318)
  - Sedation should be considered, especially if the degree of inspiratory dyspnea is severe and the patient is known to otherwise be healthy (e.g., butorphanol, 0.05-0.3 mg/kg IV).
- In cases of pharyngeal, laryngeal, or tracheal stridor with deterioration or failure to improve despite the measures described above:
  - If the obstruction is cranial to the midcervical trachea and stridor and dyspnea are severe, either anesthesia and endotracheal intubation (see p. 1292) or a tracheotomy if intubation is not possible (see p. 1344) should be considered.
  - If the obstruction is caudal to the midcervical trachea and stridor and dyspnea are severe despite the treatments mentioned above, immediate preparations should be made for tracheoscopy and/or surgical intervention.
  - If the site of obstruction is unknown, the patient must undergo radiography or direct visualization of the pharynx and larynx to determine the best intervention.

CHRONIC TREATMENT

Correction of underlying causes (as applicable):

- Brachycephalic airway surgery (nasal wedge resection, soft palate resection [staphylectomy], everted laryngeal saccule resection [laryngeal sacculectomy])
- Arytenoid lateralization (laryngeal tie-back surgery) for laryngeal paralysis
- Surgical excision of masses or polyps
- Endoscopic or surgical retrieval of foreign bodies
- Antimicrobial therapy for infectious disease

RECOMMENDED MONITORING

- Respiratory effort improvement/deterioration
- Mucous membrane color (pallor/cyanosis)
- Pulse oximetry and arterial blood gas analysis if debilitated or severely affected patient

PROGNOSIS AND OUTCOME

Dependent on the underlying disease

PEARLS & CONSIDERATIONS

COMMENTS

- Cats are much more reluctant than dogs to breathe with their mouths open. As a result, significant nasal cavity obstruction can cause marked respiratory distress in a cat, whereas a dog would simply pant more to bypass the obstruction.
- Stridor is often exacerbated by excitement and exercise.

TECHNICIAN TIPS

- Keep the environment around an acutely dyspneic animal as calm as possible. Do not force an oxygen mask on the animal if it is resisting. Sedation may help calm the animal and reduce dyspnea.
- Animals with stridor on a hot day often become hyperthermic. Be sure to check body temperature and actively cool animals with temperatures greater than 40°C or 102°F.

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Storage Diseases

BASIC INFORMATION

DEFINITION

Inherited disorders that result in intracellular accumulation of specific storage product(s) owing to a deficiency in an enzyme or cofactor necessary for further metabolism of the substance. The accumulated storage products cause subsequent cellular dysfunction. This discussion will be limited to the lysosomal storage disorders, in which the substance that fails to be processed accumulates in the lysosomes. see also online Section lll table: Storage Diseases for a summary of clinical information on these disorders.

SYNONYM

Lysosomal storage disorders

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs and cats
- Age of onset varies; typically normal at birth and develop clinical signs within first several weeks to months of life.
- Signs may not become apparent until much later in life.
- No known sex predilection

GENETICS & BREED PREDISPOSITION

- Generally have an inherited basis (mostly autosomal recessive)
- Can occur as spontaneous mutation

RISK FACTORS: Affected relatives or breeds that are at risk. Please refer to the online Section lll table: Storage Diseases, and to the suggested reading list below, for a complete list of breeds susceptible to specific disorders.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Sphingolipidoses:
  - Globoid cell leukodystrophy (Krabbe disease):
    - Deficiency: β-d-galactocerebrosidase
    - Clinical signs: multifocal; predominantly ataxia, pelvic limb paresis/paralysis. Cerebellar dysfunction may be the predominant early sign.
  - Gangliosidosis GM1 (Norman-Landing disease):
    - Deficiency: β-galactosidase
    - Clinical signs: multifocal; predominantly cerebellar dysfunction; may progress to tetraplegia
  - Gangliosidosis GM2 (Derry disease):
    - Deficiency: β-galactosidase
    - Clinical signs: multifocal; predominantly cerebellar dysfunction; may progress to tetraplegia
  - Glucocerebrosidase deficiency (Gaucher disease):
    - Deficiency: β-D-galactocerebrosidase
    - Clinical signs: multifocal; predominantly cerebellar ataxia, tremors, hyperactivity
  - Sphingomyelinase deficiency (Niemann-Pick disease):
    - Deficiency:
      - Type A: sphingomyelinase
      - Type B: cholesterol esterification deficiency
      - Type C: NPC1 mutation
    - Clinical signs: ataxia, head tremors, paraparesis, weight loss, depression
- Glycoproteinoses:
  - Fucosidosis:

        - Deficiency: α-l-fucosidase
        - Clinical signs: initially forebrain dysfunction predominates and progresses over 2-3 years to include ataxia, dysphagia, vision and hearing loss, nystagmus, and dysphonia.
            - Relatively late onset of clinical signs; neurologic dysfunction begins between 12 and 18 months of age.
            - Palpable enlargement of the ulnar nerves secondary to edema and infiltration with lipid-filled phagocytes and Schwann cells
    - Mannosidosis:
        - Deficiency: α-d-mannosidase
        - Clinical signs include skeletal abnormalities, ataxia, head tremor; possibly gingival hyperplasia.
    - Neuronal glycoproteinosis (Lafora disease):
        - Deficiency: unknown
        - Clinical signs: forebrain dysfunction predominates within the first year of life.
    - Galactosialidosis:
        - Deficiency: protective protein/cathepsin A
        - Clinical signs: predominantly ataxia
- Mucopolysaccharidoses:
    - Mucopolysaccharidosis type I (Hurler syndrome):
        - Deficiency: α-l-iduronidase
        - Clinical signs: predominantly pelvic limb gait disorder without overt neurologic deficits; patients may have hyperextensible joints and plantigrade stance; skeletal and craniofacial abnormalities may be present.
    - Mucopolysaccharidosis type II (Hunter disease):
        - Deficiency: iduronate-2-sulfatase
    - Mucopolysaccharidosis type III (Sanfilippo syndrome):
        - Type IIIA: heparan sulfate sulfamidase deficiency
        - Type IIIB: *N*-acetyl-a-D-glucosaminidase deficiency
        - Clinical signs: not well described; predominantly tremors and ataxia
    - Mucopolysaccharidosis type VI (Maroteaux-Lamy syndrome):
        - Deficiency: arylsulfatase B
        - Clinical signs: predominantly skeletal malformations (kyphosis, facial deformities); upper motor neuron paraparesis
    - Mucolipidosis II (I-cell disease):
        - Deficiency: *N*-acetylglucosamine-1-phosphotransferase
        - Clinical signs: not well described
    - Mucopolysaccharidosis type VII (Sly disease):
        - Deficiency: β-D-glucuronidase
        - Clinical signs: not well described; skeletal deformities, ataxia, corneal cloudiness
- Proteinoses:
    - Ceroid lipofuscinosis (Batten Disease):
        - Deficiency:
            - Cathepsin D[d]
            - CLN5[d]
            - CLN2 (TTP1)[d]
            - CLN8[d]
        - Clinical signs: behavioral changes and visual deficits seen initially. Progresses over several years to include seizures, ataxia, tremors, hypermetria.
            - Encephalopathic signs usually first seen at 1-2 years of age (range of disease onset 6 months-10 years)
            - A form of ceroid lipofuscinosis selectively involving the cerebellum and thalamus has been described in dogs.
            - Cats typically demonstrate rapid neurologic decline.
- Oligosaccharidoses:
    - Glycogenosis type 1a:
        - Deficiency: glucose-6-phosphatase
    - Glycogenosis type II (Pompe disease):
        - Deficiency: α-glucosidase
    - Glycogenosis type IIIa:
        - Deficiency: glycogen debranching enzyme (AGL gene)
    - Glycogenosis type IV (Andersen disease):
        - Deficiency: glycogen debranching enzyme

HISTORY, CHIEF COMPLAINT

- Normal at birth
- Clinical signs typically become apparent within the first 6 months of life and slowly progress over 1 to 2 years.

- Intention tremors are common chief complaints.
- Specific presenting complaints depend on the specific storage disease.
- May have history of affected relatives

PHYSICAL EXAM FINDINGS

- General physical examination is typically unremarkable.
- Neurologic exam findings depend on the specific storage disease; findings may include:
  - Mentation changes (behavioral changes, aggression, loss of learned behavior)
  - Menace deficits, central blindness
  - Gait abnormalities (ataxia, paresis)
  - Proprioceptive deficits
  - Intention tremors
  - Exercise intolerance
- Hepatomegaly (gangliosidosis, glycogenosis types I and III, mannosidosis, mucopolysaccharidoses types I and VII, and sphingomyelinosis) or splenomegaly (mucopolysaccharidosis type I, sphingomyelinosis) have been noted as a result of accumulation of storage products in the cells of these organs.
- May exhibit skeletal or connective tissue abnormalities (mannosidosis, mucopolysaccharidoses types I and VI, mucolipidosis type II)
- Retinal degeneration with ceroid lipofuscinosis and in cats with mucolipidosis II
- Dwarfism with gangliosidosis in English springer spaniels
- Peripheral nerve involvement associated with fucosidosis, globoid cell leukodystrophy, glycogenoses, sphingomyelinosis

ETIOLOGY AND PATHOPHYSIOLOGY

- Normally, substances undergo sequential metabolic degradation via specific lysosomal enzymes. Interruptions in these specific pathways can occur if one enzyme (or more) is deficient or dysfunctional, leading to accumulation of the substance prior to that enzymatic step.
- Accumulated byproduct(s) will lead to cellular dysfunction, presumably by cell swelling, toxic effects of accumulated material(s), or both.

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

These unusual disorders are suspected in young patients with relentlessly progressive neurologic deficits with or without associated general physical abnormalities. Confirmatory clinical tests exist for some disorders; definitive diagnosis for any of them is obtained from histologic analysis of tissue, typically at postmortem when unthrifty animals die or are euthanized.

DIFFERENTIAL DIAGNOSIS

Any slowly progressive multifocal or diffuse encephalopathy, cerebellar dysfunction, or neuromuscular dysfunction should be considered as a differential diagnosis.

- Degenerative:
  - Leukodystrophy/spongy degeneration
  - Neuronal degeneration or cerebellar abiotrophy
  - Neuraxonal dystrophy
  - Cognitive dysfunction
- Anomalous:
  - Congenital hydrocephalus
  - Caudal occipital malformation syndrome
  - Intracranial arachnoid cyst
  - Dandy-Walker syndrome
  - Miscellaneous malformations
- Infectious:
  - Fungal (*Cryptococcus neoformans*, *Coccidioides immitis*, *Histoplasma capsulatum*, *Blastomyces dermatitidis*), viral (canine distemper virus, feline immunodeficiency virus [FIV] infection, feline leukemia virus [FeLV] infection), protozoal (*Neospora caninum*, *Toxoplasma gondii*, *Hepatozoon americanum*), verminous, rickettsial, and bacterial meningoencephalitis
- Inflammatory:
  - Necrotizing meningoencephalitis of small-breed dogs

- Granulomatous meningoencephalomyelitis (GME)
- Eosinophilic meningoencephalitis

- Metabolic:
  - Organic acidurias (e.g., L-2-hydroxyglutaric aciduria in the Staffordshire bull terrier, malonic aciduria in the Maltese)
  - Mitochondrial encephalopathies (e.g., pyruvate dehydrogenase deficiency in Sussex spaniels)
  - Hepatic, renal, hypoglycemic, and electrolyte-associated encephalopathies
- Neoplastic: primary or metastatic
- Nutritional: thiamine deficiency
- Toxic: lead
- Vascular: global ischemia, thromboembolic disease

INITIAL DATABASE

- CBC, serum biochemical profile, urinalysis:
  - May reveal leukocytes containing vacuoles or storage product
  - Some disorders show evidence of multiple affected organs.
  - Performed to rule out other metabolic disorders
- Serologic titers: performed to rule out infectious diseases

ADVANCED OR CONFIRMATORY TESTING

- Supportive diagnostic tests:
  - Cerebrospinal fluid (CSF) analysis:
    - Typically normal
    - Protein level may be elevated, but nucleated cell count should remain normal.
  - CT or MRI:
    - Brain atrophy with secondary ventriculomegaly
    - Diffuse changes in tissue intensity (due to accumulation of storage products)
- Confirmatory diagnostic tests (only available for certain storage disorders) can identify specific storage products, deficient enzyme activity, and/or presence of the defective gene responsible for the disease.
- Urine assays:
  - Oligosaccharides and glycopeptides can be profiled in urine samples using thin-layer chromatography to determine the particular compound that is accumulating and being excreted.
- Enzymatic assays:
  - Measures lysosomal enzyme activity for a panel of known lysosomal enzymes
  - Performed using whole blood leukocytes, kidney or liver biopsy samples, or cultured skin fibroblasts
  - Available for some enzymes (i.e., some storage diseases) and the level of activity of an affected animal can be compared to an age-matched control.
  - Since these diseases are commonly autosomal recessive, an affected animal would have significantly decreased enzyme activity, and a heterozygous carrier would have 50% of the enzyme activity of a homozygous animal.
- Molecular genetic testing for affected gene (DNA testing):
  - The specific genetic mutation responsible for a disease may vary among different species and breeds, so molecular testing is very specific concerning breed and species for any given disease.
- Histopathologic evaluation:
  - Peripheral nerve, muscle, liver, or lymph node biopsy may be diagnostic in some cases.
  - Brain biopsy guided by CT scan
  - Postmortem/necropsy:
    - Requires use of special staining techniques to characterize the specific storage product

TREATMENT

TREATMENT OVERVIEW

- Goal is to reduce the accumulation of cellular storage products.
- Mostly limited to supportive care and maintenance of quality of life for as long as possible
- Future therapeutic options may involve gene therapy or transferring normal copies of the dysfunctional gene to the patient's cells using a viral vector. Once the functional copy of the gene becomes incorporated into the cell, it begins to produce the deficit enzyme. Has been shown effective in treatment of feline α-mannosidosis.

RECOMMENDED MONITORING

- Progressive neurologic impairment is expected.

- Monitoring for quality of life

PROGNOSIS AND OUTCOME

- Poor
- For most disorders, progressively worsening neurologic signs lead to euthanasia within the first year of life.
- For those disorders with a slower progression, progressive neurologic dysfunction leads to euthanasia or death within 1-2 years of diagnosis.

PEARLS & CONSIDERATIONS

COMMENTS

- The field of medical genetics is rapidly advancing, and genetic tests and therapies such as gene transfer therapy may provide a more favorable prognosis in the future.
- Consultation with a veterinary neurologist is recommended to obtain the most up-to-date diagnostic and treatment information available.

PREVENTION

- Maintain responsible breeding practices.
- Genetic testing is available for a limited number of these storage diseases and may be used for identifying carriers.

CLIENT EDUCATION

- Caution owners about the possibility of personality changes or aggressive behavior associated with these disorders, especially where children may be involved.
- Counsel owners concerning the progressive nature of storage disorders and likelihood of eventual euthanasia.
- Counsel breeders about the inheritance of the condition and availability of DNA testing.

SUGGESTED READING

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Stomatitis

BASIC INFORMATION

DEFINITION

Inflammation of the mucous lining of any of the structures in the mouth (storna); in clinical use, the term should be reserved to describe 'widespread oral inflammation (beyond gingivitis and periodontitis) that may also extend into submucosal tissues.

SYNONYMS

Lymphocytic-plasmacytic stomatitis, gingivostomatitis (cats); ulcerative stomatitis (dogs); alveolar, labial/buccal, sublingual and caudal stomatitis

EPIDEMIOLOGY

SPECIES, AGE, SEX: Adult cats and dogs

GENETICS & BREED PREDISPOSITION

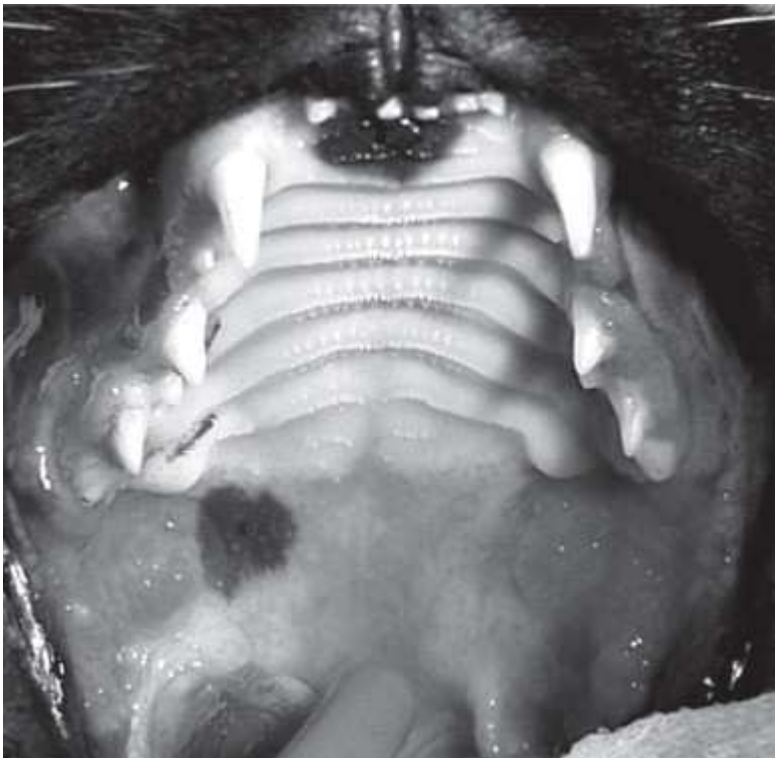
- Cats: sometimes is seen in group-housed families (may be pathogen-associated; no known genetic predispositions)
- Dogs: ulcerative stomatitis appears to be a familial disorder in Maltese dogs.

RISK FACTORS: Cats: prior exposure to viral diseases such as feline calicivirus (FCV), feline herpesvirus (FHV), or feline immunodeficiency virus (FIV)

CONTAGION & ZOONOSIS: Cats: *Bartonella henselae,* FCV, and FHV

ASSOCIATED CONDITIONS & DISORDERS

- Juvenile hyperplastic gingivitis <1 year old, presenting with severe inflammation and swelling of the gingiva of incisors, canines, and premolare; unknown if juvenile hyperplastic gingivitis can progress to adult stomatitis
- Cats with stomatitis often show resorption of multiple teeth (see p. 1104).



STOMATITIS Cat with inflammation of gingiva, alveolar mucosa, labial and buccal mucosa, and mucosa lateral to the palatoglossal folds. Note that the mucosa of the hard palate usually is not inflamed in cats with stomatitis.

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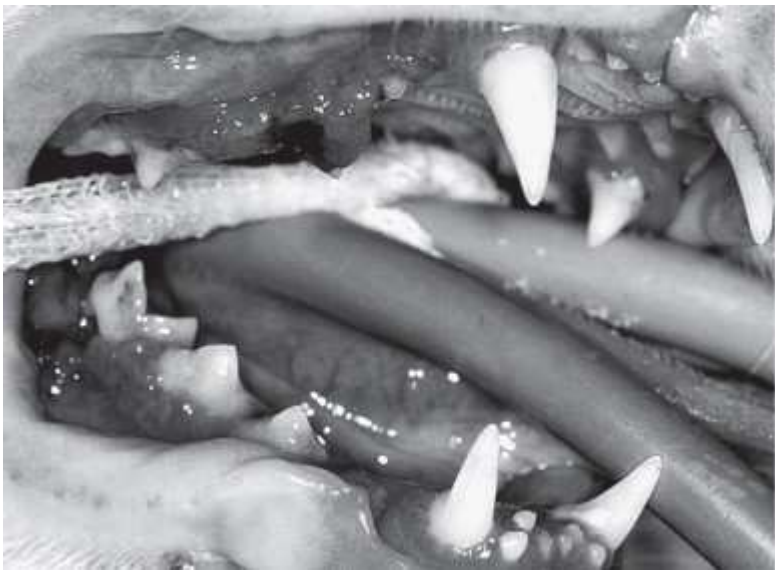
CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Dogs: ulcers most commonly found on the buccal mucosa of the lip and cheek facing plaque-laden tooth surfaces; in severely affected dogs, sometimes found on lateral margins of the tongue and on edges of the hard palate adjacent to teeth.

HISTORY, CHIEF COMPLAINT: Affected animals show signs of pain ‘when eating or when owner touches the mouth. Decreased grooming; drooling; sometimes weight loss.

PHYSICAL EXAM FINDINGS: Cats:

- Symmetric, bright red ulcerated lesions of the alveolar and buccal mucosa (rostral stomatitis) and/or the area lateral to the palatoglossal folds (caudal stomatitis)
- Lesions sometimes affect the lateral margins of the tongue extending caudally to include the palatoglossal folds.
- Commonly, poor body condition and hair coat if condition is chronic



STOMATITIS Young cat with inflammation of the gingiva, alveolar mucosa, and labial and buccal mucosa. Note proliferative changes of gingival tissue, entirely covering the crown of the right maxillary third premolar tooth.

(Copyright Alexander M. Reiter.)

Dogs:

- Oral ulcers: most commonly found on the buccal mucosa of the lip and cheek facing plaque-laden tooth surfaces
- In severely affected dogs, sometimes found on lateral margins of the tongue and on edges of the hard palate adjacent to teeth
- Halitosis, drooling, and reluctance to chew on hard treats or diets

ETIOLOGY AND PATHOPHYSIOLOGY

- Immune-mediated disease seemingly related to degree of dental plaque accumulation. Plaque bacteria play a role in the progression of the disease, and control of oral bacteria can be a critical contributor to successful management.
- The most reliable treatment in both species is extraction of teeth in affected areas of the mouth +/− extraction of all teeth, eliminating bacteria-laden dental plaque deposits.
- FCV and FHV infection may play a role in the immune system's aberrant response to plaque: 88% of stomatitis cats shed both viruses (versus 21% of cats without stomatitis). FCV-PCR is positive in 97% of cats with caudal stomatitis. Note: experimental FCV infection produces oral ulcerations but not chronic stomatitis.
- Evidence for a cause-effect relationship between *Bartonella* and feline stomatitis has not been provided.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on bilaterally symmetric inflammation that extends beyond the gingiva to include alveolar mucosa, labial and buccal mucosa, and/or mucosa lateral to the palatoglossal folds. Anesthetized examination at the time of initial diagnosis allows for coupling of confirmatory biopsy and initial dental care to reduce plaque and calculus and remove diseased teeth. Biopsy of any vesicles or mucocutaneous lesions is warranted to rule out autoimmune disease.

DIFFERENTIAL DIAGNOSIS

- Periodontal disease
- Squamous cell carcinoma or other less common neoplasia: more likely when disease is not bilaterally symmetric
- Eosinophilic granuloma: typically, isolated raised lesions on the tongue, lip, or palate
- In dogs, stomatitis may occasionally be a manifestation of autoimmune disease, including pemphigus vulgaris, bullous pemphigoid, systemic lupus erythematosus, and discoid lupus erythematosus. Look for other signs of autoimmune disease, including hematologic abnormalities, joint pain, fever, and pathologic proteinuria.
- Epitheliotropic lymphoma (mycosis fungoides)

INITIAL DATABASE

- Cats: FIV and FeLV tests; CBC, serum chemistry profile, and urinalysis are indicated for ruling out distant organ disease. Hypergammaglobulinemia due to a polyclonal gammopathy (via protein electrophoresis) is usually the most marked abnormality.
- Dogs: CBC, serum chemistry profile, urinalysis

ADVANCED OR CONFIRMATORY TESTING

- Biopsy of representative lesions; usually reported as caused by chronic inflammation, with a mixture of acute and chronic inflammatory cells (particularly lymphocytes and plasma cells). Since this pattern is expected when immune-responsive tissue is exposed to bacteria chronically, this biopsy is mainly helpful in ruling out neoplasia.
- In dogs, the characteristic location and appearance of the lesions rarely requires confirmatory biopsy except in cases where autoimmune disease or neoplasia is expected.

TREATMENT

TREATMENT OVERVIEW

Ideally, eliminate the condition by removing the plaque-retentive surfaces of the teeth and roots in their entirety; 93% of patients will be improved (80% will be clinically cured) by full-mouth or nearly full-mouth extractions. In cases where extraction is not an option, treat with strict plaque control, immunomodulators, +/− antimicrobials.

ACUTE GENERAL TREATMENT

Cats with severe generalized stomatitis:

- Antimicrobials (e.g., amoxicillin-clavulanate, 14 mg/kg PO q 12 h, and/or chlorhexidine gel or rinse 0.12% q 12 h), immunomodulators (typically a corticosteroid, such as prednisolone, 0.5-1 mg/kg PO q 24 h), and nursing care (nutritional support, grooming)
- Referral is indicated if uncertainty exists regarding the diagnosis, or if the attending practitioner is not equipped to provide necessary supportive and surgical care.
- Discuss extractions with the client and determine the client's willingness to perform full-mouth or nearly full-mouth (premolar and molars) extractions. If the client declines full-mouth extractions, schedule an appointment for anesthetized oral examination, including dental radiographs, biopsy, extraction of periodontally diseased teeth and teeth with resorption, and thorough scaling/polishing of remaining teeth. Follow with antibacterial treatment for 2 weeks, plus daily home oral hygiene (chlorhexidine gel or rinse, brushing the teeth daily, dental diet as the primary food) as soon as the cat will tolerate it.
- Reexamine the patient 2 weeks following dental treatment.
- If the cat is significantly improved, continue the home oral hygiene regimen, and reexamine the patient in 2-3 months.

Dogs with ulcerative stomatitis:

- Systemic antibacterial treatment (e.g., amoxicillin-clavulanate, 14 mg/kg PO q 12 h), chlorhexidine gel or rinse, and nursing care (soft food)
- 1-2 weeks later under general anesthesia: oral examination including dental radiographs, biopsy, extraction of periodontally diseased teeth, and thorough scaling/polishing of remaining teeth. Follow with daily home oral hygiene (daily toothbrushing, dental diet as the primary food) if the dog will tolerate it.
- If there is significant improvement, continue the chlorhexidine home care program, and reexamine the dog in 1-2 months. Excellent plaque control is the key to continued comfort of the dog. Some dogs may start to develop lesions (and oral pain) soon after initial treatment; in such cases, metronidazole may help at 20 mg/kg PO q 24 h for 1-2 weeks, then gradually reduce the dose (continuous treatment at 10 mg/kg PO q 48 h provides good control in some animals that relapse).

CHRONIC TREATMENT

Cats with severe, generalized stomatitis:

- If clinical signs and inflammation are still present, consider reinstituting oral prednisolone at 0.5-1 mg/kg PO q 12-24 h, and taper dose slowly over months to determine the lowest dose that controls clinical signs.
- If there is no improvement at all following dental treatment and prednisolone treatment, and there still are teeth in the diseased sections of the mouth, extract all remaining teeth.
- Clinical signs will persist in 20% of cats after extraction of all teeth. Refractory cases may be treated by a variety of modalities. Continuous or intermittent corticosteroids or nonsteroidal antiinflammatory drug (NSAID) treatment may provide relief, but try to avoid depot formulations owing to risk of diabetes mellitus and congestive heart failure. Cyclosporine (Neoral, 2.5 mg/kg PO q 12 h as a starting dose) shows promise in refractory cases, with up to 85% of cats showing improvement.
- CO2 laser treatment has provided apparent cures in select cases of severely proliferative disease, but therapy requires multiple anesthesias and placement of an esophagostomy tube (see p. 1267) after the first treatment to ensure caloric intake.
- Recombinant feline interferon (Virbagen Omega [Virbac]) has shown promise in treating refractory cases. In one of the most commonly used protocols, 5 MU is injected submucosally, diluted and divided as necessary to inject all inflamed areas. The remaining 5 MU are injected into a 100-mL bag of sodium chloride and frozen in ten 10-mL aliquots. The client gives 1 mL PO q 24 h for 100 days. The 10-mL fraction in use is refrigerated, and the other aliquots are kept frozen until needed.
- Azithromycin (5-10 mg/kg q 24 h for 5-21 days) has been advocated for treatment of *Bartonella*-seropositive cats. Long-term daily use of azithromycin should be approached cautiously because of its long half-life (35 hours) in cats.

Dogs with ulcerative stomatitis:

- If there is no improvement with initial treatment, extract all remaining teeth, and if necessary, start prednisone treatment (0.5-1 mg/kg PO q 12-24 h, titrating down to the lowest dose/frequency that controls clinical signs).

NUTRITION/DIET

- Soft food during healing
- Esophagostomy if severe oral discomfort precluding prehension and chewing of food (iatrogenic)

DRUG INTERACTIONS

Immunosuppressive drugs may have potentially severe side effects; adjust dose/frequency judiciously, and consult drug handbook for detailed information.

POSSIBLE COMPLICATIONS

- Failure to obtain clinical improvement: explaining this to the client at initial presentation and explaining the need for frequent treatment adjustments are important contributors to success.
- Exacerbation of preexisting infections (toxoplasmosis, FIV): due to immunosuppressive drug use

RECOMMENDED MONITORING

- Corticosteroids: monitor for evidence of diabetes mellitus.
- Cyclosporine: assess blood levels after 4-6 weeks and every 6-12 months thereafter. Target levels on a 12-hour-post blood sample are 400-600 ng/mL, but if patients are doing clinically well with a lower blood level, there is no need to increase the dose.

PROGNOSIS AND OUTCOME

Variable; response to full-mouth or near full-mouth extraction has been documented to be: 60% truly cured, 20% clinically cured

(some inflammation, no need for further therapy except home care), 13% slightly improved but needing further therapy, and 7% unimproved.

PEARLS & CONSIDERATIONS

COMMENTS

- There is no magic bullet, but extraction of teeth provides the most reliable results without long-term side effects. Extraction of teeth should be considered as an early option, not a last resort.
- In emaciated cats, rule out other causes before attributing weight loss/decreased appetite entirely to stomatitis.

PREVENTION

Good home oral hygiene from an early age may prevent development of disease in at-risk animals. However, lesions (in both dogs and cats) are often very painful, which makes animal compliance difficult.

TECHNICIAN TIPS

- Home oral hygiene is challenging in cats and dogs with painful, inflamed mouths. When teaching clients how to brush teeth, wait to start brushing until inflammation and pain are decreased with medical therapy and a professional dental cleaning.
- Performing full-mouth extractions requires a long duration of general anesthesia. To minimize anesthesia time, practice “four-handed dentistry.” Have all dental instruments available, and anticipate the surgeon's needs by having the next instrument ready and waiting.

CLIENT EDUCATION

Clients should understand that stomatitis may sometimes be controlled rather than cured. Initially, the concept of full-mouth extractions seems shocking to clients. Since full-mouth or nearly full-mouth extractions provides a “clinical cure” in 80% of cases, extraction represents the best chance of long-term relief of inflammation.

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Stifle Joint Luxation

BASIC INFORMATION

DEFINITION

Complete derangement of the stifle joint in which ligaments, joint capsule, and menisci have been damaged

SYNONYMS

Multiple ligament injury of the stifle, stifle joint luxation

EPIDEMIOLOGY

RISK FACTORS: Trauma from falls, fights, or motor vehicle accidents

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Fall, fighting, or injury caused by a motor vehicle or firearm

PHYSICAL EXAM FINDINGS

- Non-weight-bearing extremity
- Extreme stifle joint pain
- Thickened or distorted stifle
- Severe joint instability

ETIOLOGY AND PATHOPHYSIOLOGY

- Uncommon condition of the stifle joint; 12% of all cases involving ligament injuries in dogs
- Extreme unnatural stress applied to joint, causing multiple ligamentous failures
- Both cruciate ligaments, at least one collateral ligament, joint capsule, and one or both menisci are torn or avulsed.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is confirmed by clinical history, physical examination, and radiography.

DIFFERENTIAL DIAGNOSIS

Femoral or tibial fractures involving the stifle joint

INITIAL DATABASE

- Orthopedic examination to confirm stifle joint instability; palpation performed with adequate pain management
- CBC and serum biochemistry panel based on American Society of Anesthesiologists (ASA) patient classification (see p. 1372)
- Thoracic and spinal radiographs when body trauma is suspected
- Craniocaudal and mediolateral radiographs of stifle

TREATMENT

TREATMENT OVERVIEW

The goal of therapy is restoration of stifle joint (congruency, motion) and limb functions.

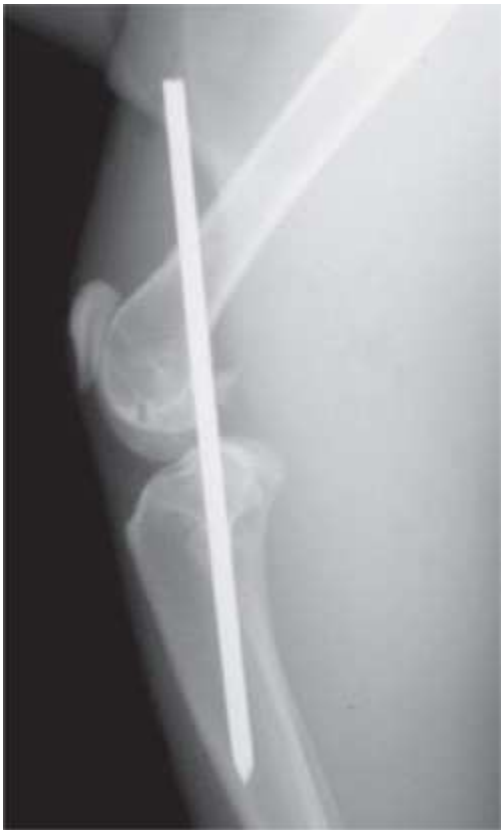
ACUTE GENERAL TREATMENT

Surgical intervention:

- Inspect and remove damaged parts of menisci.
- Suture meniscal tibial ligaments if torn and menisci are intact.
- Débride remnants of cruciate ligaments, and use intracapsular or extra-capsular repairs.
- Primary repair of collateral ligaments or replacement with synthetic sutures
- Restoration of caudal cruciate ligament function is not necessary.
- Possible transarticular pinning of the stifle joint for immobilization during initial healing of soft tissues
- Temporary transarticular external skeletal fixation, with joint fixed at normal standing angle

CHRONIC TREATMENT

- External coaptation (soft padded bandage or half splint) for 3-4 weeks
- Transarticular pin or transarticular external skeletal fixation left in position for at least 3 weeks
- Initially, exercise restriction
- Following removal of external coaptation, physical therapy is initiated to restore joint function(s).
- Increased physical activity (rehabilitation) is allowed as stifle joint function is improving (see p. 1329).



STIFLE JOINT LUXATION Transarticular pin for temporary stabilization of stifle joint derangement in a cat.

POSSIBLE COMPLICATIONS

- Persistent stifle joint instability
- Osteoarthritis secondary to trauma and instability
- Reduced range of motion due to fibrosis

RECOMMENDED MONITORING

Monthly monitoring for stifle joint stability and range of motion

PROGNOSIS AND OUTCOME

- Good for restoration of adequate joint function
- Working or athletic dogs generally do not return to preinjury status.
- If treatment fails, arthrodesis or limb amputation can be considered.

PEARLS & CONSIDERATIONS

COMMENTS

Although prognosis appears grim during initial presentation, appropriate surgical techniques will often result in satisfactory restoration of function.

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Steroid-Responsive Meningitis-Arteritis

BASIC INFORMATION

DEFINITION

Steroid-responsive meningitis-arteritis (SRMA) is a suspected autoimmune disorder characterized by inflammation of the meninges and meningeal arteries. The non-neurologic aspects of this disorder are discussed separately (see online chapter: Juvenile Polyarteritis).

SYNONYMS

SRMA, corticosteroid-responsive meningomyelitis, aseptic meningitis, beagle pain syndrome, canine juvenile polyarteritis syndrome, sterile suppurative meningitis

EPIDEMIOLOGY

SPECIES, AGE, SEX: Young adult dogs (6-18 months old), but any age is possible.

GENETICS & BREED PREDISPOSITION

- Genetic factors are possible, but have not been proven.
- Most often diagnosed in boxers, Bernese mountain dogs, and beagles; however, any breed can be affected.

RISK FACTORS: Immune response may occur secondary to environmental or infectious causes.

CONTAGION & ZOONOSIS: Infectious cause has not been demonstrated.

ASSOCIATED CONDITIONS & DISORDERS: May occur concurrently in dogs with immune-mediated polyarthritis.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Classical (acute)
- Chronic

HISTORY, CHIEF COMPLAINT

- Classical (acute): cervical hyperesthesia and rigidity, fever, stiff gait, lethargy
- Chronic: as with acute disease, but with additional complaints suggestive of spinal cord dysfunction (proprioceptive deficits, paresis, ataxia)

PHYSICAL EXAM FINDINGS

- Typical of meningitis:
  - Cervical pain and rigidity; stiff, stilted gait; fever; lethargy
- In more protracted cases: gait abnormalities, proprioceptive deficits, back pain. Other neurologic signs are less commonly reported.

ETIOLOGY AND PATHOPHYSIOLOGY

- Idiopathic: possibly an autoimmune condition
- Classical (acute): histologic analysis demonstrates moderate to marked meningitis characterized by infiltration of neutrophils, macrophages, lymphocytes, and plasma cells, as well as degenerative changes and perivascular inflammation of the meningeal arteries. Lesions are most commonly found in the cervical spinal cord.
- Chronic: histologic analysis demonstrates moderate to marked fibrosis and patchy mineralization of the meninges.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected when a patient has signs of spinal pain or (less commonly) intracranial deficits. Advanced imaging helps rule out other differential diagnoses, and cerebrospinal fluid (CSF) analysis provides the most characteristic abnormalities.

DIFFERENTIAL DIAGNOSIS

- Infectious meningitis (bacterial, viral, protozoal, fungal)
- Diskospondylitis
- Inflammatory, noninfectious meningitis (e.g., granulomatous meningoencephalomyelitis [GME])
- Intervertebral disk disease
- Neoplasia (e.g., spinal meningioma, lymphoma, malignant histiocytosis)

INITIAL DATABASE

- CBC: leukocytosis, neutrophilia with left shift; may be normal in chronic cases
- Serum biochemistry profile: usually normal
- Urinalysis: usually normal
- Survey spinal radiographs: should be normal

ADVANCED OR CONFIRMATORY TESTING

- Immunoglobulin (Ig)A (serum or CSF) is often elevated and supports the diagnosis.
- CSF analysis (see p. 1228) often reveals an elevated protein level and white blood cell count with sterile neutrophilic pleocytosis in the acute stage of disease. Chronic cases may have normal CSF or mononuclear pleocytosis.
    - CSF culture and sensitivity should be negative.
- Infectious disease titers and/or advanced imaging (MRI (see p. 1302), CT (see p. 1233), myelography (see p. 1306)) may be required to rule out other diseases.

TREATMENT

TREATMENT OVERVIEW

The cornerstone of treatment is judicious immunosuppression adjusted to optimal response with fewest/no adverse effects.

ACUTE GENERAL TREATMENT

- Prednisolone: initially 2 mg/kg PO q 24 h for 1-2 days, then reduce to 1 mg/kg PO q 24 h for 2-4 weeks, then slowly taper by 25% every 3-4 weeks to lowest effective dose.
- Consider gastrointestinal (GI) protective agents (e.g., famotidine, 0.5 mg/kg PO or IV q 12-24 h, sucralfate 0.25-1 g PO q 8 h).
- Analgesics (e.g., tramadol, 2 mg/kg PO q 8-12 h; or amantadine, 2 mg/kg PO q 24 h for 4-6 weeks)

CHRONIC TREATMENT

Additional immunosuppressive medications may be required. Consider mycophenolate (CellCept, 5-10 mg/kg PO q 12 h), azathioprine (Imuran, 2 mg/kg PO q 24 h × 5 days, then q 48 h), or cyclosporine.

DRUG INTERACTIONS

- Drug interactions or altered metabolism of medications have been reported between corticosteroids and amphotericin B, furosemide, thiazide diuretics, digitalis glycosides, cyclosporine, phenytoin, phenobarbital, and mitotane.
- All immunosuppressive drugs carry the risk of excessive immune suppression, and some may have other (e.g., bone marrow suppressant) effects.
- Corticosteroids should not be given concurrently with nonsteroidal antiinflammatory drugs (NSAIDs) or other potentially ulcerogenic medications.

POSSIBLE COMPLICATIONS

Corticosteroid side effects: polyuria, polydipsia, polyphagia, weight gain, GI ulceration, iatrogenic hyperadrenocorticism, and others.

RECOMMENDED MONITORING

- Neurologic exam every 4-6 weeks
- Ideally, CSF analysis should be repeated every 4-6 weeks prior to reduction in medication dosage.

PROGNOSIS AND OUTCOME

- Classical (acute): generally good to excellent prognosis if treated early and aggressively
- Chronic: prognosis is fair to guarded owing to frequent relapses.
- Reports indicate 60% of dogs can be cured. Remaining patients require some level of corticosteroids long-term.

PEARLS & CONSIDERATIONS

COMMENTS

- SRMA has a good to excellent prognosis when patients are treated early in disease.
- CSF analysis should be performed early in the course of disease.

TECHNICIAN TIP

The hallmark physical sign of this disorder is neck pain. Handle with care and be aware of the possibility of pain-associated aggression.

CLIENT EDUCATION

Warn owners of corticosteroid side effects (e.g., polyuria, polydipsia, polyphagia, weight gain, GI ulceration, iatrogenic hyperadrenocorticism).

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Stab Wounds

BASIC INFORMATION

DEFINITION

- Low-energy impact, penetrating injuries inflicted by sharp instruments such as knives and screwdrivers and resulting in localized tissue trauma.
- This topic covers nonaccidental/malicious injuries causing incised wounds (cuts) and/or stab wounds.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Animals of any signalment
- Animals sustaining nonaccidental/malicious physical injuries are significantly more likely to be male than female; this gender difference may apply to stab wounds specifically.

GENETICS & BREED PREDISPOSITION

- Certain breeds (e.g., Staffordshire bull terrier) have been shown to be at markedly greater risk for nonaccidental/malicious physical injuries.
- Conversely, other breeds (e.g., Labrador retriever) are at markedly lower risk.
- Whether these breed predilections apply specifically to stab wounds remains to be proven.

RISK FACTORS

- Stabbing wounds are almost invariably the result of malicious intention, although impalement injuries from falls (e.g., onto pointed fence posts) have also been described.
- Working dogs with exposure to potentially dangerous encounters may be at greater risk.
- Outdoor cats

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Usually acute onset of signs
- Victim may be a working dog recently involved in a violent encounter.
- Unless an act of violence is evident or clear malicious intent is suspected, history may be vague.
- Repeated presentations for treatment of unexplained or poorly explained injuries should raise the suspicion of nonaccidental/malicious injury.
- Chief complaint (e.g., dyspnea, skin laceration, abdominal discomfort) may suggest localization of the wound.
- Animals with a minor, previously unattended wound may present for signs associated with infection.

PHYSICAL EXAM FINDINGS

- Obvious skin laceration
- Fever or hypothermia with infection
- Dyspnea or respiratory distress with lacerations to the chest or neck
- Abdominal distension or discomfort with abdominal wounds
- Tachycardia, tachypnea, and collapse with major hemorrhage

ETIOLOGY AND PATHOPHYSIOLOGY

- Injury reflects the shape and length of the weapon, location of injury, and direction of impact.
- In addition to the initial injury, further injury can result from injudicious removal of the weapon, which may involve twisting and dragging of the blade on its tract out of the wound.
- Penetrating wounds to the thorax or neck may cause cardiovascular collapse if major vascular structures or the heart are involved.

- Tension pneumothorax can result from injury to lung or major airway strictures.
- Penetrating wounds to the abdomen may cause injury to visceral organs, resulting in vascular injury, leakage of intestinal contents, leakage of bile, or leakage of urine.
- Laceration to the diaphragm can result in herniation of visceral organs and (potentially) bowel strangulation months to years later.
- Penetrating wounds to the head may cause hemorrhage or infection in the brain or eyes.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is based entirely on history (when known) and physical identification of compatible wounds. Diagnostic testing (e.g., radiographs) help elucidate the extent of internal injury suspected from the initial exam.

DIFFERENTIAL DIAGNOSIS

- Impaling from sticks
- Arrows
- Gunshot wounds
- Hemoabdomen
- Uroabdomen
- Spontaneous pneumothorax
- Sepsis

INITIAL DATABASE

- CBC, serum chemistry profile: unremarkable unless reflective of organ damage (e.g., uroabdomen) or preexisting condition
- Survey radiography, abdominal ultrasonography: identify internal injuries

ADVANCED OR CONFIRMATORY TESTING

As needed, based on extent and location of wound(s):

- CT scan (see p. 1233)
- MRI (see p. 1302)
- Selective angiography
- Fistulography (see online chapter: Fistulography)
- Wound culture
- Esophagoscopy (see p. 1284)

TREATMENT

TREATMENT OVERVIEW

Treatment goals are to control blood loss, maintain adequate oxygenation and ventilation, control infection, and manage the wound(s).

ACUTE GENERAL TREATMENT

- Control of airway and ventilation
- Cardiovascular resuscitation with IV fluid therapy or blood products
- Surgical exploration via celiotomy, thoracotomy, or other approach indicated by injuries
- Débride and close (with a drain) minor stab wounds to the soft tissue.
- Broad-spectrum antibiotics

CHRONIC TREATMENT

Short-term antibiotic therapy

POSSIBLE COMPLICATIONS

- Unidentified laceration to the diaphragm will often result in a diaphragmatic hernia days to years later.
- Wound sepsis

PROGNOSIS AND OUTCOME

- Depends on localization and severity of injury
- Depends on response to therapy

PEARLS & CONSIDERATIONS

COMMENTS

- Because a stabbing wound is externally small, it may go undetected in an animal with only vague signs. Therefore, close inspection of the skin (including clipping of hair when necessary) is recommended when a small cutaneous wound exists in an ill animal.
- History of a recent interaction involving a sharp instrument should prompt the clinician to perform a thorough search for suspicious injuries.
- Survey radiography or advanced imaging, including CT scan or MRI, may identify internal injuries such as hematoma, abscess, or subcutaneous emphysema.
- Because removal of an embedded blade may inflict additional tissue trauma, the injured animal should be kept quiet and as immobile as possible in the field; this is immediately followed by presentation of the patient to an emergency service for stabilization and cautious withdrawal of the instrument where radiographic, surgical, and supportive care (e.g., blood transfusion) facilities are available.

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Squamous Cell Carcinoma

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

A malignant tumor arising from squamous epithelium

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Nasal planum (nonhaired, rostral, external part of nose):
  - Dog: rare site
  - Cat: squamous cell carcinoma (SCC) is the most common tumor in this site; older cats.
- Aural: generally occurs in older animals:
  - Dog: SCC is the second most common ear canal tumor (after ceruminous gland adenocarcinoma).
  - Cat: SCC may affect the pinna, often in cats with planum and periocular SCC; may also affect the ear canal, where it is the most common tumor type, equal in frequency to ceruminous gland adenocarcinoma.
- Digital:
  - Dog: SCC is the most common digital tumor, making up 35%-55% of such tumors; age between 7 and 11 years.
  - Cat: primary SCC of the digit is rare (about 10%). Digital carcinomas usually occur as metastasis from a bronchogenic carcinoma in older (mean of 13 years) cats.
- Oral:
  - SCC is one of the three most common malignant oral tumors, with nontonsillar SCC having a prevalence rate of approximately 7 per 100,000 dogs.
  - Dog: gingival area is most frequently affected, followed by lips, tongue, palate, and pharynx. Tonsillar SCC ranges in prevalence depending on the environment (urban dogs are more commonly affected). Middle-aged to older dogs are affected for most oral SCC, and there is no sex predilection. Gingival papillary SCC has been reported in very young (<1 year old) dogs.
  - Cat: SCC is the most common oral tumor in cats. SCC makes up about 75% of all feline oral tumors and occurs in the gingival and sublingual area in equal frequency. Older cats are affected; no sex predilection. Tonsillar SCC is very rare in cats.

GENETICS & BREED PREDISPOSITION

- Planum:
  - Dog: none
  - Cat: lightly pigmented animals; Siamese breed underrepresented
- Aural:
  - Dog: none
  - Cat: on pinna; found in lightly pigmented animals; Siamese breed underrepresented
- Digital:
  - Dog: approximately 75% are large-breed dogs, with around 70% having black coats. Breeds at increased risk include giant, standard, and miniature Schnauzers, Gordon setter, standard and miniature poodles, Scottish terrier, Labrador retriever, rottweiler, and dachshund. Digital SCC involving multiple digits has been reported in three related giant Schnauzers and has been reported in other large black dogs, including standard poodles, Labrador retrievers, and Gordon setters.
  - Cat: none
- Oral:
  - Dog: large dogs may be more likely to develop nontonsillar SCC than small dogs; white dogs may be predisposed to SCC of the tongue.
  - Cat: no predisposition

RISK FACTORS

- Solar exposure in white-coated cats is associated with increased risk of development of nasal planum, pinnal, and periocular SCC. Exposure to air pollution may be associated with development of tonsillar SCC in dogs. Gingival SCC has been reported to develop after oral radiation therapy in dogs. Oral SCC in cats may be associated with flea collar use, canned cat food or canned tuna consumption, and (possibly) environmental tobacco smoke. In one study, cats with SCC that were

exposed to environmental smoke were much more likely to over-express mutant p53 (a gene that when mutated can no longer function in its role as tumor suppressor) than cats with SCC living in nonsmoking environments.

GEOGRAPHY AND SEASONALITY: High altitude may increase the risk for solar exposure-induced SCC, as does living in countries with lower ozone coverage (e.g., New Zealand). Tonsillar SCC is about 10 times more likely to occur in dogs living in urban areas versus those living in rural areas.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Planum and pinna: clients may seek veterinary care because of the occurrence of crusted or ulcerated lesions or an actual mass. There may be bleeding or sneezing.
- Aural, external ear canal: there may be a visible mass, ear discharge, odor, pruritus, pain, facial nerve paralysis, head tilt, or circling. Compared to dogs, cats are more likely to present with neurologic signs.
- Digital:
  - Dog: lameness, swelling of digit, abnormal nail growth, fractured nail, licking/chewing at digit; oftentimes animals have a history of chronic nailbed infection treated with multiple different antibiotics with no improvement.
  - Cat: lameness; despite the fact that digital SCC in cats is usually metastatic from an underlying lung tumor, cats rarely have respiratory signs.
- Oral:
  - Dogs and cats may be presented for evaluation of difficulty eating, reluctance to eat, drooling, halitosis, bloody oral discharge, pawing at mouth, facial mass, oral mass, loose teeth, or weight loss. Dogs with tonsillar SCC may also be presented for evaluation of “lumps under jaw” due to large mandibular lymph node metastasis, with no other clinical signs.

PHYSICAL EXAM FINDINGS

- Planum and pinna: lesion may be proliferative or erosive; thus, mass or crusting and ulcerative lesion may be present. Regional lymph node may be enlarged.
- Aural, external ear canal: otic exam shows raised irregular mass, often ulcerated. Palpation of vertical ear canal may reveal large mass invading the area in late-stage cases.
- Digital:
  - Dog: painful swollen digit with an abnormal or absent toenail. Ulceration may be present. The regional lymph node may be enlarged.
  - Cat: swollen digit, ulcerated skin with purulent discharge; constant exsheathment, deviation, or loss of nail. About one third of animals present with multiple digits involved.
- Oral:
  - Gingival SCC: swelling or raised mass along gingival margin that may be irregular, ulcerated. Cats can have normal gingiva, with the tumor affecting the mandible/maxilla and causing a large swelling in the bone.
  - Tonsillar SCC: enlarged mandibular lymph nodes and enlarged irregular tonsils may be seen. Tonsillar enlargement is usually unilateral (see online chapter: Tonsillar Enlargement).
  - Sublingual SCC: irregular mass under tongue
- Multicentric squamous cell carcinoma in situ (MSCCIS, Bowen's disease, bowenoid in situ carcinoma [BISC]) is an uncommon disease reported mainly in cats. Lesions are multifocal and occur most commonly over the head, neck, dorsal thorax, abdomen, and proximal limbs. Lesions are found in haired and darkly pigmented skin and are not solar induced.

ETIOLOGY AND PATHOPHYSIOLOGY

- Planum and pinna: may begin as actinic keratosis and become locally invasive; low metastatic rate, possible association in some cases with papillomavirus
- Aural, external ear canal: locally invasive, more aggressive in cats than dogs; low metastatic rate (about 5%–15% in local lymph nodes)
- Digital:
  - Dog: locally invasive with digital (P3) bony destruction, low metastatic rate (5%–10% pulmonary; regional lymph node metastatic rate not well documented but uncommon; however, recent study reported 24% metastatic rate, site of metastasis not stated)
  - Cat: locally invasive with digital (P3) destruction. These are usually metastatic lesions from a pulmonary tumor. Lymph node involvement not documented.
- Oral:
  - Gingival and sublingual SCC: locally invasive with a low metastatic rate (5%–10% regional lymph nodes, 3% lung)
  - Tonsillar SCC: invasive and highly metastatic (98% regional lymph nodes, 63% lung)

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis of SCC is based upon signalment, physical examination findings, at times cytologic analysis, and most often via histopathologic evaluation from an incisional biopsy sample.

DIFFERENTIAL DIAGNOSIS

- Planum: fungal lesion (particularly *Cryptococcus* in cats), cutaneous lymphoma, mast cell tumor, fibrosarcoma, melanoma, eosinophilic granuloma, immune-mediated dermatopathy
- Aural:
  - Canal: severe hyperplasia in dogs with chronic otitis, ceruminous gland adenocarcinoma, adenoma, papilloma, polyp, plasmacytoma, basal cell tumor, melanoma, granuloma
  - Pinna: consider trauma, frostbite, insect bites; also see Planum, above.
- Digital:
  - Dog: melanoma, mast cell tumor, soft-tissue sarcoma, osteomyelitis, paronychia
  - Cat: usually metastatic lung tumor; bacterial paronychia; other primary tumors much less likely
- Oral:
  - Gingival mass in a dog: SCC, melanoma, fibrosarcoma, acanthomatous ameloblastoma (acanthomatous epulis). Less likely, osteosarcoma, plasma cell tumor, tooth root abscess, fungal disease, other primary tumors.
  - Gingival mass in a cat: SCC, fibrosarcoma, dental disease. Less likely, melanoma, other primary tumors.
  - Tonsillar mass in a dog: SCC, lymphoma. Less likely, bacterial or fungal infection.
  - Sublingual mass in a cat: SCC, foreign body, fungal infection, other neoplasia

INITIAL DATABASE

Dog, all sites:

- CBC, serum biochemistry profile, urinalysis; usually unremarkable
- Aspirate and cytologic examination from regional lymph nodes to assess for metastasis in all cases; unlikely to be positive but an easy test with prognostic value.
- Three-view thoracic radiographs to assess for metastasis; usually negative
- Fine-needle aspirate (FNA) and cytologic examination of the primary mass; it may be possible to obtain the samples on animal that is awake, but if sedation is needed, plan to biopsy as well.
  - Cytologic examination can provide a definitive diagnosis, but at times extreme inflammation of the tumor can make interpretation of the squamous cells difficult, necessitating a biopsy.

Cats:

- Planum and aural: see Dog, above. Hypercalcemia is rarely seen as paraneoplastic syndrome in ear canal SCC.
- Digital: three-view thoracic radiographs almost always reveal lung neoplasia; usually solitary mass but may be multiple. FNA and cytologic examination of the digital mass can provide a definitive diagnosis, but at times extreme inflammation of the tumor can make interpretation of the epithelial cells difficult. These cells, while usually pulmonary adenocarcinoma in origin, may have some squamous differentiation. FNA of the lung mass can confirm a lung tumor if the digit lesion is nondiagnostic.
- Oral: mandibular lymph node FNA and cytologic examination to assess for metastasis in all cases. Hypercalcemia may be seen as a paraneoplastic syndrome in some cats with oral SCC. Three-view thoracic radiographs to assess for metastasis.

ADVANCED OR CONFIRMATORY TESTING

- Incisional or excisional biopsy of the primary mass for histopathologic diagnosis
- Radiographs, CT scan, or MRI of lesion to assess for tumor extent, bone involvement, and to plan surgery or radiation therapy

TREATMENT

TREATMENT OVERVIEW

Excision of primary tumor with wide margins is often curative, as indicated by low metastatic rates in most primary locations except the tonsil. Owing to location and extent of lesion in many cases, however, wide excision may be difficult or impossible.

ACUTE GENERAL TREATMENT

Aggressive surgical resection; if margins are not complete on histologic evaluation, radiation is effective for microscopic disease.

- Planum:
  - Dog: excising the premaxilla along with the planum in cases with very large masses may provide better cosmesis.
  - Cat: excision is an excellent option if the tumor is not too extensive along the bridge of the nose or does not involve the lip or surrounding skin. Radiation, photodynamic therapy, cryotherapy, and intralesional chemotherapy (platinum drugs, 5-fluo-rocil [FU]) can be effective for small superficial lesions, with decreasing effectiveness for larger lesions. In one study, 6 out of 6 cats with large lesions had complete remission with intralesional carboplatin combined with radiation therapy (median follow-up time 9 months, with median time to recurrence or survival time not yet reached).
- Aural: total ear canal ablation with bulla osteotomy provides best survival times. In cats, the tumors can invade aggressively into the skull bones.
- Digital:
  - Dog: digital amputation; adjuvant therapy usually unnecessary
  - Cats: therapy unrewarding if metastatic lesion; if thoracic films are normal and only one digit is involved, amputation of the digit is recommended.
- Bowen's disease:
  - Systemic therapy has shown little benefit for this multifocal disease. Daily topical imiquimod has shown some efficacy in cats. This imidazoquinoline works via binding to surface toll-like receptors 7 and 8 on macrophages, which in turn leads to both innate and cell-mediated immune responses resulting in tissue-specific apoptosis. Survival times in a small series of cases (12 cats) exceeded 3 years.
- Oral:
  - Gingival: aggressive resection, including partial mandibulectomy or maxillectomy. Definitive radiation for residual microscopic disease if surgery does not provide tumor-free margins.
  - Tongue, dog: if rostral, surgical resection (40%-60% of the tongue can be removed with good function remaining, possibly more). Histologic grade predicts metastatic behavior; if high grade, consider chemotherapy.
  - Tonsillar: poor treatment options owing to invasiveness and metastatic behavior; multimodality therapy includes surgical debulking, if possible, of primary mass and involved lymph nodes, followed by chemotherapy and radiation; may extend survival times.
  - Sublingual and gingival, cat: very poor treatment options. Surgical excision usually not feasible. Radiation therapy and photodynamic therapy have been tried with limited success. Gemcitabine as a radiation sensitizer with palliative radiation has shown some short duration responses (50% complete and partial remission, with median duration 42.5 days) but may be associated with significant hematologic and normal tissue toxicity and thus cannot be recommended.
- Chemotherapy: piroxicam (0.3 mg/kg PO once daily; caution regarding gastric ulcerative effects) has some effect against gross SCC in dogs (18% complete and partial remission, 29% stable disease). Cisplatin combined with piroxicam also showed antitumor effect in dogs (55% complete and partial remission, 33% stable disease), but nephrotoxicosis is a significant concern when combining these drugs (about 40% renal toxicoses), so combining them is not recommended.

CHRONIC TREATMENT

- Cyclooxygenase (COX)-2 expression was shown in 40 out of 40 canine SCC cases, so therapy with piroxicam or other nonsteroidal antiinflammatory drugs (NSAIDs) may be of benefit.
- Only 9% of feline oral SCC cases and 0 out of 6 cutaneous SCC cases showed COX-2 expression, bringing into question the benefit of using NSAIDs for treatment of the feline disease.

PROGNOSIS AND OUTCOME

- Planum: excellent prognosis for cure if complete surgical resection. Median survival in cats with planum and/or pinna SCC: 673 days with surgery alone.
- Aural, canal: excellent prognosis for cure if treated early; unfortunately, tumors in cats have often progressed massively prior to identification, leading to a median survival time of only 3.8 months.
- Digital:
  - Dog: good prognosis with 95% 1-year and 75% 2-year survival rates. Median survival not reached in recent study (>1700 days).
  - Cat: for metastatic lesion, digital amputation median survival is only 1-2 months; for primary digital SCC, reported survival time with surgery is variable (3 weeks to 2 years).
- Oral:
  - Dogs with rostral SCC: wide surgical resection can be curative.
  - Dogs with mandibular or maxillary nonresectable SCC: radiation. Median survival time is 450 days. Control time for dogs with tumors greater than 4 cm diameter is generally shorter.
  - Dogs with tonsillar SCC: surgery and radiation. Median survival is 100 days. With surgery, radiation, and

chemotherapy (doxorubicin and cisplatin), median survival is 270 days.
- Dogs with lingual SCC: rostral masses can be cured with wide resection if low grade. Dogs with nonresectable lingual SCC can be treated with radiation therapy, but survival is generally short (i.e., median 4 months), with dogs being euthanized due to local proliferation or metastasis.
- Cats with mandibular SCC: radiation and mitoxantrone; without surgery, generally poor response; median survival is 180 days. Mandibulectomy and radiation: median survival is 14 months; euthanasia usually due to local recurrence.
- Cats sublingual: poor response to therapy; survival time <3 months.

PEARLS & CONSIDERATIONS

COMMENTS

- Planum: cosmesis and quality of life after a nosectomy are generally good to excellent, with high owner satisfaction. Early treatment when the lesion is small enough for a surgical cure is strongly recommended when possible.
- Aural:
  - Canal: complete ear ablation is needed; simple debulking is inadequate because the tumor will continue to invade inward, making a surgical cure impossible later.
  - Pinna: preneoplastic changes can extend along the entire edge of the pinna; complete pinnaectomy may be required for cure. If lesion is very small, simple removal of the affected tip of the ear can be considered, with a later decision made according to need for further excision based on histopathologic examination results.
- Digital:
  - Dog: tumors often go undiagnosed for extensive amounts of time due to treatment for a nailbed infection. Any questionable nonantibiotic-responsive digital swelling must be biopsied.
  - Cat: primary digit tumors are very rare; three-view thoracic radiographs are essential prior to surgery, because digital tumors are usually secondary.
- Oral:
  - Mandibular, maxillary, and lingual SCC in rostral locations in dogs can be cured with aggressive resection.
  - SCC in cats and in other locations in the mouth in dogs is difficult to address owing to invasiveness and/or metastasis.
  - Multimodality therapy may extend survival times, but quality of life can be an issue with the treatments:
    - Dogs with tonsillar SCC can have pronounced dysphagia and discomfort; surgical debulking may not alleviate clinical signs, and radiation therapy can contribute to local discomfort for several weeks.
    - Cats with mandibular or maxillary SCC can have temporary responses to chemotherapy and radiation, but side effects may necessitate placement of a feeding tube. The occasional cat with a small lesion may have a greatly extended survival time with surgery, radiation, and chemotherapy.
    - Case selection for multimodality treatment is important in both dogs and cats, and owners need to have realistic expectations for the success of the therapy.

PREVENTION

Planum and pinna: limit sun exposure in light-coated cats. Oral SCC in cats may be associated with flea collar use, canned cat food or canned tuna consumption, and (possibly) environmental tobacco smoke.

SUGGESTED READING

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Sporotrichosis

BASIC INFORMATION

DEFINITION

A mycotic disease caused by *Sporothrix schenckii*. The disease is caused by a dimorphic fungus and clinically manifests with chronic granulomatous skin lesions.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Cats, dogs, humans, horses, pigs, cattle. Young to middle-aged cats and dogs predominate.
- “Rose-grower's disease” in humans

RISK FACTORS

- The disease is often associated with puncture wounds, so outdoor roaming dogs are overrepresented. In cats, fighting intact males predominate in contracting the disease.
- A higher concentration of organisms exists in soils rich in decaying organic matter, barberry and rose bush thorns, sphagnum moss, tree bark, and mine timbers.
- Immune suppression allows for dissemination.
- Punctures and other wounds allow for inoculation.

CONTAGION & ZOONOSIS

- Cat-to-cat or cat-to-human transmission is considered possible, especially to immunosuppressed people (via wounds or contaminated claws). Feline sporotrichosis may be a harbinger of sporotrichosis in dogs and humans in contact with these cases.
- Dog-to-dog or dog-to-human transmission is rare to unlikely owing to low numbers of organisms found in lesions.

GEOGRAPHY AND SEASONALITY: Worldwide distribution. Temperate to tropical climates.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Three clinical forms: cutaneous, cutaneolymphatic, and disseminated. Dogs: predominantly cutaneous, cutaneolymphatic. Cats: cutaneous, cutaneolymphatic, and disseminated.

HISTORY, CHIEF COMPLAINT

- Cutaneous lesions (nodular to ulcerated)
- Possible draining tracts
- Lethargy
- Anorexia

PHYSICAL EXAM FINDINGS

- Fever: suggests possible disseminated disease and immunocompromised state
- Depression
- Cats: ≈97% of affected cats have one or multiple skin lesions, commonly on the distal limbs, head, or tail base:
  - Draining puncture wounds, abscesses, or cellulitis
  - Ulcerations, purulent exudate, and large crusted lesions
  - ≈44% of affected cats have respiratory tract signs
- Dogs: multinodular truncal or head lesions; dermal or subcutaneous:
  - Ulcerations with purulent exudate and crust formation are possible.
  - Cutaneolymphatic form: nodules on distal limb, ascending via lymphatics and associated lymphadenopathy

ETIOLOGY AND PATHOPHYSIOLOGY

- Inoculation of mycelial form of *S. schenckii* into tissues leads to production of the yeast form
- Pyogranulomatous inflammation occurs, with organisms seen in macrophages and neutrophils.
- Lymphatic dissemination to spleen, liver, lung, eyes, bones, muscles, central nervous system [CNS])
    - Lung and liver are predominant sites for dissemination in cats.
- Dissemination is rare in dogs but may occur in up to 50% of cats, especially with immune-suppressive dosages of corticosteroids.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is based on geography, history, and physical exam findings, with positive cytologic results. Suspicion also is warranted if wounds are not responding to standard antibiotic therapy.

DIFFERENTIAL DIAGNOSIS

- Deep cutaneous bacterial infection, L-form bacterial infection
- Systemic mycosis
- Leishmaniasis (dogs)

INITIAL DATABASE

- CBC, serum biochemistry profile, urinalysis: anemia, leukocytosis with neutrophilia, hypoalbuminemia, and hyperglobulinemia commonly observed
- Feline leukemia virus (FeLV) and feline immunodeficiency virus (FIV) serologic testing: positive in <1% and 8% of affected cats, respectively
- Cytologic examination from aspirates, exudates, or skin preps: diagnostic
    - Organism is small (slightly smaller than erythrocytes), round, oval, or cigar-shaped. Large numbers of organisms found in exudate in cats; small number found in dogs
- Positive bacterial cultures from secondary infection, often *Staphylococcus pseudintermedius*

ADVANCED OR CONFIRMATORY TESTING

- Histopathologic examination of nodules: diagnostic
- Fungal culture: notify laboratory of the possibility of *Sporothrix* organisms because of the infectious nature of sample to humans. Never culture suspected sporotrichosis lesions in-house (zoonosis risk).
- The Centers for Disease Control and Prevention, Atlanta, can perform fluorescent antibody testing on exudates or tissue.

TREATMENT

TREATMENT OVERVIEW

Removal of organisms, with treatment continuing for 30 days beyond apparent cure. Corticosteroids or other immunosuppressives are contraindicated.

ACUTE AND CHRONIC TREATMENT

Dogs; options include one of the following:

- Supersaturated solution of potassium iodide (SSKI) 40 mg/kg PO with food q 8 h for 30 days beyond apparent cure; *or*
- Ketoconazole 5-15 mg/kg PO with food q 8 h for 30 days beyond apparent cure; *or*
- Itraconazole 5-10 mg/kg PO with food q 12-24 h for 30 days beyond apparent cure

Cats:

- Itraconazole is the treatment of choice in cats; better absorption with suspension formula: 1.25-1.5 mg/kg (suspension) PO q 24 h for 30 days beyond apparent cure; or 5-10 mg/kg (capsules) PO q 12-24 h for 30 days beyond apparent cure.

POSSIBLE COMPLICATIONS

- SSKI can cause systemic iodination (ocular and nasal discharge, dry haircoat with scaling, vomiting, depression, collapse). If signs are mild, discontinue the medication for 1 week and reinitiate; if signs are severe, change treatment to alternative therapy.
- Ketoconazole can be hepatotoxic, especially in cats.
- Itraconazole has been found to be hepatotoxic in 10% of dogs treated with a dosage of 5 mg/kg q 12 h; better tolerated, fewer less side effects in cats.

RECOMMENDED MONITORING

With itraconazole or ketoconazole administration, monitor liver enzymes every 2-4 weeks for duration of therapy.

PROGNOSIS AND OUTCOME

- Response of cutaneous or cutaneolymphatic is fair to good. Of 266 cats treated in one study, 68 (26%) were cured, irrespective of extracutaneous signs or FIV status.
- Disseminated disease carries a guarded prognosis.

PEARLS & CONSIDERATIONS

COMMENTS

- Even after treatment is completed, use of immunosuppressive dosages of corticosteroids is contraindicated owing to reported recurrence of infection.
- Duration of therapy is often 3 months or more.
- Cats have been given iodide and ketoconazole, but because of high sensitivity, these are not recommended.

PREVENTION

- Limit outdoor roaming, especially in wooded areas.
- Castrate male cats to diminish fighting.

TECHNICIAN TIPS

- Wear gloves when handling infected animals.
- Wash hands and forearms with chlorhexidine or povidone-iodine scrub after wearing gloves.

CLIENT EDUCATION

- Sporotrichosis is a zoonotic disease, especially in cats.
- Separation of infected animals from immunosuppressed people is necessary.

SUGGESTED READING

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Spongiform Encephalopathies

BASIC INFORMATION

DEFINITION

The spongiform encephalopathies are a heterogeneous group of diseases which have in common spongiform change within the brain, seen histopathologically. Lysosomal storage diseases may also be characterized by vacuolation of neurons, but in those cases the vacuoles are lysosomes distended with storage products. In the spongiform encephalopathies, vacuoles appear empty, and if intraneuronal, they are not membrane bound.

SYNONYMS

- Gray matter disease: transmissible spongiform encephalopathies (usually named for species, e.g., bovine spongiform encephalopathy [BSE]), prion disease
- White matter disease: use of the term *spongiform encephalopathy* to describe white matter disease is being dropped to avoid confusion with prion diseases. Better terms are *spongiform leukoencephalopathies* or *spongy degeneration of white matter*. Hereditary forms have specific names such as *Canavan's disease* or *maple syrup urine disease*.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Gray matter:
  - Transmissible: cats > 2 years of age
  - Hereditary: rottweiler dogs, signs begin at 6 weeks of age and progress over 6-7 months.
- White matter:
  - Acquired: dog or cat, any age or sex
  - Hereditary: dogs or cats
    - Signs begin at 3-5 weeks and progress rapidly in silkie terriers, Shetland sheepdogs, Samoyeds, and kittens
    - Signs begin at 4-6 months and progress over 6-8 months in Labrador retrievers and dalmatians.

GENETICS & BREED PREDISPOSITION

- Gray matter:
  - Transmissible: in sheep, mice, and humans, different polymorphisms in the prion protein gene can affect risk of infection. No such evidence in cats.
  - Hereditary: appears to be autosomal recessive in rottweilers
- White matter:
  - Acquired: no predisposition
  - Hereditary: appears to be autosomal recessive or maternal (mitochondrial) inheritance

CONTAGION & ZOONOSIS

- Gray matter:
  - Transmissible: ingestion of BSE-contaminated meat or byproducts can cause variant Creutzfeldt-Jacob disease in humans and feline spongiform encephalopathy in cats.

GEOGRAPHY AND SEASONALITY

- Gray matter:
  - Transmissible: only reported in European cats but could appear anywhere BSE appears
  - Hereditary: affected rottweilers have been reported in the United States and Europe.
- White matter: none

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Can be subdivided depending on whether vacuolation occurs within the myelin sheaths in the white matter or within neurons or their processes in the gray matter. Both can then be further subdivided into hereditary and acquired

forms. The acquired white matter diseases are toxic, whereas the acquired gray matter diseases are transmissible.

HISTORY, CHIEF COMPLAINT

- Gray matter:
  - Transmissible: behavior changes (timidity or aggression) progressing to ataxia, hypermetria, and hyperesthesia to touch and sound
  - Hereditary: ataxia, paresis, progressing to severe tetraparesis.
- White matter:
  - Acquired: at lower doses, bromethalin produces pelvic limb ataxia and paresis/paralysis. Higher doses produce severe muscle tremors and seizures.
  - Hereditary:
    - Labrador retrievers develop hypermetria and spastic paresis with episodes of decerebrate rigidity progressing to quadriplegia.
    - Shetland sheepdogs, Australian cattle dogs, and kittens have motor deficits, altered mentation, and seizures.

PHYSICAL EXAM FINDINGS

- Gray matter:
  - Transmissible: as described in History, Chief Complaint
  - Hereditary: ataxia and paresis with normal reflexes most prominent in the pelvic limbs and upper airway/inspiratory stridor (due to laryngeal paralysis). Progresses to severe tetraparesis and proprioception loss.
- White matter: as described in History, Chief Complaint

ETIOLOGY AND PATHOPHYSIOLOGY

- Gray matter:
  - Transmissible: caused by prions, enigmatic infectious proteins. Abnormally folded prion proteins build up within neurons as scrapie-associated fibrils and ultimately lead to cell death. Cats were infected at the height of the BSE outbreak in Europe.
  - Hereditary: gene has not been identified. Mutations in the prion protein gene can cause a spongiform encephalopathy in humans, but this was ruled out in rottweilers.
- White matter:
  - Acquired: toxins that uncouple oxidative phosphorylation, including bromethalin and hexachlorophene
  - Hereditary: a missense mutation in the mitochondrial gene for cytochrome B has been identified in Australian cattle dogs and Shetland sheepdogs. No mutation has been identified in other breeds of dogs or cats.

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

The clinical diagnosis remains presumptive; confirmation is only possible at necropsy.

- Gray matter:
  - Should be suspected in progressive forebrain signs without other cause
  - Confirmed at necropsy
- White matter:
  - Suspected in cerebellar and long-tract signs
  - Imaging may show white matter edema.
  - Confirmed at necropsy

DIFFERENTIAL DIAGNOSIS

- Gray matter:
  - Transmissible: any cause of diffuse forebrain signs in adult cat:
    - Infectious: rabies, FIV, FIP, fungal, protozoal
    - Metabolic: hepatic, electrolytes, endocrine
    - Neoplasia: meningioma, astrocytoma, metastatic
    - Toxic: organophosphates, heavy metals
  - Hereditary:
    - Any cause of multifocal central nervous system (CNS) or peripheral nerve disease in a young dog
    - Other hereditary diseases of rottweilers: leukodystrophy, motor neuron disease, neuroaxonal dystrophy

        - Idiopathic laryngeal paralysis
        - Infectious: *Neospora*, distemper, tickborne, fungal
        - Toxic
- White matter:
    - Juvenile onset:
        - Any cause of diffuse white matter disease
        - Canine distemper
        - Lysosomal storage disease or other inborn error of metabolism
    - Neonatal onset:
        - Any cause of diffuse forebrain disease
        - Lysosomal storage disease or other inborn error of metabolism
        - Hepatic encephalopathy
        - Hypoglycemia

INITIAL DATABASE

- Neurologic exam (see p. 1311):
    - Localize lesion(s)
- CBC/serum biochemistry profile (including bile acids)/urinalysis:
    - Rule out metabolic disease and look for evidence of infection
- Brain imaging (CT or MRI; and):
    - Rule out structural disease
    - May see evidence of diffuse increase in water density of gray or white matter
- Cerebrospinal fluid (CSF) analysis:
    - Rule out encephalitis/meningitis

ADVANCED OR CONFIRMATORY TESTING

Ultimate diagnosis is only available postmortem: histopathologic lesions showing vacuolation in white matter or gray matter.

TREATMENT

TREATMENT OVERVIEW

Most are not amenable to treatment. Confirmation of gray matter spongiform encephalopathy is important for public health considerations. There are no specific treatments for any of the transmissible or hereditary spongiform encephalopathies. Treatment would be purely supportive and nonspecific, such as anticonvulsant drugs for seizures.

ACUTE GENERAL TREATMENT

Mannitol may improve the intramyelinic edema that can occur with bromethalin toxicity.

PROGNOSIS AND OUTCOME

- Prognosis for all spongiform encephalopathies is guarded to grave.
- Personality changes make animals with transmissible forms potentially dangerous.
- Hereditary forms have been inexorably progressive.
- Toxic spongiform leukoencephalopathies respond poorly to treatment but may recover if dose is low.

PEARLS & CONSIDERATIONS

COMMENTS

Transmissible spongiform encephalopathies will hopefully remain rare in dogs and cats. However, it is important to recognize them if they should occur because of their public health implications. A necropsy will be necessary to confirm a diagnosis of spongiform encephalopathy of gray matter, which should be reported to the appropriate agency.

PREVENTION

- Care with use of bromethalin rodenticides
- Do not feed bovine nervous system or byproducts to cats in BSE-endemic areas. Risk from deer with chronic wasting disease is unknown, but it would be wise to not feed deer nervous system or byproducts to cats.

CLIENT EDUCATION

Clients should be educated about transmissible spongiform encephalopathies so they can make intelligent choices regarding meat safety rather than being swayed by emotion or politics.

SUGGESTED READING

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Splenomegaly

BASIC INFORMATION

DEFINITION

Enlargement of the spleen—focal or generalized

EPIDEMIOLOGY

GENETICS & BREED PREDISPOSITION

- German shepherd, Great Dane (gastric dilatation volvulus [GDV] with splenic torsion)
- Boxer (mastocytosis)
- German shepherd, golden retriever, Labrador retriever (hemangiosarcoma)
- German shepherd (systemic mycoses, especially aspergillosis)
- Cocker spaniel (immune-mediated hemolytic anemia [IMHA])
- Bull mastiff and many others (lymphoma)
- Oriental-breed cats (feline infectious peritonitis [FIP])

RISK FACTORS: Living in endemic tickborne disease areas

GEOGRAPHY AND SEASONALITY: Tickborne diseases: more prevalent in tropical climates and during the summer

ASSOCIATED CONDITIONS & DISORDERS: Generalized lymphadenopathy (see p. 662)

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Vague and nonspecific: anorexia, lethargy, weight loss
- Related to underlying disease rather than splenomegaly
- Chronic vomition if marked splenic enlargement
- Polyuria/polydipsia: paraneoplastic hypercalcemia

PHYSICAL EXAM FINDINGS

- Palpation of abdominal mass
- Abdominal distention if severe enlargement or hemoabdomen
- Lymph node enlargement: lymphoma, ehrlichiosis, mycoses, autoimmune disorders
- Collapse, pallor, tachycardia: splenic rupture, IMHA, acute babesiosis
- Petechiae: immune-mediated thrombocytopenia (ITP)

ETIOLOGY AND PATHOPHYSIOLOGY

- Generalized splenomegaly:
  - Infiltrative disorders:
    - Neoplastic: acute and chronic leukemia, systemic mastocytosis (more common in cats), lymphoma, multiple myeloma
    - Non-neoplastic: amyloidosis
  - Congestion:
    - Smooth muscle relaxants: barbiturates, halothane anesthesia
    - Splenic torsion (alone or in association with GDV)
    - Right-sided heart failure with portal hypertension
  - Inflammatory/infectious disorders (splenitis):
    - Suppurative: hematogenous dissemination of bacterial infection
    - Necrotizing: gas-forming anaerobes associated with splenic torsion
    - Eosinophilic: hypereosinophilic syndrome (cats)
    - Lymphoplasmacytic: ehrlichiosis, infectious canine hepatitis, babesiosis
    - Granulomatous: systemic mycoses

        - Pyogranulomatous: FIP
    - Lymphoreticular hyperplasia
        - Chronic bacteremic conditions: discospondylitis, brucellosis
        - Hemolytic disorders: IMHA, ITP
    - Extramedullary hematopoiesis
- Focal splenomegaly (splenic mass)
    - Neoplastic
        - Hemangiosarcoma, hemangioma, leiomyosarcoma, fibrosarcoma
    - Non-neoplastic
        - Hematoma, abscess, nodular hyperplasia, granuloma

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Splenomegaly warrants evaluation with a CBC and serum biochemistry profile in an attempt to find a possible etiology. Diagnostic imaging helps elucidate whether the enlargement is regional or diffuse, which narrows the differential diagnosis. Based on these results, specific tests (e.g., PCR if infection is suspected) or intervention (splenic aspirate, splenectomy) can be chosen to conclude the diagnosis.

DIFFERENTIAL DIAGNOSIS

- Other cranial abdominal organomegaly
- Other nonspecific abdominal masses

INITIAL DATABASE

- CBC:
    - Regenerative anemia: IMHA, splenic rupture, blood parasites
    - Nonregenerative anemia: ehrlichiosis, retroviral infections, neoplastic bone marrow infiltration
    - Pancytopenia: ehrlichiosis, bone marrow infiltration
    - Spherocytosis: IMHA
    - Hemoglobinemia, bilirubinemia: splenic torsion, hemolysis
    - Lymphoblastosis: lymphoma, infections (rarely)
    - Blood parasites: babesiosis, acute ehrlichiosis, feline hemoplasmas
    - Thrombocytopenia: ITP, babesiosis, ehrlichiosis and other rickettsial diseases
- Urinalysis:
    - Hemoglobinuria, bilirubinuria: hemolytic disease, splenic torsion
- Serum biochemistry profile:
    - Hyperglobulinemia: FIP, multiple myeloma, ehrlichiosis
    - Hypercalcemia: lymphoma, multiple myeloma, granulomatous disease
- Imaging:
    - Abdominal radiographs: confirm abdominal mass (if sufficiently large)
    - Thoracic radiographs: assess for metastases (take ventrodorsal, left-, and right-lateral views)
    - Abdominal ultrasonography: detect abdominal effusion, define splenic architecture, confirm splenic origin (mass), delineate metastatic abdominal masses, identify abdominal effusion far centesis
- Retroviral testing (cats)

ADVANCED OR CONFIRMATORY TESTING

- Fine-needle aspiration and cytologic examination to detect infectious agents or predominant inflammatory cell type:
    - Not recommended with mixed echogenicity masses (suspicion of hemangiosarcoma) because of risk (may hemorrhage) and poor diagnostic yield (heterogenous tumor)
- Histopathologic examination of tissue after splenectomy or of tissue samples taken at the periphery of large masses
- Bone marrow aspiration
- Exploratory laparotomy
- CT (abdominal)
- PCR: *Ehrlichia,* feline hemoplasmas
- Coagulation panel: disseminated intravascular coagulation

TREATMENT

TREATMENT OVERVIEW

Since splenomegaly is a sign attributable to many different types of disorders, treatment will depend on the underlying disease process.

ACUTE AND CHRONIC TREATMENT

Selected according to the etiology

POSSIBLE COMPLICATIONS

Susceptibility to infectious diseases after splenectomy

RECOMMENDED MONITORING

Monitor for ventricular arrhythmias for up to 3 days after splenectomy (splenic masses).

PROGNOSIS AND OUTCOME

- Good to excellent with uncomplicated infections (babesiosis, ehrlichiosis)
- Guarded to grave in the case of advanced-stage (metastatic) hemangiosarcoma
- With splenic masses, prognosis cannot be determined without complete histopathologic evaluation of tissue:
    - Hematoma/nodular hyperplasia (55% of splenic masses): 83% alive 2 months post splenectomy, 64% alive at 1 year. Most deaths/euthanasia due to unrelated causes.
    - Hemangiosarcoma (40% of splenic masses): 31% alive 2 months post splenectomy, 7% at 1 year. Most deaths/euthanasia due to hemangiosarcoma progression.

PEARLS & CONSIDERATIONS

COMMENTS

- Age does not discriminate between neoplastic and non-neoplastic splenic disease.
- Clinical signs are vague.
- A common clinical error is excessive suspicion of hemangiosarcoma on the basis of a splenic mass as the only abnormality.
- Differentiate splenomegaly from hepatomegaly by ability to move the spleen caudally during abdominal palpation. Raise patient's forelimbs to facilitate examination.
- Dogs with anemia, nucleated red blood cells, abnormal red cell morphology, or splenic rupture: greater chance of having splenic neoplasia
- The spleen is an accessible organ to obtain a diagnostic sample in evaluating systemic diseases (diffuse splenomegaly).
- For histopathologic examination of splenic masses after splenectomy, a submitted tissue sample should cross from normal tissue to abnormal/mass. Ideally, the whole spleen is submitted fresh on cold packs (not frozen).
- Gross appearance at laparotomy cannot discriminate between hematoma, nodular hyperplasia, hemangioma, and hemangiosarcoma; normal ectopic splenic tissue in abdomen may falsely appear to be metastases—be careful if considering euthanasia on the operating table.

PREVENTION

Regular tick control in endemic areas

SUGGESTED READING

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AUTHOR: JOHAN P. SCHOEMAN

EDITOR: ETIENNE CÔTÉ

Splenic Torsion

BASIC INFORMATION

DEFINITION

Twisting of the pedicle of the spleen, resulting in occlusion and thrombosis of the splenic vasculature and splenic ischemia

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs: males more frequently affected

GENETICS & BREED PREDISPOSITION: Large-breed, deep-chested dogs (Great Danes, German shepherds)

RISK FACTORS: Gastric dilatation/volvulus (GDV)

ASSOCIATED CONDITIONS & DISORDERS

- GDV
- Splenic infarction

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Often vague, nonspecific signs for up to 3 weeks prior to diagnosis:
  - Intermittent vomiting, diarrhea
  - Weakness, depression
  - Anorexia
  - Abdominal distention
  - Weight loss
  - Discolored urine
- Acute collapse
- Previous episode of GDV

PHYSICAL EXAM FINDINGS

- Abdominal distention
- Abdominal mass/splenomegaly
- Any of the following may also be noted: abdominal pain, fever, dehydration, pale mucous membranes, icterus.
- If acute cardiovascular collapse: tachycardia, pale mucous membranes, prolonged capillary refill time, weak peripheral pulses

ETIOLOGY AND PATHOPHYSIOLOGY

- Etiology unknown:
  - Occurs in large-breed, deep-chested dogs
  - Associated with GDV:
    - Occurs in conjunction with GDV
    - GDV occurs after treatment of splenic torsion
- Proposed theory: repeated stretching of gastrosplenic and splenocolic ligaments, resulting in splenic hyper-motility

DIAGNOSIS

DIAGNOSTIC OVERVIEW

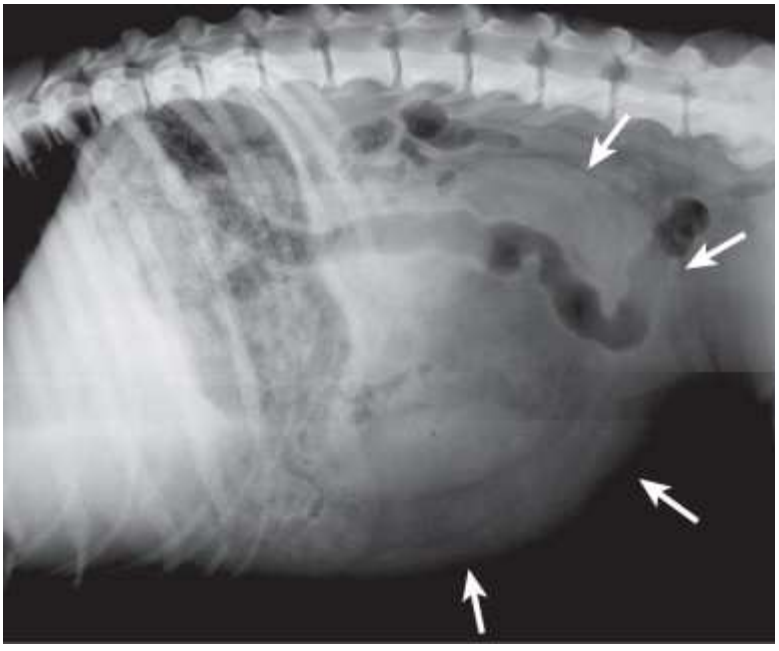
Diagnosis is suspected based on patient signalment, presenting history, and physical examination findings. Confirmation requires abdominal diagnostic imaging (radiographs, ultrasound) to demonstrate the uniformally enlarged, malpositioned spleen.

DIFFERENTIAL DIAGNOSIS

- Splenic neoplasia
- Other causes of splenomegaly (see p. 1428)
- Neoplasia of other abdominal organs (e.g., liver)
- GDV

INITIAL DATABASE

- CBC:
  - Anemia
  - Leukocytosis (neutrophilia, monocytosis: stress leukogram common)
- Serum biochemistry profile:
  - Elevated alkaline phosphatase (ALP), alanine aminotransferase (ALT), bilirubin concentrations
- Urinalysis:
  - Hemoglobinuria common
- Diagnostic imaging:
  - Survey abdominal radiographs:
    - Splenomegaly (diffuse):
      - May be the only abnormal radiographic finding
      - Often the enlarged spleen may have a "reversed C" shape.
      - Abnormal position of spleen in abdomen is common.
      - Gas bubbles may be seen within the spleen.
    - Peritoneal effusion is common and can obscure visceral detail to the point that the findings listed previously are not apparent, requiring abdominal ultrasonography.
    - Displacement of the small intestines
  - Abdominal ultrasound examination: indicated in all cases in which splenic torsion is suspected
    - Diffuse splenomegaly, appearing to curve around the hilus
    - Free abdominal fluid is generally present.
    - Diffusely hypoechoic spleen, "lacy" appearance of splenic parenchyma:
      - Linear echoes separating large hypoechoic areas. This appearance is a result of vascular congestion (hypoechoic) within the dilated sinusoids and vessels (the walls of which are the framework of the "lace").
      - Thrombi may be visible within the lumen of splenic vessels.
    - Doppler color flow:
      - Decreased blood flow through splenic veins
      - Lack of flow in regions associated with intravascular thrombi
- Electrocardiogram (ECG) if arrhythmia is noted on exam, if there is suspicion of syncope/collapse, or for postoperative monitoring



SPLENIC TORSION Lateral abdominal radiograph of a dog with splenic torsion. The characteristic "reversed C" shape of the torsed spleen is apparent *(arrowheads).*

(Courtesy Dr. Richard Walshaw.)

ADVANCED OR CONFIRMATORY TESTING

Coagulation profile: laboratory evidence of coagulopathy may exist, but a clinical bleeding problem is rarely detected.

TREATMENT

TREATMENT OVERVIEW

Splenectomy is the required treatment for this problem and should be performed as soon as the patient is stable. This time frame will depend on the clinical status of the patient at the time of presentation.

ACUTE GENERAL TREATMENT

- Preoperative patient stabilization:
  - Correction of fluid deficits and electrolyte imbalance
  - Blood products (see p. 1347):
    - Whole blood if hematocrit <20% or if acute large-volume blood loss
    - Fresh frozen plasma if coagulopathy is present
  - Treatment of cardiac arrhythmias if indicated (see p. 1165)
  - Perioperative antibiotic therapy:
    - Cefazolin, 22 mg/kg IV q 2 h
- Surgical intervention as soon as animal is stable:
  - Splenectomy without untwisting the pedicle
  - Gastropexy
- Postoperative supportive care:
  - Continuation of IV fluid and electrolyte therapy
  - Additional blood products if indicated
  - ECG monitoring:
    - Treatment of arrhythmias if indicated

POSSIBLE COMPLICATIONS

- Delay in diagnosis and treatment:
  - Splenic necrosis
  - Peritonitis/sepsis
  - Disseminated intravascular coagulation (DIC)
- Pancreatitis:
  - If distal portion of left limb of pancreas is involved in torsion of the splenic pedicle

PROGNOSIS AND OUTCOME

Good with early diagnosis and treatment; reported 100% postsurgical survival

PEARLS & CONSIDERATIONS

COMMENTS

- Splenic torsion can occur in association with GDV or as an isolated problem.
- The same type of dog that has the greatest risk of developing GDV also has an increased risk of developing isolated splenic torsion.
- Gastropexy after splenectomy for splenic torsion is indicated to prevent future GDV.

TECHNICIAN TIPS

Perioperative patient care and stabilization may involve:

- Fluid therapy and administration of blood products. Be familiar with calculations necessary for whole blood and plasma

transfusion requirements.
- ECG monitoring. Be able to recognize arrhythmias and seek appropriate veterinary assistance.
- Ensure that adequate analgesia is provided in the postoperative period.

CLIENT EDUCATION

Large-breed, deep-chested dogs that develop vague, nonspecific signs of abdominal problems (as already described in this entry) may have splenic torsion.

SUGGESTED READING

Neath PJ, Brockman DJ, Saunders HM: Retrospective analysis of 19 cases of isolated torsion of the splenic pedicle in dogs. J Small Anim Pract 38:387–392, 1997.

AUTHOR & EDITOR: RICHARD WALSHAW

Spirocercosis

BASIC INFORMATION

DEFINITION

A disease of dogs that is caused by the nematode *Spirocerca lupi* and is characterized by lesions that can affect the esophagus (with potential for esophageal malignancy), aorta, and vertebrae

EPIDEMIOLOGY

SPECIES, AGE, SEX: Primarily affects dogs. Young to middle-aged dogs overrepresented; dogs <1 year old unlikely to develop infection.

GENETICS & BREED PREDISPOSITION: Medium- and large-breed dogs predisposed

GEOGRAPHY AND SEASONALITY: This parasite is found in the southern United States and many tropical and subtropical regions. In some endemic areas, there is a disproportionately high prevalence in urban dogs compared to rural dogs, but this varies with geographic region.

CONTAGION & ZOONOSIS: Not a zoonotic disease

ASSOCIATED CONDITIONS & DISORDERS: Esophageal neoplasia (osteosarcoma, fibrosarcoma, undifferentiated sarcoma) may occur secondary to esophageal granuloma formation from the encysted worms. These dogs may also develop hypertrophic osteopathy. Thoracic aortic aneurysm may occur secondary to migration of *S. lupi* from the gastrointestinal (GI) tract into the aortic wall. Thoracic vertebral spondylitis has been reported to occur secondary to migration and granuloma formation. Salivary gland necrosis, esophageal perforation with associated mediastinitis, and pyothorax have also been reported.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Vomiting or regurgitation, odynophagia, ptyalism, weakness, respiratory difficulty, coughing, anorexia, melena, paraparesis

PHYSICAL EXAM FINDINGS: There are no pathognomonic physical examination findings. Physical examination findings are related to the area of the body affected by the parasite. In addition to the chief complaints listed above, the most common abnormalities include weight loss and fever.

ETIOLOGY AND PATHOPHYSIOLOGY

- Spirocercosis is caused by the migration of the nematode *S. lupi*. Carnivores are infected by ingestion of an intermediate host (coprophagous beetles) or other paratenic hosts (e.g., birds, hedgehogs, lizards, mice, rabbits) in which the parasite does not undergo further development during its passage.
- Adult *S. lupi* generally live within nodules in the esophagus and stomach. *Spirocerca* eggs pass with feces, where they are ingested by coprophagous beetles. The definitive host may acquire the infection by ingesting the beetle intermediate host or other paratenic host.
- The L3 larvae penetrate the stomach wall of the definitive host, and migration occurs within the walls of the gastric arteries to the thoracic aorta. From the aorta, they migrate to the esophagus. The prepatent period time from infection of the host to the first ability to detect the infection with diagnostic evaluation is approximately 5-6 months.
- Clinically significant lesions are related to the migration route and final destination site of the parasite. The most common scenario is esophageal granuloma formation.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Spirocercosis typically is suspected in a patient presented for evaluation of regurgitation and living in an area where the disease is prevalent. Thoracic radiographic findings are often supportive of the diagnosis, but direct visualization through endoscopy is required for confirmation prior to treatment.

DIFFERENTIAL DIAGNOSIS

- Regurgitation: other esophageal disorders such as megaesophagus, esophagitis, foreign bodies, esophageal stricture, gastroesophageal reflux disease
- Esophageal mass: esophageal neoplasia, granuloma of other origin
- Vomiting: both GI (inflammatory, infectious, parasitic, neoplastic, dietary) and extra-GI (metabolic, endocrine, pancreatitis) etiologies

INITIAL DATABASE

- CBC, serum biochemical profile, urinalysis; no characteristic abnormalities:
  - Anemia (53% of cases) typically normocytic, normochromic and nonregenerative
  - Leukocytosis
  - Elevation in serum creatine kinase: most common biochemical abnormality (54% of cases)
  - Increased alkaline phosphatase
  - Hyperproteinemia
- Fecal flotation:
  - Sugar flotation
  - Teleman's sedimentation:
    - May reveal characteristic small, elongated eggs
    - Variable yield; positive result in 29%-80% of cases
- Thoracic and abdominal radiographs indicated (dorsoventral and right lateral projections most accurate for thoracic films in canine spirocercosis); may reveal dorsoventral and right lateral projections most accurate for canine spirocercosis
  - Esophageal and stomach lesions (soft-tissue masses with/without calcification). A mass is typically noted in the caudal esophagus (53%-86% of cases of spirocercosis). Most affected dogs have more than one granuloma, but not all are seen radiographically.
  - Bony changes in the thoracic vertebrae
  - Evidence of metastasis when esophageal neoplasia is present
- Limb radiographs in patients with lameness or hard swelling of distal limbs, to assess for hypertrophic osteopathy

ADVANCED OR CONFIRMATORY TESTING

- Esophagoscopy and gastroscopy may allow for visualization of granulomas and for biopsy procedures. In most cases of spirocercosis, endoscopy is the confirmatory diagnostic procedure of choice.
- Thoracic CT may be useful for identifying esophageal masses and aortic aneurysm.
- Postmortem examination in patients with sudden death or who have been euthanized will also provide a definitive diagnosis.

TREATMENT

TREATMENT OVERVIEW

- Resolution of regurgitation or vomiting
- Prevent development of esophageal neoplasia or hypertrophic osteopathy.
- Prevention of sudden death due to rupture of aneurysm

ACUTE AND CHRONIC TREATMENT

- Doramectin (Dectomax [Pfizer]) 200 mcg/kg SQ q 14 days for 3 treatments
  - Treatment of choice
  - Permanent resolution/cure is expected in many or most dogs in 6 weeks' time or less.
  - Dogs with persistent lesions after 6 weeks have been treated safely and successfully using doramectin, 500 mcg/kg PO q 24 h × 6 weeks.
- Fenbendazole (50 mg/kg PO q 24 h × 5-7 days) or ivermectin (200-400 mcg/kg SQ q 14-28 days) have been used for treating spirocercosis.

POSSIBLE COMPLICATIONS

Do not use ivermectins in collies, Shetland sheepdogs, Australian shepherds, or other susceptible breeds or individuals (see pp. 625 and 706).

PROGNOSIS AND OUTCOME

Prognosis is variable:

- With appropriate treatment, cure is expected in many or most dogs in 6 weeks' time or less.
- However, presence of esophageal neoplasia, aortic aneurysm, or large masses obstructing flow of ingesta worsen the prognosis.
- Hypertrophic osteopathy worsens the prognosis (present in 39% of cases with esophageal malignancy, 0% of cases without esophageal malignancy)
- Radiographic evidence of spondylitis (68% vs. 38%) and bronchial displacement (52% vs. 17%) are significantly different between cases with esophageal malignancy versus those without malignancy, respectively.
- Sixty-three percent of dogs with spirocercosis may die or be euthanized within 1 month of admission.

PEARLS & CONSIDERATIONS

COMMENTS

- In North America and Europe, spirocercosis is a rare disease and is only considered when there is a high index of clinical suspicion.
- The characteristic lesion is a soft-tissue mass in the caudal esophagus; radiographically, foreign-body ingestion is an important differential diagnosis.
- A minority of dogs develop neoplastic transformation of esophageal granulomas (e.g., 13 out of 14 dogs with spirocercosis had esophageal masses, but only 1 out of 13 had esophageal neoplasia).

PREVENTION

Prevent dogs from eating beetles or paratenic hosts.

SUGGESTED READING

Berry WL: *Spirocerca lupi* esophageal granu-lomas in 7 dogs: resolution after treatment with doramectin. J Vet Intern Med 14:609–612, 2000.

Dvir E, Kirberger RM, Mukorera V, et al: Clinical differentiation between dogs with benign and malignant spirocercosis. Vet Parasitol 155(1-2):80–88, 2008.

Gal A, et al: Aortic thromboembolism associated with *Spirocerca lupi* infection. Vet Parasitol 130:331–335, 2005.

Kirberger RM, Dvir E, van der Merwe LL: The effect of positioning on the radiographic appearance of caudodorsal mediastinal masses in the dog. Vet Radiol Ultrasound 50(6):630–634, 2009.

Mazaki-Tovi M, et al: Canine spirocercosis: clinical, diagnostic, pathologic, and epidemiologic characteristics. Vet Parasitol 107: 235–250, 2002.

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van der Merwe LL, Kirberger RM, et al: *Spirocerca lupi* infection in the dog: a review. Vet J 176(3):294–309, 2008.

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EDITOR: DEBRA L. ZORAN

Spinal Cord Trauma

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Acute injury to the spinal cord caused by external trauma

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Common in dogs and cats
- Animals of any age, both sexes, and all breeds can be affected.

RISK FACTORS

- Unconfined
- Access to high places such as balconies

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Often documented trauma
- Abrupt-onset deficits, usually nonprogressive

PHYSICAL EXAM FINDINGS

- Focal spinal pain
- Neurologic deficits ranging from mild ataxia to paralysis
- Schiff-Sherrington posture (paraplegia with increased extensor tone in the pelvic limbs) possible with thoracic or lumbar injuries
- Presence or absence of deep pain caudal to the injury is the most important prognostic finding.
- Signs of other injuries may be present, including chest injury, abdominal injury, head injury, or orthopedic injury.

ETIOLOGY AND PATHOPHYSIOLOGY

- Causes include motor vehicle accidents, falls, bite wounds, and gunshot wounds.
- Primary injury is due to initial concussive injury to the cord and any persistent compressive injury due to displaced fracture/luxation, hematoma, or disk extrusion or unstable vertebral segments.
- Secondary injury is caused by metabolic changes, including release of free radicals that lead to progressive damage to cell membranes.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is usually suspected from a witnessed traumatic event and/or neurologic deficits indicating a spinal lesion. Plain radiography may indicate a vertebral lesion; if not, the diagnosis may remain presumptive (and treatment provided accordingly), or advanced imaging can be confirmatory.

DIFFERENTIAL DIAGNOSIS

- Acute intervertebral disk extrusion
- Pathologic fracture from neoplasia or infection
- Orthopedic injury, such as pelvic fracture

- Fibrocartilaginous embolism
- Ischemic neuromyopathy due to aortic embolus

INITIAL DATABASE

Spinal radiographs: initially perform lateral view only until vertebral instability is ruled out.

ADVANCED OR CONFIRMATORY TESTING

Myelography, CT, or MRI is indicated if plain radiographs are normal or do not correlate with clinical assessment, and to determine if there is persistent spinal cord compression if surgery is considered.

TREATMENT

TREATMENT OVERVIEW

- Treat any life-threatening injuries, such as shock.
- Prevent further spinal cord injury caused by unstable vertebral injuries.
- Minimize secondary injury.
- Decompress the spinal cord.

ACUTE GENERAL TREATMENT

- General trauma management (e.g., airway, oxygenation, IV fluids as indicated)
- Strap or tape the animal to a rigid board or gurney until an unstable vertebral injury is ruled out.
- Analgesics as needed for pain control
- Corticosteroids:
  - Methylprednisolone sodium succi-nate, 30 mg/kg IV within 8 hours of injury, 15 mg/kg IV at 2 and 6 hours later, then q 6 h for 24-48 hours
  - May slightly improve outcome with severe spinal cord injury
  - Starting treatment > 8 hours after injury is not effective and may be detrimental.
  - Other doses and other corticosteroid preparations are not indicated.
- Surgery:
  - Indicated for severe or progressive neurologic deficits and unstable vertebral injury or persistent compression of the spinal cord
  - Hemilaminectomy or dorsal laminectomy
  - Stabilization with pins or screws and bone cement, plates, or modified spinal instrumentation

CHRONIC TREATMENT

- Cage rest for 4-6 weeks on a clean, well-padded surface with good traction
- External splints are helpful for cervical and thoracolumbar injuries that do not require surgery.
- Manual bladder expression if urinary incontinence is present
- Physical rehabilitation (see p. 1329) such as passive range-of-motion and toe-pinch exercises; once spine is stable, assisted standing/walking, underwater treadmill, and swimming

DRUG INTERACTIONS

Avoid coadministration of corticosteroids and nonsteroidal antiinflammatory drugs (NSAIDs) (potentially severe gastrointestinal ulceration)

POSSIBLE COMPLICATIONS

- Decubital ulcers in nonambulatory animals
- Urinary retention in incontinent animals
- Infection in penetrating injuries, especially bite wounds
- Self-mutilation caudal to the site of injury due to paresthesia

RECOMMENDED MONITORING

- Initially evaluate neurologic status daily, including ability to urinate.
- Any deterioration indicates possible vertebral instability.

PROGNOSIS AND OUTCOME

- Voluntary movement: good prognosis
- Paralysis with intact deep pain perception: guarded prognosis
- Paralysis with loss of deep pain perception: very poor prognosis

PEARLS & CONSIDERATIONS

COMMENTS

- A common mistake is inaccurate assessment of deep pain. When there is no response to pinching with the fingers, use a hemostat to compress the digits or tail. Withdrawal of the limb indicates only an intact reflex arc (peripheral nerve and spinal segments) and does not mean the animal can feel pain. A behavioral response such as turning the head or vocalization indicates conscious perception of deep pain.
- Hemodynamic shock can affect testing of deep pain, so if initial test is negative, reassess the animal after resuscitation.

TECHNICIAN TIP

With loss of motor function, these patients may need assistance ranging in degree from simple to intensive (ambulating, urinating/defecating, eating, drinking). Providing this assistance can make the difference between a successful outcome and deterioration.

PREVENTION

Do not allow pets to roam freely or have unsupervised access to balconies and other dangerous areas.

SUGGESTED READING

Wheeler SJ, Sharp NJH: Trauma. In Wheeler SJ, Sharp NJH: Small animal spinal disorders: diagnosis and surgery, ed 2, London, 2005, Mosby-Wolfe, pp 171–191.

AUTHOR: WILLIAM B. THOMAS

EDITOR: CURTIS W. DEWEY

Spinal Cord Neoplasia

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

- Spinal tumors encompass a wide range of cancers.
- Spinal tumors can arise from vertebrae, meninges, or neuroparenchyma.
  - Vertebral neoplasia: osteosarcoma, fibrosarcoma, and hemangiosarcoma, plasma cell tumor/multiple myeloma, lymphoma, cartilaginous exostosis/osteochondroma
  - Meningeal: meningioma
  - Neuroparenchyma: peripheral nerve sheath tumors (PNST), glial tumors (oligodendroglioma, astrocytoma, oligoastrocytoma), ganglioma, nephroblastoma, ependymoma, metastatic choroid plexus carcinoma, cordoma
  - Mesenchymal tumors: myxoma/myxosarcoma, histiocytic sarcoma, infiltrative lipoma/liposarcoma
- Metastatic neoplasia: prostatic, mammary adenocarcinoma, osteosarcoma, transitional cell carcinoma, melanoma, thyroid carcinoma, pheochromocytoma

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Canine: middle-aged to older large-breed dogs:
  - Possible male predilection for meningioma (see p. 715)
  - Boxer and golden retriever predisposition for meningioma
- Feline: lymphoma; young (median age 2-3 years). Concurrent feline leukemia (FeLV) infection is common (see p. 671).

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Canine: Chronic progressive paresis and/or proprioceptive ataxia (scuffing toes, knuckling, crossing limbs). Mean duration of signs = 6 weeks, range 1 day to 1 year. In one study, duration of clinical signs prior to diagnosis is longest for intradural/extramedullary, followed by extradural. Shortest duration for intramedullary tumors.
- Alternatively, acute paresis/plegia—absent voluntary motor function
- Feline lymphoma: acute onset (often 7 days or less)
  - Hyperesthesia
- Clinical signs relate to neuroanatomic lesion: lesions affecting the cervical spinal cord present with tetraparesis, whereas lesions affecting the thoracolumbar spinal cord present with para-paresis.

PHYSICAL EXAM FINDINGS

- Location-dependent
- Often asymmetric
- Focal pain on palpation of the vertebral column
- C1-C6 spinal cord: tetraparesis/plegia, postural reaction deficits, proprioceptive ataxia, normal to exaggerated myotatic reflexes, normal withdrawal reflexes, normal to increased muscular tone, lack of muscle atrophy in all four limbs
- C6-T2 spinal cord: tetraparesis/plegia, postural reaction deficits all four limbs, short, choppy gait (forelimbs), decreased withdrawal reflexes, decreased tone, muscle atrophy in thoracic limbs; proprioceptive ataxia, normal to exaggerated myotatic reflexes, normal withdrawal reflexes, normal to increased muscular tone, lack of muscle atrophy in pelvic limbs
- T3-L3 spinal cord: paraparesis/plegia, proprioceptive ataxia, normal to exaggerated myotatic reflexes, normal withdrawal reflexes, normal to increased muscular tone, lack of muscle atrophy in pelvic limbs; thoracic limbs normal
- L4-S3: hind limb paraparesis/plegia, short-strided, crouched pelvic limb gait, postural reaction deficits, decreased myotatic and withdrawal reflexes, decreased muscular tone, muscle atrophy in pelvic limbs; decreased perineal reflex, urinary incontinence and/or fecal incontinence, decreased tail function

ETIOLOGY AND PATHOPHYSIOLOGY

- Unknown
- Canine:

  - Meningioma commonly affects cervical spinal cord
  - Osteosarcoma: secondary to radiation therapy
  - Nephroblastoma (rare): dogs <2 years old, intradural/extramedullary, between T1O and L2 vertebrae
  - Multiple cartilaginous exostosis/osteochondroma can undergo malignant transformation to osteosarcoma or chondrosarcoma.
- Feline lymphoma: FeLV infection

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Paramount to establishing a presumptive diagnosis of spinal neoplasia is advanced imaging. MRI is the gold standard imaging technique that provides exceptional resolution of pertinent anatomy, allowing detailed characterization of lesions along the neural axis. Imaging characteristics such as lesion location (extravertebral, vertebral, extradural, intradural/extramedullary, or intramedullary), lesion intensity, lesion borders, and degree of contrast enhancement may suggest a specific tumor type. Ultimately, definitive diagnosis requires histologic evaluation. Advanced imaging should be performed by a board-certified veterinary specialist (often a neurologist or radiologist) trained specifically in MRI interpretation.

DIFFERENTIAL DIAGNOSIS

- Canine: intervertebral disk herniation, diskospondylitis, infectious meningomyelitis (canine distemper virus [CDV], rabies, fungal, *Neospora caninum/Toxoplasma gondii,* bacterial), granulomatous meningoencephalitis, trauma, orthopedic disease, caudal cervical spondylomyelopathy, fibrocartilaginous embolic myelopathy
- Feline: infectious meningomyelitis (feline infectious peritonitis virus, feline immunodeficiency virus [FIV], *T. gondii,* rabies, fungal, bacterial), trauma, aortic thromboembolism, intervertebral disk herniation (rare)

INITIAL DATABASE

- CBC, serum biochemical profile, urinalysis, thoracic and abdominal radiographs, survey (plain) radiographs of the vertebral column
- Feline: serologic testing for FeLV, FIV, *Cryptococcus neoformans, T. gondii*
- Canine: serologic testing for *C. neoformans, N. caninum, T. gondii,* paired titers (cerebrospinal fluid [CSF]/serum) for CDV

ADVANCED OR CONFIRMATORY TESTING

- Advanced imaging: MRI (see p. 1302) is the gold standard for spinal cord; CT (see p. 1233), combined CT/myelography, myelography.
  - MRI characterization of the lesion may provide a presumptive diagnosis: meningioma is often characterized as a broad-based, intradural/extramedullary lesion demonstrating uniformly strong contrast enhancement and dural tail.
  - CT more sensitive for bone abnormalities (lysis or proliferation) than radiographs or may be more sensitive than MRI
- CSF analysis (see p. 1228)
- Fluoroscopic guided needle aspiration/biopsy of vertebral lesion
- Spinal lymphoma: further staging required. FeLV/FIV testing, bone marrow evaluation. Renal, lymph node, and hepatosplenic involvement common
- Presumptive diagnosis based on anatomic location and imaging characteristics:
  - Vertebral: osteosarcoma, fibrosarcoma, hemangiosarcoma, plasma cell neoplasia, lymphoma, metastatic neoplasia
  - Extradural: lymphoma, metastatic neoplasia
  - Intradural/extramedullary: PNST, meningioma, nephroblastoma
  - Intramedullary: neuroparenchymal tumors (e.g., glial cell tumors [astrocytoma, oligodendroglioma]), metastatic neoplasia
- Definitive diagnosis: histopathologic examination

TREATMENT

TREATMENT OVERVIEW

The main therapeutic option for spinal tumors remains surgery. The exception to this involves hematopoietic neoplasms such as lymphoma and multiple myeloma, in which case chemotherapy +/− radiation therapy form the foundation of treatment. The goal of surgery is to provide decompression and to obtain a histologic diagnosis. Spinal surgery should only be performed by a board-certified neurologist or surgeon.

ACUTE GENERAL TREATMENT

- Based on tumor location. However, to date, primary treatment involves surgical debulking.
- Surgical decompression of affected site(s) via hemilaminectomy/dorsal laminectomy
- Spinal tumors: palliation with corticosteroids
- Vertebral tumors: palliation with radiation, bisphosphonate, corticosteroids

CHRONIC TREATMENT

- Variable depending on tumor type
- Incompletely excised meningioma, neuroparenchymal, and vertebral tumors should receive postoperative radiation therapy.
- Spinal lymphoma: systemic chemotherapy, radiation therapy
- Plasma cell tumor/multiple myeloma: systemic chemotherapy, radiation therapy

BEHAVIOR/EXERCISE

- Postoperatively, affected animals require strict exercise restriction for 4-6 weeks.
- Additionally, controlled physical rehabilitation (see p. 1329) under the guidance of trained personnel may be beneficial during recovery from surgery.

POSSIBLE COMPLICATIONS

Radiation myelopathy

RECOMMENDED MONITORING

- Periodic neurologic examination
- Repeat imaging studies
- Chemotherapy necessitates hematologic and biochemical monitoring dictated by protocol.

PROGNOSIS AND OUTCOME

- Variable based on tumor type, completeness of resection, and severity of neurologic deficits:
  - Patients lacking both motor function and nociception (pain perception) have a grave prognosis for return of function.
- Canine:
  - Surgical resection alone: in one study of dogs with spinal tumors of various histologic types, overall median survival was 240 days.
  - Surgical resection and postoperative radiation: in one report of 9 dogs (6 with spinal meningiomas), overall median survival was 510 days.
  - Specific tumors:
    - Meningioma—based on degree of resection:
      - Surgical resection alone: median survival 19 months; ranges from <30 days-1440 days
      - Surgery with postoperative radiation significantly increases the time to recurrence (neurologic deterioration) over surgery alone.
      - Vertebral tumors: osteosarcoma and fibrosarcoma: median survival 135 days (15-600 days)
      - PNST: median survival 203 days (120-300 days)
- Feline:
  - Lymphoma (COP protocol* [see pp. 673 and 674]): if complete remission achieved, median 14 weeks; if partial remission achieved, median 6 weeks. Longer remissions may be possible with doxorubicin-containing protocols.

PEARLS & CONSIDERATIONS

COMMENTS

- Based on imaging studies, the differential diagnosis may be narrowed substantially according to the anatomic location of the lesion.
- Definitive diagnosis requires histopathologic evaluation.
- Long-term remission can be possible regardless of completeness of excision.

TECHNICIAN TIPS

- Affected animals are often recumbent and unable to ambulate, requiring soft padded bedding and frequent changes in their recumbency to prevent development of decubital ulcers. Passive range of motion of paralyzed limbs and other physical therapy exercises may be performed to assist in recovery.
- Severely affected animals may not be able to urinate and therefore require manual bladder expression or maintenance of a urethral catheter and indwelling closed urinary collection system. Development of urinary tract infection is common.
- Affected animals are often painful pre-operatively and in the early postoperative time period, necessitating analgesic therapy.

SUGGESTED READING

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Spider Envenomation

BASIC INFORMATION

DEFINITION

- Envenomating bites from widow spiders of the genus *Latrodectus.* resulting in mild to severe systemic signs including generalized muscle pain, weakness, paralysis, and death
- Envenomating bites from recluse spiders of the genus *Loxosceles,* resulting in acute onset of localized irritation and progressing to severe necrotizing wounds and occasionally systemic signs
- Bites from venomous spiders are well recognized but in general are a less common, geographic region-dependent phenomenon.

SYNONYMS

- Latrodectism: *Latrodectus* (widow spider) envenomation
- Loxoscelism, necrotic arachnidism: *Loxosceles* (brown recluse spider) envenomation

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Very young and aged animals may be more sensitive to the effects of spider venom.
- Cats are very sensitive to widow venom; mortality can exceed 90%.
- Dogs are highly susceptible to brown recluse envenomation.

RISK FACTORS: Patients with preexisting respiratory conditions (widow venom, respiratory muscles) or hematologic conditions (brown recluse, erythrocyte) may be at increased risk.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Witnessed or suspected spider on or near the animal (cats may vomit spiders)
- Specific signs are based on type of spider:
    - Widow: no to little local swelling and redness initially; reluctance to move begins <30-120 minutes after envenomation, with progressive signs of muscle pain and stiffness
    - Recluse: signs of local pain, pruritus, redness within 10-30 minutes; expanding necrotizing wound

PHYSICAL EXAM FINDINGS

- Widow: vomiting; muscle pain, rigidity, tremor, and cramping; tachypnea, atonic paralysis
- Recluse: “bull's eye” or “halo” cutaneous lesion (central vesicle; erythematous, ecchymotic periphery), progressively expanding; vesicle may be ruptured and shrunken, dark purple to black
    - Dermal lesion can range from 1-25 cm in size, depending on time line from bite.
    - Systemic signs may occur-24-72 hours, and can include hemolysis, hematuria, fever, arthralgia.

ETIOLOGY AND PATHOPHYSIOLOGY

Source:

- Widow spiders:
    - Female *Latrodectus* spp. have an hourglass-shaped red or orange marking on the abdomen. Young spiders are red in color (and venomous), progressing to black with successive molts. Males are 1/20 female size, and fangs are too short for envenomation.
    - Important *Latrodectus* spp. in the United States:
        - *L. mactans* (black widow spider, southern black widow): throughout the United States, especially in the South
        - *L. hesperus* (western black widow spider): western United States

        - *L. variolus* (northern widow spider): northern part of the United States
        - *L. bishopi* (red widow spider; red-legged widow spider): Florida
        - *L. geometricus* (brown widow spider): Florida
- Recluse spider:
    - Brown recluse (or fiddle back/violin) spider (*Loxosceles reclusa)* (distinctive violin-shaped mark on dorsal cephalothorax, neck points to abdomen). These spiders are nocturnal, not aggressive, and can be active in a wide range of temperatures. Length 6-20 mm, long legs, three pairs of eyes.
    - *Loxosceles* are found through the south and south-central regions of the United States (Texas through Georgia) but can be found as far north as Iowa, Wisconsin, and Indiana.
    - Several *Loxosceles* species that live in the western United States (*L. rufscens, L. deserta, L. arizonica)* may produce mild necrotic lesions that are not as serious as the *L. reclusa* bite.

Mechanism of Toxicosis:

- Widow spider:
    - Alpha-latrotoxin is the main toxic component of widow venom; causes release and depletion of acetylcholine, norepinephrine (and others) at motor nerve endings and postganglionic sympathetic synapses, resulting in block of neurotransmission.
- Recluse spider:
    - Recluse venom contains several proteins, polypeptides, and necrotizing enzymes including hyaluronidase, esterase, alkaline phosphatase, and 5′-ribonucleotide phosphorylase and sphingomyelinase.
    - These proteins and enzymes work in different ways, causing inflammation, local ischemia, coagulation, occlusion of small capillaries, necrosis, depletion of clotting factors (VII, IX, XI, and XII), hemolysis, platelet activation, and thromboembolic disease.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Envenomation often is not witnessed. Diagnosis then depends on physical exam findings (compatible with envenomation) in a suitable geographic zone, and a window of time for possible envenomation (e.g., pet was unobserved for the preceding several hours). No definitive confirmatory test exists; therefore, many cases of suspected envenomation may in fact be caused by completely different etiologies, and a “spider bite” often is a working diagnosis that remains unproven.

DIFFERENTIAL DIAGNOSIS

- Widow spiders:
    - Toxicologic: bromethalin, macadamia nuts, or marijuana toxicosis
    - Spontaneous, nontoxicologic: meningoencephalitis, intervertebral disc disease, CNS neoplasia
- Recluse spiders:
    - Toxicologic: snakebite, insect sting, hemolytic toxins (zinc, *Allium),* corrosive burn
    - Spontaneous, nontoxicologic: cellulitis, decubital ulcer, pyoderma, hemolytic anemia (immune mediated), thrombocytopenia (immune-mediated)

INITIAL DATABASE

- Widow:
    - Vital signs (respiratory rate and depth, heart rate, temperature)
    - CBC: leukocytosis possible
    - Serum biochemistry profile: increased creatine phosphokinase, glucose, bilirubin possible
    - Urinalysis: normal to high specific gravity, ± albuminuria
    - Blood pressure: systemic hypertension possible
- Recluse:
    - CBC: acute intra vascular hemolysis, anemia
    - Coagulation profile: evidence of bleeding disorder possible
    - Serum biochemistry profile
    - Coombs’ test: negative
    - Urinalysis: hemoglobinuria

TREATMENT

TREATMENT OVERVIEW

- Widow: all patients should be hospitalized and treated intensively. If available, antivenin is indicated in severe cases. If muscular tremor or clonus is present, muscle relaxation helps avoid hyperthermia (muscle relaxants, diazepam). Pain control and treatment according to changes in vital signs and other parameters are important.
- Recluse: treatment will depend on which one of two possible syndromes the patient experiences: local cutaneous lesions only or possible systemic manifestations, which can begin 24-72 hours after envenomation. Therefore, patients should be hospitalized for observation and treatment. Dermal complications can be long standing, and systemic manifestations are potentially fatal if left untreated.

ACUTE GENERAL TREATMENT

- Widow spider:
  - Systemic analgesia is important:
    - Opioids for severe pain (e.g., hydromorphone, 0.1-0.2 mg/kg SQ, IM, or IV once or as needed up to q 2-4 h; or buprenorphine, 0.005-0.03 mg/kg IM, IV, or SQ q 6-12 h PRN)
    - Nonsteroidal antiinflammatory drugs (NSAIDs) for moderate pain (e.g., carprofen, 1 mg/kg PO q 12 h; or etodolac, 10-15 mg/kg PO q 24 h)
  - Muscle relaxants are important to reduce or eliminate muscle rigidity/tremor:
    - Diazepam, 0.2-0.6 mg/kg IV slow PRN, or 0.25-1 mg/kg PO q 8 h
    - Methocarbamol, 55-220 mg/kg IV slow, not to exceed 330 mg/kg/day, or 20-45 mg/kg PO q 8 h (oral route, 30 minute onset)
  - Widow spider antivenin (Lyovac, equine origin [Merck]): single vial can be effective in relieving muscle involvement up to 1-3 days after envenomation; relatively inexpensive and has a good shelf life, but anaphylaxis is possible (conduct skin test first: inject small volume SQ and monitor for acute inflammation).
  - Respiratory support for hypoventilating animals; supplemental oxygen as indicated
  - IV fluids: cautious use because of volume expansion, sodium administration; systemic hypertension is common following envenomation. Monitor blood pressure.
- Recluse spider:
  - Diphenhydramine, 2.2 mg/kg PO or IM q 8 h, to relive pruritus; corticosteroids at antiinflammatory levels (e.g., prednisone 1-2 mg/kg PO q 24 h) can also be used.
  - Broad-spectrum antibiotics for secondary infection (e.g., amoxicillin-clavulanate 10-20 mg/kg PO q 12 h)
  - Monitor and measure size (progression) of lesion daily.
  - Dapsone, a neutrophil migration inhibitor, may limit severity of lesions:
    - In dogs, 1 mg/kg PO q 24 h has been suggested; caution using in cats.
  - Surgical débridement not recommended
  - IV fluids to promote fluid diuresis if hemolysis occurs (protect renal tubules)
  - Packed red blood cells (RBCs) or whole blood for hemolytic anemia
  - Monitor and treat disseminated intravascular coagulation (DIC) if present.

CHRONIC TREATMENT

Manage necrotic lesions as open wounds (recluse spiders).

POSSIBLE COMPLICATIONS

Recluse spider bites can lead to scarring as they heal.

RECOMMENDED MONITORING

CBC, platelet count, and coagulation parameters

PROGNOSIS AND OUTCOME

Fatalities rare in dogs (widow and recluse); prognosis can be guarded in cats bitten by widows.

PEARLS & CONSIDERATIONS

COMMENTS

- Many spiders are capable of inflicting an envenomating bite. In the United States, however, with the exception of widow and

recluse spider bites, most bites will not cause more than a mild local reaction, although anaphylaxis remains possible.
- Check with a local human hospital pharmacy for availability of Lyovac widow antivenin.
- Hobo spider (*Tegenaria agrestis)* is an aggressive house spider found in the Pacific Northwest, where the recluse is not indigenous. Necrotizing skin lesions are similar but less severe than those inflicted by the brown recluse; treatment approach is similar to recluse spider bite.

SUGGESTED READING

Arachnology: www.arachnology.be. Useful website for information on and identifying spiders.

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Sparganosis, Proliferative

BASIC INFORMATION

DEFINITION

Infection with the proliferating larval (metacestode) stages (spargana or plerocercoids) of pseudotapeworms (pseudophyllidean tapeworms), usually *Sparganum proliferum* or *Spirometra* spp.

SYNONYMS

Infection with these larval tapeworms may also be larval pseudophyllidiasis or larval cestodiasis. Infection with the adult stage of this parasite may be referred to as *spirometrosis*, *pseudophyllidiasis*, or *cestodiasis*.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Proliferative sparganosis may be found in dogs and cats of all ages and both sexes.

GENETICS & BREED PREDISPOSITION: Sporting/hunting breeds of dogs

RISK FACTORS

- Exposure to/contact with large stationary or slow-moving bodies of water inhabited by the first intermediate host, a copepod crustacean (*Cyclops* sp. water flea)
- Ingestion of infected transport host (rodent, reptile, amphibian, or bird)
- Direct inoculation of open wounds with flesh or meat containing plerocercoids (application of “medicinal” poultices; rare)

CONTAGION & ZOONOSIS: Sparganosis is zoonotic; thus precautions should be undertaken to prevent human infection (see Risk Factors, above).

GEOGRAPHY AND SEASONALITY: Proliferative sparganosis cases reported in dog, cat, and human in Florida, United States; dogs in Australia; and humans in Venezuela, Paraguay, Japan, Taiwan.

CLINICAL PRESENTATION

DISEASE FROMS/SUBTYPES

- There are two forms of sparganosis that occur with larval infections: nonproliferative and proliferative. Most infections are the nonproliferative form and are associated with the presence of a single, non-replicating larval stage (a sparganum) of *S. erinaceieuropaei* or *S. mansonoides* within the musculature or subcutaneous tissues of the intermediate or transport host, a common occurrence. If the nonproliferative form is ingested by a dog or cat, an adult tapeworm will develop in the small intestine of that host.
- The more rare form of the parasite, which produces proliferative sparganosis, is characterized by asexual replication of larvae (spargana) of *S. proliferum* within a variety of host tissues and the systemic migration of these larvae to other tissues, where they grow and repeat the process, ultimately resulting in the death of the host.

HISTORY, CHIEF COMPLAINT: History of free roaming; for typical complaints, see Physical Exam Findings, below.

PHYSICAL EXAM FINDINGS

- Axial musculature infection: signs of pain, diffuse swelling, progressive fore-limb lameness, and pitting subcutaneous edema
- Proliferating spargana in the thoracic cavity: dyspnea and fever
- Proliferating spargana in the peritoneal cavity: abdominal distention and/or signs of abdominal pain

ETIOLOGY AND PATHOPHYSIOLOGY

- In most instances, when infective spargana/plerocercoids within the second intermediate host (or the transport host) are ingested by the canine or feline definitive host, the plerocercoid develops to the adult pseudotapeworm within the small intestine of the dog or cat. Intestinal infection with the adult stage of this parasite, usually *Spirometra* spp. (*S.*

erinaceieuropaei or *S. mansonoides*), is a common finding in dogs and cats.

- In other instances when procercoids or spargana are ingested by the canine or feline definitive host, the plerocercoid will not undergo any further development but remains as the larval plerocercoid/spargana stage within the tissues of the canine or feline definitive host.
- The life cycle of the parasite involves both a first intermediate host, an aquatic crustacean (*Cyclops* sp.) and second intermediate host, a vertebrate host other than a fish (e.g., a frog). Paratenic or transport hosts may also be involved.
- Hermaphroditic adult tapeworm (*Spirometra* sp.) is found in the small intestine of canine or feline intermediate host. Tapeworm produces operculated ovum containing coracidium.
- Operculated egg makes contact with water.
- Coracidium emerges from the operculated egg and spins in water.
- Coracidium is ingested by aquatic crustacean (water flea). Within crustacean, coracidium develops into the first developmental stage, a procercoid.
- Crustacean containing procercoid is ingested by a second intermediate host, a vertebrate host other than a fish. Within the second intermediate host, the procercoid develops into the second developmental stage, a plerocercoid.
- The plerocercoid within the second intermediate host may be ingested by a transport or paratenic host (e.g., a small mammal such as a rodent). The plerocercoid does not undergo any further development within that host. Larval forms of *Spirometra* spp. can infect and survive in a series of transport hosts until finally consumed by a carnivore definitive host.
- In most instances, when the spargana are ingested by a canine or feline definitive host, the spargana will develop into adult pseudotapeworms within the small intestine of the host.
- In rare instances, when the spargana are ingested by a carnivore definitive host, the spargana will remain as spargana but migrate to various sites within the host tissues, where they undergo asexual replication, migrate to other tissues, and grow to repeat the process. These spargana do not mature to the adult stages when they are fed to a dog or cat.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

This very unusual disorder is diagnosed incidentally during evaluation of nonspecific abnormalities (e.g., muscle biopsy for myositis or cytologic analysis of fluid retrieved during abdominal/thoracic centesis).

DIFFERENTIAL DIAGNOSIS

- *Mesocestoides* spp. will produce a metacestode stage that undergoes a similar proliferative asexual replication in multiple tissue sites. Under the compound microscope, specimens of *Mesocestoides* will demonstrate some evidence of sucker development.
- Peritonitis
- Pleuritis
- Chronic panniculitis

INITIAL DATABASE

- CBC may reveal eosinophilia.
- Thoracic and/or abdominal radiographs: evidence of effusion
- Thoracocentesis (see p. 1338) or abdominocentesis (see p. 1193) may reveal replicating spargana:
    - Spargana may be grossly identified as being of cestode origin by the presence of calcareous corpuscles. They may be identified as being pseudophyllidean tapeworms by the absence of suckers on the developing scolex. These parasites may demonstrate the presence of two slitlike bothria instead of four suckers.

ADVANCED OR CONFIRMATORY TESTING

- Exploratory thoracotomy or laparotomy may reveal replicating spargana on histologic/cytologic analysis.
- A PCR-based assay for the detection of DNA from the spargana in host tissue is available from Oklahoma State University.

TREATMENT

TREATMENT OVERVIEW

It is extremely difficult to eliminate larval parasites (spargana or plerocercoids) from multiple tissue and organ sites, and the prognosis with systemic disease is guarded to poor.

ACUTE GENERAL TREATMENT

- If specimens are free within thoracic or abdominal cavities, these cavities may be lavaged with warm, sterile physiologic saline to physically remove as many spargana as possible.
- Mebendazole, 20 mg/kg PO q 24 h for 3 weeks, followed by praziquantel, 5 mg/kg PO q 24 h for a further 3 weeks, have not been used. These two drugs were alternated over a period of 3 months.

CHRONIC TREATMENT

- Secondary bacterial infection
- Cellulitis
- Culture and sensitivity of lesion, with appropriate antimicrobial therapy

POSSIBLE COMPLICATIONS

Since these spargana are capable of asexual replication, if one parasite is left remaining in situ, it is possible for proliferative sparganosis to return via exponential growth.

RECOMMENDED MONITORING

Thoracocentesis or abdominocentesis along with gross examination of collected specimens if effusions recur.

PROGNOSIS AND OUTCOME

The prognosis for dogs treated for proliferative sparganosis is guarded to poor.

PEARLS & CONSIDERATIONS

COMMENTS

Since this larval cestode is extremely rare, it is quite difficult to diagnose. A pathologist or parasitologist at a veterinary diagnostic laboratory may be called on to assist in the definitive diagnosis.

PREVENTION

Prevent dogs and cats from roaming and coming into contact with freshwater aquatic environments (large stationary or slow-moving bodies of water) inhabited by aquatic crustaceans. Prevent predation or scavenging of intermediate or transport hosts.

TECHNICIAN TIPS

The importance of proper sample submission cannot be overemphasized. Biopsy specimens must be submitted in 10% formalin.

CLIENT EDUCATION

Dogs and cats should never be allowed to roam freely, thus avoiding contact with infested water or ingestion of infected intermediate hosts or carrion.

SUGGESTED READING

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Soft-Tissue Sarcoma

BASIC INFORMATION

DEFINITION

A group of common tumors arising from various mesenchymal tissues, classified together because of similar biological behavior and treatment. They include fibrosarcoma, hemangiopericytoma, malignant fibrous histiocytoma, nerve sheath tumor, neurofibrosarcoma, malignant schwannoma, leiomyosarcoma, rhabdomyosarcoma, liposarcoma, myxosarcoma, lymphangiosarcoma, and synovial cell sarcoma. Although it is also a mesenchymal tumor arising from soft tissue, hemangiosarcoma is often excluded from this group because of its aggressive biological behavior.

SYNONYM

Soft part sarcomas

EPIDEMIOLOGY

SPECIES, AGE, SEX: Common in middle-aged to older dogs. Soft-tissue sarcomas at sites other than injection sites are less common in cats.

GENETICS & BREED PREDISPOSITION: In general, soft-tissue sarcomas tend to occur more commonly in larger breeds, but direct inheritance of these tumors has not been reported.

RISK FACTORS

- Certain sarcomas have been associated with metal implants, previous exposure to ionizing radiation, implanted microchips, and parasites *(Spirocerca lupi).*
- Sarcomas at injection sites have been described in dogs but are rare.

CONTAGION & ZOONOSIS: Multiple sarcomas of the head and neck have been reported secondary to combined feline sarcoma virus and feline leukemia virus infection.

ASSOCIATED CONDITIONS & DISORDERS: Hypoglycemia and diabetes insipidus have been reported as uncommon paraneoplastic syndromes in dogs with intestinal leiomyosarcoma.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Most animals present for a progressively enlarging mass noticed by the owner.
- Animals with sarcoma in certain locations will be presented because of clinical signs related to the location of the tumor. Dogs with oral tumors often present with a foul odor from the mouth, difficulty eating or prehending food, oral bleeding, or a visible oral mass. Dogs with intestinal sarcomas will often be presented because of signs related to intestinal obstruction, including vomiting and diarrhea.

PHYSICAL EXAM FINDINGS

- Visible or palpable mass. Regional lymphadenomegaly may be present secondary to inflammation caused by the tumor or (rarely) lymph node metastasis.
- Sarcomas in specific sites may present with physical exam findings related to the location of the tumor (e.g., abdominal pain, weight loss, dehydration).

ETIOLOGY AND PATHOPHYSIOLOGY

- Soft-tissue sarcomas arise spontaneously in dogs and cats. Genetic and environmental factors may be involved in tumor development, but these factors are poorly understood in companion animals.
- Specific lesions and overt clinical manifestations caused by soft-tissue sarcomas depend on location of the primary tumor and invasion into and destruction of surrounding normal structures.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Definitive diagnosis can only be confirmed via histopathologic examination, although additional tests such as diagnostic imaging are often helpful in defining the extent of the tumor. Studies show that an aggressive first surgery is more likely to result in tumor control. Therefore, an incisional biopsy should be performed first to confirm the tumor type, prior to planning definitive treatment.

DIFFERENTIAL DIAGNOSIS

- Mast cell tumors
- Other skin and subcutaneous tumors:
  - Lipoma, histiocytoma, others
- Other masses:
  - Abscess

INITIAL DATABASE

- Fine-needle aspiration and cytologic examination may help identify the type of soft-tissue sarcoma or differentiate from other tumor types.
- Thoracic radiographs to rule out pulmonary metastases
- Radiographs of the affected area may reveal involvement of underlying bone.
- Fine-needle aspirate of draining lymph nodes to help rule out metastasis

ADVANCED OR CONFIRMATORY TESTING

- CT or MRI may be necessary to delineate the local extent of the tumor and plan for surgery or radiation therapy.
- Diagnosis is based on histopathologic evaluation of tissue. Occasionally, special stains may be necessary to differentiate various types of soft-tissue sarcomas, especially with poorly differentiated tumors.
- Histopathologic grade of the tumor is necessary for determining prognosis and treatment of most soft-tissue sarcomas.

TREATMENT

TREATMENT OVERVIEW

- The goal of treatment for soft-tissue sarcomas in dogs or cats is complete eradication of the primary tumor.
- In cases where the tumor cannot be eliminated entirely, the goal of treatment is prevention or delay of the development of metastases.
- Palliative treatment options, such as palliative radiation, may help control pain or discomfort in patients with advanced tumors or when definitive treatment cannot be tolerated.

ACUTE GENERAL TREATMENT

- Surgery:
  - Commonly these tumors appear encapsulated at surgery. This can be misleading because the capsule is usually a pseudocapsule made up of compressed tumor cells, and viable tumor cells are often present beyond the extent of the pseudocapsule.
  - Surgery should be aimed at an aggressive resection of the mass with as wide a margin of normal tissue as possible from around the tumor. In situations where this is not possible because of the size and/or location of the tumor, radiation therapy may be indicated in addition to surgery.
- Radiation therapy:
  - May be used prior to surgery in situations where the tumor is not easily resectable owing to its location or size. In cases where surgery is attempted first but resection is incomplete based on histologic evaluation, these patients should be treated with radiation therapy after surgery.
- Chemotherapy:
  - May be indicated for patients with high-grade tumors, tumors in certain locations, certain tumor types, and in patients that develop metastatic disease
  - Chemotherapy drugs that have been used for soft-tissue sarcoma include doxorubicin, mitoxantrone, platinum drugs, ifosfamide, and combinations of these drugs.
- Hyperthermia:

- Oncologic hyperthermia treatment has been shown to increase response rates for macroscopic tumors treated with radiation therapy. However, such treatment has limited availability, and recurrence of tumors often occurs rapidly after treatment.

POSSIBLE COMPLICATIONS

Complications of treatments for sarcomas depend on types of treatments and location of the primary tumor:

- Surgery may result in wound complications, including infection, dehiscence, or loss of function of a limb.
- Radiation therapy can cause short-term complications in skin and mucosa involved in the radiation field (dermatitis, mucositis). Long-term complications, including bone necrosis and haircoat changes, are uncommon but are permanent when they do occur (see p. 963).
- Chemotherapy complications may include bone marrow suppression, gastrointestinal effects, and haircoat changes along with other side effects caused by specific chemotherapy drugs (see p. 963).

RECOMMENDED MONITORING

Following appropriate local treatment of the primary tumor, follow-up examination should be done on a routine basis to monitor for local recurrence and metastasis. High-grade tumors may require more frequent monitoring for metastasis during and after chemotherapy administration.

PROGNOSIS AND OUTCOME

Prognosis is variable depending on type, location, clinical stage, and histologic grade of tumor:

- Certain tumor types may have higher metastatic rates (e.g., leiomyosarcoma) or more aggressive local behavior (e.g., histologically low grade, biologically high grade sarcomas of the oral cavity).
- Soft-tissue sarcomas located in the abdomen (spleen, intestines) are typically more likely to lead to metastasis.
- Soft-tissue sarcomas in certain locations (e.g., oral tumors) may be more difficult to treat with local therapy (surgery or radiation), resulting in lower rates of local disease control.
- Soft-tissue sarcomas that are large or have metastasized at the time of diagnosis usually lead to a poor prognosis.
- Histologic grading of canine soft-tissue sarcomas is based on: (1) degree of differentiation; (2) mitotic index (0-9 per 10 high-power field (HPF), 10-19 per 10 HPF, >20 per 10 HPF); and (3) percent necrosis (0%, <50%, >50%). High-grade (grade 3) tumors are more likely to lead to metastasis. Typical metastatic rates are considered to be 40% for grade 3 tumors, up to 20% for grade 2 tumors, and 10% or less for grade 1 tumors. It is unclear whether this grading scheme is applicable in feline soft-tissue sarcomas.

PEARLS & CONSIDERATIONS

COMMENTS

Many patients with soft-tissue sarcomas can be successfully treated with wide surgical excision alone. Patients with soft-tissue sarcomas that may be more difficult to treat (oral sarcomas, grade 3 sarcomas, nonresectable tumors, etc.) should be referred for consultation with specialists, including a surgeon, oncologist, or radiation oncologist, to develop a multimodality treatment approach.

PREVENTION

In most cases, prevention of soft-tissue sarcomas is not possible. Early detection and treatment may result in easier treatment and better prognosis.

CLIENT EDUCATION

Owners should be educated to monitor their pets for the emergence of cutaneous or other masses and have them evaluated in a timely fashion. Early detection may allow for easier treatment via surgery and may help avoid the need for radiation therapy.

SUGGESTED READING

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Sneezing

BASIC INFORMATION

DEFINITION

- An explosive expiration of air from the nose for the purpose of clearing the nasopharynx. Sneezing is mediated by a central reflex as a result of stimulation of the nasal mucosa. Occasional sneezing is normal.
- Reverse sneezing is characterized by paroxysmal, forceful, and loud *inspiratory* efforts that are triggered by nasopharyngeal irritation. The syndrome, most commonly seen in small- and toy-breed dogs, is self-limiting and rarely progressive. Reverse sneezing serves to move irritating debris from the nasopharynx into the oropharynx where it can be swallowed (see p. 987).
- All causes of nasal discharge and/or irritation are potential causes of sneezing. The type and duration of the discharge varies with the underlying cause (see Etiology and Pathophysiology below).

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Young cats may have viral upper respiratory infections or nasopharyngeal polyps.
- Young unvaccinated dogs are more likely to have canine viral respiratory infections.
- Younger animals may have congenital deformities.
- Older animals are more likely to have neoplastic or dental-related causes of nasal discharge and sneezing.
- Hunting and working dogs are more likely to have nasal foreign bodies.

GENETICS & BREED PREDISPOSITION: Brachycephalic breeds have upper airway problems that may lead to sneezing and/or nasal discharge. Certain breeds can be affected by primary ciliary dyskinesia or by cleft palate/cleft lip complex.

RISK FACTORS

- Lack of adequate immunization against viral respiratory infections
- Exposure to unvaccinated animals and high-density husbandry situations
- Geographic locations where grass awns are ubiquitous
- Dental disease and poor dental care
- Immunosuppression (fungal disease)
- Compromise of nasal mucosa (secondary bacterial infections)

CONTAGION & ZOONOSIS: Viral upper and lower respiratory tract infections

GEOGRAPHY AND SEASONALITY: Geographic locations where grass awns are ubiquitous

ASSOCIATED CONDITIONS & DISORDERS: Sneezing itself can be a cause of acute nasal trauma (nose hits floor).

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Sneezing versus reverse sneezing

HISTORY, CHIEF COMPLAINT: Acute onset of paroxysmal sneezing may suggest nasal foreign bodies or early viral disease. Husbandry and management predispose to certain disorders: for example, recent boarding, exposure to new animals, and/or history of inadequate vaccination (viral infections); hunting and geographic location (nasal foreign bodies); pertinent medical history (dental disease, history of neoplasia, immunosuppression); exposure to irritating aerosols (hairspray, paints, etc.) or anticoagulants (rodenticides, pharmaceuticals).

PHYSICAL EXAM FINDINGS

- Serous, mucopurulent, or hemorrhagic discharge that may be unilateral or bilateral
- Facial deformity
- Exophthalmos
- Maxillary swelling dorsal to carnassial tooth (apical dental [“tooth root”] abscess)
- Oronasal fistula
- Ocular discharge

- Petechiation, ecchymoses
- Pawing at face

ETIOLOGY AND PATHOPHYSIOLOGY

All causes of nasal discharge and/or irritation are potential causes of sneezing. Types of nasal discharge:

- Serous: clear and watery (acellular); due to local irritation, early viral infection, allergic rhinitis, or excessive lacrimation
- Mucoid: clear and thicker (acellular with higher protein content); due to chronic noninfectious irritation and overproduction of mucus by nasal epithelial cells
- Purulent: yellow-tan, thick discharge (neutrophilic with bacteria) usually due to secondary bacterial infection
- Sanguineous: red-tinged (blood mixed with another type of discharge) due to compromise of the nasal mucosa
- Hemorrhagic (epistaxis): frank red blood due to local or systemic causes of bleeding

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

Important diagnostic elements include whether nasal discharge is present and if so, of what type; whether air flow is normal or reduced in one or both nostrils (glass slide fog test); and whether there are systemic signs of illness. These features allow the clinician to choose tests that evaluate the nasal passages specifically (e.g., rhinoscopy) or to opt for conservative treatment and monitor evolution.

DIFFERENTIAL DIAGNOSIS

- Feline viral upper respiratory tract infections (feline rhinotracheitis, feline calicivirus, *Chlamydophila felis*)
- Neoplasia (adenocarcinoma, lymphoma, undifferentiated carcinoma, osteosarcoma, chondrosarcoma, fibrosarcoma, transmissible venereal tumor)
- Foreign bodies
- Apical dental (“tooth root”) abscess
- Oronasal fistula
- Nasopharyngeal polyps
- Canine viral infections (canine distemper virus, canine parainfluenza virus, canine herpesvirus, canine adenovirus types 1 and 2)
- Mycotic infection (*Aspergillus* spp. in dogs; *Cryptococcus neoformans* in cats)
- Parasitic rhinitis (*Cuterebra* spp., *Pneumonyssoides caninum, Linguatula serrata)*
- Bacterial infections (usually secondary)
- Rhinitis (allergic/eosinophilic type I hypersensitivity, lymphoplasmacytic, chronic hyperplastic)
- Congenital defects (cleft palate-cleft lip complex, primary ciliary dyskinesis)
- Trauma
- Inhaled irritants (cat litter dust, aerosols, smoke)
- Epistaxis:
  - Local causes: mycotic infections, neoplasia, foreign body, trauma
  - Systemic causes: inherited or acquired coagulopathies, thrombocytopenia, thrombocytopathia, hypertension, vasculitides
- Nasopharyngeal stenosis

INITIAL DATABASE

- Assessment for unilateral versus bilateral nasal disease by holding a glass microscope slide close to the external nares while the patient breathes on it through its nose (mouth held closed). Presence or absence of steam on the slide suggests unilateral obstruction, bilateral obstruction, or normal air flow. Neoplasia, foreign bodies, and dental disease are often causes of unilateral nasal disease, whereas other local and systemic causes often result in bilateral disease.
- Examination of the oral cavity to look for hard-palate masses; fundic examination to look for evidence of neoplasia, fungal disease, or hypertension and associated retinal hemorrhage
- Eye globe retropulsion ± ocular ultrasound to assess for retrobulbar masses
- Blood pressure measurement to assess for hypertension
- CBC including platelet count to look for evidence of infection, inflammation, or thrombocytopenia
- Serum biochemistry profile, urinalysis
- Feline leukemia and feline immunodeficiency viral testing

ADVANCED OR CONFIRMATORY TESTING

Rocky Mountain spotted fever, *Ehrlichia,* and *Bartonella* testing, prothrombin time, partial thromboplastin time, thoracic radiographs, nasal swabs, fungal titer determinations, nasal radiography, CT (see p. 1233), rhinoscopy (see p. 1335), biopsy, deep tissue cultures, exploratory rhinotomy—as dictated by history, physical exam, and preliminary findings

TREATMENT

TREATMENT OVERVIEW

- Eliminate underlying etiology of sneezing.
- Restore normal nasal function.
- Reduce pain and discomfort.
- Provide supportive care.
- Relieve dyspnea, especially in cats who oftentimes will not readily open-mouth breathe.

ACUTE GENERAL TREATMENT

- If nasal discharge or nasal mucosal edema is causing dyspnea, oxygen therapy may be needed.
- Treatment for underlying coagulopathy (e.g., vitamin K1, 0.25-2.5 mg/kg for first-generation rodenticide intoxication or 2.5-5 mg/kg for second generation, SQ or PO divided q 12 h for 7-21 days, and fresh frozen plasma).
- Correct dehydration and electrolyte abnormalities as necessary.
- Broad-spectrum antibiotics if secondary nasal or dental infection (bacteria are rarely the primary cause of nasal disease, but secondary infection with normal nasal flora is common) or pneumonia (culture and sensitivity from the lower airways is essential if pneumonia is present). *Bartonella* has been implicated as a cause of chronic rhinitis and epistaxis; azithromycin may be used (5-10 mg/kg PO q 24 h. Start at 5 mg/kg and if tolerated, increase by 2.5 mg/kg each day to 10 mg/kg limit. After 1 week, reduce to q 48 h).
- Analgesics if painful (opiates and/or nonsteroidal antiinflammatory drugs [NSAIDs])
- Removal of animal from environmental agents (e.g., smoke, dust, allergens)
- Surgery should be considered for dental disease, neoplasia, nasopharyngeal polyps, cleft palate, foreign bodies, or traumatic causes.
- Radiation and/or chemotherapy for neoplasia
- Chemoembolization (an interventional radiology technique) of nasal tumors can be considered in cases where surgery, radiation, or chemotherapy are associated with excessive morbidity, cost, or a poor outcome.
- Rhinoscopy may be useful for removing a foreign body.
- Fungal: local or systemic treatment
- Parasitic rhinitis: ivermectin, 0.2 mg/kg SQ or PO twice 3 weeks apart, is reported to be successful; avoid in breeds susceptible to toxicosis (collies, Shetland sheepdogs, Old English sheepdogs, and others; see p. 706).
- Decongestants and cleaning of the nares (pediatric Neo-Synephrine, 1 drop in alternating nares q 24 h)
- Nasopharyngeal stenting for nasopharyngeal stenosis
- Embolization for epistaxis

CHRONIC TREATMENT

- Nutrition: cats especially may not eat if unable to smell food; consider coax-feeding (see p. 1377) or placement of a tube (e.g., esophagostomy; see p. 1267) for nutritional support.
- Analgesics
- Antibiotics for secondary infections
- In animals with chronic rhinitis, anti-histamines, inhaled corticosteroids, and systemic NSAIDs may provide some relief.

POSSIBLE COMPLICATIONS

- Anorexia (especially in cats with severe nasal congestion)
- Keratitis (feline viral upper respiratory infections)
- Upper airway obstruction following extubation after general anesthesia
- Hemorrhage following surgery or rhinoscopy
- Dehiscence of surgical site (e.g., cleft palate)
- Progression of underlying disease
- Acute nasal trauma due to paroxysmal sneezing in small, short-legged dogs whose noses may hit the floor while sneezing (e.g., dachshunds)

RECOMMENDED MONITORING

- Respiratory rate and effort; ventilation and oxygenation

- Appetite
- Ongoing hemorrhage
- Volume and nature of discharge
- Monitoring as normal for antimicrobials and NSAIDs
- Appropriate laboratory testing or diagnostic imaging, dependent on underlying disease

PROGNOSIS AND OUTCOME

- Dependent on etiology
- Good if the underlying problem is canine viral upper respiratory tract infection, foreign body, successful surgery, teeth extractions
- Guarded for feline chronic viral upper respiratory tract infections
- Guarded to good for fungal rhinitis, depending on response to therapy
- Poor if neoplasia is not amenable to surgery and radiation therapy. Interventional techniques such as chemoembolization of nasal tumors may be considered in cases where surgery or radiation are not options, or if a less invasive approach is desired.

PEARLS & CONSIDERATIONS

PREVENTION

- Isolation of cats with viral infections
- Appropriate vaccination regime and retroviral testing
- Good dental care
- Limit exposure to irritating aerosols or materials

SUGGESTED READING

Doust R, Sullivan M: Nasal discharge, sneezing and reverse sneezing. In King LG, editor: Textbook of respiratory disease in dogs and cats, St Louis, 2004, Saunders, pp 17–29.

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Snakebite

BASIC INFORMATION

DEFINITION

Injury resulting from a snake biting an animal

SYNONYM

Snake envenomation

EPIDEMIOLOGY

SPECIES, AGE, SEX: Any age or species; either sex

GENETICS & BREED PREDISPOSITION: Large-breed, outdoor dogs appear to have an increased risk.

RISK FACTORS

- Environment: exposure to outdoors in warm climates
- Behavior: curiosity

CONTAGION & ZOONOSIS

- The same snakes that are venomous to dogs and cats are venomous to humans.
- No zoonosis associated with snakebites

GEOGRAPHY AND SEASONALITY

- There are two main families of venomous snakes: Elapidae and Viperidae.
    - Elapids: coral snakes, cobras, mambas, kraits, and the tiger snake; in North America, these are found predominantly in the southeastern areas of the United States.
    - Vipers: rattlesnakes *(Crotalus* and *Sistrus* spp.) and cottonmouths and copperheads *(Agkistrodon* spp.); found throughout the United States
- Increased incidence of bites in summer months (in North America, 90% of bites occur between April and October). Toxicity increased in young or very large snakes during springtime.

ASSOCIATED CONDITIONS & DISORDERS

- Neurologic dysfunction: elapids
- Local tissue damage and possibly systemic bleeding/coagulation: vipers

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Vipers (e.g., rattlesnakes) inflict 99% of the estimated 150,000 annual snake bites of dogs and cats in North America.
- “Dry” bites possible: contain little or no toxic venom (22% of rattlesnake bites are dry; higher proportion in elapids)

HISTORY, CHIEF COMPLAINT

- Observed bite:
    - Dogs, head and neck; cats, abdomen, thorax. Common scenario: the dog cries out after sniffing in the bushes or behind a rock where snake is hidden.
- Unobserved bite: facial or neck swelling and pain after being outdoors without supervision

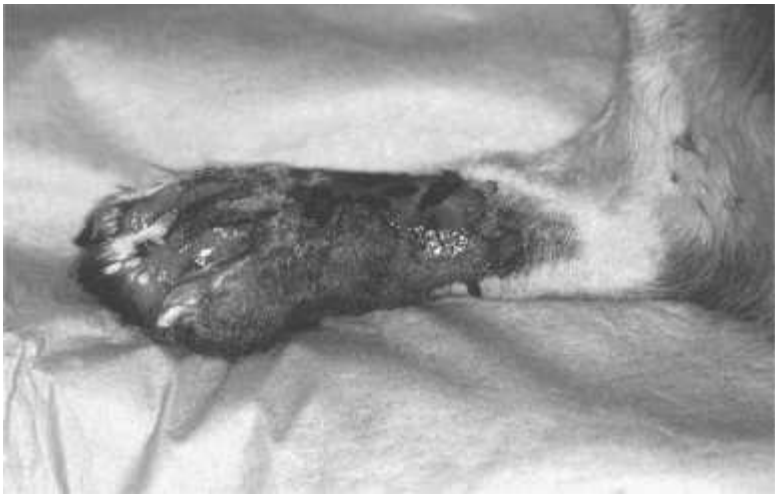
PHYSICAL EXAM FINDINGS

- Fang marks with swelling and bruising around the area may exist. The animal may show signs of mild discomfort to profound hemorrhagic and neurologic alterations. Fang marks are often difficult to find, especially in longhaired or thick-coated dogs and cats.
- Coral snakes:
    - Leave tiny fang or tooth marks with little or no local swelling
    - Signs may be delayed 1-7.5 hours.
    - Salivation
    - Vomiting
    - Convulsions
    - Quadriplegia
    - Death
- Rattlesnakes:
    - Usually leave two fang marks
    - Swelling
    - Pain
    - Erythema
    - Petechiae or ecchymoses
    - Cyanosis and tissue sloughing

SNAKEBITE Viper (rattlesnake) bite to a dog's muzzle. Note marked diffuse swelling of face and lips.

ETIOLOGY AND PATHOPHYSIOLOGY

- Elapid venom is neurotoxic and hemolytic:
    - Signs appear 1-7.5 hours after the bite was inflicted and progress rapidly.
    - Signs start with salivation, vomiting, and apprehensive behavior.
    - Signs progress to convulsions, quadriplegia, and eventually may lead to death from respiratory paralysis.
- Crotalid venom is vasculotoxic and necrogenic.
    - Bites lead to immediate regional swelling.
    - Area around the bite may have swelling, pain, erythema, ecchymosis, cyanosis, and tissue sloughing.
    - Bites are most often inflicted on the face and head and occasionally on the paws.
    - In severe cases, the tissue around the fang marks turns black within 30 minutes, and the blood oozing from the site is dark and watery.
    - Swelling typically worsens over the first 24 hours after the bite was inflicted, and the swollen tissue may be similar to a hematoma (occasionally requiring transfusion).



SNAKEBITE Viper (rattlesnake) bite to a cat's distal forelimb. Note marked swelling, moist exudation, and dark discoloration of skin, which suggests necrosis.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected when a patient develops acute swelling with bruising, often around the face (vipers), or acute neurologic dysfunction (elapids) in a geographic region known to harbor venomous snakes. Identification of puncture marks in the skin from the bite is confirmatory; in many cases the diagnosis remains presumptive.

DIFFERENTIAL DIAGNOSIS

- Other animal attacks
- Scorpion bite
- Insect bite
- Wound of unknown origin
- Intoxication with neurotoxic substance (versus elapid envenomation)

INITIAL DATABASE

- CBC with platelet count: may reveal hemoconcentration, leukocytosis, echinocytosis, or thrombocytopenia
- Serum biochemistry profile: may reveal hypokalemia, high creatine kinase
- Urinalysis: may reveal hematuria or myoglobinuria
- Coagulation profile: prolonged activated clotting time (ACT), prothrombin time (PT), partial thromboplastin time (PTT), and increased fibrin/fibrinogen degradation products (FDPs) possible
- Aerobic and anaerobic bacterial culture and sensitivity (C&S) of the wound

ADVANCED OR CONFIRMATORY TESTING

No test exists that is diagnostic for a snake bite, but echinocytes found on a blood smear are a common finding in animals with envenomation. Echinocytes are “burred” red blood cells (RBCs) that appear soon after envenomation and last 24-48 hours. These cells often precede the massive tissue swelling and necrosis that occur with serious bites.

TREATMENT

TREATMENT OVERVIEW

- Management/prevention of hypotension
- Neutralization of venom (minimizing local and systemic effects)
- Prevention of secondary bacterial infection
- Pain management
- Avoidance of iatrogenic complications, particularly during first-aid efforts in the field

ACUTE GENERAL TREATMENT

- All animals that are bitten by a snake, regardless of their apparent hemodynamic stability, should be hospitalized for a minimum of 8 hours to assess for clinical signs that may first manifest during this period.
- IV fluid therapy:
  - First line of therapy to treat hypotension or hypovolemic shock (see p. 1592) and decreased cardiac output
  - Crystalloids (e.g., lactated Ringer's solution or 0.9% NaCl) at maintenance rates (e.g., 30 mL/lb/d [65 mL/kg/d] plus deficit for extravasated fluid; estimate amount of tissue swelling) if animal is stable; or at shock rates (90 mL/lb/h [200 mL/kg/h]) if animal is in hypovolemic shock.
  - Colloids indicated for animals with hypoalbuminemia; plasma preferred because both albumin and acute phase-proteins are administered (see p. 1347).
- Antivenom (antivenin; polyvalent Crotalidae):
  - Administered immediately for viper bites; increased survival when given closer to time of bite, but beneficial effects noted for at least 60 hours after envenomization
  - A dose of up to 10 to 25 vials is routinely recommended in human cases, but very high cost (up to $400 per vial hospital cost), reduced availability, smaller animal size, and mild extent of some bites generally limit the number of vials used to 1-3.
  - Protocol:
    - Reconstitute antivenin (10 mL diluent into lyophilized antivenin). Warm to body temperature (e.g., armpit method) and not warmer. Gently swirl to dissolve over 10 to 15 minutes; avoid shaking solution.
    - Pretreat the patient (diphenhydramine, 2 mg/kg IM).
    - Dilute antivenin into 50-200 mL IV fluids, and administer test dose IV(10-20 mL over several minutes) while monitoring for anaphylaxis (see pp. 64 and 1111).
    - If no anaphylaxis, administer remainder over 1 hour while continuing to monitor.
- CroFab (polyvalent immune Fabovine) is less antigenic; dissolves more rapidly and is more potent but twice as expensive.
- Antivipmyn: similar to antivenin; obtained from Mexico
- Antibiotics (controversial): chosen empirically at first while culture results are pending; first- or second-generation cephalosporins (e.g., cefazolin, 22 mg/kg IV q 8 h)
- Analgesics: opiates for sedation and analgesia while ensuring that the animal does not develop respiratory depression; buprenorphine (0.01 mg/kg IV q 6 h) or fentanyl at a constant rate infusion (3 mg/kg IV, then 3-6 mg/kg/h)
- Corticosteroids: antiinflammatory doses (e.g., prednisone, 0.5 mg/kg/d PO, maximum 5 days) may be of benefit.
- Antihistamines: not recommended (have been shown to potentiate the toxicity of venom) except in pretreatment doses prior to antivenin administration
- Urgent airway management (critical from time of presentation to 72 hours later): prepare endotracheal tubes and tracheostomy kits when facial, neck, or tongue bites have occurred, even if swelling is initially unimpressive. see p. 1344.

CHRONIC TREATMENT

Surgical débridement of necrotic tissue is necessary in some cases.

NUTRITION/DIET

Most patients can continue to prehend and swallow despite facial bites; if not, placement of a feeding tube should be considered (see p. 1270).

DRUG INTERACTIONS

Antivenin may cause an anaphylactic reaction (see p. 64). Monitor vital signs during infusion; if signs of anaphylaxis develop, temporarily stop the infusion, and then restart the infusion at a slower rate when signs have subsided.

POSSIBLE COMPLICATIONS

Renal failure may result from myoglobinuria, hemoglobinuria, toxic nephropathy, and hypovolemic shock.

RECOMMENDED MONITORING

Monitor respiratory rate and effort as well as blood pressure (BP), electrocardiogram (ECG), coagulation status and urine output.

PROGNOSIS AND OUTCOME 

- The prognosis is worse in animals with high-venom burdens, shock, severe cardiac arrhythmias, hematologic complications, and infection.
- Nevertheless, the spectrum of severity is wide, and the majority of dog or cat snakebite victims survive without permanent

sequelae if treated early and thoroughly.
- Although death may occur in spite of the timely use of crotalid-specific antivenin, a higher survival rate has been found in dogs that received antivenin than in dogs that did not.

PEARLS & CONSIDERATIONS

COMMENTS

- With viper bites, marked worsening of tissue swelling in the 24-48 hours following the bite is common, even with excellent treatment:
  - Warn owners in advance, in order to preempt their perception that treatment is unsuccessful.
  - Prepare airway mobilization material (endotracheal tube or tracheostomy kit) if the snake bit the animal on the head or neck.
- Ineffective first-aid techniques include tourniquet application, incision and suction of the bite, electroshock of the bite, and hot or cold pack application. These maneuvers can harm the animal by fostering infection.
- Effective first aid involves minimizing exertion immediately after the bite (reducing cutaneous blood flow/venom absorption) and immediate transport to a veterinary hospital for diagnosis and treatment as outlined previously.
- Snakebites on digits or in very small animals may require 50% more antivenin on a body weight basis than bites excluding digits or in larger animals:
  - Relatively small volume of body fluid in smaller animals (higher absolute venom concentrations)
  - Difficulty attaining high antivenin concentrations in digits
- Rattlesnakes may bite for up to 30 minutes after they are killed, including death by decapitation. Therefore, the body or head of a snake that has bitten and is then killed and transported for identification should be kept in a rigid, closed container, and the head should not be handled directly.

PREVENTION

The best way to prevent snakebites is to avoid snakes.

- Vipers bite in self-defense or when they are surprised (as occurs in veterinary and human medicine), or to immobilize and consume prey, such as small rodents.
- Vipers may strike with unavoidable speed (8 ft [2.5 m]/sec) but typically for a distance corresponding only to half the snake's length (e.g., half of 3-5 ft [1-1.6 m]).
- Keeping dogs in enclosed areas with cement walls or keeping dogs on leashes while outside may help prevent contact with snakes.
- Keeping cats indoors will help to prevent their contact with snakes.
- In regions where rattlesnakes are common, courses are offered to try to teach dogs to avoid snakes.
- Bitten dogs and cats cannot be counted on to avoid snakes in the future; repeat victims occur.

CLIENT EDUCATION

Most North American snakes bite when surprised or threatened; vigilance and avoidance of snakes during warm months are the best approach to preventing bite incidents.

SUGGESTED READING

Najman L, Sashadri R: Rattlesnake envenomation. Compend Contin Educ Pract Vet 29(3):166–177, 2007.

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EDITOR: ELIZABETH ROZANSKI

Smoke Inhalation

BASIC INFORMATION

DEFINITION

Injury to the respiratory system due to breathing of harmful gases, vapors, and particulate matter contained in smoke. Neurologic dysfunction and burns may occur concurrently.

SYNONYMS

Smoke exposure, smoke intoxication

EPIDEMIOLOGY

RISK FACTORS: Exposure to closed-space fires

GEOGRAPHY AND SEASONALITY: More residential fires in winter

ASSOCIATED CONDITIONS & DISORDERS: Carbon monoxide intoxication, acute respiratory distress syndrome (ARDS), burns, secondary bacterial pneumonia, systemic inflammatory response syndrome (SIRS)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Inhalation injury generally manifests in three clinical stages:
  - Hypoxie injury
  - Neurologic compromise
  - Secondary lung injury
- Occasionally, smoke inhalation injury may be confined to the nasal passages and pharynx.

HISTORY, CHIEF COMPLAINT

- Complaint of respiratory difficulties following smoke inhalation
- Weakness, stupor, or coma following rescue

PHYSICAL EXAM FINDINGS

- Dyspnea, coughing, tachypnea, short or shallow respirations, harsh or moist airway sounds, crackles, wheezes, loud laryngeal or tracheal sounds. In milder cases, signs may be limited to the nasal cavity (inflammation-induced nasal congestion, obstruction to nasal airflow).
- Postural adaptations to respiratory distress may be seen.
- Mentation and motor dysfunction may include ataxia, weakness, depression, stupor, or coma.
- Mucous membranes may be hyperemic (due to carboxyhemoglobin [COHb], cyanide [CN], or vasodilation), pale, or cyanotic.
- Dermatologic findings include smoky smell, singed or burnt hair and skin, soot, or skin lacerations.

ETIOLOGY AND PATHOPHYSIOLOGY

Causes of respiratory injury:

- Thermal damage is usually limited to the upper-airway mucosa, owing to rapid heat dissipation. Steam, soot (particles <2.5 mm), and volatile and explosive gases, however, may also cause thermal injury to lower airways.
- Asphyxiation:
  - Atmospheric oxygen deficit due to combustion
  - Carbon monoxide (CO) toxicity: tissue hypoxia from COHb formation and subsequent decrease in the oxygen-carrying capacity of blood. A left shift of the hemoglobin-oxygen dissociation curve also reduces peripheral oxygen delivery.
  - Combustion of plastics, polyurethane, fiber, rubber, and paper produces cyanide gas, which arrests cellular respiration by binding to cytochrome a3.
  - Methemoglobinemia occurs secondary to heat denaturation of hemoglobin and release of oxides and nitrites.

- Pulmonary irritants cause direct tissue injury (dependent on particle size, water solubility, and acidity), bronchospasm, and inflammation. Leukocyte activation with cytokine release and nitric oxide upregulation lead to pulmonary vascular hyperpermeability and edema. Pulmonary hypertension and atelectasis due to acute surfactant inactivation contribute to hypoxemia.
    - Impaired macrophage function and decreased mucociliary clearance may predispose the animal to bacterial pneumonia.
- Neurologic dysfunction: central nervous system (CNS) hypoxia

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis of smoke inhalation is almost always straightforward based on history of known exposure to fire and smoke and compatible clinical signs. Diagnostic testing is useful for monitoring of progression or development, rather than initial diagnosis.

DIFFERENTIAL DIAGNOSIS

- Anaphylaxis
- ARDS
- Asthma (cats)
- Congestive heart failure (CHF)
- Pneumonia
- Pneumothorax
- Pulmonary thromboembolism
- Primary CNS disorders

INITIAL DATABASE

- Arterial blood gas (ABG) and pulse oximetry:
    - ABG may confirm hypoxemia, hypercarbia.
    - Less useful for determining tissue oxygenation in the face of carbon monoxide (CO) exposure and methemoglobinemia unless cooximetry is available
    - With smoke inhalation, standard pulse oximetry cannot evaluate the severity of hypoxemia because it does not differentiate between oxygenated Hb and COHb.
- CBC:
    - Increased packed cell volume (PCV) (hypovolemia, splenic contraction). Dogs with a more severe inhalation injury tend to have a higher PCV (mean: 58%) than milder cases (mean: 50%).
    - Neutropenia: pulmonary neutrophil sequestration.
- Serum chemistry profile:
    - May reflect hypoxic organ damage (e.g., increased hepatic enzyme levels, azotemia)
    - Electrolyte (and lactate) levels: high anion gap acidosis possible
- Thoracic radiography:
    - May be normal after initial smoke inhalation but useful to establish a baseline
    - Findings may include atelectasis, aspiration pneumonia, and pulmonary edema.

ADVANCED OR CONFIRMATORY TESTING

- Bronchoscopy (see p. 1220): may demonstrate the severity of airway damage and indicate impending airway obstruction. A bronchoalveolar lavage (cytologic examination, culture) can be helpful in stable animals to assess for secondary processes such as bacterial pneumonia.
- Transtracheal wash (see p. 1350): if secondary infection is suspected and bronchoscopy is unavailable or not feasible
- Pulmonary function testing: uncommonly used; inhalation injury may decrease functional residual capacity.

TREATMENT

TREATMENT OVERVIEW

Early oxygen supplementation is a cornerstone of treatment to optimize these patients' chances for survival. Close attention should also be paid to maintaining normal tissue perfusion and general nursing care. Additional goals are to maintain airway patency, restore normal gas exchange, and assess for and treat secondary complications such as bacterial pneumonia, ARDS.

ACUTE GENERAL TREATMENT

- High-flow humidified oxygen therapy is crucial to reverse hypoxia and accelerate CO elimination:
  - COHb half-life: 4 hours (room air) versus 1.5 hours (100% oxygen)
- Severe cases: mechanical ventilation with positive end expiratory pressure (PEEP); see p. 1362.
- Administration of IV fluids as needed to maintain normal cardiac output and tissue perfusion
- Blood or plasma transfusions may be necessary (see p. 1347).
- Fluorescein stain corneas for evidence of ulceration
- Nebulization of saline and coupage may facilitate clearance of respiratory secretions.
- Drug therapy:
  - Secondary pneumonia: prophylactic use of antimicrobials is not indicated, as it increases the risk of development of fungal or resistant bacterial pneumonias. Clinicians should monitor for development of bacterial pneumonia (worsening respiratory character or rate, purulent nasal discharge or sputum; radiographic changes; +/− transtracheal wash), justifying sampling and treatment based on cytologic and microbiologic analysis.
  - Corticosteroids: probably contraindicated
  - Nonsteroidal antiinflammatory drugs for analgesia in hemodynamically stable patients only: meloxicam, 0.1-0.2 mg/kg SQ or PO q 24 h; or carprofen, 2.2 mg/kg PO or SQ q 12 h
  - Opioids: hydromorphone, 0.05-0.1 mg/kg IV or IM q 4 h; buprenorphine, 0.01-0.02 mg/kg IV or IM q 6-8 h; or fentanyl, 1-5 mcg/kg/h IV as a continuous rate infusion, all provide effective and relatively safe analgesia.
  - Bronchodilators: albuterol, 90-mg inhaler, 1-2 puffs per large-breed dog q 8 h as needed; or aminophylline, 6-10 mg/kg IM or diluted IV q 8 h, may alleviate reflex bronchospasm.
  - Diuretics: not indicated (decrease intravascular volume without major benefits on pulmonary function and edema)
  - Specific (rarely used) antidotes include:
    - 20% sodium thiosulfate, 30-50 mg/kg IV, q 8-12 h for treatment of cyanide intoxication
    - Sodium nitrite no longer recommended (can cause methemoglobinemia).

NUTRITION/DIET

Nutritional support to preserve body condition and immune status (see pp. 1270, 1267, 1269, and 1273)

POSSIBLE COMPLICATIONS

- ARDS and respiratory failure
- Superimposed bacterial infections: common cause of deterioration
- Immediate or delayed neurologic complications

RECOMMENDED MONITORING

- Careful monitoring of airway patency, gas exchange, hydration, and cardiovascular function
- Repeat thoracic radiographs

PROGNOSIS AND OUTCOME

- The duration of smoke exposure, type of burn material, and availability of immediate oxygen supplementation impact recovery.
- Severe skin burns, other internal organ injury, and deteriorating respiratory function within 24 hours carry a poor prognosis.
- Animals with signs of neurologic dysfunction who are stable or improving at 24 hours have a good prognosis; worsening neurologic function at 24 hours is a poor prognostic indicator.

PEARLS & CONSIDERATIONS

COMMENTS

Substantial pulmonary damage may not manifest until several hours following admission.

TECHNICIAN TIPS

Early oxygen supplementation is essential; it should be administered from the time of triage. Standard monitoring for animals with respiratory distress (e.g., ABGs, pulse oximetry) may be unhelpful in animals with smoke inhalation; monitoring respiratory rate and character and follow-up radiography are superior. Good nursing care is vital, especially for patients with skin wounds (keeping clean

and uncontaminated, changing dressings, pain management) or who have neurologic deficits (protection from self-injury).

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Drobatz KJ, et al: Smoke exposure in cats: 22-cases (1986-1997). J Am Vet Med Assoc 215(9):1312–1316, 1999.

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Sinusitis and Other Sinus Disorders

Additional Images Available on Website

BASIC INFORMATION

DEFINITION

Mucosal inflammation in, or other diseases of, one or more of the sinuses: either the frontal or the maxillary sinuses in dogs and either the frontal or (even less commonly) the sphenoidal sinuses in cats

EPIDEMIOLOGY

SPECIES, AGE, SEX: Cats:

- No sex predilection
- Young to middle-aged animals for chronic idiopathic (rhino) sinusitis
- Older animals for sinus tumors
- Any age for trauma

Dogs:

- No sex predilection
- Older dogs for frontal sinusitis associated with tumors
- Young adults more commonly with aspergillosis
- Young to middle-aged dogs more often seen with chronic idiopathic sinusitis
- Any age for trauma

GENETICS & BREED PREDISPOSITION

- Cats: any breed
- Dogs: primarily dolichocephalic breeds for frontal sinusitis associated with tumors, aspergillosis, or chronic idiopathic sinusitis

ASSOCIATED CONDITIONS & DISORDERS

- Nasal tumors
- Nasal aspergillosis
- Chronic idiopathic or lymphoplasmacytic rhinosinusitis
- Nasal or frontal sinus trauma
- Abscessation of the roots of the upper fourth premolar tooth (apical dental abscess), causing maxillary sinus empyema
- Feline herpesvirus (rhinotracheitis)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: see Associated Conditions and Disorders, above.

HISTORY, CHIEF COMPLAINT

- Nasal discharge
- Intermittent sneezing
- Focal facial swelling or deformity
- Signs related to local pain:
  - Dullness or lethargy
  - Decreased movements of the head
  - Anorexia

PHYSICAL EXAM FINDINGS

- Unilateral nasal discharge of variable nature: mucoid, mucopurulent or blood-tinged; often bloody with nasal neoplasia
- If nasal cavity affected, diminished air flow through nasal passages/nares
- Focal swelling, firm enlargement, facial deformity, and/or pain with atrophy or lysis of the frontal or nasal bones:

  - Depressions or defects in frontal/nasal bone integrity from osteolysis may be noted during palpation.
  - Dogs with maxillary sinusitis from fourth premolar tooth root abscessation may have a swelling or fistulous tract and drainage from ventral to the eye on the affected side.
- Enlargement of submandibular lymph nodes is possible.
- Percussion of the sinus may induce pain or be associated with reduced resonance.

ETIOLOGY AND PATHOPHYSIOLOGY

- Sinusitis is most often secondary to another primary nasal or frontal sinus disease (as already described in Associated Conditions and Disorders, above) in which disruption of the normal nasal/sinus anatomy impairs mucociliary clearance or obstructs mucus drainage.
- Owing to physical continuity between the chambers, tumors of the frontal sinus can extend into the nasal cavity, and nasal tumors can extend in the frontal sinus.
- Mycotic sinusitis and rhinitis, mostly due to *Aspergillus fumigatus,* can affect both the nasal cavity and sinus, or either independently.
- Chronic lymphoplasmacytic inflammation in dogs can be a sequela to bacterial or mycotic infections (even after successful fungal therapy), can be idiopathic, or possibly could be related to an allergic etiology.
- Chronic lymphoplasmacytic inflammation in cats can be a sequela to bacterial, viral (feline upper respiratory tract infection complex), and (rarely) mycotic infections.
  - Like in dogs, the condition can be idiopathic in cats, possibly related to an allergic etiology.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Sinus diseases are generally associated with nasal diseases and probably secondary to nasal disease in most cases.

DIFFERENTIAL DIAGNOSIS

Nasal diseases of various origins:

- Fungal rhinitis
- Nasal neoplasia
- Dental disease/dental root infection (maxillary sinus)
- Foreign bodies
- Lymphoplasmacytic rhinitis
- Nasal mites
- Chronic viral upper respiratory tract infection in cats

INITIAL DATABASE

- For some cases, plain radiographs of the nasal cavities, sinuses, and dental roots can be helpful in the diagnosis of structural lesions such as neoplasia, fungal rhinitis/sinusitis, and dental disease but will not help discriminate among the various causes of nasal/sinus disease in other cases not involving structural changes.
- Results of a CBC, serum biochemical profile, and urinalysis are often normal.
- For cases in which there is swelling or lysis (which can be palpable) of nasal/facial bones or the frontal sinus area, fine-needle aspirate (FNA) cytologic examination can show neoplasia or inflammation.

ADVANCED OR CONFIRMATORY TESTING

- CT scan and/or MRI of the nasal cavities and sinuses can differentiate neoplasia, fungal rhinitis, and dental disease with more accuracy than plain radiographs but will not confirm the diagnosis in all cases.
- The frontal sinus can be examined by direct rhinoscopy in some dogs, but access to and visualization of the frontal sinus is often possible only in animals with severe turbinate destruction.
- Trephination of the frontal sinus for examination and biopsy may be necessary to confirm the presence of neoplasia, fungal rhinitis, or inflammation, especially if disease is confined to the frontal sinus. Trephination may also have therapeutic value for cases of fungal rhinitis (see p. 96).

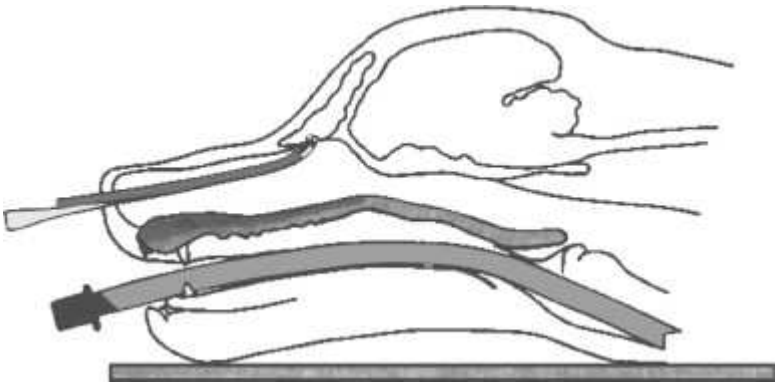
TREATMENT

TREATMENT OVERVIEW

Whenever possible, the best opportunity for resolution of sinusitis is treatment of the underlying primary disease that often exists.

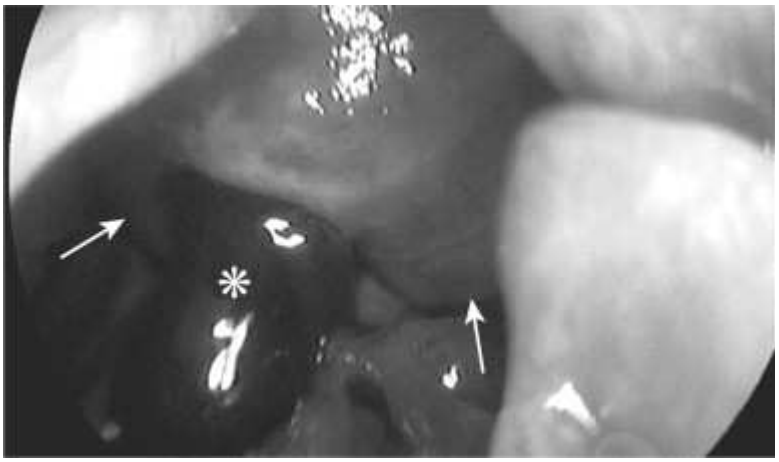
ACUTE GENERAL TREATMENT

- Direct treatment toward the causal agent:
  - Fungal sinusitis/rhinitis: antimycotic therapy (see p. 96 and online chapter: Nasal Infusion of Clotrimazole)
  - Frontal tumors: radiation therapy and, occasionally, surgical resection
  - Traumatic injuries causing fractures of the frontal bone: removal of bone fragments present in the frontal sinus and possibly reconstruction; check patency of the nasofrontal ostium (nasofrontal opening); broad-spectrum antibiotics.
  - Apical dental (tooth root) abscess: surgical extraction of the tooth, including roots, or endodontic treatment
- In acute infection, as well as in chronic idiopathic inflammation with episodes of secondary bacterial infections, oral or injectable antibiotics (e.g., amoxicillin, 20 mg/kg PO q 8 h; cefadroxil, 20 mg/kg PO q 8 h; or amoxicillin-clavulanate, 15 mg/kg PO q 12 h) and possibly mucolytics may be needed.
  - The frontal sinus is a combination of several large cavities surrounded by bone; systemically administered drugs often do not achieve high concentrations in the sinus. Even very high dosages of highly soluble drugs, preferred for systemic therapy, may not reach adequate concentrations throughout the entire sinus cavity.
  - Drug nebulization is unproven; the amount of drug delivered into the frontal sinus is unknown.



SINUSITIS AND OTHER SINUS DISORDERS Diagram demonstrating the standard position for endoscopic imaging of the frontal sinuses in the dog.

(Courtesy Dr. Cécile Clercx, University of Liège.)



SINUSITIS AND OTHER SINUS DISORDERS Endoscopic view of the frontal sinus of a dog. A large, smooth convex mass occupies the center of the image *(arrows),* and its appearance strongly suggests neoplasia. An adjacent blood vessel is seen *(asterisk).*

(Courtesy Dr. Cécile Clercx, University of Liege.)

CHRONIC TREATMENT

In cases of concomitant nasal disease, with loss of the protective filter provided by normal turbinates and decreased mucociliary clearance along the distal third of the nasal cavity, recurrent bacterial secondary infections are common and are treated each time with antibiotics and mucolytics, orally or locally (intranasal administration or aerosol delivery).

POSSIBLE COMPLICATIONS

In animals with chronic sinusitis, repeated episodes of bacterial infection can be expected.

RECOMMENDED MONITORING

Monitoring depends on etiology of the condition and persistence of clinical signs. For example, in lymphoplasmacytic inflammation of the frontal sinus after treatment of aspergillosis, diagnostic workup is warranted in cases of severe recurrence of clinical signs to differentiate between secondary bacterial infection and recurrence of aspergillosis, because the latter must be treated with antifungal agents.

PROGNOSIS AND OUTCOME

- Prognosis and outcome depend on the cause, whether the cause can be eliminated or treated, and whether there are chronic irreversible sequelae of the turbinates and sinus mucosa.
- Poor for most patients with frontal sinus tumors, which are usually malignant
- In chronic sinusitis, total cure is rarely achieved, but response to ongoing therapy is generally good.

PEARLS & CONSIDERATIONS

COMMENTS

- In acute cases, quickly find the cause, using appropriate diagnostic tests, and immediately treat the animal to avoid chronic irreversible sequelae.
- When sinusitis is related to the extension of nasal disease, it is often a chronic condition with consequent remodeling, and total cure is rare; secondary bacterial infections can always occur.

TECHNICIAN TIPS

While of low diagnostic yield, cytologic examination of nasal exudate can occasionally identify another underlying cause (e.g., cryptococcosis, rarely nasal neoplasia) of nasal cavity disease.

CLIENT EDUCATION

Treatment must be repeated when relapses, which are common in chronic idiopathic sinusitis, occur. The disease will rarely totally resolve, and most of the time, mild clinical signs persist despite treatment. If more severe signs persist, repeating a complete diagnostic evaluation is indicated, with the intent of identifying an etiologic cause.

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Sinus Tachycardia

BASIC INFORMATION

DEFINITION

An accelerated heart rate caused by rapid firing of the sinus node. Sinus tachycardia is a physiologic response to the body's needs (rather than a pathologic condition), triggered by an increase in sympathetic tone. Sinus tachycardia usually appears and subsides gradually over a few seconds; this characteristic helps set it apart from pathologic supraventricular tachycardias, which may appear and subside instantaneously.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Definition of sinus tachycardia depends on the species, breed, and age:

- Dogs > 160 beats per minute (bpm):
  - Toy breeds > 180 bpm; giant-breed dogs > 140 bpm; puppies > 200 bpm
- Cats > 240 bpm

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Primary physiologic sinus tachycardia:
  - Response to exercise, stress (restraint, anxiety), pain
- Secondary physiologic sinus tachycardia:
  - Response to underlying condition/disease:
    - Fever and infection
    - Shock and hypotension
    - Hypovolemia
    - Anemia
    - Hypoxemia
    - Heart failure and cardiac tamponade
    - Hyperthyroidism
    - Catecholamine excess (e.g., pheochromocytoma)
- Pharmacologic sinus tachycardia:
  - Response to drug administration:
    - Vagolytic drugs (atropine, glycopyrrolate)
    - Sympathomimetic drugs (beta-agonists, dopaminergic drugs)
    - Phosphodiesterase inhibitors (aminophylline, theophylline)

HISTORY, CHIEF COMPLAINT: Sinus tachycardia per se does not cause a chief complaint. The chief complaint is typically associated with the respective underlying disease (as already listed).

PHYSICAL EXAM FINDINGS

- Tachycardia
- Also possible, particularly if the cause of the tachycardia is secondary physiologic (underlying diseases listed):
  - Weak pulse or increased capillary refill time (heart failure/decreased cardiac output)
  - Pale or cyanotic mucous membranes (anemia/hypovolemia or hypoxemia)
  - Fever (infection)
  - Palpable thyroid nodule (feline hyperthyroidism)

ETIOLOGY AND PATHOPHYSIOLOGY

- Sinus tachycardia is a manifestation of the so-called fight or flight response governed by the sympathetic nervous system. Its purpose is to contribute to an increased cardiac output.
- Activation of the sympathetic nervous system increases the automatic discharge rate of sinoatrial (SA) nodal cells, either directly by activating the b1 receptors in the SA node or indirectly by stimulating the release of norepinephrine from the

adrenal gland into the circulation.
- Transient sinus tachycardia usually occurs during vigorous exercise, anxiety from restraint, fear, or pain.
- Sustained sinus tachycardia is more likely a compensatory phenomenon associated with a decreased cardiac output, hypoxia, or increased metabolic demand (fever, hyperthyroidism).
- Drug-induced sinus tachycardia (dopamine, sympathomimetics, methylxanthines, anticholinergics)

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Sinus tachycardia is suspected (and not pursued diagnostically) when environment/context is appropriate (e.g., in-hospital anxiety). If the heart rate is persistently, seemingly inappropriately elevated, the question of whether sinus tachycardia or another tachycardia is responsible should be raised. In such a situation, an electrocardiogram (ECG) provides the definitive answer.

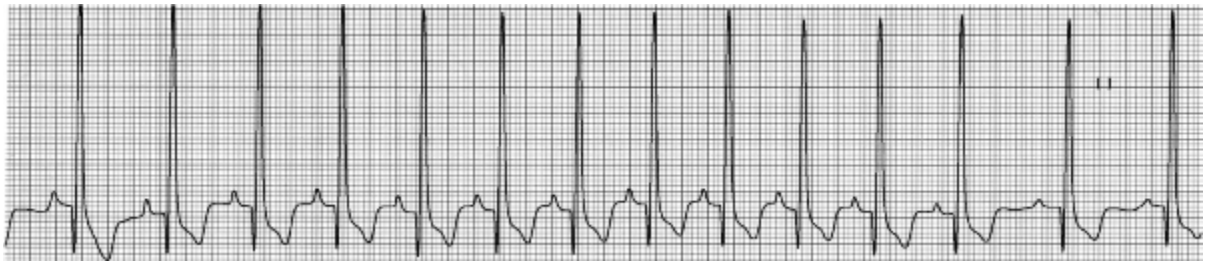
DIFFERENTIAL DIAGNOSIS

By ECG:

- Any narrow complex supraventricular tachycardia (SVT):
  - Sinus node reentry tachycardia
  - Ectopic atrial tachycardia (if normal P wave morphology)
  - In fast sinus tachycardia, the P waves cannot be distinguished from the T waves of the previous beat. In those cases, it can be difficult to differentiate sinus tachycardia from atrioventricular (AV) reentry (bypass tract-mediated supraventricular tachycardia) or AV nodal reentry tachycardia (see the text on vagal maneuver in the Initial Database section below).
  - Atrial flutter with 2:1 or 3:1 conduction
- Sinus tachycardia with bundle branch block can mimic ventricular tachycardia.

INITIAL DATABASE

- ECG (see p. 1253):
  - QRS complexes are similar to normal sinus rhythm.
  - RR interval is shorter.
  - Regular P waves with normal morphology
  - Each P wave is followed by a QRS complex in a 1 : 1 ratio.
  - At very rapid rates, the P waves might become superimposed on the preceding T waves such that the P waves are obscured by T waves.
- Physical tests:
  - Vagal maneuver: a positive response (transient, gradual slowing of sinus tachycardia over a few seconds) may increase the R-R interval enough to allow visualization of P waves. Abrupt termination of a tachycardia during a vagal maneuver (see p. 1359) suggests presence of another type of SVT, such as sinus node reentry or AV node–dependent SVT.
  - Capillary refill time (peripheral perfusion prolonged in shock or with reduced cardiac output)
- Blood pressure (BP) (hypotension)
- Oxygen saturation (hypoxemia)
- Hematocrit and hemoglobin (anemia)
- Thoracic radiography (cardiomegaly, pulmonary edema, or pleural effusion secondary to congestive heart failure [CHF])
- Echocardiography to check for cause of reduced cardiac output or CHF if present



SINUS TACHYCARDIA Electrocardiographic rhythm strip; lead II, 50 mm/sec, 10 mm/mV. Sinus tachycardia in a mixed-breed dog with chronic myxomatous atrioventricular valve disease. Normal sinus rhythm initially; acceleration to a heart rate of up to 200 bpm (sinus tachycardia) is seen in the middle of the strip, with a gradual slowing down again to 150 bpm (sinus rhythm) toward the end of the strip. The R-wave amplitude is tall, indicative of left ventricular enlargement (in this case, secondary to mitral endocardiosis), and

there is mild ST-segment depression, suggesting myocardial hypoxia. Rapid-onset sinus tachycardia, such as in this example, is usually due to catecholamine release in response to environmental stimuli (stress, excitement, etc.).

TREATMENT

TREATMENT OVERVIEW

- Treat underlying cause of sinus tachycardia (if necessary).
- Medical reduction of heart rate (β-blockers) during sinus tachycardia without knowledge of the underlying disorder can be detrimental, since the elevated heart rate might be necessary for maintaining cardiac output.

ACUTE GENERAL TREATMENT

Depends on cause of sinus tachycardia:

- Provide calming environment to reduce anxiety.
- Administer pain medication if indicated.
- Provide oxygen or hemoglobin for hypoxemic or anemic animals.
- Administer fluids or vasopressor agents to stabilize BP for animals in shock.
- Start antimicrobials (if indicated) for sepsis; reduce fever with cool fluid administration.
- Discontinue drugs that are causing sinus tachycardia.

CHRONIC TREATMENT

Address the underlying disease and:

- Manage CHF.
- Control T4 levels (correct hyperthyroidism).
- Treat other signs.

POSSIBLE COMPLICATIONS

- Acute, transient sinus tachycardia can be associated with weakness or syncope, particularly in animals with reduced cardiac function (e.g., dilated cardiomyopathy, advanced mitral/tricuspid endocardiosis) and congestive heart failure.
- Chronic sinus tachycardia may cause tachycardia-induced cardiomyopathy.

RECOMMENDED MONITORING

If the underlying cause has been identified and corrected, the sinus tachycardia should resolve.

PROGNOSIS AND OUTCOME

- Prognosis is good if underlying cause can be corrected.
- Outcome depends on underlying condition.

PEARLS & CONSIDERATIONS

COMMENTS

Sinus tachycardia is a benign “arrhythmia,” and usually should be considered a red flag that indicates an underlying cause needs to be investigated. If the heart rate does not slow down, it can be assumed that the underlying cause is not yet addressed adequately.

CLIENT EDUCATION

Avoid excessive stress or vigorous exercise in animals with reduced cardiac output and CHF.

SUGGESTED READING

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AUTHORS: ANNA R. M. GELZER, MARC S. KRAUS

EDITOR: ETIENNE CÔTÉ

Sinus Bradycardia

BASIC INFORMATION

DEFINITION

Normal sinus rhythm with heart rate less than 60-70 beats per minute (bpm) in dogs and less than 120 bpm in cats

EPIDEMIOLOGY

SPECIES, AGE, SEX: More common in dogs

GENETICS & BREED PREDISPOSITION: Physiologic sinus bradycardia is more common in brachycephalic breeds.

RISK FACTORS

- Variations of normal: athletic dogs, brachycephalic conformation
- Disorders: upper airway disease, respiratory disease, gastrointestinal (GI) disease, systemic disease, central nervous system (CNS) disease, hypothermia, hypothyroidism, sinus node dysfunction, feline dilated cardiomyopathy, end-stage heart failure
- Drug-related: normal response (e.g., β-adrenergic antagonists, diltiazem, amiodarone), inhalation anesthetics, inadvertent administration/toxicity

ASSOCIATED CONDITIONS & DISORDERS: Sinus arrhythmia (normal); sick sinus syndrome (SSS); sinoatrial (SA) block (very rare)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Physiologic: athletes, brachycephalic breeds
- Pathologic: sinus node dysfunction, intoxications, secondary to systemic disease states

HISTORY, CHIEF COMPLAINT

- Often incidental finding: owner auscults/palpates low heart rate.
- Rarely: exercise intolerance, malaise, lethargy, depression, collapse (usually with exertion). When such overt signs occur, they are commonly related to SSS (see p. 1022).

PHYSICAL EXAM FINDINGS

- Cardiac auscultation: reduced heart rate in an alert ± nervous animal:
  - <60–70 bpm in dogs
  - <120 bpm in cats
- Femoral pulse character: may be normal, reduced, or pronounced (depending on underlying etiology and chronicity of bradycardia)
- Malaise, lethargy, depression: if bradycardia is severe

ETIOLOGY AND PATHOPHYSIOLOGY

- Increased vagal tone:
  - Physiologic
    - Brachycephalic conformation (common)
    - Athlete
  - Respiratory disease (upper and/or lower respiratory tract)
  - GI disease: severe vomiting
- CNS disorders:
  - Head trauma
  - Increased intracranial pressure
  - Brainstem lesions

    - Spinal trauma
- Metabolic/systemic disorders:
    - Hypothyroidism
    - Hypothermia
    - Hypoxemia
- Intoxications:
    - Phenothiazines (although phenothiazines may instead induce hypotension and reflex tachycardia).
    - b-Adrenergic receptor antagonists
    - Digitalis
    - Diltiazem (especially injectable)
    - Quinidine
    - Narcotics
    - Amiodarone
    - Inhalation anesthetics
- Primary cardiac disease:
    - Sinus node dysfunction (from SSS)
    - End-stage heart failure
    - Feline dilated cardiomyopathy

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Electrocardiogram (ECG) is required to confirm the presence of sinus bradycardia (and thus rule out other bradycardias, such as atrioventricular [AV] block, if uncertainty exists). Further diagnostic testing is warranted if the patient is exhibiting signs of poor perfusion such as syncope, lethargy, seizures, or other nonspecific systemic disturbances. If signs of underlying disease are absent, the strong possibility of sinus bradycardia as a normal finding should be considered.

DIFFERENTIAL DIAGNOSIS

- Normal (during sleep, healthy dogs routinely have heart rates of 30-40 bpm, and healthy cats routinely have heart rates of 70 bpm).
- Other bradycardias (e.g., AV block, atrial standstill)
- Specific causes: see Etiology and Pathophysiology above

INITIAL DATABASE

- ECG: confirm clinical diagnosis.
- CBC, biochemistry panel, urinalysis may reveal evidence of systemic disease.
- Thoracic and abdominal radiographs to identify underlying respiratory, cardiovascular, or GI disorders
- Abdominal ultrasound to confirm equivocal or subtle abdominal radiographic findings (operator skill dependent)

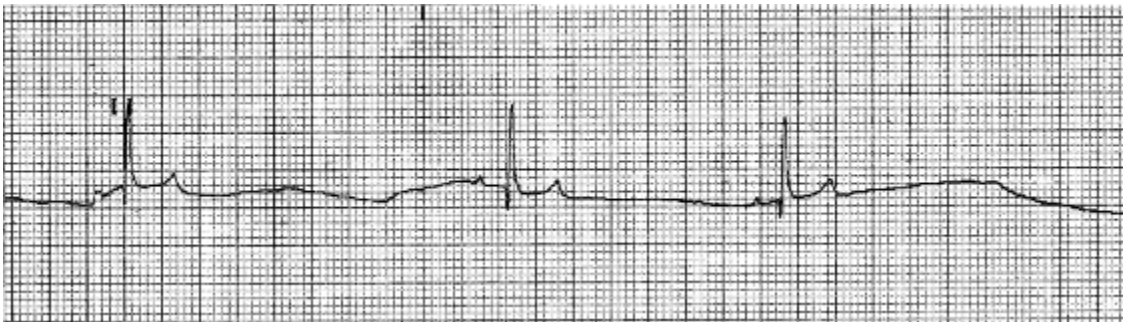
ADVANCED OR CONFIRMATORY TESTING

- Atropine response test to differentiate between vagally mediated bradyarrhythmias and those arising from a conduction disturbance
- Echocardiography to rule out underlying cardiac disease
- Serum digoxin level (if applicable)
- Complete thyroid hormone panel

TREATMENT

TREATMENT OVERVIEW

Treatment of physiologic sinus bradycardia is unnecessary. If systemic disease is identified, treatment of the underlying disease process is indicated. Patients with bradycardia causing overt clinical signs may require acute medical management or pacemaker implantation to increase heart rate, but this is rarely caused by sinus bradycardia (exception: when sinus bradycardia is part of the SSS array of arrhythmias; AV block and premature beats would also be expected concurrently).



SINUS BRADYCARDIA Sinus bradycardia/respiratory sinus arrhythmia. Incidental finding in healthy 5-year-old German shepherd dog. Heart rate = 37 bpm; lead II, 25 mm/sec, 1-cm/mV.

ACUTE GENERAL TREATMENT

- Rarely indicated
- Treat underlying problem (if applicable).
- Discontinue or taper all medications with potential to promote bradycardia.
- For animals with sinus bradycardia that are also showing critical clinical signs (recumbency, unconsciousness, etc.):
  - Administer anticholinergic agent IV (atropine sulfate, 0.04 mg/kg IV; or glycopyrrolate, 0.011 mg/kg IV).
  - If anticholinergic therapy is unsuccessful, consider IV constant rate infusion of isoproterenol (0.4 mg in 250-mL saline; slow drip to effect [prime IV line, start slowly, and increase titration based on response]) or dopamine (2-10 mcg/kg /min).
  - Rarely, emergency cardiac pacing may be required for severe refractory bradycardia.

CHRONIC TREATMENT

- Treat underlying problem (if applicable).
- Discontinue or reduce dosages of all medications with potential to induce bradycardia.
- For animals showing overt signs due to the bradycardia (very uncommon, unless SSS):
  - Propantheline bromide, 0.2-1 mg/kg PO q 8 h (variable response)
  - Theophylline, 10 mg/kg PO q 8 h (variable response)
  - Permanent pacemaker implantation

BEHAVIOR/EXERCISE

Strict exercise restriction for patients with symptomatic bradycardia

DRUG INTERACTIONS

- Propantheline bromide: use this drug cautiously in animals with suspected GI disease or autonomic neuropathy; multiple drug interactions.
- Theophylline: narrow therapeutic window, use cautiously; multiple drug interactions

POSSIBLE COMPLICATIONS

- Medical management failure common when sinus node dysfunction/SSS is present.
- Side effects of propantheline bromide or theophylline administration may be problematic.

RECOMMENDED MONITORING

- None for physiologic sinus bradycardia not causing clinical signs
- The owner monitors for signs of bradycardia: lethargy, exercise intolerance, malaise, collapse.
- Follow-up ECG 1 week after initiation of medical management, then every 1-3 months (as directed by clinical course)
- If pacemaker implantation performed, schedule a follow-up visit as directed (see p. 1022).

PROGNOSIS AND OUTCOME

- Physiologic: excellent. By definition, physiologic sinus bradycardia is not associated with clinical disease.
- Secondary: dependent on response to treatment of primary disorder

- Sinus node dysfunction/SSS:
  - Chronic response to medical therapy is generally unrewarding.
  - Good with pacemaker implantation

PEARLS & CONSIDERATIONS

COMMENTS

- Large- and giant-breed dogs may exhibit normal heart rates as low as 30-40 bpm when asleep.
- Sinus arrhythmia is often identified in conjunction with physiologic sinus bradycardia.
- A life-threatening situation can be the sudden (instantaneous) transition from sinus tachycardia to sinus bradycardia in an unconscious animal, which is associated with impending cardiac arrest.

TECHNICIAN TIPS

- Sinus bradycardia in an anxious or stressed animal (e.g., a hospitalized patient) is more likely to be pathologic and should be brought to the attention of the attending clinician.
- Sinus bradycardia is common in hospitalized patients treated with opiates (e.g., fentanyl, hydromorphone).

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Sinus Arrhythmia

BASIC INFORMATION

DEFINITION

Sinus arrhythmia is a very common form of normal heart rhythm. It is characterized by a physiologic, autonomically mediated cyclical change in sinus rate, with increase in heart rate during inspiration and decrease during expiration. On an electrocardiogram (ECG), the P-P and associated R-R intervals are “regularly irregular” due to fluctuations of the autonomic tone that result in phasic changes of the sinus node discharge rate.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Common in dogs (physiologic)
- Rare in cats (can be pathologic)

GENETICS & BREED PREDISPOSITION

- All dog breeds can display sinus arrhythmia.
- Brachycephalic breeds often have the largest variations in R-R interval (bulldog, pug, boxer, Pekinese, Lhasa apso) owing to increased inspiratory effort.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Respiratory sinus arrhythmia:
  - Physiologic fluctuation associated with respiration
- Nonrespiratory sinus arrhythmia:
  - Cyclic change in P-P interval independent of normal breathing but due to increased vagal tone:
    - Respiratory disease
    - Central nervous system (CNS) disease (increased intracranial pressure)
    - Gastrointestinal (GI) disease

HISTORY, CHIEF COMPLAINT: Respiratory sinus arrhythmia does not cause clinical signs. In animals with nonrespiratory sinus arrhythmia, particularly cats, the chief complaint is related to the underlying disease.

PHYSICAL EXAM FINDINGS

- Normal to “slow-normal” heart rate
- Regularly irregular heart rate by auscultation and pulse palpation
- Also possible but less common:
  - Upper airway noises: stridor, dyspnea, wheezes
  - Neurologic signs: depression
  - GI disturbances

ETIOLOGY AND PATHOPHYSIOLOGY

- Respiratory sinus arrhythmia: sinus node discharge rate is regulated by the autonomic nervous system. Inspiration causes a decrease in vagal tone and an increase in sympathetic tone, resulting in an increased heart rate. Conversely, on expiration there is an increase in vagal tone and a decrease in sympathetic tone, resulting in a decrease in heart rate. The fluctuation in heart rate in phase with respiration and lung volume likely optimizes pulmonary gas exchange by matching perfusion to ventilation within each respiratory cycle.
- Nonrespiratory sinus arrhythmia: autonomic influences can also cause sinus arrhythmia independent of respiration, slowing the heart rate during periods when parasympathetic tone predominates over sympathetic tone.

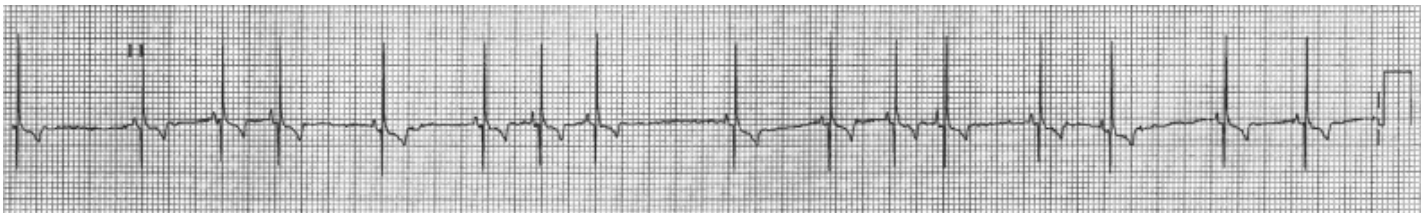
DIAGNOSIS

DIAGNOSTIC OVERVIEW

Sinus arrhythmia is a normal form of sinus rhythm with a “regularly irregular” (cyclical) pattern of increase and decrease in heart rate. Therefore, it is strongly suspected on physical exam alone, and if uncertainty exists, it can be confirmed or ruled out with ECG.

DIFFERENTIAL DIAGNOSIS

- ECG: sinus arrhythmia should be differentiated from (also see Initial Database below):
  - Sick sinus syndrome (SSS): pauses between sinus beats are longer (can be up to several seconds with SSS)
  - Slow atrial fibrillation (no P waves, “irregularly irregular” rhythm)
  - Transient sinus arrest (intermittent nature of pauses instead of cyclic pattern)
  - Atrial premature contractions (APCs): underlying rhythm may be a regular sinus rhythm frequently interrupted by APCs. Differentiation: the P wave of an APC may occur inside the preceding T wave, but such a degree of prematurity does not occur with sinus arrhythmia; APCs do not occur cyclically in concert with the patient's respirations; the heart rate during sinus arrhythmia does not exceed 140 beats/minute, but it commonly does so with APCs/atrial tachycardias.
- By auscultation alone, sinus arrhythmia may be confused with these pathologic arrhythmias. ECG is important to confirm the diagnosis.



SINUS ARRHYTHMIA Electrocardiographic rhythm strip, lead II, 25 mm/sec, 5 mm/mV; healthy dog displaying sinus arrhythmia. Average heart rate is 60-70 bpm; individual R-R intervals vary by close to 100% (range 0.6-1.2 sec).

INITIAL DATABASE

ECG:

- Morphology is similar to normal sinus rhythm:
  - Heart rate is normal to slow (<140 bpm in dogs).
  - P-P interval is variable in a “regularly irregular” fashion.
  - Variability in P-P interval is >10% and can vary up 100%.
  - Normal P wave morphology: P wave is followed by a QRS complex in a 1:1 ratio.
  - P wave amplitude may vary if wandering pacemaker is present (tall P wave after a short P-P interval, low voltage [short] P-wave after a long P-P interval).
- If sinus arrhythmia is concurrent with significant respiratory, CNS, or GI disease, specific diagnostic testing should be recommended based on the relevant abnormalities of the case.

TREATMENT

TREATMENT OVERVIEW

Sinus arrhythmia is a physiologic phenomenon and does not warrant therapy. If confirmation of the rhythm as sinus arrhythmia is needed, administration of a vagolytic agent (atropine) should result in sinus tachycardia and disappearance of sinus arrhythmia. Alternatively, excitement or exercise (sympathetic stimulation) should also result in disappearance of the sinus arrhythmia.

PROGNOSIS AND OUTCOME

Both are good.

PEARLS & CONSIDERATIONS

COMMENTS

Sinus arrhythmia is a physiologic phenomenon, most commonly indicative of a healthy cardiovascular system.

SUGGESTED READING

Hayano J, Yasuma F, Okada A, et al: Respiratory sinus arrhythmia. A phenomenon improving pulmonary gas exchange and circulatory efficiency. Circulation 94:842–847, 1996.

AUTHORS: ANNA R. M. GELZER, MARC S. KRAUS

EDITOR: ETIENNE CÔTÉ

Sick Sinus Syndrome

Additional Images Available on Website

BASIC INFORMATION

DEFINITION

One of the two most common indications for cardiac pacemaker implantation in dogs. It represents diffuse cardiac conduction system disease that displays variable degrees of sinoatrial (SA) nodal dysfunction (sinus bradycardia, sinoatrial block, or sinus arrest) and/or atrioventricular (AV) nodal dysfunction. The subsidiary pacemakers often display depressed automaticity, so prolonged episodes of sinus arrest are accompanied by asystole and syncope. Some dogs may display episodes of supraventricular tachycardia alternating with their bradyarrhythmias, producing a so-called brady-tachy syndrome.

SYNONYMS

Sinus node dysfunction (current term), SSS, bradycardia-tachycardia (brady-tachy) syndrome, chronotropic incompetence, lazy sinus syndrome, SA syncope, sluggish sinus syndrome

EPIDEMIOLOGY

SPECIES, AGE, SEX: Small-breed, older dogs

GENETICS & **BREED PREDISPOSITION:** Middle-aged to older female miniature schnauzers are most commonly afflicted. West Highland white terriers and cocker spaniels also appear to be overrepresented.

ASSOCIATED CONDITIONS & DISORDERS: Sick sinus syndrome (SSS) and chronic degenerative valvular disease often occur in the same animal because of their similar breed and age predispositions, but there is no known link between the two disease processes.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Most dogs with clinical signs from SSS are presented for episodic weakness or syncopal/seizure-like episodes.
- Some animals with severe, long-standing sinus bradycardia may develop congestive heart failure (CHF) and are presented for the evaluation of coughing, respiratory distress, or exercise intolerance.
- Some dogs are diagnosed with bradyarrhythmias and SSS during routine preventive health examination or prior to dental prophylaxis.

PHYSICAL EXAM FINDINGS

- The classic physical examination findings include a detectable bradyarrhythmia with prolonged episodes of asystole due to sinus arrest without activation of subsidiary (AV or intra-ventricular) pacemakers.
- Because of the predisposition for SSS to occur in older, small-breed dogs, many will display variable-intensity, left apical systolic murmurs of mitral insufficiency.
- Dogs with brady-tachy syndrome may have paroxysms of tachycardia followed by audible pauses.
- Unfortunately (as it obscures the diagnosis), some animals will have normal physical examinations without evidence of bradyarrhythmias, because dogs with SSS may still have some response to the elevated circulating levels of catecholamines associated with visits to the veterinary hospital.

ETIOLOGY AND PATHOPHYSIOLOGY

- To date, the etiologic basis for SSS in dogs has not been determined.
- Fibrosis and fatty infiltration with sclerodegenerative processes have been identified within the sinus node, AV node, and bundle of His in humans with SSS.
- Occlusion or degeneration of the sinus node artery could play an important role in the development of this disease.
- The absence of morphologic abnormalities in some humans with sinus node dysfunction suggests that alterations of neural innervation or neural regulation may contribute to the bradyarrhythmias.
- Autoantibodies to proteins isolated from sinus node cells have been identified in humans, suggesting an immune-mediated process in some cases of sinus node dysfunction.
- Changes in ion channels or gap junctions within the sinus node may account for the development of SSS in humans.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

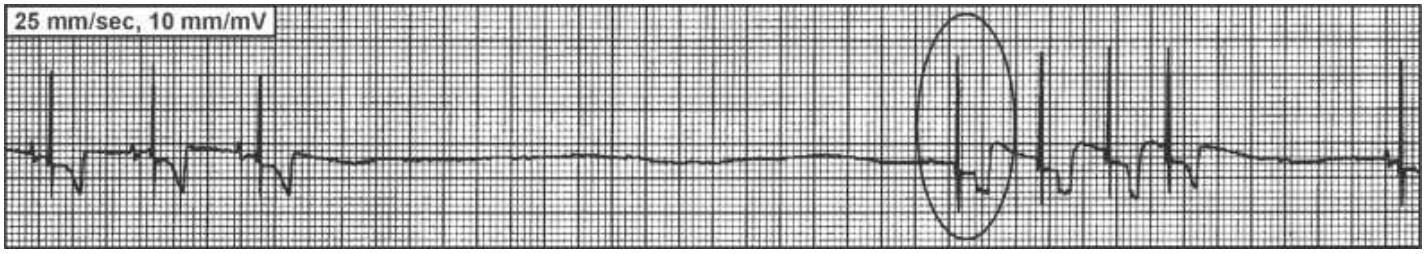
The two most common clinical contexts that would raise the suspicion of this disorder are a history of syncope in a dog of a susceptible breed, or incidental discovery of a bradycardia. The diagnosis is confirmed electrocardiographically. In some patients, an in-hospital resting electrocardiogram (ECG) is sufficient; in others, the intermittent nature of the arrhythmia mandates the use of telemetry or ambulatory ECG.

DIFFERENTIAL DIAGNOSIS

- Other bradyarrhythmias:
  - Third-degree AV block
  - Persistent atrial standstill
  - Vagally mediated bradyarrhythmias
  - Metabolic disorders that may slow SA nodal activity:
    - Hyperkalemia, see p. 556
    - Hypothermia, see p. 587
    - Hypothyroidism, see p. 588
    - Hypoadrenocorticism, see p. 573
    - Dysautonomia, see p. 325
- Seizures of any etiology (see p. 1009)

INITIAL DATABASE

- ECG: characterize the bradyarrhythmia:
  - ECG is the diagnostic test of choice for SSS.
  - Although exact criteria have not been established for the diagnosis of SSS, sinus arrest with or without variable degrees of atrioventricular block or supraventricular tachycardia should raise the suspicion of SSS.
- Atropine response test: determine if the bradyarrhythmia is wholly or partially vagally mediated. If the bradyarrhythmia is vagally mediated (i.e., physiologic), the test reveals a positive response in the form of sustained sinus tachycardia. If it is pathologic, the test reveals no change in the ECG.
  - Obtain initial ECG.
  - Administer atropine, 0.04 mg/kg IV, IM, or SQ.
  - Obtain follow-up ECG approximately 10 minutes later if administered IV, or 20-30 minutes later if administered IM or SQ.
  - An increase of at least 50% in the heart rate is expected when the bradycardia is vagally mediated and therefore physiologic but also occurs in a certain number of dogs with SSS. The absence of any response to atropine in a dog with appropriate signalment and clinical signs is strongly suggestive of SSS.
- CBC, serum chemistry profile, and urinalysis to detect underlying electrolyte imbalances or metabolic disorders that may contribute to bradyarrhythmias or seizures.
- Thoracic radiographs: cardiomegaly or CHF may develop in the face of longstanding bradyarrhythmias, especially when complicated by valvular disease in older small-breed dogs.
- Echocardiography to assess the severity of valvular, myocardial, or structural (including neoplastic) cardiac disease if present.



SICK SINUS SYNDROME A dog with bradycardia-tachycardia sick sinus syndrome displays a prolonged period of sinus arrest followed by a supraventricular escape beat *(circled complex)* and a short run of accelerated supraventricular complexes thereafter.

ADVANCED OR CONFIRMATORY TESTING

- Videotaping of episodes by the owner may help differentiate syncope from seizures if the episodes occur infrequently and are not clearly one or the other based on historic description alone.
- A 24-hour Holter monitor or cardiac event monitor may be indicated in cases where the history, clinical signs, ECG, and atropine response test are inconclusive (see p. 1287).

TREATMENT

TREATMENT OVERVIEW

- Dogs showing no overt clinical signs (arrhythmia was discovered incidentally): periodic monitoring and client education to detect progression of disease
- Dogs showing overt clinical signs such as syncope:
  - Bradycardia: increase the heart rate to alleviate the syncopal episodes.
  - Brady-tachy syndrome: therapy aimed at reducing the supraventricular tachycardia (see p. 111) may be required after resolution of the bradyarrhythmia.

ACUTE GENERAL TREATMENT

- Dogs showing no overt clinical signs: in the absence of syncope, significant cardiomegaly, or CHF, periodic ECGs and client education are

indicated. General anesthesia should be avoided, or if indispensable, should be done with concurrent temporary cardiac pacing (see p. 1320).

- Dogs showing overt clinical signs:
  - Vagolytic drugs display variable and often temporary efficacy in animals with SSS. One option is to begin with a sympathomimetic (e.g., theophylline or terbutaline), and if clinical signs persist, add a parasympatholytic (anticholinergic; e.g., propantheline):
    - Theophylline: 10 mg/kg PO q 8 h
    - Terbutaline (instead of theophylline): 0.2 mg/kg PO q 8-12 h
    - Propantheline bromide: 0.25-0.5 mg/kg PO q 8 h
  - Pacemaker implantation: dogs with overt clinical signs caused by SSS require permanent cardiac pacing if they fail to respond or become refractory to vagolytic drugs.

CHRONIC TREATMENT

- Vagolytic drugs: if animals are responsive, therapy will be maintained lifelong; refractoriness may develop over time, however.

DRUG INTERACTIONS

- Theophylline:
  - Arrhythmias may develop when used with additional sympathomimetics.
  - Cimetidine, erythromycin, allopurinol, thiabendazole, clindamycin, and lincomycin may increase its effects.
  - Phenobarbital or phenytoin may decrease its effects.
  - Enrofloxacin or ciprofloxacin inhibit the metabolism of theophylline and may promote toxicity.
- Terbutaline:
  - Arrhythmias may develop when used with additional sympathomimetics or digitalis glycosides.
  - Tricyclic antidepressants or monoamine oxidase inhibitors (MAOIs) may potentiate the vascular effects.
- Propantheline bromide:
  - Antihistamines, procainamide, quinidine, meperidine, benzodiazepines, and phenothiazines may enhance its activity.
  - Primidone, disopyramide, nitrates, and long-term corticosteroid use may potentiate its adverse effects.
  - May enhance the actions of nitrofurantoin, thiazide diuretics, and sympathomimetics

POSSIBLE COMPLICATIONS

- Tachyarrhythmias, nervousness/anxiety, vomiting, diarrhea, polyuria and polydipsia (PU/PD), and anorexia with administration of sympathomimetics
- Tachyarrhythmias, dry mouth, dry eyes, urinary hesitancy, constipation, and vomiting with administration of anticholinergics such as propantheline bromide
- Pacemakers: lead dislodgement, infection, failure to sense or oversensing, ventriculoatrial conduction, caval obstruction, or skeletal muscle stimulation (if a unipolar pacemaker is implanted)

RECOMMENDED MONITORING

- ECG: periodic monitoring or as dictated by recurrence of syncopal episodes:
  - Animals showing no overt clinical signs: every 3-4 months to evaluate for progression of bradyarrhythmia-tachyarrhythmia; atropine response test may have to be repeated.
  - Animals showing overt clinical signs: whether medical therapy or pacemaker implantation has been performed, ECGs should be repeated every 6 months to assess the long-term response to vagolytic agents or appropriate functionality of the pacemaker.
  - If clinical signs recur, reexamination including ECG is indicated immediately.
- Thoracic radiographs: every 6 months, especially in the face of valvular disease; assessment for progressive cardiomegaly and CHF, assessment of the integrity of the pacemaker.
- Pacemaker interrogation: every 6 months; evaluation of the pacing threshold, lead impedance, and battery life.

PROGNOSIS AND OUTCOME

- The risk of sudden death with SSS appears low, and some affected animals never develop clinical signs.
- If syncope is present, the episodes tend to increase in frequency over time, and the risk of sudden death is greater.
- Medical therapy is usually well tolerated, although the response is variable and in some cases short-lived.
- The prognosis and response to therapy following successful pacemaker implantation are good for animals with SSS. Episodes of syncope tend to resolve, animals become much more suitable anesthetic candidates, and episodes of supraventricular tachycardia can be managed with medications if necessary.

PEARLS & CONSIDERATIONS

COMMENTS

- Seizures and syncope can be very difficult to differentiate.
- SSS should always be on the differential list for older miniature Schnauzers, Westies, and cocker spaniels that display seizure-like activity.
- A normal heart rate at the time of examination does not exclude SSS.
- Even in the absence of syncope during Holter monitoring, many animals with SSS display significant and prolonged episodes of sinus arrest.

Analysis of the Holter recording is still warranted when no episodes have occurred during the monitoring period.

- While ventricular-based pacemakers readily alleviate the clinical signs, atrial-based pacing may be the most appropriate if AV nodal function is normal.

CLIENT EDUCATION

Artificial pacemaker implantation is most commonly performed via a transvenous approach, therefore markedly reducing the pain and recovery time for older dogs.

SUGGESTED READING

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AUTHOR: BARRET J. BULMER

EDITOR: ETIENNE CÔTÉ

Shoulder Luxation

BASIC INFORMATION

DEFINITION

Traumatic or congenital scapulohumeral luxation

EPIDEMIOLOGY

SPECIES, AGE, SEX: Traumatic luxation can occur in dogs of all sizes and ages; rare in cats.

GENETICS & BREED PREDISPOSITION: Congenital luxation occurs most often in small dogs. Toy poodles and Shetland sheepdogs appear predisposed.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Any direction for traumatic luxation; in congenital luxation, humerus is usually displaced medially.

HISTORY, CHIEF COMPLAINT: Traumatic luxations cause acute non-weight-bearing lameness. Congenital luxation will cause intermittent or continuous lameness of variable degree and associated pain.

PHYSICAL EXAM FINDINGS

- Animals that have gone through trauma can experience pain and crepitus during shoulder manipulations. Dogs carry the limb in flexion with the foot externally rotated (medial luxation) or internally rotated (lateral luxation). The greater tubercle is displaced relative to the acromion.
- Dogs with congenital luxation may be comfortable during shoulder manipulation; the joint is luxated and reduced easily.

ETIOLOGY AND PATHOPHYSIOLOGY

- Humerus is medially displaced in 75% of cases.
- Medial luxation in small dogs is congenital and associated with developmental laxity or dysplasia of the glenoid cavity; often occurs bilaterally.
- Medial luxation in large-breed dogs is caused by trauma.
- Lateral luxation is caused by trauma and is associated with disruption of the lateral joint capsule, lateral glenohumeral ligament, and infraspinatus tendon.
- Cranial and caudal luxations are rare and are caused by trauma.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Shoulder luxation is diagnosed by physical and radiographic examinations.

DIFFERENTIAL DIAGNOSIS

- Scapular neck or glenoid fractures
- Fracture of proximal humerus
- Bicipital tenosynovitis
- Supraspinatus degeneration or mineralization
- Osteosarcoma of proximal humerus
- Brachial plexus avulsion
- Nerve root signature in the forelimb

INITIAL DATABASE

- Orthopedic and neurologic evaluations

- Radiography of the scapulohumeral joint, orthogonal views
- CBC, serum biochemistry panel, urinalysis: in older dogs or trauma cases
- Electrocardiogram (ECG) and thoracic radiographs if trauma is suspected

ADVANCED OR CONFIRMATORY TESTING

- Evaluate shoulder "drawer movement" by cranial, caudal, medial, and lateral displacement of the humerus relative to the scapula.
- Test medial instability by abduction of the humerus relative to the scapula.
- Stress radiography

TREATMENT

TREATMENT OVERVIEW

The goal is to reserve integrity of the scapulohumeral joint or pain-free use of the affected limb. In the acutely luxated shoulder, closed reduction should be attempted prior to surgery. In congenital luxation with dysplasia, closed reduction is not successful.

ACUTE GENERAL TREATMENT

- Traumatic luxation without glenoid dysplasia can be reduced closed. If the joint reluxates easily during manipulation or in the postanesthetic period, surgery is indicated.
- Surgical options in traumatic luxations or congenital luxations with good joint integrity include primary repair of joint capsule/ligaments and stabilization by transposition of the biceps tendon, or prosthetic suture repair of the glenohumeral ligament. Temporary stabilization with locking plate has also been described.
- Congenital luxations with glenoid dysplasia are not suitable for closed reduction and require surgery if pain or decreased function of the limb is present. Surgical options include excision arthroplasty and shoulder arthrodesis.

CHRONIC TREATMENT

- Conservatively or surgically (biceps tenodesis, ligament prosthesis) managed dogs are immobilized with a spica splint (lateral luxations) or Velpeau sling (medial luxations) for 10-14 days (see p. 1336). Exercise is restricted for 4-8 weeks after splint or sling removal. Physical therapy with passive range-of-motion exercises and swimming are recommended after immobilization.
- Excision arthroplasty cases should be walked using a leash after surgery. Swimming or other vigorous exercise is encouraged starting 10 days after surgery.
- After shoulder arthrodesis, the limb is immobilized in a spica splint until radiographic signs of fusion are present.

NUTRITION/DIET

Dietary management to prevent or treat obesity is beneficial for long-term management.

BEHAVIOR/EXERCISE

After healing is complete, consistent daily low-impact physical activity (walking, swimming, running on soft surfaces) is recommended.

POSSIBLE COMPLICATIONS

- Seroma
- Midsubstance tearing of the biceps tendon after tenodesis
- Articular incongruity causing osteoarthritis
- Suprascapular nerve damage with prosthetic repair
- Fixation failure
- Infection

RECOMMENDED MONITORING

- With conservative management, routine reexamination of the joint is indicated to ensure stable reduction.
- Shoulder arthrodesis cases need monthly radiographic examination starting at week 6 until fusion has occurred.

PROGNOSIS AND OUTCOME

- Animals with biceps tenodesis have good to excellent outcomes in 60% (3/5 dogs), 84% (42/50 dogs), and 93% (11/12 dogs) of cases. A small number of dogs with prosthetic glenohumeral ligament (GHL) repair have had good and excellent results.
- Salvage procedures are rarely performed and may provide adequate function in small dogs; limb amputation is an option in unilateral cases.

PEARLS & CONSIDERATIONS

COMMENTS

- A Velpeau sling is contraindicated for lateral luxations due to lateral translation of the humeral head.
- Radiography helps identify articular fractures or glenoid dysplasia before joint stabilization is attempted.

SUGGESTED READING

Pucheu B, Duhautois B: Surgical treatment of shoulder instability. Retrospective study of 76 cases (1993-2007). Vet Comp Orthop Traumatol 21:368–374, 2008.

AUTHOR: BOEL A. FRANSSON

EDITOR: JOSEPH HARARI

Shock, Hypovolemic

BASIC INFORMATION

DEFINITION

Inadequate circulating blood volume due to intravascular volume loss or redistribution

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Affects all species, ages, and sex
- Underlying causes of shock may differ in different age groups (e.g., trauma may be most common in young to middle aged patients, but internal hemorrhage from a ruptured neoplasm is likely more common in older patients).

RISK FACTORS

- Free-roaming dogs and cats are more likely to sustain trauma.
- Underlying polyuria/polydipsia conditions (e.g., diabetes mellitus, chronic kidney disease) may predispose patients to severe dehydration if access to water is limited.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Absolute with actual loss of intravascular blood volume (hemorrhage)
- Relative with loss of plasma volume (severe dehydration or loss into third space)
- Minimal or no information in veterinary medicine to correlate subtype with prognosis/outcome.

HISTORY, CHIEF COMPLAINT

- Witnessed or suspected trauma (internal or external hemorrhage)
- Acute collapse (any nontraumatic type of volume loss, such as ruptured internal neoplasia or anticoagulant rodenticide intoxication)
- Abdominal distension, typically acute onset (hemoperitoneum, gastric dilatation-volvulus [GDV])
- Vomiting/diarrhea (primary gastrointestinal, commonly obstruction with foreign material or as a manifestation of gastrointestinal hypoperfusion)

PHYSICAL EXAM FINDINGS

- All cases:
  - Quiet or dull mentation
  - Tachycardia, or some cats may develop bradycardia.
  - Weak pulses
  - Pale mucous membranes
  - Tachypnea
- Possible:
  - Distended abdomen (in cases of hemoabdomen or GDV)
  - Signs of external bleeding
  - Signs of severe dehydration: enophthalmos, skin tenting, dry mucous membranes

ETIOLOGY AND PATHOPHYSIOLOGY

- Causes of excess vascular volume loss include:
  - Trauma
  - Ruptured neoplasms
  - Coagulopathies with hemorrhage into body cavities (e.g., anticoagulant rodenticide intoxication)
  - Vomiting ± diarrhea

  - Burns
  - Plasma volume loss into third space (peritoneum or gastrointestinal tract)
- Pathophysiology of hypovolemic shock:
  - A decrease in effective circulating volume leads to decreased tissue perfusion.
  - Decreased tissue perfusion leads to a decrease in oxygen supply to cells.
  - Inadequate energy consumption at the cellular level results in a conversion from aerobic to anaerobic metabolism and decreased adenosine triphosphate (ATP) production.
  - Decreased ATP production alters cellular function, leading to alterations in intracellular calcium homeostasis; this process in turn leads to direct cellular injury, enzyme activation, release of reactive oxygen species, and inhibition of oxidative phosphorylation.
  - Cell death can precipitate a cascade of events, such as activation of the coagulation cascade or bacterial translocation in the gut, which then may result in multiorgan damage and death.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is largely dependent on history and physical examination (suspected possible source[s] of fluid loss) and is confirmed with blood pressure measurement, routine laboratory testing and imaging, and response to treatment.

DIFFERENTIAL DIAGNOSIS

Other forms of shock: distributive (loss of local or systemic vascular resistance), septic, cardiogenic, neurogenic, anaphylactic, hypoxemic, or metabolic shock (specifically disrupted cellular metabolism, such as cyanide toxicity or mitochondrial dysfunction)

INITIAL DATABASE

- Packed cell volume/total solids (PCV/TS) and blood glucose: low or decreasing PCV/TS may indicate blood loss; increased PCV/TS likely indicates dehydration.
- CBC, serum chemistry profile, coagulation profile (prothrombin time and activated thromboplastin time): prolonged clotting times may indicate internal blood loss as a cause for hypovolemia and may raise concerns for anticoagulant rodenticide ingestion. Electrolyte disturbances (hypochloremia) may be present with severe vomiting or upper gastrointestinal obstruction.
- Blood pressure (BP): low BP (<90 mm Hg systolic assessed via Doppler [p. 1209] or direct arterial line [p. 1196]) is consistent with hypovolemic shock.
- Abdominocentesis (see p. 1193)/thoracocentesis (see p. 1338) with fluid analysis: if hemorrhagic effusion is obtained, intracavitary hemorrhage as a cause of the hypovolemia should be considered. Coagulation testing is recommended prior to paracentesis if an effusion is found in a young animal or if there is any possible anticoagulant rodenticide exposure.
- Abdominal and thoracic radiographs: evaluate for peritoneal effusion or gastrointestinal disease/obstruction; also scan for metastatic disease, and evaluate cardiac and pulmonary vasculature size for underlying heart disease and hydration status.
- Lactate analysis: elevated blood lactate (>2.5 mmol/L) supports hypovolemia and decreased tissue perfusion, but extraneous factors (e.g., struggling during phlebotomy) may raise lactate levels. However, increased lactate levels in a collapsed pet are vital clues.
- Mixed venous oxygen saturation: assessment of global tissue oxygenation (decreased oxygen saturation generally reflects decreased tissue oxygen delivery). May be an earlier and more sensitive indicator of patient condition and resuscitative efforts.

ADVANCED OR CONFIRMATORY TESTING

- Abdominal ultrasonography to better evaluate cause in intracavitary effusions or further evaluation for gastrointestinal obstruction (if radiography is inconclusive)
- Histopathologic examination if neoplasia is suspected

TREATMENT

TREATMENT OVERVIEW

- The primary goal is to restore circulating blood volume, thus increasing tissue perfusion. This usually means rapid and continued IV fluid or blood product administration with frequent reevaluation of patient status and parameters.
- Specific treatment of any underlying disease, such as plasma and vitamin K1 for anticoagulant rodenticide intoxication.

ACUTE GENERAL TREATMENT

- The best fluid for restoration depends on:
  - Cause of hypovolemia
  - Serum electrolyte status of animal
  - PCV/TS
- If the animal is bleeding, fresh whole blood or packed red cells ± plasma is the best replacement fluid.
- Give fluids to reach an adequate BP (systolic arterial pressure >90 mm Hg) and central venous pressure (CVP > 5 cm H2O).
- Restoration of volume can include the following fluid types:
  - Crystalloids: requires a replacement fluid (e.g., lactated Ringers, 0.9% NaCl):
    - 40-90 mL/kg IV to reach desired effect
  - Synthetic colloids (e.g., Voluven, Hetastarch):
    - 5-20 mL/kg IV to reach desired effect, up to 50 mL/kg/24 h for Voluven
  - Blood (see p. 1347)
  - Plasma may be required if massive quantities of crystalloids, synthetic colloids, or blood have been given to an animal, and the animal has developed a dilutional coagulopathy.
- Locate and control any source of hemorrhage.

CHRONIC TREATMENT

Unless cause of fluid loss is located and controlled, fluid replacement must continue past initial stabilization to meet ongoing loss and maintenance fluid needs.

POSSIBLE COMPLICATIONS

Complication of prolonged shock include:

- Renal failure
- Loss of gastrointestinal integrity, with bacteria and toxin translocation
- Myocardial dysfunction
- Brain ischemia
- Loss of vascular tone
- Systemic inflammatory response syndrome (see p. 1070)
- Disseminated intravascular coagulation
- Acute lung injury
- Sepsis

RECOMMENDED MONITORING

- Serial BP monitoring, either indirectly or directly, until goal-directed end-point is reached (systolic > 90 mm Hg).
- Monitor heart rate: persistent tachycardia may indicate inadequate fluid loading.
- Recognize that persistent hypotension or tachycardia often implies ongoing hemorrhage, systemic vasodilation, or capillary leakage and the need for continued volume resuscitation and end-point monitoring.
- Monitor PCV/TS for evidence of adequate fluid therapy.
- Utilize trends in central venous pressure as an indicator of volume status (a central multilumen catheter is also recommended for rapid fluid administration and frequent blood sampling). see p. 1227. If the CVP is <5 cm H2O, more fluids should be given. Adequate fluid resuscitation is generally present if the CVP is between 5 and 10 cm H2O.
- Repeat blood gas (including central venous oxygen saturation), electrolytes, and lactate monitoring recommended to ensure return of adequate tissue perfusion and correct electrolyte imbalances.
- Monitor for signs of end-organ damage (e.g., urine output and decreased mentation), as these may carry a poor prognosis.

PROGNOSIS AND OUTCOME

- Determined by the cause of the hypovolemia and the rapidity with which the volume deficit has been corrected
- Prolonged hypotension may cause multiple organ dysfunction, which carries a poor prognosis.

PEARLS & CONSIDERATIONS

COMMENTS

- Hypovolemic shock is a potentially life-threatening process that requires early identification and treatment.
- Tachycardia (or bradycardia in the cat) together with low BP and a known cause of fluid loss are hallmarks for diagnosis of hypovolemic shock.
- Essential elements for the successful management of hypovolemic shock are identification of the source of fluid loss and reversal/replacement of the fluid loss.
- Treatment of the underlying cause is the key to long-term success.

TECHNICIAN TIPS

- Treatment of hypovolemic shock requires a concerted effort by clinician and technical staff to quickly obtain diagnostic information, place intravenous (and ideally intraarterial) catheters, prepare IV fluid or blood-product setups, and monitor and frequently recheck patient status and parameters. This can be an exciting and rewarding disease process to treat.
- Repeated reassessment of the initial plan is of utmost importance to ensure adequate resuscitation. This means automatically rechecking the parameters discussed above (mentation, HR, BP, pulse quality, mucous membrane color, and capillary refill time) when initial treatment is completed and alerting the clinician when parameters are persistently abnormal.

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1ST EDITION AUTHOR: BENJAMIN DAVIDSON

Shearing/Degloving Wounds

Additional Images Available on Website 

Client Education Sheet Available on Website 

BASIC INFORMATION

DEFINITION

Soft-tissue injury to the limbs and tail as the result of external trauma

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs and cats of any age and either sex

RISK FACTORS: Dogs and cats that are allowed to roam in unconfined areas without supervision or leash restriction

GEOGRAPHY AND SEASONALITY: Vehicular trauma is the primary cause of external trauma; dogs and cats are most susceptible to injury in areas with high traffic.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES:

Any of the following is/are possible: laceration, contusion, crushing, shearing, penetration, perforation, avulsion, thermal injury, bite

HISTORY, CHIEF COMPLAINT

- An open wound, bleeding, or swelling to the injured area
- Presence of necrotic tissue
- Absence or avulsion of tissue
- Presence of purulent discharge
- Lameness may be noted in association with a limb injury.
- The patient may display pain by vocalization, guarding the injured area, or defensive posturing.

PHYSICAL EXAM FINDINGS

- Open wounds:
  - Skin laceration
  - Partial or complete loss of skin and underlying tissues
  - Avulsion or partial detachment of skin segments
  - Entry or exit wounds secondary to a bite, projectile, or impalement injury
  - Presence of necrotic tissue
  - Older wounds may have variable development of granulation tissue.
- Evidence of previous or ongoing hemorrhage
- Intact skin but the presence of contusion (ecchymosis/bruising)
- Local swelling due to edema, hematoma formation
- Condition and viability of the digital and metacarpal/metatarsal pads; severity of tissue trauma
- Evidence of underlying orthopedic injury:
  - Fracture
  - Joint instability associated with soft-tissue trauma
- Pain:
  - Possibly in association with manual examination of the injury or use of the affected limb(s)
- The overall health status of the animal depends on a variety of factors, including:
  - Body region(s) involved
  - Extent of the trauma
  - Degree of circulatory compromise
  - Blood loss
  - Presence of necrotic tissue/infection

ETIOLOGY AND PATHOPHYSIOLOGY

- Wounds are the result of the transfer and absorption of energy by the body; severity of trauma depends on exact type of trauma and surface area(s) absorbing the trauma.

- Lacerations may be the result of contact with a sharp, bladelike object (glass, metal, etc.) or impact against a hard-edged surface. Bite wounds may create an irregular laceration as a result of the cutting and tearing of tissues.
- Crushing wounds are the result of compression; these can result from impact with a heavy object or contact with a mechanical device; the wounds can also be caused by a powerful bite.
- Cutaneous surfaces may be stripped or avulsed from the extremity, damaging the circulation to the traumatized skin segment. This is often the result of vehicular or bite trauma.
- Shearing wounds may be the result of tangential impact with a hard surface, dragging of a body region on a hard road surface, or entrapment of an extremity beneath the tire of a moving vehicle.
- Assessment of circulation at the time of injury can be difficult. Progressive loss of circulation can result in vascular stasis and necrosis that may not be evident for 4-5 days after the initial injury.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is made from the history and physical exam, although the full extent of bony lesions and other internal injuries may only be appreciated with radiographs and/or ultrasound.

DIFFERENTIAL DIAGNOSIS

Common causes of soft tissue trauma include:

- Vehicular trauma
- Bite wounds
- Penetrating/perforating objects (gunshot, impalement)
- Sharp objects
- Thermal injuries including contact burns

INITIAL DATABASE

- CBC and serum biochemistry profile:
  - Minimum database is indicated.
- Urinalysis would be advisable in pets with extensive trauma or a history/physical findings of renal disease.
- Radiographs (two views) of the injured area:
  - Rule out underlying orthopedic trauma.
- Survey thoracic radiographs:
  - Rule out diaphragmatic hernia, lung contusions, pneumothorax, and other lesions in the face of vehicular trauma.

ADVANCED OR CONFIRMATORY TESTING

The severity of trauma will dictate whether additional diagnostic imaging techniques are required.

TREATMENT

TREATMENT OVERVIEW

Treatment goals:

- Ensure that the animal is hemodynamically stable before inducing general anesthesia, as other injuries (pneumothorax, hemothorax, diaphragmatic hernia, etc.) may be present.
- Assess severity of soft-tissue and orthopedic trauma.
- Assess wound for tissue viability.
- Provide definitive wound care and closure.
- Prevent or manage infection.
- Stabilize local fractures or joint instability.

ACUTE GENERAL TREATMENT

- Cover open wounds with a sterile dressing.
- Initiate systemic antibiotic therapy:

- Empirical therapy to provide broad aerobic coverage (e.g., cefazolin, 22 mg/kg IV q 2 h during the perioperative period)
- Definitive therapy for infected wounds should be based on the results of microbiologic culture and sensitivity (C&S) testing.

- General anesthesia is preferable for definitive wound care because both the wound and manipulations of the wound can be painful.
- Culture of infected wounds may be useful to select the most appropriate antibiotic.
- Liberally remove fur from around the circumference of a shearing wound.
- Povidone iodine or chlorhexidine surgical scrub is used for preparing the skin, alternated with swabbing the area with sterile saline impregnated sponges.
- Aseptically drape the wound.
- Explore the wound and remove nonviable tissue and foreign debris:
  - Perform copious lavage of the wound with sterile saline to remove contaminants:
    - Chlorhexidine solution (1:40 dilution) or povidone iodine solution (1:9 dilution) may be added to the sterile saline.
    - Gentle pressure lavage is useful for removal of contaminants, using a 35-cc syringe and 18-G needle.
- In the absence of infection and necrotic tissue (creating a “surgically clean” wound):
  - Skin borders can be approximated with sutures.
  - If significant incisional tension is present secondary to unresolved edema and swelling, consider partial closure or delayed primary closure.
  - Wound drainage should be established with the use of drains or leaving a portion of the wound open for drainage.
- Joint injury in association with shearing wounds:
  - Repair collateral ligament support using conventional bone screws and braided suture material; stainless steel also may be used. Persistently unstable joints may be candidates for arthrodesis.
  - Perform copious lavage for open joints; in the absence of infection, the joint capsule can be closed if feasible.
- With extensive bruising and swelling, open wound management should be considered until circulation improves, noted by resolution of these two conditions.
- Open wound management varies with severity of trauma and extent of wound. Common options include:
  - Judicious surgical débridement with resection of nonessential tissues of questionable viability
  - Especially with extremity wounds, it may be advisable to delay débridement of skin of questionable viability (daily reassessment) owing to the limited availability of loose elastic skin to facilitate wound closure.
  - Important tissue structures of questionable viability should be managed conservatively until their status becomes apparent. If necrotic, débridement is instituted.
  - Wet-to-dry dressings are considered a form of “mechanical débridement” and may be used effectively in the presence of extensive contamination/local infection. Cotton sponges are moistened with saline (or dilute povidone iodine or chlorhexidine [see above]) and are placed onto the wound. Residual necrotic tissue adheres to the cotton fibers along with partial retention of the exudate. Stripping the partially dry dressing off the wound helps remove this wound debris.
    - The author normally uses wet-to-dry dressings for no longer than 5 days: by then, they usually have accomplished their task.
    - Sedation and analgesics, including topical lidocaine, can reduce the pain associated with their removal and replacement.
  - Other suitable dressings and topical agents:
    - Hydrogel and hydrocolloid products: topical application or in the form of an occlusive dressing. Many of these products include various agents that reportedly “promote” healing.
    - Occlusive dressings are most effective when a healthy granulation bed is forming and infection/tissue necrosis are not present.
    - Absorptive dressings, including the alginates, can be used to promote healing and provide a matrix to absorb discharge.
    - Application of honey (especially Manuka honey) or sugar. These substances are both antibacterial and hydrophilic.
    - Nonadherent (low-adherent) dressings with a topical antimicrobial ointment or gel create an occlusive or partially occlusive environment.
  - A protective bandage is often required to maintain a topical dressing and minimize motion. Thicker absorptive bandages normally are used for facilitating retention of discharged from exudative wounds; lighter bandages are required as discharge progressively decreases as healing progresses.
    - Typically, bandage changes may be needed daily (1-2 times) over the first week of open wound management, with decreasing frequency over the subsequent weeks.
    - Occlusive dressings are normally changed according to the manufacturer's guidelines and the judgment of the clinician; may be changed every 3-5 days. Any cover bandage is changed accordingly.
  - Large open wounds affecting may require closure with skin grafts or skin flaps if contraction and epithelization are not suitable options:
    - In general, wounds affecting less than 90° of the extremity's circumference may heal by second intention, often within 6 weeks after injury.
  - Extensive extremity trauma with severe circulatory compromise and tissue necrosis usually necessitates amputation. The total costs of limb salvage (treatment without amputation) play a role in the decision-making process with many

pet owners.

CHRONIC TREATMENT

- Bandage and dressing changes
- Skin grafts or flaps may be needed for shearing wounds with extensive skin loss as well as nonhealing wounds.

POSSIBLE COMPLICATIONS

- Infection of the soft tissues, underlying bone, or exposed joint
- Failure to heal
- Persistent instability of a shearing wound involving a joint
- Associated fracture nonunion

RECOMMENDED MONITORING

- Bandage care and periodic wound assessment
- Serial radiographs to assess bone healing as needed

PROGNOSIS AND OUTCOME

- Massive trauma to the extremities may necessitate limb amputation.
- Progressive loss of circulation may necessitate serial débridement of the wound or eventual amputation.
- Many shearing wounds will heal by second intention.
- As noted, failure to heal usually necessitates wound closure with a skin graft or flap.
- Severe joint injury/instability may require eventual arthrodesis.
- Wound contracture or the loss and inhibition of function secondary to scarring usually requires surgical intervention combined with physical therapy.
- Loss of the weight-bearing metacarpal or metatarsal pad usually warrants reconstruction, either by digital pad transfer or pad grafts when applicable.

PEARLS & CONSIDERATIONS

COMMENTS

- Most cases of soft-tissue trauma that are presented to veterinarians are relatively simple to manage.
- Confusion occasionally arises with extensive wounds, for which the full extent of the injury is difficult to assess at presentation.
- In the face of infection, open wound management provides optimal drainage and facilitates daily inspection of the entire wound.
- Combined closure techniques can be used effectively together. In some cases wounds can be supported while second intention healing progresses. If the wound does not close after 6 weeks, the wound likely will be smaller; closure may be accomplished using a smaller local flap or skin graft.
- In general, the goal of wound care is to promote formation of a healthy wound bed. In open wound management, the formation of granulation tissue is a key indicator of underlying tissue viability. Moreover, the wound may then be a suitable candidate for surgical closure.
- With the formation of a healthy granulation bed, systemic antibiotics are usually discontinued unless they are indicated for a related/unrelated infection.
- Surgical closure of problematic wounds may be more cost-effective than prolonged open wound management.

PREVENTION

Most wounds occur in pets that are permitted to roam unsupervised. Confining the pet to the house or yard or accompanying the pet on a leash dramatically reduces risks associated with vehicular trauma, bites, and malicious injury.

CLIENT EDUCATION

- Discuss the safety and prevention issues noted above.
- In open wound management, many willing owners can be trained to perform simple bandage changes and manage wound drains. Costs can therefore be reduced.

SUGGESTED READING

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AUTHOR: MICHAEL PAVLETIC

EDITOR: RICHARD WALSHAW

Shar-Pei Fever

BASIC INFORMATION

DEFINITION

A familial, sterile, systemic inflammatory disorder characterized by recurrent fever, swelling of the tibiotarsal joints, and renal amyloidosis

SYNONYM

Familial amyloidosis of Chinese shar-pei dogs. Resembles familial Mediterranean fever of humans.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Young adults, 1 to 5 years old

GENETICS & BREED PREDISPOSITION: Shar-pei dogs; unknown pattern of inheritance

ASSOCIATED CONDITIONS & DISORDERS: Vasculitis may occur concurrently.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Early stage: fever, tibiotarsal (hock) swelling
- Late stage: signs of renal amyloidosis, hepatic amyloidosis, or amyloid deposition in other organs

HISTORY, CHIEF COMPLAINT

- Early stage: signs due to intermittent fever lasting 24-36 hours (e.g., lethargy, inappetence)
- Late stage: signs of renal and liver failure; signs include vomiting, anorexia, lethargy, polyuria and polydipsia (PU/PD), and weight loss.

PHYSICAL EXAM FINDINGS

- Early stage: fever (103°F-107°F; 39.4-41.7°C); palpable swelling of tibiotarsal joints; swollen muzzle may be present.
- Late stage:
  - Signs of dehydration, halitosis, weight loss, and other manifestations of chronic kidney disease (see p. 207)
  - If nephrotic syndrome is present: ascites, peripheral edema possible; dyspnea may also develop secondary to pulmonary thromboembolism or (rarely) pleural effusion, which is generally small in volume.
  - Liver disease; icterus, hepatomegaly, signs of dehydration, weight loss

ETIOLOGY AND PATHOPHYSIOLOGY

- Elevated levels of the cytokine interleukin 6 alpha (IL-6a) are thought to lead to chronic overproduction of acute-phase reactant proteins (APP), the precursors of amyloid A.
- Amyloid is then deposited in many organs, and its presence in the kidneys usually leads to renal failure and death. Historically, renal amyloid deposition in shar-pei fever was thought to occur mainly in the medulla (unlike most other forms of renal amyloidosis); newer findings suggest that glornerular deposition is common and may surpass medullary deposition.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Shar-pei fever is a diagnosis of exclusion. The diagnosis is suspected in shar-peis presenting with a history of episodes of fever and lameness. A workup is directed toward detecting organ damage and ruling out other causes of fever, polyarthritis, azotemia, or liver disease.

DIFFERENTIAL DIAGNOSIS

- Polyarthritis (see p. 894)
- Lyme disease, ehrlichiosis (see, and 334)
- Other causes of fever (see, p. 389)
- Other causes of renal and liver disease

INITIAL DATABASE

- CBC may show an inflammatory leukogram and (in the presence of chronic kidney disease) nonregenerative anemia.
- Serum biochemistry profile: azotemia (blood urea nitrogen [BUN], creatinine elevation) if renal insufficiency; hypoalbuminemia and hypercholesterolemia with nephrotic syndrome
- Urinalysis: proteinuria possible. If proteinuria is present, culture and sensitivity (C&S) are indicated to rule out urinary tract infection and a urine protein/creatinine ratio to detect pathologic proteinuria, a hallmark of glomerular disease.
- Blood pressure (BP) measurement: to rule out systemic hypertension in cases with renal involvement
- Other tests to consider depending on signs and geographic location: *Borrelia*, *Ehrlichia*, *Leptospira*, and fungal titers; heartworm antigen test; and survey radiographs to screen for evidence of metastatic or fungal disease

ADVANCED OR CONFIRMATORY TESTING

- Abdominal ultrasound exam to evaluate kidney, liver, and other abdominal organs and screen for thrombi from urinary loss of antithrombin
- Renal biopsy: majority of these animals have moderate to severe amyloid deposition in the renal medulla; approximately two-thirds also have glomerular deposition of amyloid. This distribution helps increase diagnostic yield, because glomerular density is greatest in the cortex, and a renal biopsy must be limited to the renal cortex (i.e., the biopsy instrument must be oriented parallel to the long axis of the kidney) to avoid lacerating a renal arcuate artery.
- Consider a liver biopsy (generally safer than renal biopsies), especially if there are clinical and biochemical signs of hepatic dysfunction. Assessment of albumin level, coagulation parameters, and a platelet count must be performed first and abnormalities corrected prior to biopsy.
- Tissue biopsy is the only way to document the presence of amyloid (using Congo red stains).

TREATMENT

TREATMENT OVERVIEW

The three phases of treatment are acute care, prevention of deterioration, and supportive care in advanced cases as follows:

- Supportive care using nonsteroidal antiinflammatory drugs (NSAIDs) during fever and lameness episodes
- Attempt to prevent further amyloid deposition and subsequent organ failure with the use of colchicine.
- Management of chronic kidney or liver disease associated with late-stage disease is difficult and largely supportive.

ACUTE GENERAL TREATMENT

- If fever >105○F, the patient may need hospitalization and intensive antipyretic management (see pp. 389 and 480).
- Presentation in early stage, temperature £105°F (40.6°C): NSAIDs for fever (e.g., carprofen, 2.2 mg/kg PO q 12 h)
- Presentation in late stage, immediate supportive care:
  - Judicious use of IV fluids for volume resuscitation/rehydration and diuresis if renal failure. If nephrotic syndrome is present, fluids may worsen edema and be contraindicated.
  - Antacids if vomiting, anorexia, or other evidence consistent with uremic gastropathy (e.g., famotidine, 0.5 mg/kg PO or IV q 12-24 h)
  - Antihypertensives if systemic hypertension (e.g., enalapril 0.5 mg/kg PO q 24 h and/or amlodipine, 0.125-0.25 mg/kg PO q 24 h)

CHRONIC TREATMENT

- Colchicine, 0.03 mg/kg PO q 24 h for 2 weeks; if no gastrointestinal (GI) signs, may increase to 0.03 mg/kg PO q 12 h
  - Used in people with familial Mediterranean fever; no controlled trials in shar-pei dogs
  - Recommend early in the course of the disease to prevent or delay the development of amyloidosis; no effect on fibrosis once established
- Renal disease: see pp. 450, 205, and 207.
- Liver disease: dogs can respond to supportive care and colchicine therapy.

DRUG INTERACTIONS

Colchicine given with NSAIDs may increase myelosuppressive effects.

POSSIBLE COMPLICATIONS

- Colchicine in humans can cause anorexia, vomiting, diarrhea, renal failure, hepatotoxicity, pancytopenia, and paralysis.
- Vomiting and diarrhea have been reported in dogs taking colchicine and may resolve with dose reduction.

RECOMMENDED MONITORING

Periodic CBC, serum biochemistry profile, and urinalysis with urine protein/creatinine ratio

PROGNOSIS AND OUTCOME

- Early stage: guarded to fair long-term prognosis; colchicine may improve survival.
- Late stage: very poor; most dogs die of renal failure, and thromboembolism and hepatic rupture have also been reported.

PEARLS & CONSIDERATIONS

COMMENTS

- Shar-pei dogs with episodic fever are at high risk of developing amyloidosis.
- The most common cause of renal failure in shar-pei dogs is renal amyloidosis.

PREVENTION

- Removal of affected dogs from the breeding pool
- Colchicine treatment may help prevent or delay amyloidosis once early stage of disease is confirmed with biopsy.

CLIENT EDUCATION

- Closely monitor temperature of an animal during a fever episode.
- Monitor the patient's lab work if treating with colchicine.
- Inform the owner of the guarded long-term prognosis.

SUGGESTED READING

DiBartola SP, et al: Familial renal amyloidosis in Chinese shar-pei dogs. J Am Vet Med Assoc 197:483–487, 1990.

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EDITOR: SUSAN M. COTTER

Sepsis and Septic Shock

BASIC INFORMATION

DEFINITION

Sepsis is the occurrence of systemic inflammation in response to infection (see p. 1070). It generally implies systemic circulation of infectious agents (e.g., bacteremia). *Septic shock* is defined as sepsis with concurrent hypotension that is refractory to fluid therapy and requires vasopressor therapy.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs and cats of any age and either sex may develop sepsis or septic shock.

RISK FACTORS

- Animals with established infections
- Animals with diseases resulting in immunosuppression (such as hyperadrenocorticism or diabetes mellitus)
- Noninfectious diseases that may predispose an animal to bacteremia include neoplasia, glucocorticoid therapy, trauma, surgery, cytotoxic therapy, IV and urinary tract catheters, burns, and hematologic abnormalities (e.g., leukocyte function defects).

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Sepsis and early septic shock initially present a *hyperdynamic phase* characterized by increased metabolic processes: tachycardia, fever, warm extremities, injected mucous membranes, and a bounding pulse. If unchecked, the hyperdynamic phase progresses to a more critical and potentially terminal *hypodynamic phase* of septic shock characterized by normothermia or hypothermia, pallor, cool extremities, a weak or absent pulse, and decreased mentation.

HISTORY, CHIEF COMPLAINT: Complaints vary depending on the source of sepsis. Animals with abdominal sources of sepsis may present with vomiting, anorexia, or abdominal pain, while those with thoracic sepsis often present with a history of coughing, labored breathing/dyspnea, or respiratory distress. Sepsis from an occult source (anywhere in the body) may not produce localizing signs, and some animals with sepsis present with only vague signs of general malaise, such as anorexia and lethargy.

PHYSICAL EXAM FINDINGS

- General:
  - Hyperthermia (>104°F [>40°C]): fever in response to infection (hyperdynamic phase)
  - Hypothermia (<100.4°F [<38°C] in dogs, <100°F [<37.8°C] in cats): advanced stages, usually with visible lethargy, mental depression, or collapse (hypodynamic phase)
  - Tachycardia (although bradycardia may be present in cats with septic shock): by definition, as part of the systemic inflammatory response syndrome
  - Tachypnea, dyspnea: as compensation for metabolic acidosis, as a manifestation of pain, or with primary respiratory disease (e.g., pneumonia) as the source of sepsis/septic shock
  - Pulse and mucous membrane alterations:
    - Injected/red mucous membranes and bounding pulse (hyperdynamic phase)
    - Pale mucous membranes, slow capillary refill time (>3 seconds), weak pulse (hypodynamic phase)
  - Collapse (hyperdynamic or hypodynamic phase)
- Specific signs may indicate the source of infection, such as:
  - Abdominal pain or a distended abdomen (if present, abdominal source of sepsis is suspected)
  - Swollen limb or an infected cutaneous wound

ETIOLOGY AND PATHOPHYSIOLOGY

- Generalized infection leads to the release of inflammatory mediators, including tumor necrosis factor alpha (TNF-α), interleukin 1 (IL-1), and IL-6. These and other inflammatory mediators increase microvascular permeability, cause leakage of fluid from the vascular space, and lead to reduced effective circulating volume.
- Excessive nitric oxide production via the inducible nitric oxide synthase pathway results in arterial and venous vasodilation, reduced systemic vascular resistance, and eventually hypotension. Tachycardia and increased cardiac output occur as compensatory mechanisms for these changes, though these compensatory effects may be negated by reduced myocardial

contractility as a result of inflammatory mediators with myocardial depressant properties (e.g., TNF-α).
- Other physiologic changes in sepsis include stimulation of the coagulation cascade, reduction in endogenous anticoagulants such as protein C and antithrombin, hypoalbuminemia from changes in microvascular permeability and reduced production by the liver, and lung injury secondary to atelectasis or acute respiratory distress syndrome (ARDS).
- Ultimately, if left to progress, these serious changes lead to further reduced tissue perfusion and decreased oxygen delivery to tissues. Deprived of oxygen, tissues sustain terminal cellular injury, leading to the development of multiple organ failure (see p. 732) and death.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Sepsis should be suspected in a patient with two or more of the four following characteristics: an elevated or low temperature, tachycardia, tachypnea, and leukopenia or leukocytosis and/or the presence of bands and a documented infection. Septic shock should be considered in a septic patient who is hypotensive despite adequate fluid resuscitation.

DIFFERENTIAL DIAGNOSIS

Causes of:

- Fever (see p. 389)
- Abdominal pain without an infectious basis (pancreatitis, reno/ureterolithiasis, neoplasia)
- Abdominal distention (organomegaly, neoplasia, obesity, gastrointestinal [GI] obstruction, ascites secondary to cirrhosis or right-sided heart failure, hyperadrenocorticism)

INITIAL DATABASE

- CBC: neutrophilia (medium term) or neutropenia (acute sepsis) and the presence of band forms and toxic changes in neutrophils; thrombocytopenia suggests a hypercoagulable state or early disseminated intravascular coagulation (DIC).
- Serum biochemistry panel:
    - Azotemia (prerenal or renal—correlate to urine specific gravity >1.035 or <1.035, respectively).
    - Elevated liver enzymes (alanine aminotransferase [ALT] and aspartate aminotransferase [AST]) often occur secondary to hepatic hypoperfusion, hepatic thromboembolism, or bacterial showering from a compromised GI tract.
    - Hyperbilirubinemia due to sepsis-induced cholestasis or hemolysis (assess hematocrit)
    - Hypoalbuminemia: common as a result of reduced hepatic synthesis (in favor of acute phase protein production) and increased microvascular permeability
    - Hypoglycemia: common (changes in hepatic gluconeogenesis versus insulin-like growth factor [IGF] production).
- Elevated lactate is an important marker of hypoperfusion and is often elevated in dogs with sepsis.
    - Hyperlactatemia (>3.5 mmol/L) often resolves quickly following initiation of fluid therapy.
    - Increasing lactate despite fluid resuscitation is a negative prognostic indicator and should lead the clinician to seek superior treatment modalities or alternate reasons for deteriorating status.
- Urinalysis with culture and sensitivity (C&S) to help rule out genitourinary source of sepsis. Urine is obtained by cystocentesis to prevent contamination, unless pyometra, ascites, or a bleeding disorder is suspected.
- A coagulation profile helps identify animals with coagulopathy including DIC.
- Diagnostic imaging, including chest and abdominal radiographs and/or abdominal ultrasound, are often necessary to further elucidate the source of sepsis.

ADVANCED OR CONFIRMATORY TESTING

- Abdominocentesis (see p. 1193) should be performed in animals with abdominal effusion and fever. A neutrophilic effusion with intracellular bacteria is diagnostic of septic effusion, which essentially always warrants surgical intervention. The glucose level of septic abdominal fluid is typically <50 mg/dL (<2.8 mmol/L).
- Thoracocentesis to identify septic pleural effusion is indicated in animals with pleural effusion and fever.
- Echocardiography is indicated in animals whose source of fever is difficult to identify, especially when a new-onset murmur is noted in the absence of anemia. Echocardiographic lesions of the aortic valve are often consistent with bacterial endocarditis; less so mitral valve changes, which may be due either to infection or sterile myxomatous valve disease/endocardiosis.
- Blood cultures (four samples: aerobic and anaerobic, both drawn at time 0 and 2 hours later) are indicated in any critically ill animal that develops a fever, neutropenia, neutrophilia with a left shift, a new cardiac murmur, or other signs suggestive of sepsis that cannot be explained by a known preexisting condition.
- Arterial blood gas (ABG) measurement often may identify hypoxemia and metabolic acidosis, conditions commonly associated with sepsis and that may be corrected with treatment.

TREATMENT

TREATMENT OVERVIEW

- Hemodynamic resuscitation to correct intravascular volume deficits and maintain organ perfusion. IV fluids (crystalloids and colloids) are the mainstay of therapy.
- Eradication of the inciting infection using source control measures (e.g., surgery) and systemic antibiotic therapy
- A future direction and goal is modulation of the inflammatory response with interventions that target its specific mediators. Specific agents to target the inflammatory response are not readily available in veterinary medicine but continue to be a subject of intense research in the field of human medicine.

ACUTE GENERAL TREATMENT

- Antibiotic therapy: essential for successful treatment of sepsis. Two commonly used empirical combinations are a cephalosporin (cefazolin, 22 mg/kg IV q 8 h); a fluoroquinolone (enrofloxacin, 10 mg/kg [5 mg/kg in cats] diluted 1:1 in saline and given slowly IV q 24 h); and metronidazole (10 mg/kg given slowly IV q 8 h) or ampicillin (22 mg/kg IV q 6 h) along with an aminoglycoside (gentamicin, 6 mg/kg IV q 24 h, only when rehydrated/optimal renal function). Definitive antimicrobial treatment is based on C&S. Cardiovascular support: IV fluids to address hypotension/hypovolemia; crystalloids (e.g., lactated Ringer's solution, 0.9% NaCl) with or without a colloid (e.g., Hetastarch) are titrated to correct deficits (up to 90 mL/kg per hour initially in dogs and up to 70 mL/kg per hour in cats) until heart rate, blood pressure (BP), mentation, pulse quality, and capillary refill time have normalized. Central venous pressure (CVP) measurement is valuable if available (see p. 1227). If hypoperfusion persists despite appropriate fluid therapy, consider dobutamine (2.5-10 mcg/kg/min IV), dopamine (5-10 mcg/kg/min IV), norepinephrine (0.01-1 mcg/kg/min IV), or vasopressin (0.01-0.04 U/min IV).
- Surgery: after hemodynamic stabilization of the patient, a search for surgically correctable sources of infection is indicated and can be curative. (Coagulation abnormalities: see p. 1549.)
- Support of organ function: increased oxygen delivery to the tissues is critical to prevent organ dysfunction. Provide supplemental oxygen if hypoxemia is present, and mechanical ventilation if Pao2 < 60 mm Hg despite oxygen supplementation. GI dysfunction may lead to gastric ulcer formation or bacterial translocation; gastric protectants (e.g., famotidine, 0.5-1 mg/kg IV q 12 h) are routinely administered to reduce the risk of developing a gastric ulcer, while antibiotic therapy (as described previously) addresses bacterial translocation. Renal dysfunction associated with sepsis and septic shock may lead to oliguria and renal failure. Maintenance of mean arterial BP at >60 mm Hg using IV fluids and vasopressors may reduce the risk of acute renal failure.

NUTRITION/DIET

After stabilization, enteral nutrition is considered superior to parenteral nutrition in preservation of gut function and integrity, but parenteral nutrition should be considered in animals that are not expected to begin eating within several days.

POSSIBLE COMPLICATIONS

Recognized complications of sepsis and septic shock include DIC, MODS, acute renal failure, pulmonary thromboembolism, ARDS, and intractable hypotension leading to cardiac arrest.

RECOMMENDED MONITORING

- Heart rate and pulse quality: hourly or as indicated by case evolution
- Respiratory rate, mentation, BP, and central venous pressure: hourly or as dictated by case evolution
- Continuous electrocardiogram (ECG): all animals with ventricular arrhythmias or those that are persistently tachycardic despite therapy
- Hematocrit, total protein, and electrolyte concentrations; body weight; urine output; and fluid Cytologic examination from indwelling closed suction drains are evaluated daily.
- Repeat CBC and biochemistry profile every 48 hours.

PROGNOSIS AND OUTCOME

- Reported mortality from sepsis in animals ranges from 30%-70%.
- Severity of underlying disease and choice of antibiotic therapy are important factors influencing mortality in animals with sepsis.

SUGGESTED READING

Otto CM: Clinical trials in spontaneous disease in dogs: a new paradigm for investigations of sepsis. J Vet Emerg Crit Care 17(4):359–367, 2007.

Scroggin RD, Quandt MS: The use of vasopressin for treating vasodilatory shock and cardiopulmonary arrest. J Vet Emerg Crit Care 12(2):145–157, 2009.

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Separation Anxiety

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Physical or behavioral signs of distress exhibited by the animal only in the absence of (real absence) or lack of access to the client (virtual absence). Distress can manifest with destruction, elimination, vocalization, withdrawal, and salivation.

EPIDEMIOLOGY

Prevalence has been estimated at 14% of dogs seen in the average United States private practice.

SPECIES, AGE, SEX: Dogs reported > cats; age of onset usually overlaps with social maturity (dogs: 12-36 months old; cats: 24-48 months old)

RISK FACTORS

- Trauma during a client's absence (e.g., fire, burglary) can precipitate a sudden onset of separation anxiety.
- The popular beliefs that dogs with separation anxiety are “spoiled,” are “only dogs,” or have never “learned” to be left alone are incorrect.

ASSOCIATED CONDITIONS & DISORDERS

- Phobias (see p. 875): commonly coexistent
- Probability of separation anxiety given a diagnosis of storm or noise phobia in a dog: 87% and 88%, respectively

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Chief complaints range from minor (a chewed slipper) to major (walls chewed through) destruction, urination, defecation, puddles of saliva, salivary staining, primary self-mutilation (e.g., a chewed leg) or secondary self-mutilation (e.g., injury incurred when breaking out of a crate or through a window).
- Vocalization, while common, is often unrecognized (e.g., no near neighbors).
- Observant clients may see earliest manifestations of separation anxiety begin when signs of impending absence occur (e.g., client putting on a coat, drinking while moving).
- Dogs with separation anxiety have routinely experienced unexplained diarrhea or have been previously considered as candidates for inflammatory bowel disease.
- Some dogs with separation anxiety freeze and withdraw from all action and interaction when left. These animals are underdiagnosed but suffering.

PHYSICAL EXAM FINDINGS: Self-induced during anxiety:

- Broken teeth
- Lingual, nasal, buccal, cutaneous lacerations
- Torn or broken claws
- Abdominal palpation: evidence of ingestion of drywall, plastic, and other such items
- Weight loss possible if chronic condition; clients may not notice that weight loss occurred until the animal begins to recover and gains weight because the anxiety increased activity (e.g., pacing).

ETIOLOGY AND PATHOPHYSIOLOGY

- Multiple mechanisms likely, given the wide variety of anxiety manifestations
- Greater duration of the disorder may lead to more signs, more intense signs, and worse response to treatment.
- Dogs, like humans, may have “susceptibility genes” for the development of problematic anxieties.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is based virtually entirely on history; physical exam findings may be supportive but are not required for the diagnosis to be established.

DIFFERENTIAL DIAGNOSIS

- Generalized anxiety disorder (GAD), panic disorder: many signs are similar to separation anxiety, but in animals with separation anxiety, signs occur only around or during owner's absence.
- Attention-seeking behavior: signs occur only in the owner's presence and generally improve with proper management (ignoring the signs while they occur and rewarding good behavior by interacting with the pet).
- Incomplete housetraining: signs are confined to inappropriate elimination and occur continually (daily for months or more).
- Age-associated destruction and elimination problems (youth or old age)
- Pseudocyesis-like reaction: destructive behavior is typically confined to bedding, occurs after an ovariohysterectomy, and responds to hormonal supplementation.
- Systemic medical conditions can produce changes in behavior, including hyperthyroidism (cats), hypothyroidism (dogs), neurologic disease (some seizure disorders, rare brain tumors, rabies, etc.), and urinary tract disorders.

INITIAL DATABASE

- A complete and detailed history is the cornerstone of diagnosis.
- The most powerful diagnostic tool for separation anxiety is a video camera. Animals should be videotaped when left alone.
  - Identification of distressed but nondestructive animals
  - Identification/ruling out provocative stimuli for the destructive animals
  - Assessment of improvement by comparison with a later videotape
- Neurologic exam: no abnormalities expected.
- CBC, serum biochemistry panel, urinalysis ± thyroid profile: results should be within normal limits but may also reflect ongoing or chronic stress.

ADVANCED OR CONFIRMATORY TESTING

If neurologic signs are present or develop, a full neurologic evaluation including spinal fluid analysis and imaging (CT scan or MRI) may be indicated (see pp. 1311, 1233, and 1302).

TREATMENT

THERAPEUTIC OVERVIEW

The ultimate goal is to change the behavior of the pet so it no longer responds to being left alone with any of the signs of anxiety. Instead, it should be calm in these circumstances.

ACUTE GENERAL TREATMENT

- Separation anxiety is a veterinary emergency. Until medications can take effect, or if clients are unwilling to use medication, pets must not be left alone. Options include dog and cat sitters, daycare, boarding, or bringing the pet to work if possible.
- Reward any spontaneous decrease in reactivity.
- Implement behavior modification designed to teach the pet to relax. Substitute a new and calming rule structure for the pet that panics. Ensure that clients understand what pet anxiety looks like, and teach them to avoid rewarding it. Accidental reinforcement of anxiety-related behaviors occurs frequently (e.g., clients arrive home and think their frantic pet is just glad to see them).
- Clients should not respond to any nonspecific sign of anxiety and only engage with the pet if it is sitting calmly and quietly. Talking to the pet calmly can often help to induce future calmer behaviors. Then clients can add to the behavior modification by gradually teaching the dog or cat that it can be gradually left for incrementally increasing amounts of time.
- Pets should be rewarded with praise and food treats when calm, and the pace of the behavior modification must proceed at an appropriate rate that will allow improvement. If the pet is distressed, the owner is trying to progress too quickly. If panic, noise phobia, or storm phobia coexist (see p. 875), consider alprazolam (dogs, 0.01-0.1 mg/kg [likely most effective range: 0.02-0.04 mg/kg] PO q 4-6 h PRN; cats, 0.0125-0.025 mg/kg PO q 12-24 h PRN; some published sources recommend a tenfold higher dose, which is an error), with a half to a full dose given 2 hours before the expected provocative event and repeated 30 minutes beforehand. If the pet panics when the owner leaves for work in the morning, he/she can give the pet a half to a full dose when awakening in the morning, and then give the same dose 30 minutes prior to departure. An alternative (though more sedative and likely to cause more side effects) is diazepam (dogs, 0.5-2 mg/kg PO q 4-6 h PRN; cats, 0.2-0.4 mg/kg PO q 12-24 h PRN).

CHRONIC TREATMENT

- Dogs should be taught to relax while making eye contact with their owners as a new default behavior when the dogs encounter a situation about which they are anxious or unsure. Clients should learn to monitor facial cues, body postures, pupil size and shape, and respiratory behavior associated with relaxation. Periodic videotaping that clients then watch with their veterinarian is priceless.
- Avoid exposing dogs to circumstances likely to distress them (e.g., boarding dogs in a kennel if they have never enjoyed or experienced this).
- Desensitization to the triggers can be accomplished if two criteria can be met: triggers can be identified, and they can be reproduced faithfully in a systematic and incremental fashion. Beware that many dogs only learn to react earlier if "gradual departure" desensitization programs are inappropriately conducted.
- Dogs and cats should be crated as part of treatment only if they voluntarily and routinely use and enjoy their crates. Crates may represent entrapment to some animals and will make these animals worse.
- Once the pet has improved, it is important that the owners continue the behavior modification as a consistent and kind rule. A decreased or ablated response to an inciting trigger as evidenced by a reduction in or elimination of somatic signs of sympathetic arousal is the desired goal.
- Once developed, humane treatment of separation anxiety will likely require long-term treatment with antianxiety medications:
    - Amitriptyline: dogs, 1-2 mg/kg PO, q 12 h for a minimum of 30 days; cats, 0.5-1 mg/kg PO, q 12-24 h for a minimum of 30 days; tricyclic antidepressant (TCA) drug and first drug of choice in mild cases; inexpensive
    - Clomipramine (Clomicalm): dogs, 2-3 mg/kg PO q 12 h for a minimum of 8 weeks; cats, 0.5 mg/kg PO q 24 h for a minimum of 8 weeks; TCA drug and the only medication licensed for use for separation anxiety. Most successful when the behaviors have a ritualistic component or elimination component.
    - Selective serotonin reuptake inhibitor (SSRI) drugs: fluoxetine (Prozac/Reconcile; dogs, 1 mg/kg PO q 24 h for 8 weeks minimum; cats, 0.5 mg/kg PO q 24 h for 8 weeks minimum) or sertraline (Zoloft; dogs, 1 mg/kg PO, q 24 h for 8 weeks minimum; cats, 0.5 mg/kg PO q 24 h for 8 weeks minimum) can be successful in situations where other medications have been less helpful.
    - The minimal total treatment time for using medication with behavior modification is 4-6 months. Drugs should not be stopped too early.

DRUG INTERACTIONS

- Benzodiazepines, TCAs, and SSRIs can all be combined at lower-than-normal dosages if needed, but the potential for sedation and interaction must be evaluated.
- TCAs and SSRIs should not be given with monoamine oxidase inhibitors (MAOIs) that are found in many flea and tick collars and dips as well as in some cognitive dysfunction medications.

POSSIBLE COMPLICATIONS

- Abrupt cessation of medications with short half-lives is not recommended for the TCAs and SSRIs; wean over 10-14 days.
- TCAs should be used cautiously or not at all in animals with heart disease.
- Cats and dogs receiving serotonergic medications can manifest "serotoninlike syndromes (see p. 1427)," with hyperactivity, unpredictability, and ultimately seizures. This is an extraordinarily rare side effect.

RECOMMENDED MONITORING

- Owners can abuse benzodiazepines. Abuse can be limited by frequent follow-up appointments and not allowing automatic refills.
- Examination, CBC, serum chemistry profile, urinalysis, ± thyroid profile are indicated q 6-12 months for animals receiving long-term medication.
- Clients should learn to monitor heart rate digitally, since the first sign of cardiac side effects of medications can be an unremitting tachycardia.

PROGNOSIS AND OUTCOME

- Prognosis is improved by early diagnosis and aggressive treatment and by client compliance. Frequent and thorough communication between clinician and client so the treatment plan can be adjusted according to the animal's response and needs is essential.
- With chronic separation anxiety, treatment may be lifelong, especially if there are other comorbid anxiety-related conditions.

PEARLS & CONSIDERATIONS

COMMENTS

If a veterinarian is not comfortable treating a case of separation anxiety, the animal should be referred to a specialist (see www.dacvb.org for a listing in the United States).

TECHNICIAN TIP

Most veterinary staffs have no one with formal experience in behavior modification. Resources to help inform support personnel include the Association of Pet Dog Trainers (www.APDT.com) and the Society of Veterinary Behavioral Technicians (www.SVBT.org).

PREVENTION

- Early intervention for diagnosis and treatment
- Veterinarians should screen for behavioral problems as a routine part of every appointment. Otherwise, left untreated, separation anxiety worsens.
- When selecting breeding stock, clients should assess both medical and behavioral patterns of the pet's family members. Liability for anxiety disorders is likely heritable.

CLIENT EDUCATION

- Most behavioral conditions are due to chemical and functional abnormalities. These pets are distressed; they are not vindictive, jealous, spoiled, or disobedient.
- Under no circumstances should pets with behavioral problems be “punished,” physically “disciplined,” or “corrected.” These techniques only render the animal more anxious.
- Clients should expect treatment to be long term (at least 6 months) and possibly lifelong if the condition has been ongoing and/or severe.
- Relapses may occur with treatment discontinuation or added Stressors. When such Stressors are anticipated, premedication may be helpful.

SUGGESTED READING

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Landsberg GM, et al: Effectiveness of fluoxetine chewable tablets in the treatment of canine separation anxiety. J Vet Behav: Clin Appl Res 3:12–19, 2008.

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Semilunar Valve Insufficiency

BASIC INFORMATION

DEFINITION

Diastolic incompetence of the aortic valve and/or pulmonic valve

SYNONYMS

Aortic insufficiency (AI) or aortic regurgitation (AR); pulmonic insufficiency (PI) or pulmonic regurgitation (PR)

EPIDEMIOLOGY

SPECIES, AGE, SEX: May affect dogs and cats of any age and either sex

GENETICS & BREED PREDISPOSITION: Only when associated with an inciting cause (e.g., subaortic stenosis in Newfoundland dogs)

RISK FACTORS

- Aortic insufficiency: subvalvular aortic stenosis, aortic stenosis, ventricular septal defect, tetralogy of Fallot, infectious endocarditis, cardiac catheterization, aortic valve balloon valvuloplasty, aortic dilation
- Pulmonic insufficiency: pulmonic stenosis, patent ductus arteriosus, pulmonary hypertension, infectious endocarditis, heartworm disease, cardiac catheterization, pulmonic valve balloon valvuloplasty

GEOGRAPHY AND SEASONALITY: see Endocarditis, Infective, p. 346; Heartworm Disease, Cat, p. 474; Heartworm Disease, Dog, p. 477.

ASSOCIATED CONDITIONS & DISORDERS

- Severe AI may cause volume overload of the left ventricle and ultimately may lead to left-sided congestive heart failure. Such severe AI is rare in dogs and cats.
- Pulmonic insufficiency, even if severe, essentially never produces volume overload of the right ventricle.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Aortic insufficiency:
  - Isolated AI: uncommon
  - Secondary AI: underlying causes: see Risk Factors above
- Pulmonic insufficiency:
  - Isolated trivial PI: relatively common in dogs of all ages and either sex; uncommon in cats
  - Secondary PI: underlying causes: see Risk Factors above

HISTORY, CHIEF COMPLAINT

- Aortic insufficiency:
  - Often an incidental finding; no overt clinical signs
  - If severe: respiratory distress, cough, exercise intolerance, weakness, collapse
  - Signs of the causative cardiac disorder may predominate
- Pulmonic insufficiency:
  - Virtually never associated with clinical signs
  - If severe: respiratory distress, cough, cyanosis, exercise intolerance, weakness, collapse, abdominal distention
  - Signs of the causative disorder may predominate.

PHYSICAL EXAM FINDINGS

- Aortic insufficiency:
  - No abnormal findings if AI is trivial to mild
  - If moderate to severe:
    - Cardiac auscultation reveals a soft, low-frequency holodiastolic murmur over the left heart base (4th-5th intercostal space [ICS]) with radiation to right hemithorax.
    - Bounding peripheral pulses in some instances (dependent upon quantity of AI and underlying etiology)
  - If sufficiently severe to cause congestive heart failure (CHF): dyspnea, cough, pale mucus membranes, lethargy, pulmonary crackles
- Pulmonic insufficiency:
  - No abnormal findings if PI is trivial to moderate
  - If severe, and/or if concurrent pulmonary hypertension:
    - Cardiac auscultation reveals a low-frequency, diastolic/decrescendo murmur over the left heart base (3rd-4th ICS).
  - If sufficiently severe to cause CHF (rarely under any circumstance, and virtually never without a complicating factor such as pulmonary hypertension):
    - Pulse quality may be decreased.
    - Dyspnea, cough, dull lung sounds, abdominal fluid wave, pale mucous membranes, lethargy

ETIOLOGY AND PATHOPHYSIOLOGY

- Isolated semilunar valvular insufficiency:
  - Usually mild, rarely associated with clinical disease (especially PI)
  - Presumed mild congenital valvular malformation
- Aortic valve incompetence secondary to other causes:
  - Subaortic stenosis:
    - Poststenotic turbulence distorts valve endothelium such that valve closure is ineffective.
  - Valvular aortic stenosis (rare), infectious endocarditis:
    - Malformed valve leaflets do not coapt/close normally.
  - Ventricular septal defect (membranous):
    - Base of aortic valve is poorly supported owing to absent basal septal tissue, causing sagging and partial prolapse of the aortic valve in diastole.
- Pulmonic valve incompetence secondary to other causes:
  - Pulmonic stenosis: malformed pulmonic valve leaflets do not coapt/close normally.
  - Heartworm disease: physical blockage of pulmonic valve closure by worms
- Volume overload and increased end-diastolic ventricular and atrial pressures if AI or PI severe:
  - Predisposes to CHF and ultimately myocardial failure

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Clinically significant semilunar valve insufficiency is suspected when a diastolic murmur is identified on physical examination. More commonly, trivial semilunar valve insufficiency is identified incidentally during an echocardiogram and is of little or no consequence. Doppler echocardiography is necessary to noninvasively confirm the presence of this disease process and define the etiology. Further testing is often indicated if a pathologic disease process is identified; however, isolated semilunar valve insufficiency (in the absence of structural valvular or myocardial lesions) is rarely clinically significant.

DIFFERENTIAL DIAGNOSIS

- Normal
- Differentiate isolated semilunar insufficiency from specific causes (see Etiology and Pathophysiology above).

INITIAL DATABASE

- Echocardiogram: confirm diagnosis, identify underlying conditions, and qualitatively assess degree of insufficiency.
- Thoracic radiographs: normal if insufficiency mild:
  - AI: if moderate to marked: left ventricular enlargement, left atrial enlargement, distended pulmonary veins, pulmonary edema
  - PI: if marked (and especially when associated with severe pulmonary arterial hypertension): right ventricular enlargement, pleural effusion, distended caudal vena cava
  - Findings consistent with primary disorder
- Blood pressure: assess hemodynamic consequence of valvular insufficiency.

- CBC, serum biochemistry panel, urinalysis usually unremarkable with mild insufficiency but varies with underlying etiology

ADVANCED OR CONFIRMATORY TESTING

- Tests to rule out specific acquired diseases such as infective endocarditis and heartworm disease (see pp. 346, 474, and 477)
- Angiogram: confirmation of echocardiographic findings (rarely necessary)

TREATMENT

TREATMENT OVERVIEW

Treatment of semilunar valve insufficiency is oriented towards the underlying etiology and severity of the disease process. Isolated semilunar valve insufficiency rarely requires treatment, whereas treatment of semilunar valve insufficiency secondary to endocarditis (see p. 346) may require aggressive multimodal therapy.

ACUTE GENERAL TREATMENT

- None if insufficiency is mild/moderate
- Treat primary cause of insufficiency if applicable (e.g., antimicrobial therapy for semilunar valve insufficiency secondary to endocarditis)
- Manage CHF if present (see pp. 468, 470)

CHRONIC TREATMENT

- Dependent on underlying cause and presence or absence of CHF
- Prevent progressive cardiac remodeling and myocardial failure.

NUTRITION/DIET

Reduce dietary sodium if CHF present.

BEHAVIOR/EXERCISE

Exercise moderation for patients that develop CHF

POSSIBLE COMPLICATIONS

- Refractory CHF
- Systemic hypotension
- Azotemia (especially in patients with preexisting renal compromise and/or those receiving aggressive diuretic therapy)

RECOMMENDED MONITORING

Implemented as needed based on severity of disorder:

- Systemic blood pressure
- Renal function (with diuretics)
- Serum digoxin levels (measure 6-8 hours post administration)
- Repeat echocardiograms regularly (frequency dependent on the severity of insufficiency).

PROGNOSIS AND OUTCOME

- Excellent for mild to moderate PI and mild AI without evidence of ventricular or atrial dilation
- Guarded to poor for patients with marked AI/PI and CHF

PEARLS & CONSIDERATIONS

COMMENTS

- Auscultation of soft, low-frequency diastolic murmurs may be enhanced by positioning patient in left lateral recumbency and placing stethoscope bell on the dependent side of the chest wall over the heart base.
- The detection of small jets of semilunar valve insufficiency requires a high-quality echocardiograph.
- The presence of mild or moderate aortic insufficiency, even if inaudible, may add weight to a diagnosis of mild subaortic stenosis in a patient with echocardiographic results that are otherwise equivocal.
- With increasingly sensitive color-flow Doppler echocardiography, semilunar valve insufficiency can be detected in a progressively larger proportion of the normal dog and cat population; the volume of insufficiency and its impact on the ventricle are more important than simple presence or absence.

PREVENTION

see Endocarditis, Infective, p. 346; Heartworm Disease, Cat, p. 474; Heartworm Disease, Dog, p. 477.

TECHNICIAN TIPS

Auscultation of diastolic murmurs requires careful auscultation in a quiet environment. Minimizing ambient background noise, limiting respiratory tract interference, and reducing patient movement are strategies that may promote auscultation of diastolic murmurs.

SUGGESTED READING

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Nakayama, et al: Prevalence of valvular regurgitation in normal beagle dogs detected by color Doppler echocardiography. J Vet Med Sci 56:5, 1994.

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Seizures

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

A seizure is the clinical manifestation of abnormal, excessive, and/or hypersynchronous neuronal activity in the cerebral cortex. The location and extent of this abnormal neuronal activity determines the clinical appearance of the seizure. In clinical practice, seizures must be differentiated according to whether they are of extracranial or intracranial origin.

SYNONYMS

Convulsion, epileptic seizure, ictus

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Both sexes, dogs and cats, all ages
- Dogs: 6 months to 5 years (primary epilepsy); older dogs (brain tumor); young dogs (intoxication, metabolic, malformation)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Partial seizures (previously called *petit mat):* focal or asymmetric sensory or motor activity affecting any part of the body (e.g., facial twitching, chomping of the mouth); can be associated with autonomie signs (e.g., salivation, vomiting)
  - Simple (no alteration of consciousness) or complex (alteration in mentation and/or behavioral abnormalities; also called *psychomotor seizures)*
- Generalized seizures (previously called *grand mat):* diffuse, bilateral motor activity with loss of consciousness
- Status epilepticus: continuous seizure activity lasting for 5 minutes or more or repeated seizures with failure to return to normality in between
- Cluster seizures: two or more seizures within 24 hours

HISTORY, CHIEF COMPLAINT

- Any combination of uncontrollable, involuntary, excessive, or reduced motor activity; alteration in consciousness; behavioral disturbance and autonomie signs (e.g., salivation, urination, defecation, piloerection)
- A seizure is transient and starts and ends abruptly.
- Postictal disturbances frequently follow the seizure (e.g., confusion, pacing, blindness, ataxia).
- The motor activity can be bilateral and diffuse (e.g., generalized tonic/clonic seizure) or minor and subtle (e.g., facial twitching).

PHYSICAL EXAM FINDINGS

- The animal is often normal between episodes.
- Complete neurologic examination (see p. 1311) is mandatory:
  - Presence of any neurologic deficits after complete resolution of the seizure (interictal period) is important. Interictal neurologic deficits are an indication of a structural intracranial lesion, such as inflammation or neoplasm.
  - A patient that shows no interictal neurologic deficits, however, may have either a primary brain disturbance as the cause of seizures or, less likely, an extracranial cause for the seizures.
- Evidence of systemic illness is often present in cases where seizures are the result of intoxication (e.g., bradycardia, gastrointestinal [GI] signs) or metabolic diseases (e.g., anorexia, lethargy, vomiting).

ETIOLOGY AND PATHOPHYSIOLOGY

Etiology:

- Intracranial:

- Idiopathic epilepsy: based on exclusion of all known causes
- Primary epilepsy: genetic, common in dogs, rare and poorly documented in cats, possible ion channel mutation
- Persistent interictal deficits: structural forebrain lesion, including infectious encephalitis (e.g., viral, fungal, other), noninfectious encephalitis (e.g., granulomatous meningoencephalitis, necrotizing meningoencephalitis), brain tumor, vascular insult (e.g., stroke, feline ischemic encephalopathy), head trauma, degenerative diseases (e.g., storage disease), and malformation (e.g., cyst, hydrocephalus)

- Extracranial (or reactive): seizure secondary to a transient systemic or toxic insult to a normal brain. Systemic causes include hypoglycemia (e.g., insulinoma), encephalopathy (e.g., portosystemic shunt), and hypocalcemia (e.g., hypoparathyroidism, eclampsia). Many toxins can cause seizures at the advanced stage (e.g., ethylene glycol, metaldehyde, lead). For most toxins, there is progression from shaking to trembling to (finally) seizuring.

Pathophysiology:

- An alteration in neuronal excitability causes a paroxysmal depolarizing shift (PDS). This PDS may be secondary to inadequate neuronal inhibition (neurotransmitters GABA and glycine) or to excessive neuronal stimulation (neurotransmitters glutamate and aspartate) or can be a combination of both.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

- Seizure is the most common neurologic disorder in small animals.
- Ensure that the episodes truly are seizures: a thorough history and description are essential. Asking the owner to provide a video clip of the episode can be very useful.
- Once episodes are confirmed to be seizures, all patients undergo a comprehensive medical evaluation, and if no causes of extracranial/reactive seizures are identified, advanced imaging of the brain and cerebrospinal fluid (CSF) analysis are warranted.

DIFFERENTIAL DIAGNOSIS

- Syncope: sudden loss of consciousness and muscle tone, usually without motor activity and without postictal signs (fast and complete recovery). Syncopal events last <1 minute (otherwise fatal), whereas seizures may last several minutes. Clues of a cardiac problem may be present on examination (e.g., heart murmur, arrhythmias).
- Metabolic diseases: seizures are usually preceded by other signs (e.g., confusion, change in behavior, weakness).
  - Hypoglycemia (e.g., insulinoma): diagnosed rapidly with a simple blood glucose evaluation
  - Hypocalcemia: causes muscle cramping, spasms and fasciculation, and weakness and irritability rather than “true” seizures; diagnosed rapidly with simple blood total calcium or ionized calcium evaluation
  - Hepatic encephalopathy: episodes usually last hours, often associated with food intake.
  - Polycythemia: may cause weakness, confusion, collapse, and even a vascular event in the brain; diagnosed rapidly with hematocrit > 60%-65% (sight hounds >70%).
  - Kidney failure: at advanced stages, evident on physical exam (anuria) and/or blood work and urinalysis (concurrent azotemia and isosthenuria)
- Narcolepsy/cataplexy: animal “falls asleep” but can be awakened; usually associated with excitement or food.
- Sleep disorder: excessive “jerky” movements occurring exclusively during sleep. The animal can be awakened and exhibits normal wakening behavior (i.e., no postictal signs).
- Obsessive/compulsive behavior (e.g., “fly biting”): complex behavior that is usually goal directed and/or can be interrupted; more common in dogs. Affected dogs often have other behavioral problems (e.g., separation anxiety).
- Movement disorders: Focal motor signs are not associated with loss of consciousness or postictal signs. One of these signs is the “head bob,” which is occasionally seen in Doberman pinschers, boxers, bulldogs and occasionally in other breeds (movement of the head from side to side or up and down); another sign is dyskinesia in the bichon frise.

INITIAL DATABASE

- Fundic examination (see p. 1313): clues include papilledema (as can be seen with optic neuritis/encephalitis); retinal hemorrhage or detachment (which would suggest hypertension, polycythemia, or coagulopathy); lesions of chorioretinitis suggestive of a systemic infection (e.g., ehrlichiosis, toxoplasmosis, neosporosis, fungal disease).
- CBC, serum biochemistry panel, and urinalysis: evaluate for hypoglycemia, electrolyte imbalance (e.g., hypocalcemia), signs of liver or kidney disease, anemia, polycythemia, and calcium oxalate monohydrate crystals in antifreeze toxicity.
  - Usually normal in cases of primary brain disease
  - After severe seizures or status epilepticus, hyperglycemia (or rarely, hypoglycemia if prolonged seizures last for more than 20 minutes), increased liver enzymes (reduced perfusion or congestion), increased creatine kinase (CK; muscular damage or necrosis), and metabolic acidosis are typical.

- Electrocardiogram (ECG): evaluate for arrhythmias.
- Thoracic and abdominal radiographs: usually unremarkable
- Serum bile acids assay: indicated if hepatic encephalopathy is suspected and/or if a young animal presents with seizures. More than 90% of dogs and cats with portosystemic shunts have abnormal 2-hour postprandial serum bile acid levels.

ADVANCED OR CONFIRMATORY TESTING

- Portable electrocardiogram (ECG; cardiac event monitor or Holter monitor) if distinction between syncope and seizure is unclear on history and physical exam. Helps rule in (severe tachycardia or severe bradycardia occurs during episode) or rule out (cardiac rhythm is normal during episode) a cardiac arrhythmia as the cause of episodic clinical signs. Important prior to proceeding to general anesthesia, as for advanced imaging or CSF tap.
- Advanced imaging of the brain (MRI or CT scan (see p. 1302 and p. 1233)): brain tumor, multifocal lesions suggestive of inflammation, vascular lesion. MRI is slightly more sensitive. Radiographs of the skull are unrewarding except in cases of head trauma or palpable skull abnormalities.
- CSF analysis: often nonspecific but can be helpful in confirming brain disease or inflammation
- Serologic testing (e.g., fungal diseases, *Toxoplasma, Neospora,* and others; selection based on physical findings and initial database)
- Tests for toxins if exposure (e.g., plasma lead concentration, serum cholinesterase level)
- Electroencephalogram (EEG): limited availability; usefulness has yet to be proven.

TREATMENT

TREATMENT OVERVIEW

- Control or elimination of the underlying cause is the overarching long-term goal but is not possible in all cases.
- Reduction in seizure frequency and severity is a principal goal; acceptable seizure control for the owner (e.g., could be <1 seizure per 6-8 weeks) without significant side effects from the medication.
- For cluster seizures (more then two seizures per 24 hours) and status epilepticus: stopping the seizures and preventing others.
- Cluster seizures and status epilepticus are medical emergencies.

ACUTE GENERAL TREATMENT

For emergency situations (cluster or status):

- Identify and address any immediately reversible causes:
  - Hypoglycemia (blood or serum glucose < 40 mg/dL [<2.2 mmol/L]): administration of dextrose 2 g/kg IV. If using 50% dextrose, this equals 4 mL/kg, which must then be diluted with 5-10 times as much 0.9% saline or other sterile isotonic fluid by volume prior to administration to reduce the risk of phlebitis.
  - Hypocalcemia (blood or serum calcium < 6 mg/dL [<1.5 mmol/L]): administration of 10% calcium gluconate IV at a dose of 0.5-1.5 mL/kg or 5-15 mg/kg slowly to effect over a 15- to 30-minute period. Monitor ECG for onset of bradycardia, ventricular arrhythmia, or shortening of the QT interval, any of which justifies temporarily stopping the infusion. Total dose is the amount required to stop clinical signs.
  - Dextrose and calcium should not be administered unless a deficiency is documented.
- To stop the seizure and if reversible causes are absent: diazepam, 0.5-1 mg/kg IV bolus; can be repeated safely if seizure activity persists. Animals receiving phenobarbital may require 2 mg/kg of diazepam. Diazepam lasts only 20-30 minutes; further seizure activity must be prevented by one of the following steps:
  - Diazepam (2 mg/kg) can also be administered rectally either in the hospital or at home by the owner.
- To prevent another seizure:
  - Identify and control any known causes (e.g., antidote if known intoxication: pralidoxime or atropine for organophosphate; others).
  - Administer loading dose of phenobarbital (total mg = desired serum concentration (µg/mL) × BW (kg) × 0.8 L/kg): IV bolus of 10-20 mg/kg slowly; will reach an optimal serum level immediately. Monitor the patient carefully for excessive sedation if combined with diazepam.
  - Administer diazepam as a constant rate IV infusion (CRI): 0.5-1 mg/kg/h; can be added to 0.9% sodium chloride (NaCl) in an in-line burette; reduced by 25% every 4-6 hours if the seizures are controlled. Do not prepare more than 2 hours at a time, because diazepam is adsorbed by plastic and degraded by light.
  - Give diazepam boluses: alternative to a CRI; give 2 IV boluses of 1 mg/kg 30 minutes apart, followed by an IV bolus of 0.5 mg/kg 30 minutes and 60 minutes later.
- If seizures persist, administer propofol via IV bolus of 1-6 mg/kg to effect followed by an IV CRI of 2-8 mg/kg/h; then reduce the dose by 25% every 4-6 hours if the seizures are controlled; adequate monitoring is recommended.
- Provide supportive care and reestablish homeostasis.

- Thiamine (cofactor for glucose metabolism) 25-50 mg IM can be administered.

CHRONIC TREATMENT

Depends on underlying cause. Initiation of long-term, oral anticonvulsant drug therapy (e.g., phenobarbital, potassium bromide) is often required (see p. 353).

POSSIBLE COMPLICATIONS

- Seizures may continue despite adequate anticonvulsant drug therapy.
- Status epilepticus and death
- Hyperthermia, noncardiogenic pulmonary edema
- Neuronal damage if long, severe, or frequent seizures
- Hypersensitivity to phenobarbital; hepatotoxicity, rare bone marrow aplasia or blood dyscrasia, skin lesions (see p. 871)

RECOMMENDED MONITORING

- Phenobarbital serum level 3 weeks after initiation, change in dosage, signs of toxicosis or poor seizure control
- Bromide level after loading dose (if applicable), 3 to 4 months after initiation, and change in dosage; toxicity or poor control
- CBC and serum biochemistry panel every 6 to 12 months

PROGNOSIS AND OUTCOME 

- Good to guarded, depending on the cause:
  - Approximately 25% of dogs are refractory to treatment.
  - Owners should have realistic expectations.
- Many patients need lifetime medication and follow-up appointments.

PEARLS & CONSIDERATIONS 

COMMENTS

- A structural forebrain lesion rather than primary epilepsy should be suspected in seizuring dogs younger than 6 months or older than 5 years, and in seizuring cats.
- Status epilepticus is a medical emergency and needs to be treated intensively.
- Most animals will need long-term or lifelong treatment, and some animals may be refractory to treatment.

CLIENT EDUCATION

Understanding your pet's epilepsy: www.canine-epilepsy.net. College of Veterinary Medicine, University of Missouri; accessed Feb 26, 2010.

SUGGESTED READING

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Sebaceous Adenitis

BASIC INFORMATION

DEFINITION

Sebaceous adenitis (SA) is a destructive inflammatory disease of the sebaceous glands.

SYNONYM

Granulomatous sebaceous adenitis

EPIDEMIOLOGY

SPECIES, AGE, SEX: Uncommon in dogs, rare in cats; more common in young-adult to middle-aged dogs (1.5-7 years)

GENETICS & BREED PREDISPOSITION: Any breed can be affected, but the condition appears to be inherited in Akita, Samoyed, and standard poodle (autosomal recessive) dogs. Other breeds frequently reported to have SA are English springer spaniel, Hungarian Vizsla, German shepherd, Lhasa apso, Hovawart, and Bernese mountain dog.

ASSOCIATED CONDITIONS & DISORDERS: Pyoderma (see p. 951) and *Malassezia* dermatitis (see p. 682)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- The condition may appear differently in individual breeds, with marked variability depending on severity. Two clinical presentations exist:
  - Generalized SA: in long-coated breeds, such as Akita and standard poodle
  - Multifocal SA: in short-coated breeds, such as Hungarian Vizsla and in cats
- SA can also be subclinical and only identifiable by histologic examination in predisposed breeds.

HISTORY, CHIEF COMPLAINT: Progressive areas of hair loss, poor haircoat, excessive scaling, and musty odor. Pruritus is variable but may be marked, especially if secondary bacterial or *Malassezia* dermatitis is present.

PHYSICAL EXAM FINDINGS

- Generalized SA: presents with dramatic amounts of scaling. Typically, scales are adherent to hairs (follicular castings), coat, and skin and are often dry to the touch. Hypotrichosis on the top of the head, back of the neck, and dorsum is observed as the disease progresses. In chronic cases, hyperkeratotic skin is observed. The dorsal midline and ears are usually the first and most affected areas. In the Akita, where the disease can be more severe, fever, anorexia, and lethargy have been reported.
- Multifocal SA: this clinical presentation seen in Vizlas is strikingly different and presents with coalescing patches of scaly alopecia and annular plaques, with adherent scales developing mainly on face, head and trunk.

SEBACEOUS ADENITIS When hairs are epilated, follicular casts adhere to hair shafts.

(Courtesy Dr. Caroline de Jaham.)

ETIOLOGY AND PATHOPHYSIOLOGY

- Cause and pathogenesis are uncertain, but mechanism may be a genetically inherited cell-mediated immune reaction against the sebaceous glands.
- Initial defect could be a cornification disorder or abnormalities in cutaneous lipid metabolism that affect sebum production.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

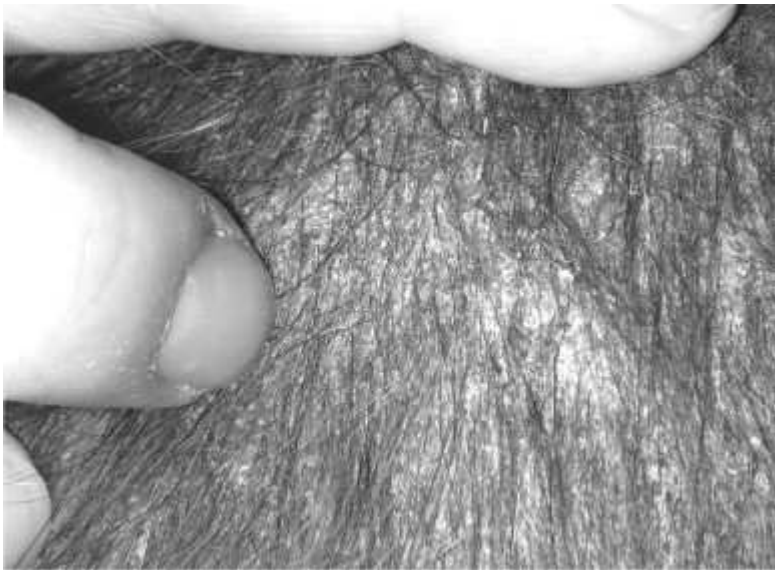
The diagnosis is suspected based on physical appearance of large amount of adherent scaling and a dull, sparse haircoat in a predisposed breed. Such findings warrant skin biopsies, which are confirmatory. Deep skin scrapings, fungal cultures, and skin cytologic examination should be done prior to obtaining skin biopsies, to identify complicating/concurrent factors.

DIFFERENTIAL DIAGNOSIS

- Generalized form: cornification disorders (primary seborrhea, ichthyosis), pyoderma, *Malassezia* dermatitis, demodicosis, dermatophytosis, endocrinopathies, leishmaniasis
- Multifocal form: pyoderma, demodicosis, dermatophytosis, zinc-responsive dermatosis, pemphigus foliaceus

INITIAL DATABASE

- Cytologic examinations to assess for presence of secondary bacterial or *Malassezia* infection
- Skin scrapings (for parasites) and dermatophyte culture: generally negative with sebaceous adenitis
- CBC, serum biochemistry profile, urinalysis, and endocrine function tests: no abnormalities expected



SEBACEOUS ADENITIS Note the poor-quality haircoat with adherent scales over the dorsum in this 4-year-old Akita-cross dog.

(Courtesy Dr. Caroline de Jaham.)

ADVANCED OR CONFIRMATORY TESTING

Histopathologic findings are diagnostic. Affected areas show a pyogranulomatous inflammation around the sebaceous glands. Sebaceous glands are in various stages of being destroyed. Marked orthokeratotic hyperkeratosis is present. In late-stage disease, the inflammation resolves, leaving an absence of sebaceous glands.

TREATMENT

TREATMENT OVERVIEW

SA is incurable; however, control of clinical signs (for patient comfort, reduction of risk of secondary infections, and esthetics) can be reached with topical and/or systemic therapy. The mainstay of topical treatment involves the use of keratolytics. Nutritional supplements may be beneficial but are unproven.

ACUTE GENERAL TREATMENT

- Treat bacterial infections with appropriate systemic antibiotic therapy. An acceptable empirical choice initially is cephalexin, 22-30 mg/kg PO q 12 h for 3 weeks.
- There is no gold standard for treatment of SA in dogs; a variety of protocols has been published, all with variable efficacy.
- Mild cases: intensive topical therapy leads to effective (although partial in most cases) control of scaling: keratolytic shampoos and emollient rinses; weekly baby oil soaks prior to shampoo are effective in dissolving the keratin. Weekly baths are needed at first (6-8 wks), but the frequency usually can be decreased to every 2-3 wks when signs improve.
- For more stubborn cases, topical application of 50%-75% propylene glycol as a rinse daily, then decrease frequency as needed.
- For more severe or refractory cases, options include:
    - Synthetic retinoids (isotretinoin, acitretin): 1-3 mg/kg PO q 12-24 h until remission (approximately 6 wks); then the lowest, most infrequent dose (reported effective in Vizsla, variable results in other breeds). Hepatotoxicity, hypertriglyceridemia and keratoconjunctivitis sicca are common, and monitoring is indicated.
    - Cyclosporine: effectively reduces sebaceous gland inflammation, alopecia, and follicular casts at 5 mg/kg PO q 24 h for 4 months, then gradual dose reduction that maintains clinical control. A combination of systemic cyclosporine and topical treatments further improves the skin and coat condition.

NUTRITION/DIET

- Omega-3 fatty acids PO q 24 h (180 mg of eicosapentaenoic acid per 5 kg body weight).
- Vitamin A, 8000-10,000 IU PO q 24 h is listed, but only weak clinical evidence of benefit.

DRUG INTERACTION

Ketoconazole potentiates cyclosporine activity; adjust dosage to reduce risk and monitor serum cyclosporine levels

RECOMMENDED MONITORING

Animals on synthetic retinoids should have liver enzyme activity and triglyceride levels monitored q 1-2 months and tear production monitored q 3 weeks for first 2 months, then q 1-2 months). Cyclosporine serum levels should remain in therapeutic range.

PROGNOSIS AND OUTCOME

- Early diagnosis and treatment improve the prognosis for long-term control.
- Even though the disease is not lethal, dogs with SA are sometimes euthanized because the treatment is lifelong and labor intensive. A clinically and cosmetically acceptable result is sought but not always obtained.

PEARLS & CONSIDERATIONS

COMMENTS

- Subclinical states of SA may progress with time. Early diagnosis can be done with skin biopsies.
- Hair regrowth can be straight rather than curled and of a different color in affected standard poodles.

TECHNICIAN TIPS

Do not scrub—or wipe with alcohol or antiseptic—the biopsy site prior to performing skin punch biopsies. Scales on the skin surface and follicular casts, which are important in making the diagnosis, may be removed. For the same reason, do not shave; gently clip the hair with scissors if necessary. Handle biopsy samples gently, avoiding squeezing or crushing.

PREVENTION

Discourage the breeding of affected animals. Screening is performed via histologic analysis of at least two 6-mm skin biopsies taken from skin with scaling and hair loss, or if no lesions are present, on the dorsal midline between the neck and lumbosacral region. see https://secure.offa.org/sainfo.html for details.

CLIENT EDUCATION

- A clinically and cosmetically acceptable result is not always obtained despite treatment.
- The Orthopedic Foundation for Animals (OFA) provides a database and guidelines on canine sebaceous adenitis. For information and registration: www.offa.org.

SUGGESTED READING

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Sarcoptic Mange

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

A nonseasonal, highly contagious, intensely pruritic cutaneous infestation caused by a small, obligate, burrowing mite, *Sarcoptes scabiei* var. canis.

SYNONYMS

Canine scabies, sarcoptic acariosis

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs (all breeds, both sexes, all age) are commonly affected.

RISK FACTORS: The disease is more common in dogs that have been in animal shelters, pet shops, dog shows, boarding, grooming or dog daycare facilities, as well as stray dogs and dogs living in the country where infested foxes or coyotes roam near farm buildings.

CONTAGION & ZOONOSIS

- Transmission occurs most commonly from direct contact with an infested dog or wild canidae but can also occur from a contaminated environment and fomites.
- Humans exposed to an infested dog can develop a pruritic papular eruption which will resolve when the mites are eradicated from the animal. Although quite rare, a dog may acquire the parasite from a human infested with *S. scabiei* var. humanis.
- Dog-to-dog transmission is best avoided by preventing direct contact and administering scabicidal drugs promptly to affected dogs (mites die within several days).

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: The primary complaint is pruritus. In more chronic cases, the condition can present as nonseasonal intense pruritus that has responded poorly to various dermatologic therapies, including corticosteroid therapy.

PHYSICAL EXAM FINDINGS

- Typically, the ear margins, elbows and hocks, ventral abdomen, chest, and eventually legs (the dorsum is usually spared) will show intense pruritus, papules, erythema, crusting, excoriations, and alopecia.
- A positive pinnal-pedal reflex (scratching action with the dog's hind limb when the examiner firmly rubs the edge of the dog's pinna between thumb and forefinger) is seen in 82% of dogs with sarcoptic mange but observed in only 7% of dogs with pruritus caused by other diseases.

ETIOLOGY AND PATHOPHYSIOLOGY

- The life cycle lasts approximately 3 weeks, and adult mites usually survive off the host for up to 6 days at room temperature.
- *S. scabiei* var. canis is not totally host specific, given that it has been isolated from foxes, coyotes, and rarely from immunosuppressed cats.
- Infestation with *Sarcoptes* mites (as for many other parasitic infestations) leads to a hypersensitivity reaction, the latter being responsible for the intense pruritus in sensitized dogs. The precise incubation period is not known, but in first-time infections, the first clinical signs are usually expected a few weeks after exposure.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

- The diagnosis is suspected from the history and clinical signs; a positive pinnal-pedal reflex is strongly suggestive of the disease. Consider *S. scabiei* infestation when presented with any dog with an apparent sudden onset of intense itching.

DIFFERENTIAL DIAGNOSIS

- Ectoparasites *(Cheyletiella, Otodectes,* fleas, lice, chiggers)
- Hypersensitivities (flea bite and other ectoparasite hypersensitivities, atopic dermatitis, adverse food reaction, contact hypersensitivity)
- Pyoderma
- *Malassezia* dermatitis

INITIAL DATABASE

- Confirmation of the diagnosis relies on a positive skin scraping (mites, mite eggs, or mite fecal pellets) or occasionally on dermatohistopathologic analysis of biopsies or fecal flotation. The ear margins, the elbows or hocks, and unexcoriated papules are the preferred sites for scrapings. However, the mites are notoriously difficult to find.
- Test for the pinnal-pedal reflex.

ADVANCED OR CONFIRMATORY TESTING

- A serodiagnostic (ELISA) test is available in some European countries for the diagnosis of canine scabies. Sensitivity = 82%-92%, specificity = 92%-**96%.**
- Therapeutic trials with reliable scabicides are essential to confirm or rule out scabies in pruritic dogs with negative skin scrapings.

TREATMENT

TREATMENT OVERVIEW

- The goal of treatment is to thoroughly eradicate the mites. Affected and all in-contact dogs should be treated with a scabicide regardless of presence or absence of clinical signs.
- All clinically suspected *S. scabiei* cases should be treated even if multiple skin scrapings are negative.
- Traditional topical scabicides (lime sulfur, amitraz, organophosphates) have been largely replaced by the labeled and off-label use of macrocyclic lactones.

ACUTE GENERAL TREATMENT

- Selamectin (Revolution/Stronghold [Pfizer]) and moxidectin/imidacloprid (Advantage Multi/Advocate [Bayer]) are approved as topical scabicides once every 30 days for 2 treatments, although many veterinary dermatologists recommend a minimum of 3 treatments at 2-week intervals.
- The off-label use of ivermectin, one of the most useful diagnostic and therapeutic tools in canine scabies in the 1980s and '90s, remains a therapeutic alternative but should never be used in collies or related breeds with a high prevalence of MDR1 (ABCB1) mutation (see p. 706). The injectable product (Ivomec 1% injection for cattle and swine [Merial]) is usually given at a dosage of 0.3 mg/kg PO or SQ q 7-14 days for a 4-6 week course of treatment. The 0.5% alcohol based pour-on ivermectin formulation (Ivomec Pour-on for cattle [Merial]) is also effective and practical when applied to the interscapular skin q 14 days at 0.5 mg/kg for 2-3 treatments.
- Concomitant antibiotic therapy may be required if secondary pyoderma is present. Cephalexin at a dose of 22-30 mg/kg PO q 12 h for 30 days typically is a good choice.
- Short-term corticosteroid therapy may be required in severely pruritic dogs. Prednisone can be used at 0.5-1 mg/kg PO q 24 h for the first 2-3 days and then weaned down.
- The use of an environmental acaricidal is generally not required, although grooming equipment and bedding can be treated with an appropriate acaricidal spray.

POSSIBLE COMPLICATIONS

In collies, Australian shepherds, and many other canine breeds carrying the MDR1 (ABCB1) mutation, intoxication can occur with dosages of ivermectin or other off-label macrocyclic lactones that are tolerated by normal dogs. Pretreatment testing for the gene mutation (and/or selection of alternate treatment) is recommended in at-risk breeds (see p. 706).

RECOMMENDED MONITORING

Follow-up examination, including skin scrapings and cytologic analysis, are recommended if clinical signs persist or worsen 1-2 months after initiating scabicidal treatment.

PROGNOSIS AND OUTCOME

- It can take 2 to several weeks for complete resolution of pruritus. In some dogs, an increase in pruritus (probably associated with an immunogenic response to the dying mites) may occur in the first few days after treatment.
- Prognosis is good.
- In humans, the zoonotic infestation is transient, with the pruritic papular eruption resolving when the mites are eradicated from the dog.

PEARLS & CONSIDERATIONS

COMMENTS

- Crusting of the elbows, hocks, and pinnal ear margins accompanied by intense pruritus are strongly suggestive of *S. scabiei.*
- Look for a pinnal-pedal reflex, and treat for scabies if this reflex is noted.
- "Feline scabies" is caused by a different parasite, *Notoedres cati;* however, cats in close contact with dogs affected with *S. scabiei* var. canis may be temporary reservoirs for the mite and occasionally develop transient pruritus. Rarely, immunosuppressed cats may develop persistent pruritic lesions when infested with *S. scabiei* var. canis.
- Owing to cross-sensitization, a positive intradermal skin test response to house dust mite antigen is seen in 75% of dogs with a confirmed diagnosis of scabies. All clinical signs resolve following acaricidal therapy, and all intradermal reaction to dust mites are generally negative within 6 months of the original diagnosis. This illustrates the importance of ruling out scabies prior to testing for atopic dermatitis.

CLIENT EDUCATION

Humans transiently affected with *S. scabiei* mites may develop a pruritic papular eruption, especially on the arms or trunk. This should spontaneously resolve within 3 weeks when the mites are eradicated from the dog. Persistent problems should prompt the person to consult a physician.

TECHNICIAN TIPS

- Sarcoptic mange has zoonotic potential. Therefore, ideally, lesions on affected animals should not be held or touched directly, and the hospital environment should be decontaminated.
- An acaricide (e.g., pyrethrin) is indicated for disinfecting surfaces such as exam tables and floors, but with patients that have low mite burdens, these surfaces may be adequately treated using routine disinfectants.
- Environmental treatment (e.g., home environment) is rarely performed, except for the dog's bedding.

SUGGESTED READING

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Salt Toxicosis

BASIC INFORMATION

DEFINITION

Salt (sodium chloride, table salt, NaCl) toxicosis results when an excessive amount of sodium has been ingested, intake of potable water is limited, and/or free water translocates from the vasculature into the gut following osmotically active agents.

SYNONYMS

Water deprivation, sodium ion toxicosis, osmotic hypernatremia, salt poisoning

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs (all breeds, both sexes, all ages) are more commonly evaluated for salt toxicosis than cats. RISK FACTORS

- Use of table salt as an emetic, a technique which is now contraindicated for this reason
- Availability of homemade play dough in pet's environment
- Swimming and drinking seawater when availability of potable drinking water is limited (or incidentally during persistent exercise)
- Dehydration (places animals at higher risk)
- Vomiting (inability to maintain hydration despite polydipsia)
- Outdoor dogs in cold climates/frozen water (climate-dependent)

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Owner description of typical risk factor (see above)
- Lack of drinking water or vomiting of water after ingesting excessive amounts of salt
- Polydipsia, vomiting, ataxia, tremors, and seizures within 1-4 hours after ingestion

PHYSICAL EXAM FINDINGS

- Polyuria and polydipsia (PU/PD)
- Vomiting, diarrhea, signs of abdominal pain
- Signs of dehydration
- Sinus tachycardia (secondary to dehydration)
- Depression, ataxia, tremors, seizures, potentially altered mentation
- Hyperthermia possible (secondary to tremors, seizures)

ETIOLOGY AND PATHOPHYSIOLOGY

Source:

- Sources of excess sodium chloride for animals include homemade play dough and modeling clay, table salt (used as an emetic or simply ingested), improperly mixed feed or formula, ice melts, paintballs (22% of canine ingestions caused hypernatremia), sea water, hypertonic saline solutions, sodium bicarbonate, and sodium phosphate enemas.
- Osmotically active agents include polyethylene glycol and some sugar alcohols such as glycerol, maltitol, and sorbitol. Sources relevant to veterinary medicine include activated charcoal, paint balls, gummy candies, glaucoma prescriptions, sugar-free candy, and bulk artificial sweeteners.

Mechanism of Toxicosis (also see p. 559):

- Signs of toxicosis appear when serum sodium is >170 mEq/L (vomiting, polydipsia), and central nervous system (CNS) signs such as tremors and seizures begin when serum sodium is > 180 mEq/L (typical normal range in healthy dogs: 145-157 mEq/L).

- Hypernatremia creates a hypertonic state in the extracellular fluid (ECF). Initially, water shifts from the interstitium to the vasculature and then from intracellular fluid (ICF) to the ECF to maintain equilibrium.
- The CNS is particularly vulnerable to initial tissue shrinkage as water leaves the ICF, resulting in microvascular trauma and potential demyelination, with a rapid rise to severe hypernatremia.
- Sodium passively crosses the blood-brain barrier into the cerebrospinal fluid (CSF). Once in the CSF, excess sodium affects neuronal function by inhibiting glycolysis, leading to decreased energy production. Sodium requires active transport to move from the CSF back to the serum; decreased energy production limits this process. In the brain, a compensatory response to dehydration is the formation of idiogenic osmoles or solutes 24 hours or more after onset of hypernatremia. With rapid rehydration, these osmotically active solutes cause an influx of water into the brain, resulting in cerebral edema, seizures, permanent neurologic dysfunction, and possibly death.
- Excess sodium is irritating to gastrointestinal (GI) mucosa and can cause gastroenteritis and dehydration.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A tentative diagnosis is made based on history (excessive sodium intake, water deprivation, and/or ingestion of an osmotically active agent), compatible clinical signs (polydipsia, vomiting, tremors, seizures), or both. Diagnosis is confirmed by documentation of an elevated serum sodium level.

DIFFERENTIAL DIAGNOSIS

Toxicologic (see common sources for excessive sodium chloride ingestion, above)

Spontaneous, nontoxicologic (see p. 559):

- Water deficit:
  - Primary hypodipsia, diabetes insipidus (central/nephrogenic), high ambient temperature, fever, restricted water access
- Hypotonic fluid loss:
  - GI loss, third-space loss (peritonitis, pancreatitis), cutaneous (burns), osmotic diuresis (diabetes mellitus, mannitol infusion), chemical diuretics, acute and chronic kidney disease (CKD)
- Solute gain:
  - Hyperaldosteronism
  - Hyperadrenocorticism

INITIAL DATABASE

- CBC: stress leukocytosis
- Serum biochemistry profile:
  - Hypernatremia: serum sodium >170 mEq/L
  - Hyperchloremia
  - Hyperalbuminemia
  - Decreased serum $Hco3^{-}$ possible (metabolic acidosis)
  - Azotemia possible (prerenal)
- Thoracic radiographs: pulmonary edema possible (with concurrent sodium and water load, especially if there is preexisting heart disease)

ADVANCED OR CONFIRMATORY TESTING

- NaCl can be analyzed in vomitus, food, water; may help determine the source and concentration of NaCl (rarely needed clinically)
- Postmortem: brain sodium (> 1800 ppm)

TREATMENT

TREATMENT OVERVIEW

The cornerstone of treatment is judiciously timed reduction of serum sodium. Patients presented within 24 hours of ingestion may be decontaminated (induction of vomiting, but no administration of activated charcoal) and treatment aims for rapid sodium excretion/dilution. Patient presentation after >24 hours requires careful lowering of serum sodium concentrations to avoid iatrogenic

CNS injury.

ACUTE GENERAL TREATMENT

- Decontamination of patient:
  - Induction of vomiting (see p. 1364) if the animal is not showing clinical signs, and it is performed within 30 minutes of ingestion.
  - DO NOT administer activated charcoal. It does not adsorb NaCl, and some preparations contain substantial amounts of sodium.
- Replacement of water and electrolytes:
  - When the hypernatremia is acute (<24 hours), calculate the amount of free water needed:
  - Free water deficit (liters) = body weight (kg) × 0.6 × ([present serum Na concentration/previous or normal range serum Na concentration] – 1). Replace 50% of the water deficit in the first 24 hours using sterile 5% dextrose solution IV. Replace the remaining deficit in the next 24-48 hours using the same fluid type (5% dextrose), avoiding excessively rapid decreases (see Chronic Treatment, below).
- Facilitation of renal excretion of sodium:
  - 5% dextrose at 3.7 mL/kg/h IV in dogs can decrease serum sodium at about 1 mEq/L/h; 0.45% NaCl with 2.5% dextrose is also suitable (slower decrease).
  - Furosemide, 1-2 mg/kg IM or IV q 6 h (correct dehydration first).
- Supportive care:
  - Control seizures with diazepam: 0.5-2 mg/kg IV PRN.
  - Control tremors with methocarbamol: 55 mg/kg slowly IV PRN.
  - Manage acidosis with sodium bicarbonate (PRN).
  - Warm water enema (5-10 mL/kg) or oral water can help correct free water deficit and thus correct hypernatremia. This works well when hypernatremia is due to osmotically active agents (not readily absorbed, e.g., activated charcoal, glycerol, gummy candies, etc.)

CHRONIC TREATMENT

Do not decrease serum sodium concentration faster than 0.5 mEq/L/h. A rapid drop in serum sodium concentrations can cause water influx into the CNS, and cerebral edema.

POSSIBLE COMPLICATIONS

Permanent CNS damage (osmotic demyelination, microvascular trauma) if excessively rapid correction of longstanding (>24 hours) hypernatremia

RECOMMENDED MONITORING

- Serum electrolytes: cornerstone of diagnostic testing during treatment
- Hydration status/body weight
- CBC (for hematocrit)
- Serum biochemistry profile (serum proteins)
- Acid-base status

PROGNOSIS AND OUTCOME

- Poor if serum sodium > 180 mEq/L and seizures are present
- Good if treated early and intensively

PEARLS & CONSIDERATIONS

COMMENTS

- A widely used homemade play dough recipe contains 2 cups of flour, 1 cup of table salt, and 0.5-1 cup of water; ingestion by dogs is a common cause of severe hypernatremia.
- Minimum lethal dose of NaCl in dog = 4 g/kg; minimum toxic dose = 1.9 g/kg. Equivalents: 1 tsp NaCl = 6 g; 1 lb table salt = 454 g.
- A 10-lb (4.5-kg) dog needs to eat 3.4 tsp (18 g) of homemade play dough to reach a minimum toxic dose of NaCl.
- In patients that are less severely affected, frequent access to small amounts of drinking water may be sufficient to lower serum sodium levels.

TECHNICIAN TIP

Do not use salt to induce vomiting.

SUGGESTED READING

Barr JM, Khan SA, McCullough SM, et al: Hypernatremia secondary to homemade play dough ingestion in dogs: a review of 14 cases from 1998 to 2001. J Vet Emerg Crit Care 14(3):196–202, 2004.

Donaldson CW: Paintball toxicosis in dogs. Vet Med 98(12):995–997, 2003 Dec.

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Salmonellosis

BASIC INFORMATION

DEFINITION

Infection of susceptible patients with pathogenic *Salmonella* spp.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Many species can be infected, including cats, dogs, and people.
- Cats appear to be more resistant to *Salmonella* infection.
- Younger animals are more commonly affected.

RISK FACTORS

- Young, stressed, or immunocompromised patients
- Feeding raw or undercooked meat products, eggs, or diets
- Overcrowded, unsanitary, or stressful conditions
- Concurrent gastrointestinal (GI) infections
- Antibiotic therapy

CONTAGION & ZOONOSIS

- Infected dogs and cats are a major risk to people, especially immunocompromised persons.
- Risk to people increases if pets are eating raw meat diets.
- Undercooked meat is also a risk for people if ingested.

ASSOCIATED CONDITIONS & DISORDERS: Focal organ infections following clinical or subclinical infection:

- Abscesses, pneumonia, pyothorax
- Meningitis
- Osteomyelitis
- In utero infection resulting in abortion, stillbirth, weak puppies or kittens

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Up to 30% of dogs and 18% of cats are subclinical carriers.
- Acute enterocolitis
- Chronic diarrhea rare
- Septicemia/endotoxemia
- Cats may develop chronic, febrile illness

HISTORY, CHIEF COMPLAINT

- Watery to mucoid diarrhea with or without blood
- Straining or increased urgency to defecate
- Vomiting
- Anorexia and lethargy
- Weight loss

PHYSICAL EXAM FINDINGS

- Fever
- Abdominal pain

- Dehydration, possibly severe
- Pale mucous membranes, tachycardia, tachypnea, weakness, weak pulses if septicemic
- Conjunctivitis in cats

ETIOLOGY AND PATHOPHYSIOLOGY

- *Salmonella* spp: gram-negative, facultative anaerobic, motile, non-spore-forming rods from the family Enterobacteriaceae.
- Most common route of transmission is through contact with infected food, water, or fomites.
- Bacterium survives for long periods, up to 6 weeks, in environment.
- Clinical signs occur secondary to mucosal invasion and epithelial injury:
  - *Salmonella* spp. also produce an enterotoxin, resulting in secretory diarrhea.
- Organism persists in phagocytic cells of intestinal mucosa and mesenteric lymph nodes, liver, and spleen:
  - Results in persistent shedding for 3-6 weeks after infection
- Bacteremia and endotoxemia may occur in association with mucosal invasion, resulting in systemic infection and possibly the systemic inflammatory response syndrome (SIRS).
- Persistence and severity of infection depend on the patient's immune status.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is based on the isolation of *Salmonella* from feces in conjunction with appropriate clinical signs, or isolation from blood or infected tissues.

DIFFERENTIAL DIAGNOSIS

- Viral diarrhea: parvovirus, coronavirus, rotavirus
- Bacterial diarrhea: *Clostridium, Campylobacter* enteritides
- GI parasites
- Dietary indiscretion
- Septicemia due to other causes

INITIAL DATABASE

- CBC, biochemistry profile, and coagulation changes are generally nonspecific or represent signs of endotoxemia/sepsis:
  - Neutropenia with left shift and toxic neutrophils in acute phase or systemic disease
  - Neutrophilia if chronic illness
  - Nonregenerative, possibly hypo-chromic anemia may be noted.
  - Thrombocytopenia in severe cases, with septicemia leading to disseminated intravascular coagulation (DIC)
  - Hypoproteinemia due to GI loss
  - Sometimes hyponatremia and hyperkalemia (similar to hypoadrenocorticism)
  - Hypoglycemia, azotemia, or hyperbilirubinemia suggest endotoxemia/sepsis.
  - Prolonged coagulation times in severe cases with DIC
  - Fecal flotation, direct smear, and parvoviral ELISA test as needed to address differential diagnosis

ADVANCED OR CONFIRMATORY TESTING

- Fecal bacterial culture:
  - Best results using enrichment broth or selective culture media
  - Positive fecal culture establishes infection but not necessarily that signs are due to salmonellosis, since subclinical carriers are common.
  - Positive culture from blood, bile, or other normally sterile samples is more strongly indicative of salmonellosis.
  - False-negative results are possible, since organism grows fastidiously.
- Serologic testing is used in establishing diagnoses in human salmonellosis but is not routinely used in animals.

TREATMENT

TREATMENT OVERVIEW

Treatment consists of supportive care without antibiotics for mild to moderate cases of gastroenteritis. For severe gastroenteritis or

systemic disease, aggressive therapy with antibiotic use is warranted. No therapy is usually recommended for asymptomatic carriers.

ACUTE GENERAL TREATMENT

- Depends on severity of illness
- Mild cases are often self-limiting and require only supportive therapy.
- Intravenous fluid support, including plasma or colloids if necessary, recommended if dehydrated or septicemia is present
- Antibiotic therapy is controversial:
    - May induce carrier state and prolong fecal shedding of organisms
    - Antibiotics are indicated if severe hemorrhagic diarrhea is present, if the patient is depressed or febrile, if evidence of sepsis exists, if the patient is immunosuppressed and shows GI signs, or if positive blood cultures are obtained. Duration of treatment corresponds to time to resolution of fever, shock, or other signs of complications.
    - The most effective and least likely antibiotic to develop resistance is enrofloxacin (5-10 mg/kg PO or slow IV q 24 h in dogs; 4-5 mg/kg PO or slow IV q 24 h in cats).
    - Others reported to be effective include trimethoprim-sulfa (15 mg/kg PO q 12 h) or amoxicillin (22 mg/kg PO q 8 h).
    - Antibiotic therapy should initially be administered for 10 days, but some cases may require long-term administration.

RECOMMENDED MONITORING

Monitor carefully for signs of sepsis or SIRS (see pp. 1591 and online chapter: Systemic Inflammatory Response Syndrome).

PROGNOSIS AND OUTCOME

- Prognosis for mild cases is good; infections may resolve spontaneously or with supportive care only.
- Prognosis for septicemic patients is guarded; potential disease complications include dehydration, electrolyte imbalances, sepsis, septic shock, SIRS, and DIC.

PEARLS & CONSIDERATIONS

COMMENTS

Patients fed raw food diets are at increased risk of salmonellosis:

- *Salmonella* isolated from 66%-80% of samples of raw food (e.g., bones and raw food [BARF] diet).
- *Salmonella* isolated from 30%-93% of stool samples from dogs fed these diets (thus, there is an increased risk for human exposure and infection).

PREVENTION

- Avoid feeding raw or undercooked meat diets.
- Isolate infected animals, and practice good hygiene.

CLIENT EDUCATION

- Owners should be informed that this is a zoonotic disease, and humans are very susceptible.
- Avoid eating undercooked meats.

SUGGESTED READING

Greene CE: Salmonellosis. In Greene CE, editor: Infectious diseases of the dog and cat, ed 3, St Louis, 2006, Saunders Elsevier, p 355.

Morley PS, Strohmeyer RA, Tankson JD, et al: Evaluation of the association between feeding raw meat and *Salmonella enterica.* infections at a Greyhound breeding facility. J Am Vet Med Assoc 228:10, 2006.

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Salmon Poisoning

BASIC INFORMATION

DEFINITION

A febrile rickettsial infection of dogs in the Pacific northwestern United States and Pacific coastal Canada, associated with ingestion of raw fish

SYNONYM

Neorickettsia helminthoeca infection

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs: any age, both sexes affected

RISK FACTORS: Exposure to a fresh brackish stream or beach is commonly elicited in the history.

GEOGRAPHY AND SEASONALITY: Infections are limited to the habitat range of the intermediate snail host *(Oxytrema silicula)* in western British Columbia, Washington, Oregon, northern California, and more sporadically in areas where fish carrying the causative organism, *N. helminthoeca,* migrate or are transported. Dogs have the greatest access to dead fish during spawning seasons (late summer to early winter).

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Acute, severe febrile illness 5-7 days after fish ingestion; often fatal
- A more moderate illness may be seen as late as 14-33 days after exposure, particularly with the Elokomin fluke fever disease variant.

HISTORY, CHIEF COMPLAINT

- Acute onset of anorexia and lethargy associated with fever
- Vomiting and bloody diarrhea common
- Oculonasal discharge occasionally reported

PHYSICAL EXAM FINDINGS

- Fever
- Lymphadenopathy
- Signs of hypovolemic shock (tachycardia, collapse, poor pulse quality)

ETIOLOGY AND PATHOPHYSIOLOGY

- Dogs acquire the causative organism (*N. helminthoeca),* and therefore the disease, from a fluke parasite *(Nanophyetus salmincola)* carried in the kidneys of salmon, and rarely other fish or salamanders.
- Rickettsial infection transmitted when flukes mature in the canine gastrointestinal (GI) tract:
  - Fluke maturation in the GI tract involves release of the rickettsiae, which are taken up into macrophages and disseminate to lymph nodes (especially mesenteric).
  - Replication of the organism occurs in the lymph nodes, and this is where the lesions are most profound (other than the inflammatory response that occurs in the GI mucosa when flukes and rickettsiae elicit an immune response).
- Systemic rickettsial replication results in clinical disease in dogs.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is typically based on compatible clinical signs (fever, hemorrhagic gastroenteritis, lymphadenopathy) in a dog with a history of fish ingestion, finding flukes on a fecal exam, or response to doxycycline therapy.

DIFFERENTIAL DIAGNOSIS

- Parvoviral enteritis
- Ehrlichial infections
- Hemorrhagic gastroenteritis
- Sepsis (e.g., due to foreign body perforation, cholangiohepatitis)
- Pancreatitis
- Neoplasia, especially GI lymphoma

INITIAL DATABASE

- CBC and serum biochemical findings are inconsistent but may include thrombocytopenia, lymphopenia, eosinophilia, hypoalbuminemia, and elevated alkaline phosphatase.
- Operculated fluke eggs are most easily seen on fecal sediment exam but may be seen on direct smear or fecal flotation.

ADVANCED OR CONFIRMATORY TESTING

- Giemsa-stained lymph node aspirates may reveal intracytoplasmic rickettsial bodies.
- Abdominal ultrasound often reveals moderate to marked mesenteric lymph node enlargement.

TREATMENT 

TREATMENT OVERVIEW

Affected patients should be hospitalized and treated with intravenous fluids, supportive care, and parenteral then oral doxycycline. The flukes should also be eliminated via treatment with praziquantel.

ACUTE GENERAL TREATMENT

- Hospitalization is recommended for intravenous fluid support and alleviation of vomiting and diarrhea.
- Mild cases: rickettsial infection can be treated with oral doxycycline (10 mg/kg q 12 h) or tetracycline (22 mg/kg q 8 h) for 7-14 days.
- Severe cases, particularly with vomiting/diarrhea: parenteral doxycycline (5-10 mg/kg IV q 12 h until oral form is tolerated) or ampicillin (20-30 mg/kg IV q 6 h). Oxytetracycline (7 mg/kg IV q 8 h × 3 days) has also been effective.
- Praziquantel (10-30 mg/kg PO or SQ once) is effective for elimination of the fluke.

POSSIBLE COMPLICATIONS

Parenteral oxytetracycline has been rarely associated with acute renal failure.

PROGNOSIS AND OUTCOME 

- Prognosis is fair to good in aggressively managed cases; improvement is usually noted within 2-3 days after treatment initiation but may take up to a week.
- Death is likely within 5-10 days if the disease remains untreated.

PEARLS & CONSIDERATIONS 

COMMENTS

- Salmon poisoning is an important cause of fever, lymphadenopathy, and severe GI signs in dogs in the Pacific northwestern United States and Pacific coastal Canada.
- Clinical signs are similar to hemorrhagic gastroenteritis, but affected dogs are typically febrile.
- Fecal direct and sedimentation exams and treatment with doxycycline are recommended in febrile dogs when possible ingestion of raw fish is noted in disease-endemic regions.

PREVENTION

Restrict canine access to raw fish in the Pacific Northwest.

CLIENT EDUCATION

Early aggressive treatment is required for salmon poisoning, or death is likely.

SUGGESTED READING

Gorham JR, Foreyt WJ: Salmon poisoning disease. In Greene CE, editor: Infectious disease of the dog and cat, ed 3, St Louis, 2006, Saunders Elsevier, p 198.

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Salivary Gland Disorders

BASIC INFORMATION

DEFINITION

- Sialocele: accumulation of saliva that has leaked from a salivary gland or its duct into subcutaneous or submucosal tissue and consequent tissue reaction to saliva
- Sialadenitis: inflammation of a salivary gland
- Sialadenosis: noninflammatory, nonneoplastic enlargement of a salivary gland
- Necrotizing sialometaplasia: squamous metaplasia of the salivary gland ducts and lobules, with ischemie necrosis of the salivary gland lobules
- Salivary neoplasia: benign or malignant lesion arising from salivary glandular or ductal tissue

SYNONYMS

- Sialocele: salivary mucocele; ranula (sublingual sialocele)
- Necrotizing sialometaplasia: salivary gland necrosis or infarction

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Sialocele: typically dogs between 2 and 4 years old; in fewer than 20 of 4000 dogs
- Sialadenitis: typically older dogs
- Sialadenosis and necrotizing sialometaplasia: dogs of all ages, most often 3-8 years old
- Salivary neoplasia: older dogs (mean-10 years old); prevalence in cats almost twice that in dogs

GENETICS & BREED PREDISPOSITION

- Sialocele: German shepherds, miniature poodles overrepresented
- Sialadenosis and necrotizing sialometaplasia: small dog breeds (especially terriers) predisposed
- Salivary neoplasia: spaniel breeds and poodles predisposed

RISK FACTORS: Sialocele: oral trauma and activity of young dogs; however, experimental duct ligation, duct laceration, rupture of the mandibular salivary gland capsule with damage to glandular tissue, and subcutaneous injection of mucocele fluid have not caused salivary mucoceles in healthy dogs, suggesting a developmental predisposition in some dogs.

ASSOCIATED CONDITIONS & DISORDERS: Necrotizing sialometaplasia: *Spirocerca lupi* infestation (esophageal granulomas), megaesophagus, esophagitis, esophageal diverticulum, giardiasis, autoimmune sialadenitis

CLINICAL PRESENTATION

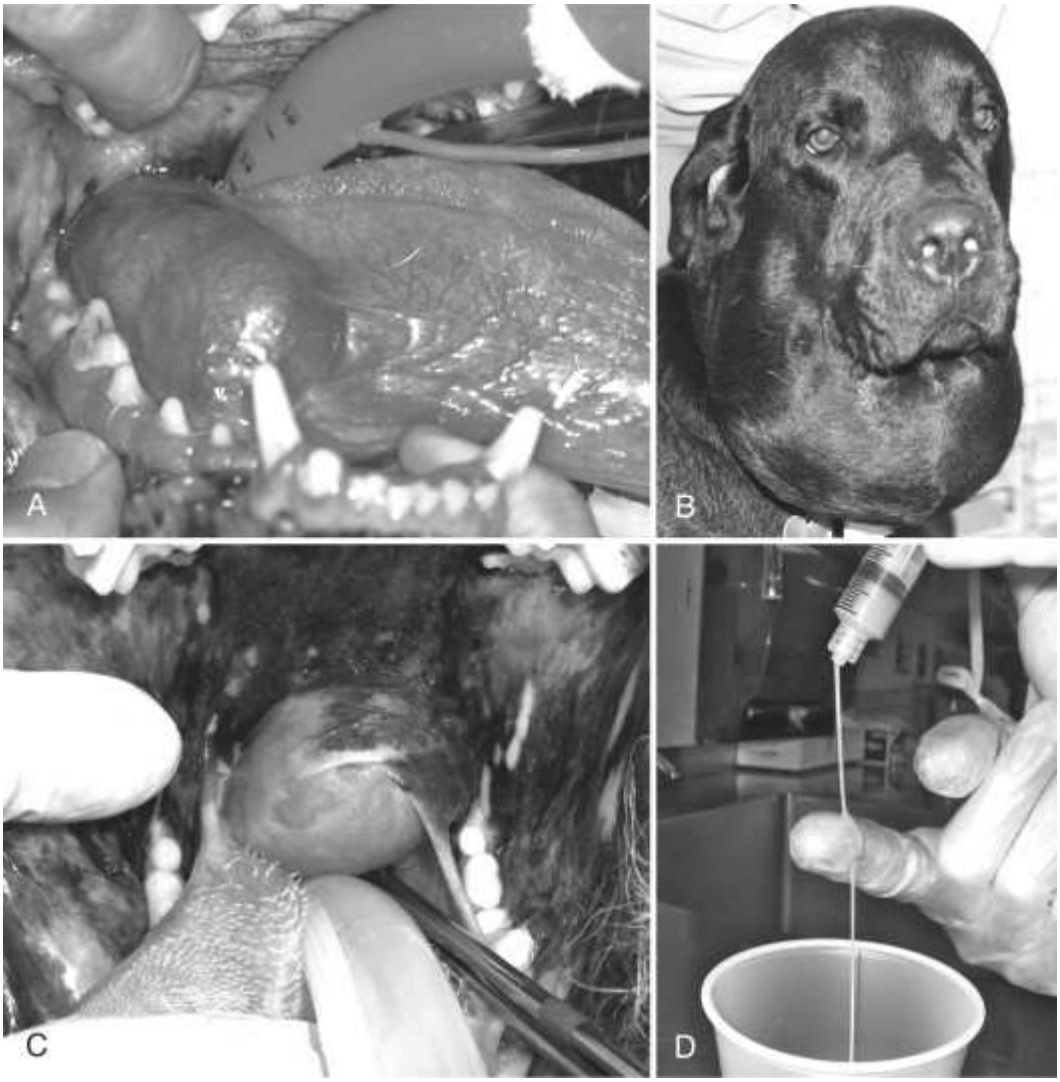
DISEASE FORMS/SUBTYPES

- Sialocele:
  - Sublingual sialocele (ranula): in sublingual tissue
  - Cervical sialocele: in intermandibular or cervical area; most common
  - Pharyngeal sialocele: in pharyngeal wall
  - Zygomatic sialocele: in orbit
- Salivary neoplasia: carcinoma or adenocarcinoma most common

HISTORY, CHIEF COMPLAINT

- Sialocele:
  - Acute, painful intermandibular swelling: initial stage of cervical salivary mucocele resulting from an inflammatory response; uncommon presentation
  - Swelling in the cranioventral neck region: cervical salivary mucocele at later stages when inflammation has subsided (more common presentation); typically found incidentally by owner; slowly enlarging or intermittently large, fluid-filled,

and usually nonpainful.
    - Ptyalism, blood-tinged saliva secondary to masticatory trauma, poor prehension of food, and reluctance to eat: sublingual salivary mucocele
    - Dyspnea/dysphagia secondary to pharyngeal obstruction: pharyngeal salivary mucocele
    - Periorbital mass and either enophthalmos or exophthalmos: zygomatic salivary mucocele (infrequently reported in dogs)
- Sialadenitis:
    - Painful swelling (dependent on location) along the vertical ear canal, caudal to the mandible, or orbital/retrobulbar area, with exophthalmos
    - Lymphadenopathy, fever
    - Pain associated with palpation of the affected gland
    - Pain associated with mouth opening
    - Dysphagia secondary to pain or enlarged inflamed gland that physically inhibits mouth opening
- Sialadenosis:
    - Regional swelling (dependent on location), exophthalmos, but no apparent pain
    - Retching and gulping elicited by mild excitement and occurring several times a day
    - Weight loss, reluctance to exercise, snorting, lip smacking, nasal discharge, hypersalivation, inappetence, depression
- Necrotizing sialometaplasia:
    - Depression, nausea, anorexia
    - Hypersalivation, persistent swallowing, lip smacking
    - Retching, gagging, regurgitation, chronic vomiting, weight loss
    - Cough, tachypnea, dyspnea, abdominal respiration
    - Painful swelling caudal to the mandible, pain associated with mouth opening
- Salivary neoplasia:
    - Sometimes painful swelling (dependent on location) around the vertical ear canal or caudal to the mandible
    - Exophthalmus from orbital or retrobulbar swelling
    - Pain on palpation of the involved gland
    - Pain associated with mouth opening
    - Dysphagia secondary to pain or neoplastic gland that physically inhibits mouth opening



SALIVARY GLAND DISORDERS Sialoceles in dogs: **A**, Sublingual (right-sided). **B**, Cervical (originating from the right side). **C**, Pharyngeal (left-sided). **D**, Nontransparent, stringy, brownish fluid aspirated from a sialocele.

PHYSICAL EXAM FINDINGS: All: see also History/Chief Complaint, above.

- Sialocele:
  - Fluid-filled, generally painless swelling in the cervical, sublingual, pharyngeal, or periorbital region
  - Patient otherwise normal with no signs of systemic disease
  - Sublingual gland most commonly affected
- Sialadenitis:
  - Pain upon palpation of the gland
  - Pain upon gentle retropulsion of the eye through closed eyelids
  - Systemic signs of inflammation: fever, malaise, inappetence
  - Mucopurulent discharge may be noted at the duct opening in the oral cavity.
  - Soft palate asymmetry from an enlarged, inflamed zygomatic salivary gland
  - Zygomatic and mandibular glands most commonly affected
- Sialadenosis:
  - Usually bilateral salivary gland enlargement
  - Mandibular gland most commonly affected
  - Exophthalmos if zygomatic gland affected
  - Hypersalivation, retching, and gulping but no signs of pain
- Necrotizing sialometaplasia:
  - Enlarged, painful, hard salivary gland
  - Mandibular gland most commonly affected
  - Very sensitive upon palpation of pharyngeal area
  - Dyspnea, cough, reverse sneezing

- Hypersalivation, lip smacking, persistent swallowing, retching, vomiting
- Weight loss

- Salivary neoplasia:
  - Painful swelling in the cervical, periauricular, or periorbital region; distinct mass; rarely any fluid accumulation
  - Pain upon gentle retropulsion of the eye through closed eyelids
  - Occasionally cancer cachexia or signs of other paraneoplastic disorders
  - Parotid and mandibular glands most commonly affected

ETIOLOGY AND PATHOPHYSIOLOGY

- Sialocele:
  - Contrary to a true cyst which is lined by epithelium, a sialocele represents a tissue reaction to extravasation of saliva from a gland/duct complex and has a nonepithelial, nonsecretory lining consisting primarily of fibroblasts and capillaries.
  - Damage to salivary gland or duct associated with orofacial trauma may cause leakage of saliva into adjacent tissues. Generally this leakage is self-limiting and does not lead to mucocele.
  - The defect is most often associated with the portion of the sublingual gland/duct complex caudal to the lingual nerve.
- Sialadenitis:
  - Salivary gland inflammation with enlargement. Sialoliths may be a contributing factor, since they can occur in dogs and are reported commonly in humans with sialadenitis. The associated ductal obstruction can lead to inflammation of the glandular tissue.
- Sialadenosis:
  - Sialadenosis: salivary gland enlargement without cytologic or histologic abnormalities. Excessive saliva production may be associated with increased parasympathetic activity or changes in sympathetic innervation.
  - No evidence of cytologic or histologic abnormalities in affected salivary glands; usually no abnormalities noted upon esophageal endoscopy
- Necrotizing sialometaplasia:
  - Squamous metaplasia of salivary gland ducts and lobules, with ischemic necrosis of the salivary gland lobules
  - Neurogenic pathogenesis suspected to be associated with abnormalities of the vagal nerve
  - Associations with *Spirocerca lupi* infestation, megaesophagus, esophagitis, esophageal diverticulum, giardiasis, autoimmune sialadenitis
- Salivary neoplasia:
  - No cyst or mucocele formation unless there is saliva accumulation secondary to ductal obstruction

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Among other signs, the presence of any swelling in the periorbital, sublingual, intermandibular, subhyoid, parotid, pharyngeal, and cranioventral neck regions; exophthalmos; or being unable or reluctant to open the mouth should prompt suspicion of disease of the salivary gland/duct complex. Fine-needle aspiration for cytologic evaluation is valuable (particularly for sialoceles: saliva-like fluid). Definitive diagnosis for all others requires biopsy and histologic evaluation.

DIFFERENTIAL DIAGNOSIS

- Edema, cyst, seroma, hematoma, abscess
- Trauma, foreign body, sialolith
- Lymphadenitis, neoplasia affecting lymph nodes
- Aural or ocular neoplasia

INITIAL DATABASE

- Sialocele:
  - Fine-needle aspiration and cytologic evaluation: clear or nontransparent, stringy, sometimes blood-tinged, often brownish fluid with a very low cellular content
  - Mucin and amylase analyses of the fluid are not reliable diagnostic procedures.
  - If cervical sialocele appears on ventral midline, place patient in exact dorsal recumbency (awake, sedated, or anesthetized):
    - Sialocele usually shifts to the originating side and is more easily mobile on the originating side.
    - Essential for correct identification of the affected side if surgical intervention is contemplated
- Sialadenitis, sialadenosis, necrotizing sialometaplasia, salivary neoplasia:
  - Fine-needle aspiration of gland and cytologic evaluation (zygomatic salivary gland may require per os aspiration)

- Fine-needle aspiration of regional lymph nodes
- Bacterial culture and sensitivity
- Three-view thoracic radiographs to rule out conditions associated with necrotizing sialometaplasia and thoracic metastasis

ADVANCED OR CONFIRMATORY TESTING

- Regional radiographs or ultrasonography if sialolith is suspected or palpated
- Sialography: radiographic contrast study of a salivary gland/duct complex; most common indication for a sialogram is to determine the location of a salivary gland/duct defect in patients with sialocele.
- CT (see p. 1233), MRI (see p. 1302)
- Incisional biopsy for histopathologic evaluation

TREATMENT

TREATMENT OVERVIEW

Combination of immediate relief through aspiration or incision for some disorders is followed by surgical excision, radiation therapy, or others depending on diagnosis.

ACUTE GENERAL TREATMENT

- Sialocele:
  - Needle drainage of mucocele; not recommended as repeat treatment option owing to rapid recurrence and risk of iatrogenic infection
  - Complete removal of involved salivary gland/duct complex with ligation of remaining duct and drainage of sialocele and surgical site
  - Marsupialization of a sublingual or pharyngeal sialocele (creation of a large window in the mucosa overlying the swelling to allow for intra-oral drainage of saliva) is not as effective as removal of the involved gland/duct complex because granulation tissue may result in closure of the window.
- Sialadenitis, sialadenosis and necrotizing sialometaplasia:
  - Surgical removal of the affected salivary gland produces minimal if any improvement.
  - If needle aspirate yielded mucopurulent fluid, per os or percutaneous drainage to alleviate mucopurulent fluid accumulation and associated pressure causing discomfort:
    - Percutaneous drainage using a closed suction system rarely required
    - Per os drainage following stab incision using a #15 scalpel blade through the soft palate into the affected zygomatic salivary gland (hemostatic forceps can be used to enlarge the stab wound and facilitate drainage)
- Salivary neoplasia:
  - Complete excision of a salivary neoplasm: only if entirely intracapsular, otherwise not recommended
  - Surgical debulking procedure recommended if part of a multimodality treatment plan that involves cytoreduction of the neoplasm
  - Pain management

CHRONIC TREATMENT

- Sialadenitis, sialadenosis, and necrotizing sialometaplasia:
  - Pain management, antibiotics (based on culture and sensitivity of the fluid/tissue aspirate), nonsteroidal antiinflammatory drugs, antiinflammatory doses of glucocorticosteroids, and control of internal parasites have resulted in favorable responses in some cases.
  - Phenobarbital administration (1-2 mg/kg PO q 12 h) has resulted in dramatic improvement in some cases, providing more support for a neurogenic pathogenesis.
- Salivary neoplasia:
  - Radiotherapy
  - Surgical debulking

POSSIBLE COMPLICATIONS

- Injury to the lingual nerve during removal of mandibular/sublingual gland/duct complex (lingual nerve is located dorsal and rostral to the gland/duct complex)
- Recurrence of mucocele due to failure of having completely excised all affected gland(s)
- Seroma/hematoma formation due to failure of having appropriately drained the sialocele and surgical site
- Injury to major neurovascular structures during incisional biopsy procedures

- Ocular trauma associated with the zygomatic salivary gland during drainage of mucopurulent fluid
- Failure to completely excise all affected tissue (any salivary neoplasm)
- Ocular complications of radiotherapy if ipsilateral eye is in the treatment field

RECOMMENDED MONITORING

Surgical site for evidence of seroma/hematoma formation

PROGNOSIS AND OUTCOME

- Sialocele: excellent with complete removal of the gland/duct complex, with appropriate drainage of the sialocele and surgical site
- Sialadenitis: excellent/good, depending on identification of initiating cause and response to treatment
- Sialadenosis: excellent/good with phenobarbital treatment
- Necrotizing sialometaplasia: good/guarded, depending on response to medical treatment (such as phenobarbital)
- Salivary neoplasia: guarded/poor; treatment is generally considered palliative.

PEARLS & CONSIDERATIONS

COMMENTS

- Sialocele:
  - Placement of the patient in exact dorsal recumbency can lateralize cervical sialoceles that otherwise seem to be on the ventral midline, which is essential for knowing which side to approach surgically.
  - Sialoliths are concretions of calcium phosphate or calcium carbonate and may occur with chronic sialocele.
  - The intimate anatomic association of the sublingual and mandibular salivary glands and their ducts requires removal of both structures when a sialocele affects one of them.
  - If left untreated, a sialocele may result in:
    - Physical problems associated with a large cranioventral cervical mass
    - Trauma, ulceration, secondary infection
    - Dysphagia (sublingual sialocele), dyspnea/dysphagia (pharyngeal sialocele), exophthalmos, strabismus, and other ocular complications (zygomatic sialocele)
- Sialadenitis, sialadenosis, and necrotizing sialometaplasia:
  - Be careful to differentiate these conditions from salivary neoplasia, as they can have similar clinical signs.
  - Complete surgical excision of affected salivary gland/duct complexes is virtually impossible, often unhelpful, and usually not necessary.
  - Be mindful of the many neurovascular structures in anatomic areas where drainage of salivary glands is required.
  - It is speculative whether sialadenitis or sialadenosis can progress to necrotizing sialometaplasia.
- Salivary neoplasia:
  - Be careful to differentiate this from sialadenitis, sialadenosis, and necrotizing sialometaplasia, as they can produce similar clinical signs.
  - Complete excision of a salivary neoplasm is unlikely and may increase morbidity; generally lesions are large and invasive at the time of diagnosis.
  - Be mindful of the many neurovascular structures in anatomic areas where salivary gland neoplasms are likely to occur.
  - Salivary neoplasia should be staged according to the TNM system (see p. 692) to permit appropriate prognostication and treatment plan.

TECHNICIAN TIPS

Technicians should be able to distinguish lymph nodes from salivary glands upon neck palpation.

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Tularemia

BASIC INFORMATION

DEFINITION

Acute zoonotic bacterial infection caused by fastidious gram-negative aerobic intracellular coccobacilli, *Francisella tularensis* subsp. *tularensis* (type A [more virulent]) or subsp. *holarctica* (type B); uncommon to rare in occurrence

SYNONYMS

Rabbit fever, deerfly fever, *Brucella* or *Pasteurella tularensis*

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Affects > 100 species of wild and domestic mammals, amphibians, arthropods, birds, and humans
- Seroprevalence indicates latent infection is common in dogs and cats in endemic areas.
- Clinical disease occurs occasionally in cats and rarely in dogs.
- Cats often severely affected; dogs more resistant and milder signs; puppies and kittens more susceptible than adults

RISK FACTORS: Exposure to ticks or wild rabbits or rodents; humans at greater risk include veterinarians, farmers, hunters, landscapers, meat handlers, cooks, and laboratory personnel.

CONTAGION & ZOONOSIS: Highly infectious zoonotic disease; the infectious dose for humans is <100 organisms via cutaneous or conjunctival exposure and <10 for inhalation. Transmission occurs through direct contact with infected animals, their tissues or excrement, or contaminated fomites; cat bites or scratches; insect bites (mosquitoes, biting flies, ticks); ingestion of contaminated food (esp. meat) or water; inhalation of aerosolized organisms (bacterial cultures, contaminated plant material).

GEOGRAPHY AND SEASONALITY: Throughout the Northern Hemisphere; occurs in distinct endemic areas, with a few cases in bordering areas; sporadic disease with 100-200 human cases per year in the United States

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Subclinical to mild to fatal disease approximately 2-7 days after exposure
- Cats often present with severe acute disease with nonspecific signs: lethargy, anorexia
- Dogs may present with anorexia, lethargy, weakness, and mucopurulent oculonasal discharge
- Recent contact with rabbits or rabbit carcasses is common.

PHYSICAL EXAM FINDINGS

- Cats: usually severe illness characterized by fever, lymphadenopathy, oral or lingual ulcerations, splenomegaly, hepatomegaly, icterus. Occasionally, milder nonfatal form of disease may present as chronic draining cutaneous lesions.
- Dogs: fever, lymphadenomegaly and oculonasal discharge

ETIOLOGY AND PATHOPHYSIOLOGY

- *F. tularensis* is a highly infectious gram-negative intracellular bacterium found in water and mud.
- Two disease cycles are noted: a terrestrial cycle associated with transmission of type A (subsp. *tularensis)* from infected rabbits, ticks (eastern and central United States), and biting flies (western United States); and an aquatic cycle, associated with transmission of type B (subsp. *holarctica)* from infected aquatic mammals (muskrat, beaver, voles) via contamination of water by carcasses or excrement or mechanical transmission by biting insects.
- Transmission occurs through inoculation (cat or insect bite), ingestion, inhalation, or contact with skin or conjunctiva (able to penetrate intact skin).
- At the site of inoculation, the organism multiplies locally and spreads to local lymph nodes, resulting in regional lymphadenopathy.

- Bacteremia with seeding of the organism to multiple organs throughout the body may follow, particularly in cats and humans.
- *Francisella* is an obligate intercellular organism: it invades and replicates in macrophages, facilitating persistence and systemic dissemination.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Tularemia should be considered in acutely febrile patients with regional or generalized lymphadenopathy, especially in endemic areas and/or if oral ulcerations or cutaneous abscesses are present.

DIFFERENTIAL DIAGNOSIS

- Plague *(Yersinia pestis)*
- Pseudotuberculosis *(Yersinia pseudotuberculosis)*
- Nocardiosis
- Mycobacterial infection
- Pasteurellosis

INITIAL DATABASE

- CBC: panleukopenia or leukocytosis with toxic neutrophils, thrombocytopenia
- May have elevated liver enzymes (alanine aminotransferase [ALT]) and hyperbilirubinemia

ADVANCED OR CONFIRMATORY TESTING

- Serologic test: fourfold increase in titer or single markedly high titer (=1:160 in humans); false positives may occur because of cross-reactivity with *Brucella* and *Yersinia*
- Definitive diagnosis: demonstration of organism by PCR, direct fluorescent antibody, or culture of organism from tissue biopsy or aspirate samples (use caution during diagnostic sampling and specimen handling: organism highly infectious).

TREATMENT

TREATMENT OVERVIEW

- Antimicrobial treatment for eradication of *Francisella* organisms and supportive care for accompanying conditions (dehydration, septic shock)
- Cats must be treated early and intensively; treat presumptively while awaiting test results.
- Canine cases are often self-limiting, requiring only supportive care.
- Wear barrier attire and stringently avoid cutaneous contact with infected animals or splatter/aerosolization of patient blood, tissue, and excrement to prevent transmission of disease to contact humans and other animals.

ACUTE AND CHRONIC TREATMENT

- Supportive therapy, including IV fluid administration (see also Sepsis, p. 1014)
- Specific treatment of choice is aminoglycoside antimicrobial (gentamicin, streptomycin). Nephrotoxic: patients must be well hydrated prior to aminoglycoside administration: IV fluid therapy prior to treatment is advised.
- Alternative agents: fluoroquinolones, tetracyclines, erythromycin, chloramphenicol
- Gentamicin, ciprofloxacin, or doxycycline most commonly used for treating humans
- β-Lactam antibiotics, azithromycin are not effective.
- Clinical relapse in humans reported more commonly after treatment with bacteriostatic antimicrobials (tetracycline, chloramphenicol) than with bactericidal agents
- Gentamicin, 4-8 mg/kg IV, SQ, IM q 8-12 h; or 8-12 mg/kg q 24 h for 7-10 days. Ensure hydration and normal renal function prior to treatment to reduce risk of nephrotoxicity; in animals with chronic kidney disease, decrease dose of aminoglycoside or choose another antibiotic.
- Enrofloxacin, 2.5-5 mg/kg PO, SQ, IV q 12-24 h; if IV, dilute with saline and administer slowly.
- Doxycycline, 5-10 mg/kg PO q 12-24 h; or 5 mg/kg IV q 24 h for minimum of 14 days

DRUG INTERACTIONS

- Aminoglycosides: use with extreme caution with other drugs that are excreted by the kidneys or are potentially nephrotoxic or ototoxic. Diuretics or cephalosporins given concurrently with aminoglycosides may increase toxicity.
- Tetracyclines: do not administer rapidly IV (may cause collapse).
- Fluoroquinolones: may alter metabolism of other drugs, leading to toxicity (e.g., theophylline); avoid >5 mg/kg/d enrofloxacin in cats.

POSSIBLE COMPLICATIONS

- Sepsis (see p. 1014)
- Disseminated intravascular coagulation (DIC; see p. 315)
- Renal failure

RECOMMENDED MONITORING

- Monitor for DIC and other complications of sepsis.
- Monitor serum blood urea nitrogen (BUN) and creatinine, as well as urine sediment, of patients receiving aminoglycosides.

PROGNOSIS AND OUTCOME 

- Rapidly fatal in untreated cats with overt clinical signs
- Self-limiting infection in most dogs
- Rapid resolution of fever follows administration of appropriate antibiotic.

PEARLS & CONSIDERATIONS 

COMMENTS

- May be underreported in dogs because of the mild, self-limiting nature of disease.
- Highly infectious and zoonotic
- CDC Class A pathogen; potential bioterrorism agent
- Tularemia awareness is important for veterinarians to (1) recognize, treat, and prevent disease in animal patients; (2) prevent disease exposure to themselves and other people in contact with infected animals; and (3) recognize potential bioterrorism in unexplained increase in cases.
- Tularemia is a reportable disease in most U.S. states; many states require immediate reporting (within 3 hours). Reporting regulations vary by country, state, and within-state region and may change. Veterinarians should verify infectious-disease reporting regulations for the areas in which they practice.

PREVENTION

- Tick, mosquito and biting fly control
- Limit exposure to rabbits, rodents, and other wild mammals.
- Currently, no licensed vaccine, although great effort to develop human vaccine underway.

TECHNICIAN TIPS

- Tularemia is extremely infectious and readily transmitted from infected animals to humans.
- Strict protective measures should be used in handling animals, their bedding, and all laboratory samples.
- Use of hoses to clean cages of infected animals, or blow dryers or fans in the proximity of the patient, is contraindicated. Resulting aerosols may cause exposure by inhalation and subsequent pneumonic tularemia, the most highly fatal form of the disease in people.

CLIENT EDUCATION

- Multiple reports of transmission to humans from infected cats (cat bite, cat scratch, cutaneous contact) and from pet prairie dogs.
- No recorded transmission from infected dog to humans, but the possibility is not excluded.

SUGGESTED READING

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Tritrichomonas Infection

BASIC INFORMATION

DEFINITION

Infection of the ileocolic and colonic mucosa with the protozoan parasite, *Tritrichomonas foetus,* causing chronic large-bowel diarrhea in susceptible young cats. The organism is a similar but distinct member of the protozoan family that causes early embryonic death and abortions in cattle.

EPIDEMIOLOGY

RISK FACTORS: The predominant risk factors appear to be age and population density. The infection is most prevalent in kittens and cats < 2 years of age housed in shelters and catteries. In one study of cats in a cat show, nearly 30% of the cats were asymptomatic carriers.

CONTAGION & ZOONOSIS: Zoonotic transmission has not been described.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Chronic large-bowel diarrhea that is refractory to standard antibiotic or antidiarrheal therapy and often progresses over time to liquid, fetid small-bowel diarrhea. Infected cats are often in good flesh, have a normal appetite and activity level, and are feline leukemia virus/feline immunodeficiency virus (FeLV/FIV) negative.

PHYSICAL EXAM FINDINGS: There are no specific physical exam findings. Affected kittens may have a reddened, protruding anal mucosa due to recurrent bouts of diarrhea and straining. Affected adult cats may have a normal physical examination, other than abnormal fecal odor and character.

ETIOLOGY AND PATHOPHYSIOLOGY

- *T. foetus* is a single-cell flagellated protozoan found in the colon of domestic cats.
- No cysts are formed, but the parasite is passed in the feces as a trophozoite.
- Infection occurs by direct fecal-oral transmission of the trophozoites.
- The pathophysiologic mechanism has not been described, but in one case, colonic biopsies revealed severe lymphocytic plasmacytic colitis with multifocal disruption of the surface epithelium.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Suspected in cats from population-dense environments presenting with chronic diarrhea. The confirmatory test of choice is a microscopic fecal exam.

DIFFERENTIAL DIAGNOSIS

- Giardiasis or enteritis due to other protozoan parasites
- Intestinal parasitism
- Idiopathic colitis or inflammatory bowel disease
- Bacterial colitis
- Dietary intolerance or sensitivity
- Antibiotic responsive diarrhea

INITIAL DATABASE

- Microscopic evaluation of fresh fecal preparations for trophozoites is diagnostic:
  - Fecal saline suspension (by mixing a speck of feces with a drop of saline on a microscope slide and covering with coverslip) or fecal smear of fresh feces
  - Directed motility of organisms, which are 10-25 µm long and flagellated

- Differentiation: unlike *Giardia* spp., trophozoites of *T. foetus* have an undulating membrane and demonstrate directed movement across the slide. *Giardia* spp. form cysts (which may also be seen on fecal suspensions, smears, and flotations), but *T. foetus* does not. Motility of *Giardia* is "falling leaf" or movement in place, which helps distinguish it from trichomonads.
- Main problem is that chronic diarrhea may make finding trophozoites difficult; in one study, only 20% sensitivity was reported.

- Minimum database (CBC, panel) is typically within normal limits.
- Fecal flotation to rule out other parasites
- Imaging (radiographs and ultrasound): generally unremarkable

ADVANCED OR CONFIRMATORY TESTING

- PCR to amplify *T. foetus* rDNA in the feces
- Protozoal culture of feces using the *T. foetus* pouch. This method can be especially helpful if chronic diarrhea makes finding trophs more difficult as a result of dilution of numbers; it increases the numbers of organisms so easy identification is possible.

TREATMENT

TREATMENT OVERVIEW

Treatment aims to resolve diarrhea and eradicate infection.

ACUTE AND CHRONIC TREATMENT

- Standard antiprotozoal and antidiarrheal therapies are ineffective for the eradication of *T. foetus* infection and the management of associated chronic diarrhea.
- Oral ronidazole (a nitroimidazole antimicrobial), 30-50 mg/kg PO q 24 h for 2 weeks. This powdered drug is not approved for use in cats and must be compounded to achieve appropriate dose forms. Reports indicate resolution of *T. foetus-associated* diarrhea and eradication of the infection (based on PCR studies). However, adverse effects (e.g., neurotoxicity) are relatively common with use of ronidazole, and it must be stopped immediately if signs of neurotoxicity are observed.

PROGNOSIS AND OUTCOME

- Historically, most cats diagnosed with chronic diarrhea resulting from *T. foetus* infection have had apparent resolution of the diarrhea within 2 years of onset. Chronic *T. foetus* infection following resolution of clinical signs appears to have been common.
- There appears to be an inverse correlation between housing density and the interval to the resolution of *T. foetus-associated* diarrhea.

PEARLS & CONSIDERATIONS

COMMENTS

Consider *T. foetus* as a differential diagnosis in kittens or young cats with chronic small- or large-bowel diarrhea, particularly if they are housed with other cats or have come from a shelter or cattery.

SUGGESTED READING

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Trigeminal Neuritis

BASIC INFORMATION

DEFINITION

An idiopathic, self-limiting inflammatory condition that involves the motor and sensory branches of the trigeminal nerve and (on occasion) the sympathetic innervation to the eye (i.e., Horner's syndrome)

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs most commonly affected; rare in cats

GENETICS & BREED PREDISPOSITION: No sex or breed predilection, although golden retrievers have been reported to be overrepresented.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Bilateral paralysis of the masticatory muscles that primarily affects the mandibular branch of the trigeminal nerve

HISTORY, CHIEF COMPLAINT: Acute or subacute onset of an inability to close the mouth. The dog cannot prehend food, may hypersalivate, and has difficulty drinking water.

PHYSICAL EXAM FINDINGS

- Bilateral paralysis of the masticatory muscles
- Affected dogs are bright and alert and do not appear as though they are in pain. They have no other detectable neurologic abnormalities.
- In some cases, there is decreased facial sensation bilaterally, and Horner's syndrome may be observed.
- Trismus/inability to open the mouth does not occur with trigeminal neuritis.

ETIOLOGY AND PATHOPHYSIOLOGY

- Most common neurologic cause of an inability to close the mouth in the dog
- Etiology is unknown, but extensive bilateral nonsuppurative inflammation, demyelination, and, in some cases, axonal degeneration of all portions of the trigeminal nerve and its ganglion, with no brainstem lesions, have been reported at necropsy.
- Complete recovery is observed in 2-3 weeks (rarely, may take several months), with no drug therapy being reported as useful.
- Facial sensation is usually preserved. Occasionally, Horner's syndrome may be observed, presumably because the postganglionic sympathetic axons course with the ophthalmic branch of the trigeminal nerve.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is based on characteristic clinical signs, absence of other neurologic deficits, and elimination of the possibility of orthopedic (mandibular, temporomandibular joint) disorders. Advanced diagnostic testing is generally reserved for cases showing additional or unusual neurologic deficits, when spontaneous resolution does not occur, or if rabies is possible (quarantine/euthanasia).

DIFFERENTIAL DIAGNOSIS

- Rabies
- Traumatic mandibular injury
- Inflammatory or infectious central nervous system (CNS) disease

INITIAL DATABASE

CBC, serum chemistry profile, urinalysis: usually within normal limits

ADVANCED OR CONFIRMATORY TESTING

- Cerebrospinal fluid (CSF) analysis may be normal or show mild increases in protein concentration. Lymphocytic pleocytosis is rarely observed.
- Electromyography may reveal increased insertional activity and other mild changes.
- CT scan or MRI of the brain: within normal limits
- Trigeminal nerve biopsy: not recommended

TREATMENT

TREATMENT OVERVIEW

Spontaneous resolution usually occurs in 2-3 weeks with no treatment.

ACUTE GENERAL TREATMENT

- Maintenance of hydration and alimentation is critical.
- Percutaneous gastrostomy may be helpful in severe cases (see p. 1270).
- Feeding canned food gruel is most helpful, since tongue function is maintained.

CHRONIC TREATMENT

Signs will typically resolve spontaneously in 2-3 weeks but in some cases will take months to totally normalize.

POSSIBLE COMPLICATIONS

- Dehydration
- Weight loss

RECOMMENDED MONITORING

- Hydration status
- Food intake

PROGNOSIS AND OUTCOME

Excellent for recovery

PEARLS & CONSIDERATIONS

COMMENTS

- If signs do not resolve in the 2-3-week period, other differentials should be considered.
- If sensory deficits are observed, the recovery period may take longer.

CLIENT EDUCATION

- Signs are typically self-limiting and should resolve in 2-3 weeks.
- Suggested feeding protocols

SUGGESTED READING

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Tricuspid Valve Dysplasia

BASIC INFORMATION

DEFINITION

Congenital cardiac abnormality involving the right atrioventricular (AV) valve (tricuspid valve) and characterized by any or all of the following: thickening of leaflets, foreshortening of chordae tendinae, fusing or underdevelopment of right ventricle (RV) papillary muscles, tethering of particularly the septal leaflet to the underlying ventricular muscle, and redundancy of the parietal leaflet

SYNONYMS

Congenital tricuspid valve malformation, Ebstein anomaly (specific form of tricuspid valve dysplasia [TVD])

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs and cats
- Present at birth; however, affected individuals are identified at any age based on when the heart murmur is detected.
- Either sex

GENETICS & BREED PREDISPOSITION: Identified in several breeds, notably Labrador retrievers

ASSOCIATED CONDITIONS & DISORDERS

- Typically an isolated congenital heart defect
- Atrial septal defect (ASD), patent foramen ovale, mitral valve dysplasia, ventricular septal defect (VSD), pulmonic stenosis (PS), and patent ductus arteriosus have coexisted.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Often no clinical signs are detectable by the owner (incidental discovery of heart murmur on routine physical exam).
- Severe forms of the disease cause exercise intolerance, abdominal distension, dyspnea (secondary to pleural effusion), poor appetite, and weight loss.

PHYSICAL EXAM FINDINGS

- Right-sided systolic heart murmur of tricuspid regurgitation (significantly softer or even inaudible over the left precordium)
- Rarely a soft diastolic murmur of tricuspid stenosis
- Tachycardia possible
- Jugular venous distension and pulsation if severe disease
- Abdominal palpation: hepatomegaly and a peritoneal fluid wave if right-sided congestive heart failure (R-CHF) is present
- Femoral pulses: usually normal; weak with severe disease associated with poor cardiac output
- Lung auscultation: usually normal; muffled lung sounds if pleural effusion
- Mucous membrane color: usually normal; pale with poor cardiac output; cyanotic if concurrent patent foramen ovale or septal defect

ETIOLOGY AND PATHOPHYSIOLOGY

- During embryonic development, tricuspid valve leaflets are almost exclusively derived from ventricular myocardium by a process of undermining the RV inner wall:
  - The inner layer of RV myocardium is undermined from the remainder to form a skirt in which perforations appear in the apical portion.
  - These perforations enlarge until only the papillary muscles remain, and the initially muscular chordae tendinae become fibrous.
  - Abnormalities during this process lead to TVD.

- An autosomal dominant mode of inheritance with reduced penetrance has been found to date only in the Labrador breed:
  - Affected Labrador retrievers that have been studied thus far (from different families) all had the same susceptibility locus identified, suggesting a founder effect.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Physical examination findings are highly suggestive; echocardiography is required for confirmation and delineation of the defect's extent/structure, as well as associated defects.

DIFFERENTIAL DIAGNOSIS

- Tricuspid valve endocardiosis/myxomatous valve disease: older dogs; concurrent more severe myxomatous mitral valve disease/endocardiosis generally is present.
- Tricuspid valve endocarditis: very rare in dogs and cats, associated with systemic illness and fever (can be waxing and waning); focal valve thickening or vegetation

INITIAL DATABASE

- Echocardiogram (see p. 1251):
  - Diagnostic test of choice
  - Two-dimensional (2-D) mode defines degrees of tricuspid valve leaflet thickening, adherence of the septal leaflet to the interventricular septum, redundancy of the parietal leaflet, presence of hyperechoic fibrous tissue at the annulus resulting in stenosis, and right atrial and right ventricular dilation.
  - Doppler echocardiography documents the presence and degree of tricuspid regurgitation and presence/severity of tricuspid stenosis.
  - Concurrent defects can be identified.
- Thoracic radiographs:
  - Normal in mild disease
  - Evidence of right atrial and right ventricular enlargement in moderate to severe disease
  - Enlargement of the caudal vena cava and possible pulmonary hypoperfusion in severe disease
  - Hepatomegaly, peritoneal effusion, and less commonly, pleural effusion can occur in severe cases (such as in R-CHF).
- Electrocardiogram (ECG; see p. 1253):
  - Normal in mild disease
  - May exhibit fragmentation or splintering of the QRS complex, with a normal mean electrical axis
  - Less commonly, classic right axis deviation of the QRS complex as seen with right ventricular dilation
  - P waves may be tall and wide.
  - May exhibit ventricular preexcitation or supraventricular tachycardias associated with accessory pathway conduction (e.g., see online chapter: Wolff-Parkinson-White Syndrome).

ADVANCED OR CONFIRMATORY TESTING

- Generally not required
- Holter monitoring to document intermittent tachyarrhythmias (see p. 1287)

TREATMENT

TREATMENT OVERVIEW

Goals of treatment are to control R-CHF if present, control associated tachyarrhythmias, and consider surgical valve reconstruction in severe cases.

ACUTE GENERAL TREATMENT

- Abdominocentesis (see p. 1193) or abdominal drainage (see p. 1192) for severe peritoneal effusion to relieve abdominal pressure that can inhibit diaphragmatic movement
- Cage rest for severe R-CHF
- Antiarrhythmic treatment for acute control of supraventricular tachyarrhythmias

CHRONIC TREATMENT

- Careful diuretic administration for CHF (furosemide, 1-2 mg/kg PO q 8-12 h; spironolactone, 1-2 mg/kg PO q 12 h)
- Low-dose angiotensin-converting enzyme (ACE) inhibition may be helpful (e.g., enalapril or benazepril, 0.1-0.25 mg/kg PO q 12-24 h)
- Pimobendan, 0.25 mg/kg PO q 12 h in the face of RV myocardial failure (very advanced stages)
- Digoxin, 0.0055 mg/kg PO q 12 h, adjusting based on serum digoxin concentrations, for certain supraventricular tachyarrhythmias; consultation with a cardiologist is recommended
- Exercise restriction
- Nutritional management (see below)

NUTRITION/DIET

- A high-quality, reduced-sodium diet (<90 mg sodium/100 kcal) in the face of congestive heart failure
- Nutritional management of cardiac cachexia (adequate calorie intake for disease state, highly digestible foods [see p. 168])

DRUG INTERACTIONS/CONTRAINDICATIONS

- Be careful about compromising renal perfusion, owing to excessive diuretic administration and poor forward cardiac output from the disease.
- Coadministration of spironolactone and ACE inhibitors can theoretically lead to hyperkalemia, although concurrent furosemide administration generally causes potassium wasting.

POSSIBLE COMPLICATIONS

- Excessive diuresis, causing decreased forward output and weakness
- Electrolyte abnormalities and azotemia secondary to diuresis and renal hypoperfusion
- Hypoalbuminemia secondary to cardiac cachexia and continued peritoneal effusion

RECOMMENDED MONITORING

- Monitor for signs of R-CHF (peritoneal effusion, decreased exercise tolerance, decreasing muscle mass).
- Monitor for tachyarrhythmias (ECG, Holter monitoring if necessary).
- If the animal is receiving a diuretic and other CHF therapy, monitor the serum chemistry profile every 5-7 days after medication adjustments are made and every 3 months thereafter.

PROGNOSIS AND OUTCOME

- Better than is typically found in the literature
- Dogs with mild disease and even many with moderate disease can live a normal lifespan.
- Dogs with severe disease will have shortened lifespans, but some can live several years (5 or more years is possible).

PEARLS & CONSIDERATIONS

COMMENTS

- TVD appears to be inherited as an autosomal dominant trait with reduced penetrance in Labradors, meaning it may be transmitted by the sire or the dam, and the extent to which offspring are affected is individually variable.
- Carefully auscult dogs over the right precordium to detect this disease.
- Prognosis in animals with isolated TVD is better than initially thought, although the lifespan of dogs with severe disease is still shortened.
- Major complications in severe disease include CHF and tachyarrhythmias.
- Concurrent congenital heart defects are not common but, if present, generally worsen the prognosis.

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Tremors and Myoclonus

BASIC INFORMATION

DEFINITION

- Tremor: involuntary oscillating contraction of opposing muscle groups: may occur during rest or movement and typically disappears during sleep.
- Myoclonus: single or multiple shocklike contraction of a muscle group: may occur singly or repetitively, regularly or irregularly, and does not stop during sleep.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dependent on underlying cause.

- Dogs: puppies (hypomyelination/dysmyelination, familial myoclonus): young adults (see p. 592); older adults (senile tremors)
- Cats: kittens (hypomyelination)

GENETICS & BREED PREDISPOSITION

Dogs:

- Maltese, West Highland white terriers, other small-breed white or nonwhite dogs (see p. 592)
- Doberman pinscher, English bulldog, Shetland sheepdog, boxer: idiopathic head tremors
- Labrador retriever: idiopathic head tremor, familial myoclonus
- Great Dane, mastiff: orthostatic tremor
- Springer spaniel, Samoyed, chow chow, weimaraner, Lurcher, Bernese mountain dog, dalmatian: hypomyelination/dysmyelination
- Scottish terriers: central axonopathy

Cats:

- Siamese: hypomyelination

RISK FACTORS: Exposure to tremorgenic drugs or toxins

CONTAGION & ZOONOSIS: Dogs: distemper virus (dog-to-dog transmission)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Generalized more common than localized
- Resting tremor
- Action tremor
- Intention tremor

HISTORY, CHIEF COMPLAINT

- Tremor may worsen with exercise and abate with rest or sleep.
- Littermates may be affected:
  - Tremor associated with hypomyelination/dysmyelination typically begins between 12 days and 3 weeks of age. Signs worsen with exercise but often resolve with rest.
- Exposure to tremorgenic toxins
- Insulin therapy for diabetes mellitus, suggesting hypoglycemia
- Recent (preceding weeks/months) history of respiratory disease, ill thrift, or adoption from a shelter, suggesting canine distemper-associated myoclonus
- Recent whelping, suggesting hypocalcemia
- Seizures (must be differentiated from tremor/myoclonus)

- Idiopathic head tremors are episodic and may be confused for focal seizures. They are often precipitated by excitement or particular head positions, and owners may describe a characteristic “yes” or “no” movement of the head and normal consciousness with tremors, in contrast to the tonicclonic or gum-chewing motions of seizures.
- Orthostatic tremor is a fine tremor of the muscles that occurs only while standing and subsides when walking, running, or in recumbency.
- Scottish terriers with central axonopathy develop tremors and ataxia at 10-12 weeks of age.

PHYSICAL AND NEUROLOGIC EXAM FINDINGS

- The presence of tremors or myoclonus may be the only abnormality on the physical or neurologic examination.
- Ataxia, paresis, and proprioceptive deficits may be present, suggesting a central (brain, spinal cord) lesion.
- Seizures, stupor, and coma may be seen concurrently with intoxication or metabolic derangement.
- Ocular tremors and menace deficits often accompany idiopathic tremor syndrome.
- Intention tremor (i.e., tremor precipitated by the onset of voluntary movement, such as responding to a command) if associated with a fine head tremor, dysmetria, and nystagmus, is characteristic of cerebellar disease.
- Pelvic limb tremors in older dogs (senile tremors)

ETIOLOGY AND PATHOPHYSIOLOGY

Primary:

- Idiopathic tremor syndrome: immune-mediated (see p. 592)
- Hypomyelination, dysmyelination: congenital
- Lysosomal storage diseases: congenital
- Cerebellar disease
- Idiopathic head tremors
- Senile tremors

Systemic:

- Intoxication (mycotoxins [see p. 144]. hexachlorophene, heavy metals, organophosphates [see p. 792], metaldehyde [see p. 720], pyrethrins [see p. 958], others)
- Drug administration (fentanyl/droperi-dol, epinephrine, metoclopramide, diphenhydramine, isoproterenol, numerous illicit drugs)
- Metabolic (hypocalcemia, hypoglycemia, hepatic or uremic encephalopathy, hyperthyroidism)
- Infectious (canine distemper)

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A presumptive diagnosis is often made based on the signalment, history, and clinical findings.

DIFFERENTIAL DIAGNOSIS

- Shivering
- Tetany
- Weakness
- Seizure
- Specific causes according to etiology

INITIAL DATABASE

- Complete physical and neurologic examination
- CBC, serum biochemistry, and urinalysis to assess for metabolic etiologies
- Serum T4 (hyperthyroidism in cats)

ADVANCED OR CONFIRMATORY TESTING

Cerebrospinal fluid (CSF) analysis: may be normal or reveal increased numbers of leukocytes (usually lymphocytes) with increased levels of protein, reflecting a nonsuppurative meningoencephalitis

TREATMENT

TREATMENT OVERVIEW

Identify and treat the underlying cause of tremors.

ACUTE GENERAL TREATMENT

- General and/or specific treatment for intoxication
- Discontinue drug therapy if suspected to be causing tremors.
- Correct metabolic and electrolyte abnormalities.
- Sterile inflammatory tremor syndromes often respond to corticosteroid therapy.
- Orthostatic tremor usually improves with phenobarbital or gabapentin administration.

CHRONIC TREATMENT

- Long-term corticosteroid therapy is often necessary for inflammatory tremor syndromes.
- Supportive care aimed at keeping animals safe and ensuring adequate caloric and water intake.

POSSIBLE COMPLICATIONS

Prolonged tremors may result in hyperthermia, hypoglycemia, dehydration, and anorexia.

RECOMMENDED MONITORING

Follow-up exam and serial diagnostic studies as directed by the animal's clinical progression

PROGNOSIS AND OUTCOME

- Tremors associated with idiopathic tremor syndrome usually resolve within days of the initiation of corticosteroid therapy:
  - Treatment should be continued for 2-3 months.
  - Relapses may occur.
- Male springer spaniels with hypomyelination are nonambulatory and generally do not recover.
- Female springer spaniels and other breeds with hypomyelination/dysmyelination usually recover completely between 2 and 12 months of age.
- Idiopathic head tremors may improve and become less frequent over time and rarely cause any clinical dysfunction.
- Senile tremors also generally do not interfere with normal function.
- Central axonopathy in Scottish terriers is progressive and associated with a poor prognosis.
- Lysosomal storage diseases are usually fatal.
- Toxin and drug-induced tremors resolve if the animal survives the initial event.

PEARLS & CONSIDERATIONS

CLIENT EDUCATION

- Owners should be warned that excitement and exercise often precipitate or worsen tremors.
- Many tremor syndromes have a known or suspected inherited basis, and these animals should not be bred.

SUGGESTED READING

Garosi LS, Rossmeisl JH, de Lahunta A, et al: Primary orthostatic tremor in Great Danes. J Vet Intern Med 19(4):606–609, 2005.

AUTHOR: GREG KILBURN

EDITOR: ETIENNE CÔTÉ

Transmissible Venereal Tumor

BASIC INFORMATION

DEFINITION

A contagious, neoplastic disease transmitted by transplantation of viable tumor cells during coitus

SYNONYMS

Canine condyloma, contagious lymphoma, contagious venereal tumor, infectious sarcoma, Sticker's sarcoma, transmissible venereal sarcoma, venereal granuloma

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Species: canids—dogs, foxes, coyotes, jackals
- Age: mostly young, sexually active animals; average age 4-5 years
- Sex: females > males

GENETICS & BREED PREDISPOSITION

- Higher prevalence in mixed-breed dogs

RISK FACTORS

- More commonly occurs in free-roaming sexually active dogs
- Grows more rapidly in neonatal or immunosuppressed dogs

CONTAGION & ZOONOSIS

- By definition, transmissible venereal tumor (TVT) is contagious among members of the family Canidae. It has not been identified as a zoonotic disease, although personal protection apparel (exam gloves, etc.) is recommended when examining and treating TVT lesions.

GEOGRAPHY AND SEASONALITY

- Worldwide distribution
- Greatest prevalence in tropical and subtropical urban environments

ASSOCIATED CONDITIONS & DISORDERS

- Urinary tract infections (UTIs; due to presence of TVT in the vestibulovagi-nal junction of females) and phimosis (males; inability to extrude the penis from the prepuce). Both conditions interfere with voiding of urine.
- Tumors are easily traumatized and ulcerated; secondary bacterial infection is a common sequela.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Initial persistent or intermittent bloody genital discharge (often foul smelling), constant licking, genital malformation, or swelling
- Eventually, masses can be seen protruding either from vulva or penis.
- Clinical signs of TVT typically last 40-100 days but may last longer depending on the tumor size and location, immune status of the animal, and occurrence of secondary bacterial infections.

PHYSICAL EXAM FINDINGS

- Nodular lesions in the external genitalia

- Solitary or multiple masses progressing to cauliflower-like, papillary, multilobulated, or pedunculated masses
- Appearance is typically gray or pinkish gray.
- Texture is firm but friable; masses bleed easily when manipulated, resulting in genital bleeding in both sexes.

Definitive diagnosis is by histologic classification of a biopsy specimen (after formalin fixation and staining with hematoxylin and eosin) and immunochemistry testing to determine degree of malignancy.

TREATMENT

TREATMENT OVERVIEW

The goal of treatment is elimination of the tumor. Spontaneous regression occurs in experimental and clinical cases.

ACUTE GENERAL TREATMENT

- The rationale for surgical removal of the tumor is to induce an immune response as well as mechanically remove the mass. A small TVT may be surgically excised without relapse, but tumor regrowth frequently occurs over a very short period of time following excision of large tumors (>2 cm).
- Chemotherapy with vincristine at 0.025 mg/kg IV (highly corrosive if extravascular) once weekly for 6 weeks until complete tumor regression is the treatment of choice for metastatic or multifocal TVT.
- Radiation therapy is effective (100% cure with a single radiation dose) when appropriate facilities are available.

CHRONIC TREATMENT

Electrochemotherapy with bleomycin has been tried for vincristine-resistant TVT.

BEHAVIOR/EXERCISE

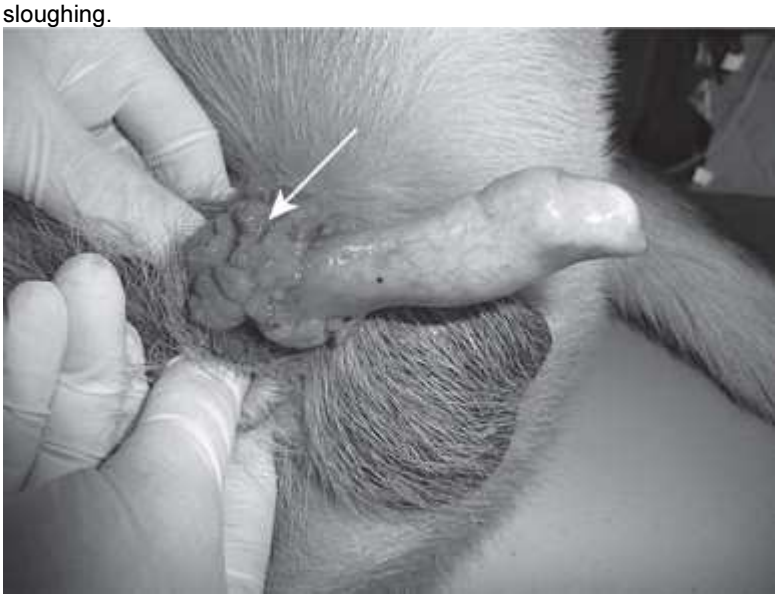
- Breeding should be avoided when TVT is present (contagion risk).
- Erection from excitement with preputial extrusion of the penis with a TVT tumor may result in paraphimosis.

DRUG INTERACTIONS

Severe bronchospasm has been reported in humans when vinca alkaloids are used in combination with mitomycin C.

POSSIBLE COMPLICATIONS

- Extravasation injuries associated with perivascular injection of vincristine can range from irritation to necrosis and tissue sloughing.



TRANSMISSIBLE VENEREAL TUMOR Transmissible venereal tumor *(arrow)* surrounding the bulbus glandis of an intact male dog. Prepuce was difficult to retract over the penis owing to size of tumor relative to size of preputial opening.

- Combined chemotherapy with vincristine presents more side effects (vomiting, diarrhea, and neutropenia) than vincristine alone.

RECOMMENDED MONITORING

- Monitor for efficacy (tumor reduction).
- Monitor for toxicosis, using peripheral neuropathic clinical signs, CBCs with platelets, and liver tests before, during, and after treatment.

PROGNOSIS AND OUTCOME 

Despite the location or pattern of metastasis, the prognosis for TVT is excellent with recommended therapy.

PEARLS & CONSIDERATIONS 

COMMENTS

With any kind of vaginal or preputial bleeding:

- Cytologic examination for TVT cells
- Visual examination of clitoral fossa and preputial fornix for gross TVT lesions

PREVENTION

Pet dogs should avoid contact with stray dogs.

CLIENT EDUCATION

In areas were TVT is endemic, pet dogs should be confined and spayed or neutered to reduce the risk of disease transmission.

SUGGESTED READING

Feldman EC, Nelson RW: Brucellosis and transmissible venereal tumor. In Canine and feline endocrinology and reproduction, ed 3, St Louis, 2004, Elsevier Saunders, pp 924–927.

AUTHOR: ROSA MARÍA PÁRAMO RAMIREZ

EDITOR: MICHELLE A. KUTZLER

Transitional Cell Carcinoma

BASIC INFORMATION

DEFINITION

Neoplasms arising in the bladder parenchyma of epithelial origin; relatively common in dogs but rare in cats

SYNONYM

TCC

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs: typically, older adults (median age 11 years). Females appear at higher risk than males.
- Cats: rarely affects older adults, males at increased risk

GENETICS & BREED PREDISPOSITION: Scottish terriers (up to 20-fold increased risk), Shetland sheepdogs, West Highland white terriers, wirehaired fox terriers, Airedales, beagles, and collies have higher incidence.

RISK FACTORS

- Dogs: female predominance. Exposure to herbicides and insecticides associated with an increased risk; worsened in the presence of obesity, possibly due to accumulation of “inert ingredients.” Spot-on flea products do not appear to increase risk. Cyclophosphamide administration may increase risk.
- Cats: possibly associated with chronic urinary tract infection (UTI). Older cats at greatest risk.

ASSOCIATED CONDITIONS & DISORDERS

- Bacterial cystitis
- Hypertrophic osteopathy
- Urethral obstruction
- Bladder atonia/hypotonia

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Most common form is invasive cancer into muscularis, most often in trigone region
- Early form of superficial cancer may be identified that may be more responsive to therapy.

HISTORY, CHIEF COMPLAINT

- Pollakiuria (common)
- Hematuria (common)
- Stranguria (common)
- Tenesmus (occasional)
- Abdominal pain (occasional)
- Abdominal distension (occasional)
- Lameness and joint thickening (rare; associated with hypertrophic osteopathy)

PHYSICAL EXAM FINDINGS

- Abdominal tenderness +/−
- Caudal abdominal mass +/−
- Urethral mass on rectal exam +/−
- Distended urinary bladder +/−

- Abdominal distension with fluid wave if bladder ruptured (rare)

ETIOLOGY AND PATHOPHYSIOLOGY

- Bladder mass most commonly occurs in trigone region.
- Urethral or prostate involvement is common, often leading to obstruction.
- Lymph node metastasis present in approximately 15% of cases.
- Distant metastasis common (49% at death)
- Metastatic sites include lymph node, lung, liver, kidney, spleen, uterus, gastrointestinal (GI) tract, bone, muscle, cystocentesis needle tracts.
- Secondary bacterial urinary infection common

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Middle-aged to older animals with signs of recurrent UTI should be screened for bladder masses, and dogs of at-risk breeds —particularly Scottish terriers— should be screened early. Diagnosis should be made as early as possible to achieve the best outcome.

DIFFERENTIAL DIAGNOSIS

- Pollakiuria, stranguria, hematuria:
  - UTI
  - Urolithiasis
  - Feline lower urinary tract disease/interstitial cystitis
  - Other bladder tumor such as botryoid rhabdomyosarcoma (in young, large-breed dogs) or leiomyosarcoma
- Abdominal distension/tenderness or abdominal mass:
  - Mass in spleen, mesenteric lymph node, or retroperitoneal space
  - Ruptured splenic or hepatic mass with hemoperitoneum
  - Abdominal trauma or coagulopathy with peritoneal or retroperitoneal bleeding
  - Rectal mass
  - Prostatic abscess, cyst, or neoplasia
  - Pyelonephritis
  - Hydronephrosis or hydroureter
- Radiographic:
  - Other bladder neoplasm or radiolucent urolithiasis
  - Ruptured splenic, renal, or hepatic mass with hemoperitoneum
  - Traumatic bladder rupture
- Ultrasonographic :
  - Papillary cystitis
  - Leiomyosarcoma
  - Botryoid rhabdomyosarcoma
  - Lymphoma (rare)
  - Other rare carcinomas or sarcomas
- Urinalysis:
  - UTI
  - Urolithiasis
  - Other bladder tumor
  - Idiopathic renal hematuria

INITIAL DATABASE

- CBC, chemistry profile: no specific findings supportive of TCC. Azotemia, hyperkalemia may occur with urethral or ureteral obstruction.
- Urinalysis: proteinuria and hematuria are most common. May be complicated by secondary bacterial UTI with pyuria, bacteruria. Cystocentesis has been associated with needle-tract neoplastic cell implantation; recommend catheterization or free-catch for urine collection.
- Veterinary bladder tumor antigen test (VBTA): approximately 85% sensitive for TCC but only 45% specific in the presence of other urinary tract disease. As such, it is a good screening test but does not confirm the presence of TCC.
- Abdominal radiographs: bladder mass is possible to visualize, but this is unusual. Bladder distension may be seen, and with rupture, possible peritoneal or retroperitoneal fluid may be present.

- Thoracic radiographs: metastasis may be present. Pulmonary lesions my be nodular interstitial, unstructured interstitial, cavitated, or alveolar in appearance; bone lesions possible.
- Abdominal ultrasound: bladder mass or wall thickening with possible metastasis to abdominal organs or nodes; prostate or urethra are commonly involved.

ADVANCED OR CONFIRMATORY TESTING

- Cytologic analysis or biopsy from guided diagnostic catheterization or biopsy from cystoscopy necessary for diagnosis
- Contrast cystography/ureterography may be used to delineate ureteral involvement and impending urethral obstruction.
- VBTA does not confirm, only suggests, TCC.

TREATMENT

TREATMENT OVERVIEW

The therapeutic goal is to alleviate clinical signs, control the primary mass, and prevent or delay metastasis

ACUTE GENERAL TREATMENT

- Surgically manage urinary bladder rupture if present (see p. 1135)
- Surgically remove lesions at bladder apex if operable. Surgery may be of greater benefit in cats.
- Address complicating bacterial UTI with antimicrobials (see p. 276).
- Begin chemotherapy to palliate clinical signs and address metastatic disease: See p.677 for conversion table of body weight to body surface area.
  - Piroxicam, 0.3 mg/kg PO once daily if renal function is normal. Can be used alone or in combination with:
  - Mitoxantrone, 5 mg/m^2 IV q 21 days for 4 cycles; *or*
  - Doxorubicin, 30 mg/m^2 IV q 21 days for 4 cycles (dogs); or 1 mg/kg IV q 21 days (cats and small dogs)
  - CBC and blood urea nitrogen (BUN)/ creatinine/urine specific gravity should be checked prior to each dose, and CBC checked 1 week later.
  - Cisplatin cannot be recommended in combination with piroxicam due to nephrotoxicity.
  - Intravesicular therapy of BCG or thiotepa used in humans has been poorly effective in veterinary patients.
- If bladder distended initially, maintain urinary drainage to avoid detrusor hypotonia (see pp. 104 and 1131)
- Address electrolyte imbalances if present secondary to obstruction (see pp. 1131 and 556)

CHRONIC TREATMENT

- Continue piroxicam indefinitely.
- May repeat mitoxantrone after first four doses if clinical signs recur.
- Cumulative doxorubicin doses greater than 180-240 mg/m^2 are associated with increased risk of cardiotoxicity.
- Urinary diversion surgery or intraluminal stenting may prolong life if urethral obstruction is imminent.

NUTRITION/DIET

Feeding vegetables may help prevent bladder transitional cell carcinoma.

DRUG INTERACTIONS

- Avoid combining drugs with similar toxicity profiles, such as cisplatin and piroxicam.
- Piroxicam should not be given in combination with corticosteroids or other nonsteroidal antiinflammatory drugs.

POSSIBLE COMPLICATIONS

- Neutropenia, thrombocytopenia, sepsis, and renal injury secondary to chemotherapy
- GI ulceration or nephrotoxicity secondary to piroxicam
- Urethral or ureteral obstruction secondary to tumor growth

RECOMMENDED MONITORING

- Monitor CBC prior to every chemotherapy treatment and 7-10 days later.
- Monitor BUN, creatinine, and urine specific gravity for renal function every 3-12 weeks.
- Monitor frequently for UTI.

PROGNOSIS AND OUTCOME

This disease is locally aggressive with a significant metastatic potential.

Dogs:

- Median reported survival treated with piroxicam alone is approximately 6-7 months.
- Median reported survival treated with piroxicam and mitoxantrone is approximately 12 months, with or without surgery.
- Median reported survival treated with surgery alone is approximately 3.5 months.

Cats:

- Median reported survival approximately 8.5 months
- Surgical resection may improve prognosis significantly in cats.

PEARLS & CONSIDERATIONS

COMMENTS

- Repeated urinary tract signs or infection, especially in older animals, warrants further screening for TCC
- Early detection is critical for best response to treatment.
- VBTA test may allow early detection in geriatric at-risk breeds of dogs with lower urinary tract signs.
- Definitive diagnosis necessary for prognosis and therapeutic decisions; requires cytologic examination or biopsy.
- Bacterial UTI is a frequent complication.

PREVENTION

see Nutrition/Diet

TECHNICIAN TIPS

Because cystocentesis can allow peritoneal seeding and accelerate metastasis, it should be avoided in older dogs (especially in predisposed breeds) with signs of dysuria prior to screening for TCC by imaging or VBTA.

CLIENT EDUCATION

- Signs are subtle and nonspecific, so advanced diagnostics and imaging are most useful early.
- Urethral obstruction is often the life-limiting complication, and urinary diversion may be beneficial.

SUGGESTED READING

Henry CJ: Management of transitional cell carcinoma. Vet Clin North Am Small Anim Pract 33:597–613, 2003.

Wilson HM, et al: Clinical signs, treatments, and outcome in cats with transitional cell carcinoma of the urinary bladder: 20 cases (1990-2004). J Am Vet Med Assoc 231:101–106, 2007.

Greene SN, et al: Evaluation of cisplatin administered with piroxicam in dogs with transitional cell carcinoma of the urinary bladder. J Am Vet Med Assoc 231:1056–1060, 2007.

Raghavan M, et al: Evaluation of the effect of dietary vegetable consumption on reducing risk of transitional cell carcinoma of the urinary bladder in Scottish terriers. J Am Vet Med Assoc 227:94–100, 2005.

AUTHOR: JEFFREY BRYAN

EDITOR: LEAH A. COHN

Transfusion Reactions

BASIC INFORMATION

DEFINITION

Adverse effects from infusion of blood products are well recognized. They are classified as immunologic or nonimmunologic and further categorized as acute (minutes to 48 hours later) or delayed (days to weeks later).

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs and cats of any age and either sex

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Acute immunologic:
  - Acute hemolytic transfusion reaction (AHTR): antibodies to donor red blood cells (RBCs) are present in recipient plasma (incompatible blood type).
  - Nonhemolytic febrile reaction: recipient antibodies against donor leukocyte or protein antigens
  - Anaphylaxis: recipient hypersensitivity/immune reaction to donor leukocyte, major histocompatibility complex, or protein antigens
- Acute nonimmunologic:
  - In vitro hemolysis: improper handling of blood (freezing, overheating, mixing with nonisotonic solutions, inappropriate infusion devices)
  - Volume overload: excessively rapid or large-volume infusion, particularly in cats, puppies, and small dogs or in those with compromised cardiac or renal function.
  - Contaminated blood: lack of aseptic collection or storage, long transfusion times (>4 hours), and subclinical infection of donor
  - Citrate intoxication: rapid large-volume infusions of whole blood or plasma in small animals or those with liver failure
  - Hyperammonemia: high ammonia levels in stored blood in animals with hepatic failure
- Delayed immunologic:
  - Development of antibody that shortens lifespan of transfused RBCs
  - Occurs within 3 days to several weeks
- Delayed nonimmunologic:
  - Transmission of infectious diseases from donors

HISTORY, CHIEF COMPLAINT: Current (acute reaction) or recent (delayed reaction) transfusion of whole blood, packed RBCs, or platelet-rich plasma

PHYSICAL EXAM FINDINGS: In most instances, the first manifestations of a transfusion reaction include only one or two of the physical signs listed for each. If unnoticed, however, these signs may quickly worsen, with additional signs occurring as the reaction worsens.

- Acute immunologic:
  - RBC: vomiting, fever, anaphylaxis (lethargy, urticaria, pruritus, tachypnea/dyspnea), hemolysis (pallor, tachycardia, weakness), tremors, salivation hypotension (weak pulse), pigmenturia, ventricular arrhythmias, apnea
  - Platelet/leukocyte: fever, vomiting
  - Plasma proteins: urticaria, edema, pruritus, erythema
- Acute nonimmunologic:
  - Contamination: sepsis (fever, weak pulse, tachycardia), hemoglobinuria, vomiting
  - Disseminated intravascular coagulation possible (hemorrhage, thrombosis; see p. 315)
  - Improper collection, in vitro hemolysis: vomiting
  - Volume overload: dyspnea, tachypnea, tachycardia, new-onset cough (dry, soft at first), vomiting (rarely)
  - Citrate toxicity: uncommon; vomiting, tremors, tetany
- Delayed immunologic:
  - RBC: recurrence of clinical signs of anemia sooner than expected (shortened RBC survival)
  - Platelet: melena, epistaxis, ecchymoses (thrombocytopenia: post-transfusion purpura)
- Delayed nonimmunologic:

- Disease transmission; signs reflect pathogen transmitted.

ETIOLOGY AND PATHOPHYSIOLOGY

- Immunologic: specific cellular or protein fraction in blood transfused to sensitized recipient:
  - Acute: animals receiving incompatible blood (A/B incompatibility in cats; or rarely Mik) or dogs sensitized by prior transfusion, usually dog erythrocyte antigen (DEA) 1.1 incompatibility (or rarely other antigens)
  - Delayed: previously transfused animals with antibodies to minor RBC antigens
- Nonimmunologic: results from contamination, improper handling, or cytokine activation in the blood product

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Clinical signs of transfusion reaction usually appear during or immediately after the transfusion. Signs that develop after several days (delayed reaction) may need to be differentiated from recurrence of the disorder that warranted transfusion originally (e.g., hemolysis) and from complications of the disease or its treatment (e.g., sepsis). Additional testing, if necessary, is selected based on the type and severity of the reaction.

DIFFERENTIAL DIAGNOSIS

- Hemolysis: rule out underlying hemolytic diseases (see p. 71).
- Fever: rule out acute hemolytic transfusion reaction, sepsis, underlying inflammatory diseases.

INITIAL DATABASE

- CBC, serum biochemistry panel, urinalysis:
  - Hemoglobinemia (after centrifuging, serum is pink; repeat blood sampling to rule out hemolysis from blood collection).
  - Bilirubinemia (serum often icteric if bilirubin > 1 mg/dL [>17 mmol/L])
  - Leukocytosis
- Urinalysis: hemoglobinuria, bilirubinuria
- Hypocalcemia (citrate toxicity); only ionized calcium is reduced.
- Blood pressure (BP) measurement (see p. 1209): rule out hypotension.
- Thoracic radiographs: if volume overload is suspected (rule out pulmonary edema)

ADVANCED OR CONFIRMATORY TESTING

- Acute hemolytic transfusion reaction: centrifuge recipient blood to check for evidence of hemolysis; repeat major cross match (see p. 1234); Coombs' test on recipient.
- Inspect transfused unit for dark discoloration, clots, air bubbles, or hemolysis to detect contaminated blood; Gram stain and culture (aerobic/ anaerobic).
- Examine blood from bag or administration set for in vitro hemolysis.

TREATMENT

TREATMENT OVERVIEW

Treatment is tailored to the type and severity of the reaction. Often, slowing or stopping the transfusion is sufficient, while in other cases pharmacologic therapy may be necessary (see reaction types below). Identification and correction of the cause of reaction are indicated (when possible), and supportive care should be provided while clinical signs resolve.

ACUTE GENERAL TREATMENT

- Acute hemolytic transfusion reaction: stop the transfusion and treat for shock (IV fluids, vasopressor agents if persistent hypotension, ± glucocorticoids)
- Urticaria: antihistamines (e.g., diphenhydramine, 2 mg/kg IM) and/or short-acting corticosteroids (e.g., dexamethasone sodium phosphate, 0.2 mg/ kg slow IV); temporarily halt transfusion until signs resolve.
- Nonhemolytic febrile reaction without cardiovascular or respiratory compromise (temperature rise of 2○F [1○C]): slow rate of transfusion. Discontinue if fever persists or worsens.
- Volume overload (pulmonary edema): halt transfusion and give IV diuretics (furosemide, 2 mg/kg IV) and oxygen.

- Sepsis: halt transfusion and obtain samples for culture; IV antibiotics; IV fluids.

POSSIBLE COMPLICATIONS

- Acute immunologic hemolytic reactions and reactions to infected blood may be severe and require a rapid and intensive response. Most other transfusion reactions, when detected early, respond well to conservative management.
- Acute hemolytic transfusion reaction/ contaminated blood: arterial hypotension and shock, renal failure, disseminated intravascular coagulation
- Volume overload: hypoxemia

RECOMMENDED MONITORING

- Monitor mentation, temperature, and vital signs throughout and following the transfusion.
- Monitor hematocrit/total protein before and after the transfusion.

BEHAVIOR/EXERCISE

Limit activity during the transfusion.

PROGNOSIS AND OUTCOME

- Stable animals: good with early recognition and intervention
- Severely ill: guarded

PEARLS & CONSIDERATIONS

COMMENTS

- Pretreating with antihistamines or corticosteroids will not prevent immunologic hemolytic reactions.
- Severe reactions usually occur during or shortly after transfusion.
- Most acute hemolytic transfusion reactions can be prevented by using DEA 1.1-negative canine blood donors (in nontyped recipients); and in cats, using matched blood donors.
- With the recent discovery of new RBC antigens (Mik in cats; Dal in dogs), it has been suggested that routine cross-matching should be considered in all cats and all previously transfused dogs requiring blood products.
- Cross-matching detects antibodies against donor RBCs. Nonimmune reactions or reactions due to antibodies attacking white blood cells (WBCs), platelets, or proteins will not be detected by cross-matching.

TECHNICIAN TIPS

- Inspect all units prior to infusion; discard if discolored. Monitor patients closely during the transfusion. Transfusion administration checklists can assist staff in patient monitoring and early recognition of potential reactions.
- All technical staff should be familiar with signs of transfusion reactions.

PREVENTION

- Type all donors, screen for infectious diseases, and use a sterile collection technique.
- Type all recipients if possible.
- Cross-match all cats and dogs that have had previous transfusions.
- Never use outdated or hemolyzed products.
- Consider the animal's underlying diseases when choosing component and administration rate.
- Follow strict guidelines for storage, handling, and administration of blood products.
- Monitor transfusions carefully.

SUGGESTED READING

Bracker KE, Drellich S: Transfusion reactions. Compend Contin Educ Pract Vet 27(7):500–512, 2005.

AUTHOR: LILIAN CORNEJO

EDITOR: SUSAN M. COTTER

Tracheobronchitis (Infectious): Dogs

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

An acute, highly contagious, generally benign respiratory disease complex of dogs. Common manifestations include cough, oculonasal discharge, and occasionally bronchopneumonia. For more information regarding cats, see p. 1431.

SYNONYMS

Kennel cough, canine respiratory disease complex, canine croup

EPIDEMIOLOGY

SPECIES, AGE, SEX: Common in dogs: puppies more prone to pneumonia. Often infectious tracheobronchitis is a multi-etiology syndrome that can involve viruses, bacteria, *Mycoplasma* spp, and other infectious agents. *Bordetella* spp (see p. 144) can infect multiple species, including felines, wildlife, and rodents.

RISK FACTORS: Exposure to other dogs; affected animals usually have a history of boarding, grooming, or being in environments with many other dogs (e.g., dog parks, veterinary hospitals).

CONTAGION & ZOONOSIS

- Highly contagious among canines
- *B. bronchiseptica* zoonosis can occur, mainly in immunocompromised humans

ASSOCIATED CONDITIONS & DISORDERS: Pneumonia (rare)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Most dogs develop a typical mild "classic" clinical disease characterized by coughing, even though the dog is otherwise normal.
- Unvaccinated puppies or adult dogs may develop a more severe disease with bronchopneumonia and rhinitis.

HISTORY, CHIEF COMPLAINT: Classic:

- Sudden-onset deep, hacking cough often followed by terminal retch (may be misinterpreted by client as vomiting).
- Owners often believe the dog has "something stuck in its throat."
- Appetite and demeanor are not affected, although excessive coughing may cause mild lethargy.

Bronchopneumonia: see p. 887

PHYSICAL EXAM FINDINGS

- Physical exam is often unremarkable in dogs with classic disease, other than an easily inducible cough on tracheal palpation and mild nasal or ocular discharge.
- Bronchopneumonia: fever, depression, tachypnea, dyspnea, cyanosis. Wheezes, crackles, rales on lung auscultation may be present.

ETIOLOGY AND PATHOPHYSIOLOGY

Infectious causative agents include *B. bronchiseptica,* canine parainfluenza virus (CPIV), canine influenza, and canine adenovirus 2 (CAV-2). Other agents that are implicated include canine herpesvirus (CHV) and occasionally canine distemper virus (CDV). Clinical disease is often the result of multiagent infections, and the most frequent multiagent infection includes *B. bronchiseptica* with CPIV or canine adenovirus (CAV, CAV-2):

- CPIV damages the respiratory epithelium of the upper respiratory tract and trachea. Alone, it primarily causes a dry cough and serous nasal discharge. Incubation period is 3-10 days.
- Canine influenza is an emerging viral disease that is highly contagious and typically found in kennels and settings where dogs are in close contact. Since this is an emerging disease with no preexposure, all ages are susceptible.
- CAV-2 replicates and damages epithelial cells in the nasopharynx, tonsils, trachea, and unciliated bronchial epithelium. Incubation period is 3-6 days.
- *B. bronchiseptica* is a gram-negative coccobacillus that replicates on respiratory ciliary epithelial cells and produces toxins that can paralyze cilia and impair local phagocytosis, allowing colonization by opportunistic pathogens. Incubation period is approximately 6 days.
- *Mycoplasma* spp. infections (see online chapter: Mycoplasma/Ureaplasma Infections) can develop secondarily and cause bronchopneumonia.
- Transmission of all three primary pathogens is via airborne transmission or oronasal contact.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Clinical diagnosis is often made based on historical and physical signs, vaccination history, and history of recent exposure to other dogs. However, in more complicated cases, additional tests including blood work and imaging may be indicated to determine the extent and severity of disease.

DIFFERENTIAL DIAGNOSIS

- Pulmonary signs:
  - Fungal pneumonia
  - Aspiration pneumonia
  - Pulmonary neoplasia
  - Pulmonary thromboembolism
  - Lung lobe torsion
- Cough:
  - Collapsing trachea
  - Chronic bronchitis
  - Heartworm disease
  - Nasopharyngeal foreign body
  - *Oslerus osleri* infection
  - Pulmonary or mediastinal neoplasia
  - Pulmonary edema
  - Left atrial enlargement due to chronic left heart disease

INITIAL DATABASE

- For dogs with a simple cough, diagnosis is typically made according to history, physical examination, and possibly response to therapy.
- For dogs with suspected pulmonary involvement, routine blood and urine tests, thoracic radiographs, and transtracheal wash (see p. 1350) are indicated.
- CBC, serum biochemistry panel, and urinalysis are often unremarkable, especially in dogs with simple infection. CBC may show an inflammatory leukogram with left shift in complicated bronchopneumonia.
- Thoracic radiographs are usually normal in dogs with cough only. Puppies and adults with pulmonary signs may show diffuse or focal bronchial or alveolar pattern ± evidence of hyperinflation or atelectasis, or complete lobar consolidation.
- Transtracheal wash cytologic examination is characterized by excessive neutrophils and may demonstrate bacterial colonization.

ADVANCED OR CONFIRMATORY TESTING

Bacterial or *Mycoplasma* spp. isolation, or virus isolation can be performed on nasopharyngeal or tracheal swabs or on transtracheal wash fluid, although such testing is virtually never necessary or helpful in formulating a treatment plan.

TREATMENT

TREATMENT OVERVIEW

- In simple clinical disease, the goal of treatment is cough suppression and prevention of secondary infection; the cough resolves spontaneously, generally in 7-10 days.
- In bronchopneumonia, the goals are to identify and eradicate bacterial agents involved, improve air movement, and maintain respiratory epithelial health.

ACUTE GENERAL TREATMENT

- In patients with simple clinical disease, antibiotic treatment is often not necessary; most dogs with a healthy immune system can recover from the disease spontaneously.
- Antibiotic selection in bronchopneumonia should be based on culture and sensitivity (C&S) results.
- Empirical antibiotics may be used in the absence of C&S or while results are pending. In bronchopneumonia, appropriate antibiotics are given 7-28 days beyond resolution of clinical and radiographic signs, depending on severity of disease. Empirical choices can include one of the following:
  - Amoxicillin/clavulanic acid: 12-25 mg/kg PO q 8-12 h
  - Ampicillin: 30 mg/kg IV or SQ q 6-8 h
  - Azithromycin: 5-10 mg/kg PO q 24 h
  - Trimethoprim-sulfa drugs: 15 mg/kg PO or IV q 12 h
  - Enrofloxacin: 10-20 mg/kg PO, SQ, or IV q 24 h
  - Antibiotics effective against *B. bronchiseptica* include azithromycin, enrofloxacin, and doxycycline, 5-10 mg/kg PO q 12 h
- Antitussives:
  - Hydrocodone: 0.22 mg/kg PO q 6-12 h PRN
  - Butorphanol: 0.5 mg/kg PO, SQ, or IM q 6-12 h PRN
  - Dextromethorphan (available in over-the-counter human cough suppressants): 1-2 mg/kg PO q 6-8 h. Warn owners to avoid products that contain other ingredients such as antihistamines and decongestants.
- Dogs with bronchopneumonia may require further therapy, including bronchodilators, aerosol therapy, and supportive care (see p. 887).

PROGNOSIS AND OUTCOME

Prognosis in dogs with simple disease is excellent. Prognosis for those with bronchopneumonia is guarded to good, depending on age of animal and severity of disease.

PEARLS & CONSIDERATIONS

PREVENTION

- Vaccination (CPIV, CDV, CAV-2: modified live); part of many commercial combination canine vaccines (DHLPP). CPIV vaccine is also available as intranasal formulation with *Bordetella.*
- Parenteral and intranasal vaccines against *B. bronchiseptica:* duration of immunity is variable and can be short (3-6 months).

TECHNICIAN TIPS

- Wear gloves, wash hands, and strictly isolate patients to prevent spread to other hospitalized dogs.
- Clean nasal and ocular discharge with a warm, moist cloth.
- Warm food to enhance smell when offering food (see p. 1377).

CLIENT EDUCATION

- To prevent disease, limit exposure to other dogs, especially in high-density populations such as boarding kennels, shelters, and dog parks.
- If exposure is unavoidable, recommend vaccination 5-14 days prior to potential risk.

SUGGESTED READING

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AUTHOR: THOMAS MITCHELL POTTER

EDITOR: DOUGLASS K. MACINTIRE

1ST EDITION AUTHOR: SHANNON T. STROUP

Tracheal Avulsion

BASIC INFORMATION

DEFINITION

Disruption of the continuity of, or a tear in, the trachea

SYNONYMS

Tracheal laceration, tracheal rupture, tracheal transection

EPIDEMIOLOGY

SPECIES, AGE, SEX: Reported primarily in small dogs and cats; there is no age or gender predilection.

RISK FACTORS

- Choke chains
- Overinflation of an endotracheal tube cuff
- Cervical trauma

ASSOCIATED CONDITIONS & DISORDERS: Can lead to pneumomediastinum, pneumothorax, and/or subcutaneous emphysema

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- History of trauma or recent general anesthesia and subsequent dyspnea
- Intermittent, continuous, or progressive respiratory distress

PHYSICAL EXAM FINDINGS

- Increased respiratory effort:
  - Decreased heart and breath sounds on thoracic auscultation if pneumothorax is present
- Subcutaneous emphysema: inflated, crepitant subcutaneous space
- Precipitation of severe dyspnea with neck flexion

ETIOLOGY AND PATHOPHYSIOLOGY

- Direct injury to the trachea due to either blunt or penetrating trauma to the cervical or thoracic area
- Violent hyperextension of the head and neck can lead to stretching of the trachea and may cause tracheal transection:
  - The carina and lungs are a fixed point that is stronger than the tracheal wall.
  - As the trachea is stretched, the intrathoracic trachea ruptures cranial to the carina.
- The dorsal tracheal membrane is the most common location for a tear from overinflation of an endotracheal tube cuff.
- Peritracheal tissues can maintain tracheal continuity.
- Initial dyspnea may persist, worsen, or resolve until subsequent stenosis or displacement causes return of clinical signs.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis of tracheal avulsion is suggested by a patient with a history of cervical trauma or recent anesthesia, especially in the presence of subcutaneous emphysema, pneumomediastinum, or obvious radiographic disruption of the trachea.

DIFFERENTIAL DIAGNOSIS

- Tracheal foreign body
- Collapsing trachea
- Tracheal stenosis
- Tracheal neoplasia or mass
- Laryngeal paralysis
- Laryngeal collapse
- Tracheobronchitis
- Pneumothorax/pneumomediastinum from other causes
- Pulmonary disease

INITIAL DATABASE

- Results of CBC, serum biochemistry panel, and urinalysis are usually unremarkable.
- Radiographs of the neck (lateral view) may show discontinuity of the tracheal wall. Site of rupture may be obscured by the humeri or scapulae, requiring retaking of radiographs with the fore-limbs repositioned.
- Cervical and/or thoracic radiographs may show peritracheal air accumulation, subcutaneous emphysema, and/ or pneumomediastinum.
    - Pneumothorax is rare.
    - Tracheal stenosis can be seen in chronic cases.

ADVANCED OR CONFIRMATORY TESTING

Tracheoscopy is useful in documenting tracheal rupture, especially tears in the dorsal tracheal membrane, if a radiographic diagnosis is not definitive.

TREATMENT

TREATMENT OVERVIEW

- Stabilize animal.
- Repair or resect damaged trachea or stenosis to resolve respiratory distress.
- Note that surgery is not always needed, and follow guidelines for conservative versus surgical management.

ACUTE GENERAL TREATMENT

- Oxygen supplementation if dyspnea (see p. 1318)
- For animals with respiratory distress, induction of anesthesia or heavy sedation and intubation per os or through a cervical tracheal laceration (if present) are indicated to quickly gain control of the airway:
    - Intubation through a cervical laceration/avulsion is accomplished in similar fashion to tracheostomy.
    - Distal cervical tracheal lacerations may require retrieval of the distal trachea from the thoracic inlet via traction sutures.
- Thoracocentesis may be indicated if pneumothorax is present (see p. 1338).
- Prepare the animal for exploration of all structures in the injured area to determine extent of injury and provide the opportunity for primary repair.
- Treat any other additional wounds.
- Antibiotics are indicated, especially if traumatic injuries are present.
    - Coverage against skin organisms *(Staphylococcus* or *Streptococcus* spp.) is considered most important.
        - Ampicillin, 22 mg/kg PO or IV q 8-12 h; cefazolin, 22 mg/kg PO or IV q 12 h; or clavulanic acid/ amoxicillin, 12.5-25 mg/kg PO q 8-12 h (dogs), 62.5 mg PO q 8-12 h (cats)
        - Enrofloxacin, 5-20 mg/kg PO or IV q 24 h if concerns about gram-negative organisms (maximum 5 mg/kg PO q 24 h in cats)

CHRONIC TREATMENT

- Closure and débridement of tracheal laceration:
    - Surgery is indicated for repair of tracheal defects if:
        - The cause is from injury associated with contamination (e.g., bite wounds or other penetrating injury).
        - The animal is not improving or getting worse with conservative (nonsurgical) treatment.
        - There is stenosis or stricture causing respiratory difficulty.
- Resection of damaged or stenotic trachea and anastomosis of normal ends:
    - Minimize tension.
    - May need to use tracheal tubes/stents

- Use a tape neck splint to hold the neck in a flexed position to reduce tension on the trachea postoperatively:
  - Try to keep the splint in place for 2 weeks if it is needed.

POSSIBLE COMPLICATIONS

- Dehiscence may occur if excessive tracheal suture tension is present.
- Narrowing of the tracheal lumen due to scar tissue may occur secondary to tracheal anastomosis.

RECOMMENDED MONITORING

- Monitor for respiratory distress.
- Drainage of the peritracheal area may be indicated if area is contaminated.
- Small areas of tracheal granulation tissue may be removed through a bronchoscope at periodic examinations during the healing period.
- Removal of tubes/stents is indicated when a healed mucosal surface is present.

PROGNOSIS AND OUTCOME

- Prognosis is good for long-term resolution of clinical signs.
- Stenosis of the tracheal lumen may be a complication postoperatively.

PEARLS & CONSIDERATIONS

COMMENTS

- Trauma is the most common cause of tracheal avulsion in small dogs.
- Overinflation of the endotracheal tube is the most common cause of tracheal rupture in cats:
  - Tracheal tears can occur from over-inflation of either low-volume/high-pressure cuffs or high-volume/ low-pressure cuffs.

TECHNICIAN TIPS

Have a sterile endotracheal tube readily available in case the trachea within the sterile field needs to be intubated. It is also worthwhile to have an extra-long endotracheal tube handy if the avulsed trachea needs to be temporarily bridged.

CLIENT EDUCATION

Recurrence of clinical signs is possible secondary to tracheal stenosis.

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AUTHOR: MICHAEL B. MISON

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Toxoplasmosis/Neosporosis

BASIC INFORMATION

DEFINITION

Infections with *Toxoplasma gondii* or *Neospora caninum,* obligate intracellular coccidian parasites that infect mammals, including humans

EPIDEMIOLOGY

SPECIES, AGE, SEX: Cats and other members of the Felidae family are definitive hosts for *T. gondii*

- Warm-blooded mammals serve as intermediate hosts.
- More severe disease can affect trans-placentally infected kittens.
- Cats of any age can be affected.

N. caninum infections have been seen in dogs, cattle, sheep, goats, horses, and deer but not in cats.

- Dogs are both intermediate and definitive hosts.
- Puppies are more severely affected by disease, but dogs of any age can be affected.
- Cats have demonstrated antibodies to *N. caninum* in field conditions but are not known to develop clinical neosporosis

GENETICS & BREED PREDISPOSITION: All breeds seem to be equally susceptible to toxoplasmosis. German short-haired pointers, Labrador retrievers, boxers, golden retrievers, basset hounds, and greyhounds may be more susceptible to neosporosis.

RISK FACTORS: Immunosuppression (e.g., from glucocorticoids or antineo-plastic drugs) or concomitant illnesses, such as ehrlichiosis, canine distemper, feline leukemia virus (FeLV), feline immunodeficiency virus (FIV), feline infectious peritonitis (FIP), or *Mycoplasma haemofelis* infection. Immuno suppression is not consistently found in cases of neosporosis.

CONTAGION & ZOONOSIS: Toxoplasmosis is zoonotic. The zoonotic potential of *N. caninum* is not known.

- A cat negative for *T. gondii-specific* antibodies is at greatest risk for developing oocyst shedding in feces, and is a danger to a susceptible owner, especially if it goes outside where it may ingest the intermediate host.
- A healthy cat positive for *T. gondii*-specific antibodies is of little risk to its owner, as it is unlikely to shed oocysts again if exposed.

GEOGRAPHY AND SEASONALITY

- Worldwide
- About 30% of cats and dogs in the United States have antibodies against *T. gondii*
- There is a higher prevalence of antibodies against *N. caninum* in rural or farm dogs than urban dogs.

CLINICAL PRESENTATION

In dogs, the clinical presentation of toxoplasmosis and neosporosis may be identical.

DISEASE FORMS/SUBTYPES

- Unaffected cat
- Clinically ill dog (toxoplasmosis or neosporosis) or cat (toxoplasmosis)

HISTORY, CHIEF COMPLAINT

Toxoplasmosis:

- Cats with clinical illness commonly present with anorexia, lethargy, respiratory distress, and ocular signs.
- Dogs and cats can present with anorexia, vomiting, diarrhea, weight loss, lethargy, dyspnea, ocular signs, lameness, and signs of central nervous system (CNS) dysfunction (seizures, paresis, cranial nerve deficits).

- Stillborn kittens

Neosporosis:

- Older dogs may present with dermatitis, respiratory signs (cough, dyspnea), gastrointestinal (GI) signs, or neurologic signs (lameness, seizures).
- In young dogs (<6 months), acute ascending paralysis is typical. Dysphagia, incontinence, and muscle atrophy are also seen.

PHYSICAL EXAM FINDINGS

Toxoplasmosis:

- Prenatally infected kittens: hepatomegaly, ascites, dyspnea, and fever
- Postnatal infection in cats is characterized by uveitis, chorioretinitis, dyspnea, icterus, ascites, fever, stiff gait, hyperesthesia, and neurologic deficits (spinal cord or brain).
- As definitive hosts, most cats with *T. gondii* harbor the organism with no adverse effect and no clinical signs.
- Young dogs (1 year or less) have generalized infections resulting in fever, icterus, dyspnea, and tonsillitis.
- Older dogs more commonly have neuromuscular signs, including muscle atrophy, stiffness, abnormal gait, and multifocal neurologic deficits involving the spinal cord or brain (seizures, ataxia, lower motor neuron [LMN] signs, cranial nerve deficits).
- Arrhythmias or, rarely, heart failure may be present in some older dogs.

Neosporosis:

- Puppies are more severely affected and show ascending rigid paralysis, with hind limbs worse than forelimbs:
  - Muscle atrophy and stiffness, muscle contractures leading to arthrogryposis and hyperesthesia. Cervical weakness, dysphagia, and variable CNS signs may also be seen.
- Older dogs may have LMN flaccid paralysis or show multifocal CNS signs (cranial nerve deficits, seizures, blindness).
- Systemic signs include fever, dyspnea, cough, skin lesions, vomiting, icterus, cardiac arrhythmias, megaesophagus, and regurgitation.

ETIOLOGY AND PATHOPHYSIOLOGY

- *T. gondii* exists in three infectious stages: sporozoites, tachyzoites, and bradyzoites:
  - Sporozoites occur in oocysts, which are excreted in a cat's feces, whereas tachyzoites and bradyzoites occur as tissue cysts.
- Transmission can occur through ingestion of infected tissues or ingestion of oocysts in contaminated food or water; transmission can also occur congenitally.
- The enteroepithelial life cycle (and thus fecal shedding) occurs only in cats.
- Cats are infected by ingestion of intermediate hosts infected with tissue cysts:
  - Bradyzoites are released in the GI tract from tissue cysts during digestion.
  - The bradyzoites penetrate the small intestinal epithelium and initiate asexual stages, eventually forming oocysts. These oocysts are passed in feces.
- The extraintestinal life cycle occurs in all hosts including cats:
  - After ingestion of oocysts or tissue cysts, the organism invades the small intestine and spreads to many extraintestinal tissues through blood and lymph, where it causes a focal necrosis. The CNS, muscles, liver, lungs, and eyes are commonly affected.
  - The organism localizes in tissues as cysts, resulting in chronic infection. These cysts may rupture, resulting in clinical relapses during immunosuppression.
- The life cycle of *N. caninum* involves three infectious stages: tachyzoites, tissue cysts found primarily in the CNS, and oocysts:
  - Tissue cysts and tachyzoites are found in intermediate hosts.
  - Transmission is suspected to occur through ingestion of shed oocysts, ingestion of infected tissues, and transplacentally.
  - Transplacental transmission may be the predominant route in dogs.
  - The organism and associated necrosis may be found in macrophages, polymorphonuclear cells, spinal fluid, and neural cells (brain, spinal cord, peripheral nerves, retina) as well as other cells, causing focal necrosis.

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

The diagnosis of either one of these diseases relies mainly on identifying appropriate clinical signs in patients with positive antibody

tests. It is possible (but unusual) to identify the organism in tissue or fluid samples.

DIFFERENTIAL DIAGNOSIS

- Uveitis: infectious (FeLV, FIV, FIP [coronavirus]), immune-mediated, trauma
- Respiratory signs: feline asthma, pneumonia (bacterial, *Mycoplasma,* parasitic, fungal), pulmonary edema, neoplasia, heartworm disease, trauma
- Hepatic: hepatic lipidosis (cats), cholangiohepatitis (cats), infectious hepatitis, neoplasia, toxic hepatopathy
- GI: infectious (bacterial, viral, parasitic), dietary, endocrine (hypoadrenocorticism), obstructive, pancreatitis.
- Neurologic signs: meningoencephalitis (FeLV, FIV, FIP, canine distemper, ehrlichiosis, Rocky Mountain spotted fever, rabies, fungal disease, parasitic disease, thiamine deficiency [cats], immune-mediated disease)
- Neuromuscular: hepatozoonosis, Lyme borreliosis, immune-mediated disease (polyradiculoneuritis, polymyositis)

INITIAL DATABASE

- CBC, serum biochemistry profile, urinalysis:
  - Nonregenerative anemia, neutrophilic leukocytosis, lymphocytosis, monocytosis, eosinophilia possible (toxoplasmosis)
  - Leukopenia (lymphopenia, neutropenia, degenerative left shift) possible in cats severely affected with toxoplasmosis
- Serum biochemistry profile may show elevated alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase, bilirubin, amylase, lipase, and creatine kinase (CK). Hyperglobulinemia, hypoalbuminemia, and hypoproteinemia may also be present with toxoplasmosis.
- Proteinuria and bilirubinuria may be present in cats with toxoplasmosis.
- Dogs with neosporosis may have elevated CK and AST secondary to muscle disease.
- Liver enzymes may be elevated with hepatic involvement in neosporosis.
- Radiographs:
  - Thoracic radiographs may show a diffuse interstitial to alveolar pattern and mild pleural effusion.
  - Abdominal radiographs may show hepatomegaly, ascites, masses in the intestines, or mesenteric lymph nodes.
- Other tests:
  - Fecal examination with Sheather's sugar solution may not reveal oocysts in clinically ill cats.
  - Cytologic examination of ascitic fluid, tracheal washes, and pleural fluid may reveal tachyzoites.

ADVANCED OR CONFIRMATORY TESTING

Toxoplasmosis:

- Clinical confirmation comes from serologic testing combined with clinical response to medications and exclusion of other causes for clinical signs:
  - Serologic testing: ELISA tests designed specifically for dogs or cats should be used. A fourfold rise in immunoglobulin (Ig) G over a 2-3 week period or a high IgM titer suggest active infection.
  - The presence of a positive IgM may not be reliable, but 80% of cats with clinical disease associated with toxoplasmosis have positive IgM titers.
  - IgG reflects only past exposure (positive in 30% of the cat population), but a positive titer along with appropriate clinical signs may suggest toxoplasmosis.
- Organism detection: *T. gondii* can be detected using PCR on tissue or blood and aqueous humor samples.

Neosporosis:

- Serologic testing with indirect FA, ELISA, and direct agglutination tests can confirm neosporosis:
  - Serologic testing can be done on cerebrospinal fluid (CSF).
  - Organism detection with histologic or cytologic examination
  - *N. caninum* may be found in CSF or tissue samples.
- Both organisms can be grown in cell culture and in mice.
- CSF analysis and aqueous humor may have elevated protein levels and leukocytes in both toxoplasmosis and neosporosis.

TREATMENT 

TREATMENT OVERVIEW

Treatment is predominantly supportive, with antimicrobials as appropriate for the organism. Drugs suppress replication of *T. gondii* and are not completely effective at killing the organism. There is limited information for effective treatment of neosporosis.

ACUTE AND CHRONIC TREATMENT

- Toxoplasmosis: clindamycin is the treatment of choice in dogs and cats.
- Neosporosis should be treated early in the disease with the same drugs used for treating toxoplasmosis. Treatment should continue at least 2 weeks after resolution of clinical signs.
- Clindamycin (dogs): 10-20 mg/kg PO q 12 h for at least 2 weeks
- Clindamycin (cats): 12.5 mg/kg PO q 12 h for a minimum of 2-4 weeks
- Alternatively, trimethoprim-sulfonamide: 15 mg/kg PO q 12 h for 2-4 weeks may be used if the patient cannot tolerate clindamycin. Barring corneal ulceration, uveitis may be treated with 1% prednisolone acetate ophthalmic drops.

POSSIBLE COMPLICATIONS

- Clindamycin may cause anorexia, vomiting, and diarrhea with higher doses.
- Trimethoprim-sulfonamides are associated with bone marrow suppression (anemia, leukopenia, thrombocytopenia), keratoconjunctivitis sicca (KCS), depression, immune-mediated disease, cutaneous drug eruptions, renal failure, GI signs, and hepatotoxicosis (especially in Doberman pinschers). Reduce dose of trimethoprim sulfa in renal insufficiency and avoid use in hepatic disease, anemia, leukopenia, and congenital bleeding disorders.
- In cases of fulminant infection, some patients do get worse after antimicrobials are started.

RECOMMENDED MONITORING

Serial recheck examinations at 2 days and 1 week after initiation of therapy and again at 2 weeks after resolution of signs and prior to discontinuation of therapy

PROGNOSIS AND OUTCOME

- In most cases, clinical signs of systemic illness usually begin to resolve within 1-2 days after institution of therapy.
- Uveitis should resolve in 1 week with therapy.
- Neuromuscular deficits should partially resolve within 2 weeks of initiation of therapy; however, some signs may be permanent. Animals may survive acute disease if treated intensively and rapidly.
- Guarded for complete resolution of neuromuscular signs
- Clinical improvement is not likely in severe cases of neosporosis with muscle contracture.
- Older puppies (>16 weeks) and adult dogs generally respond better to treatment for *N. caninum.*

PEARLS & CONSIDERATIONS

COMMENTS

- Examine and treat all dogs in a litter for neosporosis if one littermate is diagnosed.
- No drug will clear the organism, and relapses may occur.
- Toxoplasmosis-associated chorioretinitis in cats can be treated with topical glucocorticoids.
- Precautions are often adequate for preventing zoonosis, and immunocompromised individuals need not necessarily be separated from their cats.
- Toxoplasmosis in cats with FIV is most often reactivation of latent infection rather than a newly acquired one.

PREVENTION

- Clean litter boxes daily (oocysts need 1-5 days to sporulate and become infective).
- Disinfect litter boxes with boiling water at least once weekly.
- Cover outdoor sandboxes.

CLIENT EDUCATION

- Wash hands and surfaces after handling raw meat or cleaning litter boxes.
- Wear gloves when gardening, and wash vegetables and hands thoroughly to prevent contamination from soil.
- Do not eat undercooked meat or unpasteurized dairy products.
- Boil drinking water from unreliable sources.
- Pregnant women must avoid contact with soil, cat litter, raw meat, and cats excreting oocysts.

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Tooth Resorption

BASIC INFORMATION

DEFINITION

Loss of tooth substance due to resorption by osteoclast-like cells (odontoclasts)

SYNONYMS

Feline odontoclastic resorptive lesion (FORL), odontoclastic resorptive/resorption lesion, resorptive/resorption lesion, external root resorption, cervical line erosion/lesion, feline caries, neck lesion. (Note: The term *neck lesion* is a topographical distinction only. The terms *erosion* and *caries* are inappropriate because the dental defect is resorptive in nature and not caused by acidic or bacterial insult.)

EPIDEMIOLOGY

SPECIES, AGE, SEX: Resorption can occur in any mammalian deciduous or permanent tooth, but the condition affecting multiple or all permanent teeth is seen predominantly in domestic cats 4 years of age and older, with reported prevalence rates ranging between 25% and 75%.

GENETICS & BREED PREDISPOSITION: No obvious breed predisposition; purebred cats have been reported to develop tooth resorption at a younger age compared to other breeds.

RISK FACTORS

- Periodontal disease
- Trauma from occlusion
- Dietary composition
- Increased vitamin D levels in commercial diets

GEOGRAPHY AND SEASONALITY: Worldwide

ASSOCIATED CONDITIONS & DISORDERS

- Thickening of bone at the alveolar margin (alveolar bone expansion)
- Abnormal extrusion of teeth (particularly canine teeth)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Tooth resorption is classified based on severity (stages 1-5) and radiographic appearance (types 1-3; see http://avdc.org):

- Dentoalveolar ankylosis (ankylotic fusion between root and bone)
- Root replacement resorption (resorption followed by bone replacement)
- Inflammatory resorption (vascular and inflamed granulation tissue filling a resorptive defect)

HISTORY, CHIEF COMPLAINT: Patients may present with “red spots” on their teeth (crown defect filled with granulation tissue), repetitive lower jaw motions (jaw opening reflex), fractured crowns, root remnants, and missing teeth. These animals may also have difficulty eating hard food and may refuse to drink cold water. The majority of cats are diagnosed with tooth resorption from dental radiography.

PHYSICAL EXAM FINDINGS: Oral examination can reveal crown defects filled with vascular and inflamed granulation tissue, fractured crowns, root remnants, bulging gingiva in areas of missing teeth, thickening of bone at the alveolar margin, and abnormal extrusion of the canine teeth.

ETIOLOGY AND PATHOPHYSIOLOGY

- Suggested causes include periodontal disease, anatomic peculiarities, mechanical trauma, increased vitamin A and vitamin D intake, abnormal calcium homeostasis, and viruses causing immunosuppression.
- Association of multiple tooth resorption in cats with excessive dietary intake of vitamin D:
  - Histologic examination of healthy teeth from cats with tooth resorption on other teeth shows periodontal ligament degeneration, hypercementosis, decreased width of the periodontal space, and dentoalveolar ankylosis, indicating that inflammatory cells may not play a primary role in the development of tooth resorption.
  - A prospective study showed that cats with tooth resorption have significantly increased serum levels of 25-hydroxyvitamin D, compared to cats without tooth resorption; these findings indicate that cats with tooth resorption must have had a higher intake of dietary vitamin D, compared to cats without tooth resorption.
  - Recently the nuclear vitamin D receptor has been implicated in tooth resorption in cats.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Changes may be visible during intraoral examination, but these lesions are only the tip of the iceberg. What lurks below the gum line cannot be appreciated without diagnostic imaging. Full-mouth dental radiography is of utmost importance in identifying and assessing tooth resorption in cats.

DIFFERENTIAL DIAGNOSIS

- Periodontal disease
- Fractured teeth
- Root remnants
- Tooth resorption due to local causes (e.g., apical abscess, orthodontic tooth movement, trauma, neoplasia)
- Caries (dogs)

INITIAL DATABASE

Preanesthetic CBC, serum biochemistry profile, urinalysis

ADVANCED OR CONFIRMATORY TESTING

Full-mouth (intraoral) dental radiographs (see p. 1246)

TREATMENT

TREATMENT OVERVIEW

Goals of treatment are to make the mouth free of pain, preserve masticatory function, and prevent abscess formation and local osteomyelitis.

ACUTE GENERAL TREATMENT

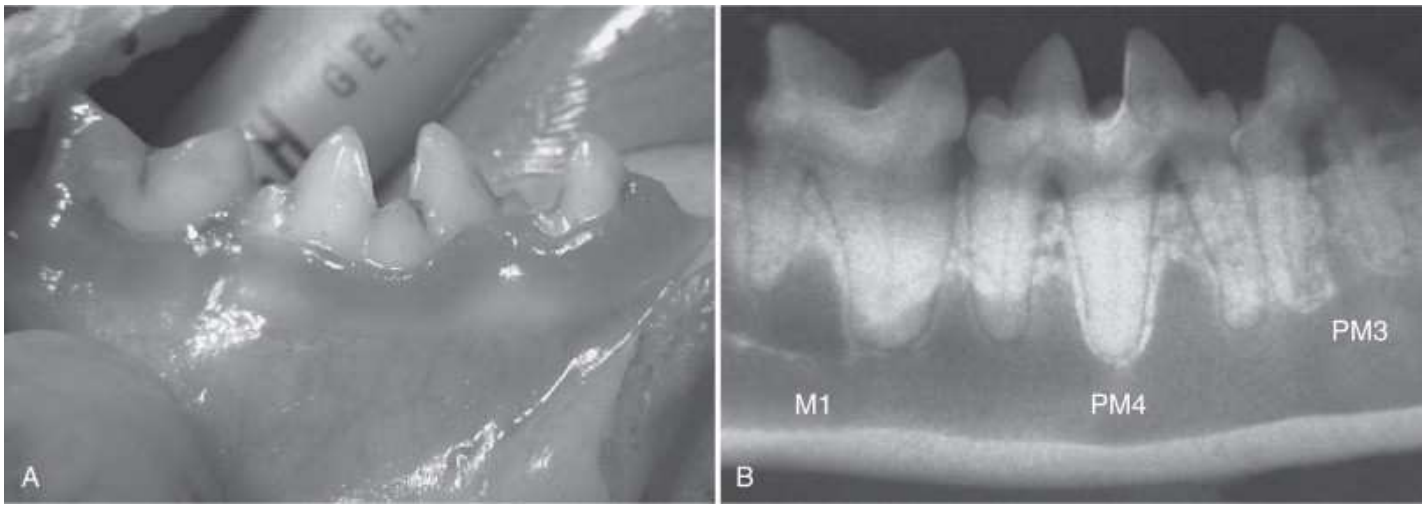
- Closed or open extraction of root remnants and teeth affected by resorption
- Flaps should be closed with synthetic absorbable suture material.
- Administration of antibiotics is not usually necessary after tooth extraction unless another medical condition or extensive tissue trauma at the extraction site is present.
- Pain management: regional nerve block(s) intraoperatively (0.3-0.4 mL of 0.5% bupivacaine per block) followed by opioid medications upon extubation (hydromorphone, 0.1 mg/ kg IM) and opioid medications post-operatively for 3-4 days (butorphanol, 0.2-0.4 mg/kg PO q 8 h; or buprenorphine, 0.01-0.02 mg/kg buccal transmucosal q 8 h); transdermal fentanyl patch (25 mcg) if multiple extractions were performed.

POSSIBLE COMPLICATIONS

- Fractured teeth and roots
- Root remnants
- Regional trauma due to improper extraction technique
- Infection
- Future development of resorption on other teeth

RECOMMENDED MONITORING

- Examination in 2 weeks to evaluate extraction sites
- Clinical examination and full-mouth dental radiography once per year



TOOTH RESORPTION A, Clinical picture of right mandibular third and fourth premolars and first molar in a cat; rostral is to the right. Generalized

moderate gingivitis with focalized gingival hyperplasia; possible tooth resorption on third premolar and first molar; fourth premolar shows gemination (division of a tooth bud, resulting in the formation of partially or completely separated crowns). **B**, Radiograph of same area. Generalized mild to moderate horizontal alveolar bone loss; tooth resorption on third premolar (PM3; inflammatory resorption near cervical region and furcation; dentoalveolar ankylosis and replacement resorption at distal root) and first molar (M1; inflammatory resorption near cervical region on mesial tooth surface); geminated fourth premolar (PM4) does not show obvious radiographic signs of tooth resorption.

PROGNOSIS AND OUTCOME

- Excellent for extraction site healing
- Fair with regard to preventing the development of resorption on other teeth

PEARLS & CONSIDERATIONS

COMMENTS

- Usually more than one tooth is affected.
- Dental radiography is an invaluable tool in diagnosing tooth resorption that is missed on clinical examination.

PREVENTION

There is no reliable prevention strategy available at this time.

CLIENT EDUCATION

Inform clients about the likelihood of development of resorption on other teeth and the need for continued clinical and radiographic monitoring.

SUGGESTED READING

Booij-Vrieling HE, et al: Inflammatory cytokines and the nuclear vitamin D receptor are implicated in the pathophysiology of dental resorptive lesions in cats. Vet Immunol Immunopathol 132:160, 2009.

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AUTHOR & EDITOR: ALEXANDER M. REITER

Tooth Fractures

BASIC INFORMATION

DEFINITION

Fracture of dental enamel, dentin, and/ or cementum; common in both dogs and cats

SYNONYMS

Dental fracture; “slab” fracture: fracture of the buccal (or lingual/palatal) surface of a tooth

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs: canine and maxillary fourth premolar teeth are commonly affected (due to trauma).
- Cats: more commonly in canine teeth (due to trauma) or any other teeth (weakened by tooth resorption; see p. 1104)

RISK FACTORS

- Dogs: chewing on bones, ice cubes, nylon toys, cow hooves, rocks
- Cats: high-rise syndrome (see p. 529 and online chapter: High Rise Syndrome, Craniofacial), vehicular trauma, tooth resorption

ASSOCIATED CONDITIONS & DISORDERS: Attrition (wear from tooth-to-tooth contact), abrasion (wear due to contact of teeth with nondental materials such as bones), pulpitis (pulpal inflammation), displacement injuries (tooth luxation or avulsion; see p. 1100), tooth resorption (commonly seen in cats), and caries (bacterial infection causing tooth demineralization)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: American Veterinary Dental College (AVDC) Tooth Fracture Classification (http://avdc.org/) based on location (crown [portion of the tooth covered by enamel], crown-root, or root) and presence of pulp exposure (uncomplicated or complicated):

- Enamel infraction: incomplete fracture (crack) of the enamel without loss of tooth substance
- Enamel fracture: fracture with loss of crown substance confined to the enamel
- Uncomplicated crown fracture: fracture of the crown that does not expose the pulp
- Complicated crown fracture: fracture of the crown that exposes the pulp
- Uncomplicated crown-root fracture: fracture of the crown and root that does not expose the pulp
- Complicated crown-root fracture: fracture of the crown and root that exposes the pulp
- Root fracture: fracture involving the root

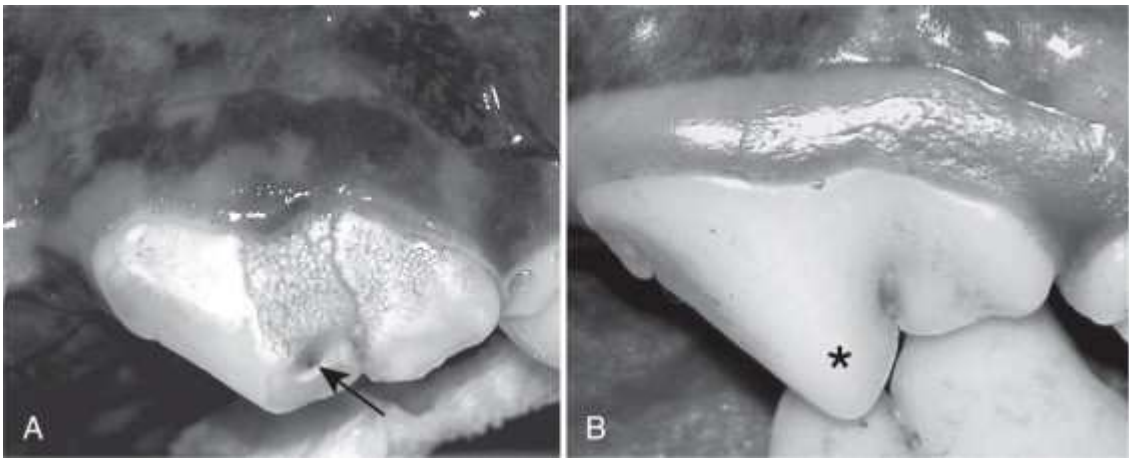
HISTORY, CHIEF COMPLAINT

- Tooth fractures are commonly noted as incidental findings on routine physical examination.
- History of falling from a height, vehicular trauma, fights with other animals, aggressive chewing tendencies, or other unknown trauma

PHYSICAL EXAM FINDINGS

- Commonly no overt clinical signs, especially if fracture is uncomplicated
- Oral bleeding with complicated fractures
- Hypersalivation with acute complicated fractures
- Appetite rarely affected; chewing on opposite side results in greater calculus accumulation on affected side.
- Calculus may obscure a slab fracture of the maxillary fourth premolar; compare with crown height and shape of the contralateral tooth.
- Acute pulp exposure: red spot in tooth defect ± bleeding from exposed pulp, painful on probing
- Chronic pulp exposure: dark brown/ black spot in tooth defect, asymmetric calculus accumulation (greater on affected side),

regional facial swelling ± draining tracts at mucogingival junction or through skin



TOOTH FRACTURES A, Slab fracture of left maxillary fourth premolar in a dog. The main cusp is fractured off; there is pulp exposure *(arrow)* and moderate calculus accumulation. Amount of calculus indicates fracture occurred more than 1-2 months prior to the visit, but bleeding pulp tissue indicates fracture may not be older than 6-12 months. **B**, Normal left maxillary fourth premolar for comparison. The tooth (notably the main cusp *[asterisk])* is structurally intact; mild calculus accumulation in developmental groove.

(Copyright Dr. Alexander M. Reiter.)

ETIOLOGY AND PATHOPHYSIOLOGY

- Uncomplicated fracture: exposure of dentinal tubules causes sensitivity and may allow bacterial access to the pulp. Odontoblasts may respond by forming tertiary dentin, sealing off exposed tubules.
- Complicated fracture: pulp exposure results in pulpitis and bacterial infection; most will develop pulp necrosis and periapical disease (e.g., apical abscess; see p. 10).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Often the diagnosis of a fractured tooth is straightforward from visual inspection, though it may be difficult to determine whether the fracture is complicated or involves the roots from physical examination alone. A sedated/anesthetized oral examination and dental radiography are essential. It is important to avoid waiting for the patient to show clinical signs of oral discomfort, at which time the disease process may be advanced.

DIFFERENTIAL DIAGNOSIS

- Abrasion/attrition
- Tooth resorption
- Caries
- Displacement injury (luxation/avulsion)

INITIAL DATABASE

CBC, serum chemistry panel, urinalysis: generally unremarkable (preanesthetic)

ADVANCED OR CONFIRMATORY TESTING

- Anesthetized oral examination using a dental explorer (#11/12, 17, or 23) to determine pulp exposure
- Dental radiographs (see p. 1246): indicated to identify extent of lesion and state of adjoining teeth. Possible findings include structural crown and/or root defect, arrested root development (open root apex, wide root canal when compared with healthy contralateral tooth), diffuse root canal mineralization, apical root resorption, and/or periapical lucency.

TREATMENT

TREATMENT OVERVIEW

Endodontic or exodontic (extraction) therapy is indicated for fractured teeth with pulp exposure. Fractured teeth with no pulp exposure require radiographic evaluation and monitoring, since they may also develop endodontic disease. A "wait-and-see" approach for fractured teeth with pulp exposure is below the standard of care, because tooth fractures cause discomfort and invite infection of endodontic and periapical tissues.

ACUTE GENERAL TREATMENT

- Uncomplicated crown fractures may not require treatment, or may benefit from sealing dentinal tubules of exposed dentin with a bonding agent. Fractures extending below the gumline (crown-root fractures) may require periodontal surgery to prevent focal periodontal pocketing.
- Acute complicated crown fracture: vital pulp therapy (partial pulpectomy, direct pulp capping, and restoration) within 48 hours of pulp exposure; administer antibiotics (e.g., intraoperative ampicillin, 22 mg/kg IV q 6 h; followed by amoxicillin/clavulanic acid, 14 mg/kg PO q 12 h × 7 days; or clindamycin, 5.5 mg/kg PO q 12 h × 7 days).

CHRONIC TREATMENT

- Chronic, complicated crown fractures (adult animals): root canal therapy or extraction (extraction of large, firmly rooted teeth causes more postoperative morbidity than root canal therapy)
- Recently fractured (<2 weeks) teeth in immature animals (<18 months old) may be treated by vital pulp therapy in an attempt to achieve root lengthening and apical closure (apexogenesis).

POSSIBLE COMPLICATIONS

Uncontrolled force during extraction of crown-root segments can result in:

- Fracture and incomplete removal of the tooth/root, resulting in formation of an apical abscess (see p. 10)
- Trauma to soft tissues (eye, brain, tongue, salivary gland ducts, and neurovascular structures)
- Transposition of tooth/root fragments into the mandibular/infraorbital canal and nasal passages
- Iatrogenic jaw fracture

RECOMMENDED MONITORING

Vital pulp therapy and root canal therapy require follow-up radiography under sedation/anesthesia at 6 months postoperatively and yearly thereafter.

PROGNOSIS AND OUTCOME

- In periodontally sound teeth (teeth without concurrent periodontal pockets or bone loss), root canal therapy fails in only 6% of treated roots (dependent on skill of the operator).
- Animals likely to continue abusive chewing habits may benefit from placement of prosthodontic metal crowns.

PEARLS & CONSIDERATIONS

COMMENTS

- Functionally significant teeth (i.e., those teeth on which the animal depends for chewing, prehending, cosmesis, or other functions—the importance of which varies from patient to patient) should be preserved with endodontic therapy rather than being extracted.
- Although root canal therapy can be performed for almost any dog tooth, endodontic therapy in cats is often not feasible because of size, except for the canine teeth.
- Dental radiography is an important diagnostic tool in determining appropriate treatment.

PREVENTION

Appropriate chew toys will allow for decreased plaque and calculus accumulation without fracturing teeth. Owners should avoid very hard treats and toys such as real bones, nylon bones, ice cubes, cow hooves, and rocks.

TECHNICIAN TIPS

- Technicians can help prevent tooth fractures with proper education. Discuss appropriate chewing habits, treats, and toys during wellness visits.
- Technicians may be the first to notice subtle tooth fractures during professional dental cleanings. Bringing these fractures to the veterinarian's attention and becoming accustomed to taking dental radiographs of fractured teeth are important parts of oral health provision.

CLIENT EDUCATION

Root canal therapy causes less postoperative discomfort than tooth extraction.

SUGGESTED READING

Clarke DE: Vital pulp therapy for complicated crown fracture of permanent canine teeth in dogs: a three-year retrospective study. J Vet Dent 18:117, 2001.

Kuntsi-Vaattovaara H, et al: Results of root canal treatment in dogs: 127 cases (1995-2000). J Am Vet Med Assoc 220:775, 2002.

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Tooth Displacement Injuries

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

- Concussion and subluxation: injuries to the periodontal tissues, with little or no tooth loosening or displacement and with mild hemorrhage and edema in the periodontal space. Usually do not require treatment.
- Luxation: partial displacement of the tooth in an axial (intrusion, extrusion) or lateral direction, usually accompanied by extensive injury to the pulp and periodontal ligament and (except in case of extrusion) fracture of the alveolar bone as well as soft-tissue laceration
- Avulsion: complete displacement of the tooth out of the alveolus, with total tearing of periodontal fibers and shearing of the pulp neurovascular supply
- Replantation/reimplantation: replacement of the tooth in its alveolar socket

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Occasionally reported in dogs and cats
- More common in dogs than cats, with lateral luxation following fights with other animals most commonly reported
- Maxillary incisor and canine teeth are most commonly affected.

RISK FACTORS

- Loss of attachment due to periodontitis or other diseases causing alveolar bone lysis
- Young age: alveolar bone and periodontal ligament of teeth of young animals more resilient than the same tissues of older individuals

ASSOCIATED CONDITIONS & DISORDERS: Trauma: other oral, cranial, thoracic or abdominal injuries

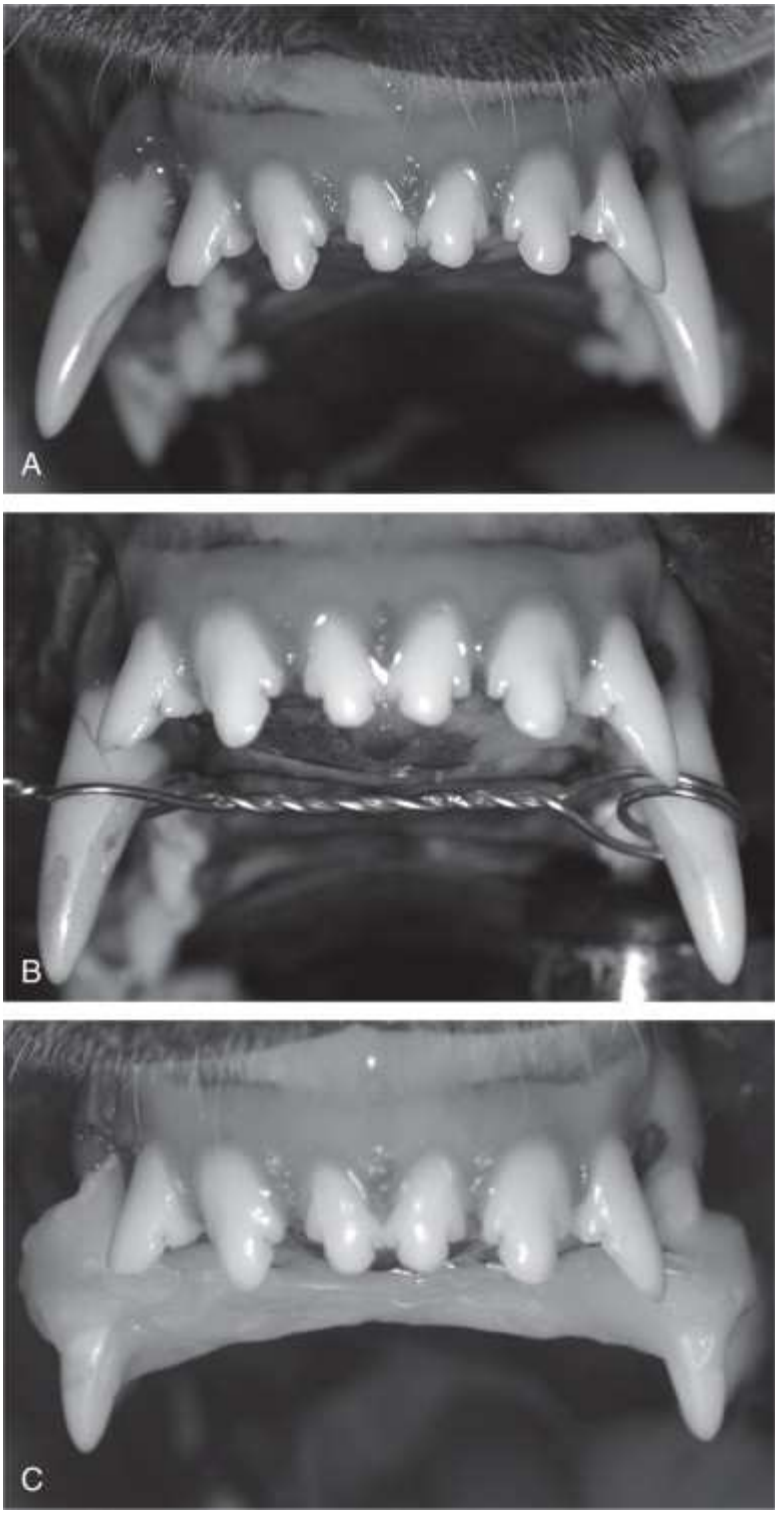
CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Owners usually report a recent traumatic event and oral hemorrhage.
- Anorexia, oral pain, continuous licking, and abnormal facial profile may be present.

PHYSICAL EXAM FINDINGS

- Lateral luxation: hemorrhage from the periodontal space, abnormal mobility and displacement of the tooth crown in a labial direction, laceration of gingiva and alveolar mucosa
- Extrusive and intrusive luxation: tooth elongation or shortening, with increased or decreased mobility; hemorrhage from the periodontal space
- Avulsion: empty alveolar socket, eventually filled with blood clots and debris
- All: evaluate teeth adjacent to a displaced tooth for structural defects or abnormal mobility, which may indicate periodontal trauma, root fracture, or bone fracture.



TOOTH DISPLACEMENT INJURIES A, Lateral luxation of right maxillary canine tooth in a dog, following a fight with another dog. **B**, Wire placement following replantation of luxated tooth. **C**, Completed splint after placement of cold-cured composite resin over the wire.

(Courtesy Dr. Margherita Gracis.)

ETIOLOGY AND PATHOPHYSIOLOGY

Energy and direction of impact determine type of displacement. A frontal impact may cause concussion or subluxation if mild to moderate, or cause luxation or avulsion if severe. A horizontal force usually causes lateral displacement, and an oblique force causes extrusion. Intrusion follows an impact in an axial direction.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis of more severe tooth displacement requires a thorough oral, periodontal, and radiographic examination. Diagnosis of dental concussion and subluxation may be difficult or impossible to make because clinical and radiographic signs may be mild or absent.

DIFFERENTIAL DIAGNOSIS

- Increased tooth mobility and displacement (lateral luxation): root fracture, bone fracture, neoplasia
- Decreased tooth mobility (intrusive luxation): incomplete tooth eruption, root replacement resorption, dentoalveolar ankylosis
- Tooth elongation (extrusive luxation): buccal bone expansion and idiopathic tooth extrusion
- Missing tooth (avulsion): congenital or acquired (postextraction) missing tooth, unerupted tooth, crown-root fracture with retained root tip

INITIAL DATABASE

Routine preoperative blood work; no specific associated abnormalities expected

ADVANCED OR CONFIRMATORY TESTING

Dental radiographs (see p. 1246) of the affected tooth and surrounding tissues; intraoral techniques are preferred over extraoral techniques, to avoid superimposition with other structures of the head.

TREATMENT

TREATMENT OVERVIEW

Treatment goals include prompt tooth replantation, bone fracture reduction (lateral luxation), and treatment of periodontal and pulpal injuries. Replantation requires a minimum level of surgical skills and competence and should be performed at the emergency visit. For endodontic treatment, the case should be referred to a veterinary dentist.

ACUTE GENERAL TREATMENT

- Keep avulsed tooth moist in commercial tissue culture media, cold low-fat milk, or egg albumin (raw egg white) until replantation.
- Start systemic tetracycline hydrochloride (20 mg/kg PO q 8 h for 4 weeks) or amoxicillin (22 mg/kg PO q 12 h for 4 weeks) immediately.
- Induce general anesthesia if patient is stable.
- Obtain dental radiographs to evaluate the extent of injury.
- Rinse alveolus and tooth root with sterile saline. To avoid damage to viable periodontal fibers, do not scrape the root surface, and do not use chlorhexidine solution.
- Soak the avulsed tooth in 5% doxycycline solution for 5 minutes before replantation.
- Gently replant the tooth manually, and confirm its position radiographically.
- Suture lacerated soft tissues with thin, absorbable suture material.
- After scaling and polishing, splint the replanted tooth to adjacent teeth with or without wire reinforcement using an acid-etch resin technique and cold-cured composite or acrylic resin applied to 1-3 teeth mesially and distally.
- Perform temporary root canal treatment with calcium hydroxide or anti-inflammatory medicaments (e.g., 1% triamcinolone) to inhibit inflammatory root resorption (optional).
- Smooth the splint, and check the occlusion before recovery from anesthesia.
- Orthodontically move an intruded tooth into position over a few weeks.

CHRONIC TREATMENT

- Remove the splint 1-2 weeks (avulsion and extrusion) or 4-6 weeks (lateral luxation and intrusion with extensive bone fracture) after replantation.
- Perform definitive root canal therapy at the time of splint removal.

BEHAVIOR/EXERCISE

Limit chewing activity on toys and other hard materials while a splint is in place.

POSSIBLE COMPLICATIONS

- Pulp necrosis, pulp infection, tooth discoloration, root canal obliteration
- Inflammatory root resorption, replacement resorption, dentoalveolar ankylosis
- Loss of marginal alveolar bone

RECOMMENDED MONITORING

Regular radiographic follow-ups for several years after replantation

PROGNOSIS AND OUTCOME

- Good prognosis after immediate replantation followed by proper endodontic treatment
- Poor prognosis after delayed replantation, long-term and rigid splinting, and delayed endodontic treatment
- In humans, concussion injuries have the best prognosis, followed by subluxation and extrusion. Lateral luxation, intrusion, and avulsion show the highest incidence of complications.

PEARLS & CONSIDERATIONS

COMMENTS

- Tooth luxation and avulsion are dental emergencies. Immediate replantation and splinting are mandatory for successful treatment.
- Severed pulp tissue may survive for 2 hours in an extraoral environment. Periodontal fibers survive 30 minutes if dry and 1-3 hours if kept moistened.
- In most instances, endodontic treatment is necessary after replantation.
- Displaced deciduous teeth should be extracted rather than replanted.
- Extraction of displaced permanent teeth is an alternative to replantation.

CLIENT EDUCATION

- Recommend soft diet and daily oral hygiene when an oral splint is in place.
- Discuss the need for endodontic treatment, radiographic follow-ups, and possible complications before tooth replantation is performed.

SUGGESTED READING

Andreasen JO, Andreasen FM, Andersson L: Textbook and color atlas of traumatic injuries to the teeth, ed 4, Ames, IA, 2007, Wiley-Blackwell.

Gracis M, Orsini P: Treatment of traumatic dental luxation in six dogs. J Vet Dent 15:65, 1998.

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Tonsillar Disorders

BASIC INFORMATION

DEFINITION

Abnormal structure or function of the palatine tonsils, usually manifest as increased size, often with protrusion from the tonsillar fossa

SYNONYM

Palatine tonsillar disorders

EPIDEMIOLOGY

SPECIES, AGE, SEX: Occasionally seen in dogs; less frequent in cats. No known sex predilection. Acute tonsillitis appears to be more frequent in animals <1 year of age.

CONTAGION & ZOONOSIS

- Group A *Streptococcus pyogenes* ("strep throat" in humans) does not cause signs of tonsillitis in dogs or cats.
- Rates of infection in dogs or cats from contact with infected humans appear low; in rare circumstances, infected dogs or cats not showing clinical signs may serve as a source of reinfection to humans in the household.

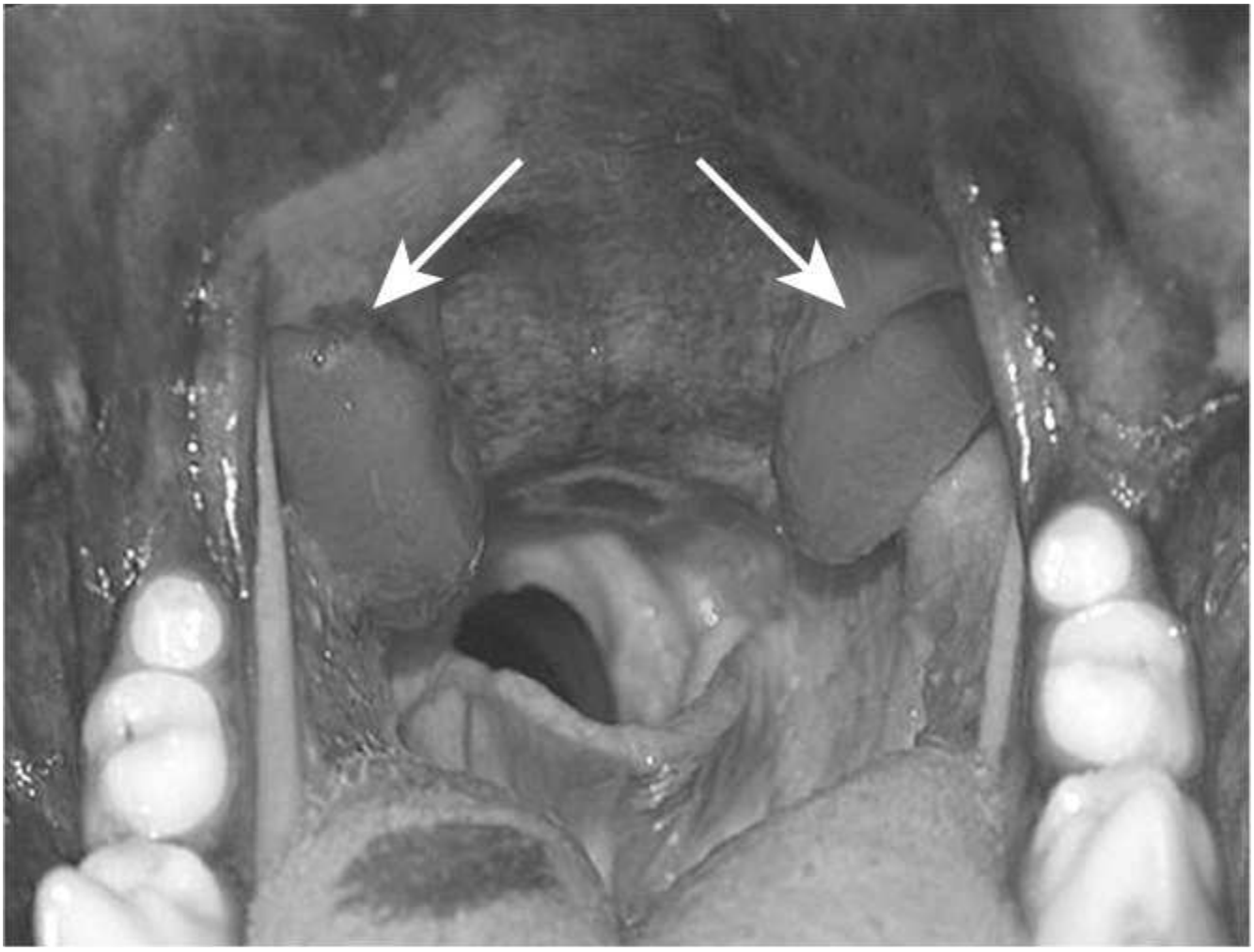
CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Tonsillar enlargement often is an incidental finding; when present, signs may include dysphagia/retching, coughing, ptyalism, and inappetence. The clinical signs of the underlying disease may often be more clinically significant than the signs attributable to tonsillar enlargement.

PHYSICAL EXAM FINDINGS: Bilaterally or unilaterally enlarged palatine tonsils; with tonsillitis, the tonsils are often bright red and protruding from the tonsillar crypts. There may be petechiae or a purulent exudate on the tonsils or in the tonsillar crypts. Fever is common with infectious disease.

ETIOLOGY AND PATHOPHYSIOLOGY

- The palatine tonsils are sentinels for exposure to antigens that enter through the mouth and nose; unlike lymph nodes, they have no afferent drainage region and therefore, reactive tonsillar enlargement arises from exposure through the oral cavity.
- Primary tonsillitis: bacterial or viral colonization of the lymphatic tissue of the tonsils. The tonsils are a common portal of entry for enteric bacteria and viruses.
- Secondary tonsillitis: results from chronic pharyngeal irritation, such as recurrent vomiting, regurgitation, or coughing; may also result from chronic pharyngitis secondary to elongated soft palate, immunosuppression from feline immunodeficiency virus (FIV), chronic contamination of the oropharynx with pathogenic bacteria in cases of chronic periodontal disease, or licking of distant infected sites such as skin or anal sacs.
- Swallowed foreign bodies such as grass awns or wood splinters may become lodged in the tonsillar crypt.
- Tonsillar cyst: embryonic remnant
- Neoplasia: squamous cell carcinoma (SCC) or lymphoma may develop from the epithelial or lymphoid components of the tonsils, respectively.



TONSILLAR DISORDERS Intraoral view of a dog with marked bilateral enlargement of the tonsils *(arrows)*.

DIAGNOSIS

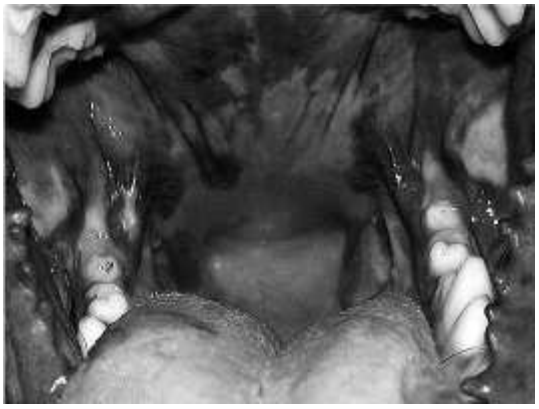
DIAGNOSTIC OVERVIEW

Most cases of bilateral tonsillar enlargement are benign and secondary to such processes as licking infected material. The diagnostic goal is to rule out neoplasia. If a single tonsil is irregular and enlarged, suspect squamous cell carcinoma or foreign body. If both tonsils are enlarged, along with other lymphoid tissues such as peripheral lymph nodes, suspect lymphoma. Suspected neoplastic cases can be confirmed with fine-needle aspirates or biopsy.

DIFFERENTIAL DIAGNOSIS

Symmetric/bilateral tonsillar enlargement:

- Primary tonsillitis:
  - Bacteria: streptococci, staphylococci, coliforms, canine infectious tracheobronchitis
  - Viruses: feline panleukopenia, canine distemper, infectious canine hepatitis, rabies
  - Parasites: *Pneumonyssoides caninum* nasal mites
- Secondary tonsillitis:
  - Pharyngeal irritation: chronic vomiting, regurgitation, or coughing
  - Anatomic abnormalities: elongated soft palate, cleft palate
  - Oropharyngeal contamination: anal sac disease (licking at distant site), pyoderma (licking at distant site), possibly periodontal disease
  - In racing greyhounds, lymphoid hyperplasia of the tonsils and tonsillar enlargement are associated with respiratory disease and poor performance.



TONSILLAR DISORDERS Intraoral view of tonsils in a normal dog for comparison.

Unilateral tonsillar enlargement:

- Foreign body (e.g., grass awn or splinter in tonsillar crypt)
- Tonsillar cyst

Unilateral or symmetric/bilateral tonsillar enlargement:

- Neoplasia: tonsillar lymphoma or SCC

INITIAL DATABASE

- CBC, serum biochemistry profile, and urinalysis to identify underlying systemic disease
- Feline leukemia virus (FeLV) and FIV testing of cats

ADVANCED OR CONFIRMATORY TESTING

- Bacterial culture and sensitivity (C&S) or virus isolation in cases of primary tonsillitis that fail to respond to routine antibiotics
- General anesthesia and tonsillar fine-needle aspirate (FNA) cytologic examination or biopsy:
    - Specific indications: unilateral tonsillar enlargement or tonsillar enlargement that does not resolve (or worsens) despite identification and treatment of underlying disease

TREATMENT

TREATMENT OVERVIEW

- Treat the underlying disease
- Tonsillectomy is only indicated with the following:
    - Chronic recurrent tonsillitis unresponsive to antibiotic therapy and elimination of source of antigen (e.g., licking infected area)
    - Marked tonsillar enlargement interfering with swallowing or breathing
    - Neoplasia

ACUTE AND CHRONIC TREATMENT

- Primary tonsillitis with no identifiable etiology: broad-spectrum antibiotics if necessary (e.g., ampicillin or amoxicillin at 20 mg/kg PO q 8-12 h, 10-14 days)
- Chronic tonsillitis: antibiotic therapy based on C&S results
- Foreign-body retrieval
- Tonsillar lymphoma: chemotherapy for lymphoma
- SCC: surgical excision followed by chemotherapy (e.g., doxorubicin or epirubicin and cisplatin or carboplatin) and radiation therapy
- Incidentally discovered bilateral/symmetric tonsillar enlargement is often most appropriately treated with only monitoring (watchful waiting) while the underlying cause is sought and treated.

PROGNOSIS AND OUTCOME

- Tonsillitis: good prognosis, usually resolves with underlying disease
- Neoplasia: poor long-term prognosis

PEARLS & CONSIDERATIONS

COMMENTS

- Therapeutic intervention for enlarged tonsils is rarely required.
- The most common cause of symmetric/bilateral tonsillar enlargement is a reactive change in response to oral exposure to antigen, such as the pet licking his/her anal sacs or genitalia. Therefore, diagnostic investigation and treatment should focus on these processes first, then on the tonsils only if necessary.

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Gunnarsson L, et al: Experimental infection of dogs with the nasal mite *Pneumonyssoides caninum.* Vet Parasitol 77:179–186, 1998.

Montague AL, et al: A study of greyhounds with tonsillar enlargement and a history of poor racing performance. Vet J 164:106–115, 2002.

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Toad or Lizard Intoxication

BASIC INFORMATION

DEFINITION

Toxicoses associated with exposure to toads of the genus *Bufo;* generally characterized by severe neurologic and cardiovascular effects (hypersalivation/foaming, head shaking, tremors, ataxia, collapse, seizures, cardiac arrhythmias, and death)

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs are more likely to mouth the toads than are cats.

GEOGRAPHY AND SEASONALITY

- In the United States, the greatest number of cases is seen in Florida. Cases occur across the United States (California to New England, Florida to Ohio), Hawaii and the Caribbean.
- Wet conditions (e.g. hurricanes, high rainfall) may predispose to increased *Bufo* numbers.
- Peak months are June through September.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Witnessed or suspected exposure (mouthing by the dog or cat; some dogs will swallow the toad)
- Hypersalivation, head shaking
- Sudden onset of collapse, seizures

PHYSICAL EXAM FINDINGS

- Hypersalivation/foaming
- Head shaking
- Vomiting
- Tachypnea
- Ataxia
- Seizures
- Stupor
- Pale mucous membranes or cyanosis
- Cardiac arrhythmias:
    - Sinus tachycardia
    - Bradycardia; atrioventricular (AV) block

ETIOLOGY AND PATHOPHYSIOLOGY

- Two species of toads have been associated with poisonings:
    - *Bufo marinus* (cane toad, marine toad, giant toad): sizes of 4-9.5 inches (10-25 cm); found in southern tips of Florida and Texas, much of the Caribbean, and Hawaii
    - *B. alvarius* (Colorado River toad): sizes 3-7 inches (8-18 cm); found in southeasternmost California, across the southern half of Arizona, and southwesternmost New Mexico
- Modified parotid glands (skin glands) of toads excrete several toxins known as *bufogenins,* including marinobufagin and bufotoxins. Clinical signs are likely caused by a combination of toxins
    - Action of bufogenins and bufotoxins is similar to that of cardiac glycosides (such as digitalis [see p. 175 and online chapter: Digoxin Toxicosis]), which inhibit Na+/K+-ATPase activity in myocardial cells; this process leads to increased intracellular calcium and blockage of sodium channels, resulting in cardiac anhythmias.
    - Secondary toxins in the parotid secretions may include bufotenins, serotonin, 5-hydroxytryptophan, powerful hallucinogenic tryptamines (found in *B. marinus* and *B. alvarius),* or catecholamines and could be responsible for such other signs as gastrointestinal (GI) upset, tremors, hyperthermia, and seizures

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Tentative diagnosis is based on observed or suspected exposure to a toad and acute onset of a startled, agitated, and hypersalivating patient. Digoxin irnmunoassay may aid confirmation of exposure in questionable cases.

DIFFERENTIAL DIAGNOSIS

- Cardiac glycoside toxicity (e.g., digoxin/digitalis, foxglove, lily of the valley)
- Illicit or prescription drug intoxication

INITIAL DATABASE

- Blood pressure (BP; see p. 1209):
  - Hypotension is common and may require treatment.
- Electrocardiogram (ECG; see p. 1253):
  - Various cardiac arrhythmias
- Serum potassium:
  - Hypokalemia or hyperkalemia may be present

TREATMENT

TREATMENT OVERVIEW

Management is based primarily on whether the toad has been merely mouthed and released (rinse the mouth immediately) or has been chewed and/ or swallowed (more aggressive intervention and cardiac and neurologic monitoring/management are indicated). Common effects requiring treatment include bradycardias or tachycardias, hypotension, electrolyte disturbances, and seizures.

ACUTE GENERAL TREATMENT

- Immediately rinse the patient's mouth with running water for 5 minutes.
- If a toad has been ingested and the animal is not showing overt clinical signs of toxicosis:
  - Induction of vomiting:
    - Hydrogen peroxide 3%, 0.25-0.5 mL/kg PO once; *or*
    - Apomorphine, 0.04 mg/kg IV, IM, SQ, or conjunctivally
  - Administration of activated charcoal:
    - Dose according to packaging label of product (e.g., 10 mL of activated charcoal suspension PO made from 2 g activated charcoal suspended in 10 mL tap water).
- IV fluids ± colloids to correct shock and hypotension
- Correct hyperkalemia or hypokalemia if present (see pp. 556 and 577).
- Control seizures with diazepam (0.5-1 mg/kg IV) or barbiturates as needed.
- Monitor and control anhythmias:
  - Atropine, 0.02-0.04 mg/kg IV or IM, for significant bradycardia. Do not use atropine to treat hypersalivation alone because it can predispose the patient to arrhythmias.
  - Propranolol, 0.02-0.06 mg/kg via slow IV, or other beta-blocker only for extremely rapid, sustained sinus tachycardia. Reflex tachycardia may occur secondary to hypotension and must not be suppressed; correct hypotension before treating tachycardia.
  - Lidocaine, 2 mg/kg IV bolus followed by 50-80 mcg/kg/min (constant rate infusion) for ventricular tachyarrhythmias
- Oxygen supplementation for severe cases (see p. 1318):
  - Address cerebral edema if suspected (collapsed or comatose patient: furosemide [dog, cat], 1-2 mg/kg IV; mannitol [dog, cat], 0.25-1 g/kg IV over 15-20 min).
- Digibind (Glaxo Wellcome), a digoxin-specific Fab fragment for poorly responsive or deteriorating animals:
  - Determine serum digoxin levels for dosing Digibind. Empirically, can use multiple vials with minimal risk (good safety profile; see online chapter: Digoxin Toxicosis).
  - High cost and large amounts needed for treatment may make Digibind impractical in many cases.

RECOMMENDED MONITORING

- ECG, blood pressure, oxygen tension

- Neurologic status
- Serum potassium

PROGNOSIS AND OUTCOME

Good if signs are mild; guarded if both neurologic and cardiac signs develop

PEARLS & CONSIDERATIONS

COMMENTS

- Exposure to other North American toads such as *B. americanus* (American toad), *B. boreas* (western toad), *B. cognatus* (Great Plains toad), *B. terrestris* (southern toad), *B. valliceps* (Gulf Coast toad), and *B. woodhousei*(Woodhouse toad) may result in only mild hypersalivation; severe systemic signs are unlikely.
- Several species of salamanders and newts (e.g., California newt) may contain tetrodotoxin in their skin and muscles. Ingestion can cause vomiting, muscle weakness, ataxia, hypotension, bradycardia, and an ascending paralysis with respiratory arrest. Treatment is centered on supportive care.
- Gila monsters *(Heloderma suspectum)* and the Mexican beaded *lizard (Heloderma horridum)* are two venomous lizards found in North America. Gila monsters are found in the southwestern part of the United States, while the Mexican bead lizard is found in the southwestern part of Mexico and Guatemala. The lizards' bites tend to be defensive; they will hang on after biting, so they can inflict considerable mechanical trauma in addition to envenomation. The venom can cause local pain, weakness, vomiting, muscle fasciculation, hypotension, and tachycardia or anaphylaxis. Treatment consists of wound irrigation, antibiotics, analgesia, management of hypotension if present, and monitoring for systemic signs. Antivenin is not commercially available.
- Blue-tailed skinks *(Plestiodon* [formerly *Eumeces]* spp., family Scincidae) are anecdotally reported to cause acute vocalization, ataxia, hypersalivation, labored respirations, and generalized weakness in cats; not all ingestions cause clinical signs. While this American lizard is endemic east of the Mississippi River from Michigan and Ontario southward, most reports are from Florida, and clinical cases appear to respond to general supportive treatment; little is known regarding a toxic principle

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Ticks

BASIC INFORMATION

DEFINITION

Ectoparasites that feed on the blood of their hosts and can be divided into hard (ixodid) and soft (argasid) ticks. Ixodid ticks are highly parasitic, produce more progeny, and infest larger areas compared to argasid ticks.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Ixodid ticks (*Ixodes*, *Dermacentor*, *Rhipicephalus*, *Amblyomma*, *Haemaphysalis* spp.) are more commonly found on dogs than on cats.

RISK FACTORS: Canine hunting breeds (greater environmental exposure)

CONTAGION & ZOONOSIS: Infected animals may act as a source of transmission to other animals and people.

GEOGRAPHY AND SEASONALITY: Ixodid ticks:

- *Ixodes scapularis* (black-legged tick): the Midwest and the northeastern and southeastern parts of the United States; borreliosis [Lyme disease] (also transmitted by *I. pacificus*)
- *Dermacentor variabilis* (American dog tick): throughout North America but most commonly found along the Atlantic Coast in areas of shrub and beach grass; Rocky Mountain spotted fever, tick paralysis, tularemia
- *Rhipicephalus sanguineus* (brown dog tick): widely distributed throughout North America; babesiosis, ehrlichosis, and tick paralysis
- *Amblyomma americanum* (lone star tick): found throughout the southeastern and south central states; tularemia
- *Haemaphysalis* spp. (yellow dog tick): Africa and Asia

Argasid ticks:

- *Otobius megninii* (spinous ear tick) in arid areas of North America, South America, India, and South Africa

ASSOCIATED CONDITIONS & DISORDERS

- Anaplasmosis
- Babesiosis
- Borreliosis (Lyme disease)
- Ehrlichiosis
- Rocky Mountain spotted fever
- Tick paralysis
- Tularemia

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Ticks can injure animals by producing tick paralysis through their secretions, causing localized irritation via bites, producing hypersensitivity reactions, and serving as vectors for bacterial, viral, protozoal, and rickettsial diseases.

HISTORY, CHIEF COMPLAINT: Owners note a tick infestation. Generally the patient is either in or has traveled to an area known to be tick-infested.

PHYSICAL EXAM FINDINGS: Presence of ticks noted on the skin. Clinical signs vary from none to the presence of a nodule at the site of tick attachment or systemic signs of tickborne diseases (ehrlichiosis, Lyme disease, Rocky Mountain spotted fever, babesiosis, tick paralysis, tularemia). Ticks are most commonly found on the pinnae of the ears or within the interdigital spaces.

ETIOLOGY AND PATHOPHYSIOLOGY

- Heavy infestations can lead to significant blood loss.
- Several types of neurotoxins produced by a variety of ticks affect the lower motor neurons of the spinal cord and cranial nerves and produce a progressive ascending flaccid paralysis (tick paralysis).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is based on noting the presence of ticks on the skin and then evaluating for localized and/or systemic disease if appropriate historical and/or physical signs exist.

DIFFERENTIAL DIAGNOSIS

Tickborne systemic disorders:

- Tick paralysis
- Rocky Mountain spotted fever: caused by *Rickettsia rickettsii*; causes a necrotizing vasculitis
- Ehrlichiosis: caused by *Ehrlichia canis* (other species exist also); vasculitis, hematologic disorders, and facial dermatitis
- Lyme disease: caused by *Borrelia burgdorferi*; in dogs: fever, neurologic signs, polyarthritis
- Tularemia: vectors are *D. andersoni*, *D. variabilis*, *D. occidentalis*, and *A. americanum*

INITIAL DATABASE

- Examine the entire skin for ticks, paying special attention in the ears and between the toes.
- Perform a complete physical examination; if clinical signs and history warrant, specific (serologic) testing should be done for the various tickborne diseases.

TREATMENT

TREATMENT OVERVIEW

Treatment should involve the efficient removal of attached ticks, performing proper environmental control measures, and treating localized reactions or transmitted diseases.

ACUTE GENERAL TREATMENT

- Tick removal as soon as possible:
  - Soak the tick in isopropyl alcohol while it is still attached to the animal's skin. Then, using a pair of hemostats, grasp the head parts at the surface of the skin and apply firm traction with a gentle twist.
- Effective approved antiparasitic treatments for dogs include Fipronil (Frontline) and acaricidal collars containing amitraz (Preventic). Fipronil (Frontline) may be effective for tick control in cats.
- Repeated spraying of the internal (kennel) and external environments with approved pesticides may be effective for controlling or eliminating infestations with *R. sanguineus*.

PROGNOSIS AND OUTCOME

Prognosis is good, but reinfestation can occur if preventive measures to prevent exposure are not undertaken.

PEARLS & CONSIDERATIONS

PREVENTION

- Avoid environments with large tick populations.
- May require strict indoor sequestration
- Selamectin (Revolution) is effective in control of *R. sanguineus* and *D. variabilis* on dogs and is safe to use on cats. Imidacloprid-permethrin (Advantix) is effective in controlling *D. variabilis* when applied monthly on dogs.
- Immunotherapy with a tick vaccine has been proposed.
- Tick habitats can be destroyed by cutting and burning brush and grass, cultivating land, and rotating pastures.
- Grassy and shrubbed areas can be treated with appropriately registered pesticides in urban areas; application is done in the spring and repeated once during midsummer.

CLIENT EDUCATION

- Inform clients that tick control/prevention can be challenging because ticks have long lifespans, are widely prevalent in the environment, have remarkable reproductive capabilities, and spend short time periods on their hosts.
- Infected animals may act as a source of transmission to people.

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Tick Paralysis

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

An acute, rapidly progressive generalized lower motor neuron (LMN) paralysis that results from neuromuscular blockade due to a salivary neurotoxin produced by certain gravid, female tick species

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Any age or breed; both sexes
- North American tick paralysis *(Dermacentor* ticks) affects dogs but not cats; Australian tick paralysis *(Ixodes* ticks) affects dogs and cats.

GENETICS & BREED PREDISPOSITION: Any species; incidence is rare in the cat.

RISK FACTORS: Tick exposure CONTAGION & ZOONOSIS: Some ticks may cause tick paralysis in humans; animal-to-animal or zoonotic transmission does not occur.

GEOGRAPHY AND SEASONALITY

- Recognized worldwide; most in-depth reports from the United States and Australia
- Incidence is most frequent in the summer months.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- History of hind limb and then forelimb stiff gait that progresses to flaccid paralysis
- Mentation, behavior, and ability to urinate and defecate remain normal.

PHYSICAL EXAM FINDINGS

North America *(Dermacentor* spp. ticks):

- Hind limb weakness rapidly progressing to generalized weakness, then complete flaccid paralysis. Tail wag often is preserved.
- Cranial nerve involvement is rare, but nystagmus or mild facial palsy may be observed.
- Pain sensation is preserved, but hyperpathia is rare.
- Voice change and intercostal muscle paresis can be observed, potentially leading to ventilatory failure (respiratory paralysis).

Australia *(Ixodes* spp. ticks):

- Hind limb weakness rapidly progressing to generalized weakness, then complete flaccid paralysis. Tail wag often is preserved.
- Pain sensation is preserved, but hyperpathia is rare.
- Signs of facial paralysis, dysphagia, and megaesophagus are common and may be profound.
- Autonomic signs (mydriasis, peripheral vasoconstriction, arterial and pulmonary hypertension) can be observed. If left undiagnosed, respiratory paralysis and death may ensue.

ETIOLOGY AND PATHOPHYSIOLOGY

- Gravid female tick of the species *D. variabilis* (Eastern wood or dog tick), *D. andersoni* (Rocky Mountain wood tick) in the United States, and *Ixodes holocyclus* in Australia.
- Adult *D. variabilis* and *D. andersoni* female ticks elaborate the neurotoxin; adult female, nymphs, and larvae of *Ixodes* ticks are incriminated.

- The neurotoxin is secreted by the engorged feeding female tick; the toxin either inhibits depolarization in the terminal portions of motor nerves or blocks the release of acetylcholine (ACh) from the motor nerve terminals at the neuromuscular junction.
- The toxin may affect both the motor and sensory nerve fibers by altering ionic fluxes that mediate action potential production.
- In most cases, hind limb weakness begins days after tick attachment, 5-9 rapidly followed by generalized weakness and complete flaccid paralysis as well as areflexia within 24-72 hours.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis rests entirely on finding tick(s) in an animal with compatible clinical signs. Delay to finding and removing tick(s) can affect prognosis markedly.

DIFFERENTIAL DIAGNOSIS

- Polyradiculoneuritis
- Early stages of botulism
- Fulminant myasthenia gravis

INITIAL DATABASE

- Response to tick removal is confirmatory: patient's rapid clinical improvement after tick removal (within 24 hours for *Dermacentor* spp. and return to normalcy in 48-72 hours; clinical signs may initially progress for 24-48 hours after tick removal for *Ixodes* spp.)
- Exclusion of other causes of rapidly progressive LMN diseases (see Differential Diagnosis, above)
- Hematologic and biochemical profiles are usually normal

ADVANCED OR CONFIRMATORY TESTING

- Chest and abdominal radiographs are usually normal (exception: megaesophagus *[Ixodes* spp.])
- Electromyography:
  - Shows no evidence of denervation
  - Amplitude of evoked motor potentials is markedly reduced.
  - Repetitive stimulation does not cause further decrement in amplitude.
- Nerve conduction velocity (motor and sensory) may be slightly slower; terminal conduction times may be prolonged.

TREATMENT

TREATMENT OVERVIEW

Since tick removal is both diagnostic and therapeutic, additional treatment consists of supportive care until the clinical signs resolve.

ACUTE GENERAL TREATMENT

- Tick removal can be curative; remember to remove the head, since the toxin resides in the salivary glands.
- Insecticide if ticks are not found
- Whole-body shaving if long-haired patient (tick search)
- Hyperimmune serum (0.5-1 mL/kg IV): recommended for binding circulating neurotoxin and preventing further progression in the dog; caution regarding anaphylaxis risk.
- Autonomic dysfunction can be treated with a combination of phenoxybenzamine hydrochloride, 1 mg/kg as a 0.1% solution given IV over 15 minutes q 12-24 h; and acepromazine, 0.05-0.1 mg/kg IV q 6-12 h.
- Oxygen and ventilatory support necessary for animals with respiratory compromise.

CHRONIC TREATMENT

- Supportive care
- Physical therapy
- Sanitation
- Provision of food and water
- Recurrence is possible with reexposure

DRUG INTERACTIONS

Avoid aminoglycosides (associated with neuromuscular blockade).

POSSIBLE COMPLICATIONS

- Respiratory paralysis (especially with recurrent exposure)
- Decubital ulcers
- Aspiration pneumonia

RECOMMENDED MONITORING

- Respirations
- Urination/defecation
- Progression of signs

PROGNOSIS AND OUTCOME

- Highly dependent on timely identification and removal of tick(s)
- Excellent if rapid removal of *Dermacentor* tick (in United States); fatal if undiagnosed/untreated
- Guarded with *Ixodes* ticks (Australia); fatal if undiagnosed/untreated

PEARLS & CONSIDERATIONS

COMMENTS

- Consider time of the year in the differential diagnosis.
- Note rapid (24-72 hours) progression to areflexic flaccid paralysis, which should raise the suspicion of tick paralysis and prompt a meticulous examination of the skin and coat.
- Make sure whole tick is removed, because the toxin lies in the tick's head (salivary glands).
- Make sure the animal is shaved if heavily funed so that identifying the tick(s) (if present) is easier.

TECHNICIAN TIP

Identifying and removing a tick (including mouth parts) from the skin of a patient with a presumptive diagnosis of another neuromuscular disease can be lifesaving.

PREVENTION

- Avoid tick exposure.
- Use insecticides at appropriate doses.
- Avoid reexposure.

SUGGESTED READING

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Thyroid Carcinoma

BASIC INFORMATION

DEFINITION

Most common malignant neoplasm of the thyroid gland. Thyroid carcinomas are uncommon in dogs, accounting for 1.2%-4% of all canine tumors. They are very rare in the cat.

SYNONYM

Thyroid adenocarcinoma

EPIDEMIOLOGY

SPECIES, AGE, SEX: Usually older dogs; median age at diagnosis is 9-10 years; no sex predilection.

GENETICS & BREED PREDISPOSITION: Any breed; beagles, boxers, and golden retrievers may be at increased risk.

RISK FACTORS: Radiation exposure; possibly iodine deficiency or excess

ASSOCIATED CONDITIONS & DISORDERS

- Hypothyroidism
- Hyperthyroidism
- May occur as part of multiple endocrine neoplasia syndromes

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Histologic classification:
  - Follicular cell origin; papillary, follicular, compact or anaplastic
  - Medullary tumors (parafollicular or C-cell carcinomas) are rare.
- Functional classification:
  - Hypofunctional (30%), normal function (60%), or hyperfunctional (10%)

HISTORY, CHIEF COMPLAINT

- Ventral cervical mass, cough, dysphagia, dysphonia, dyspnea, facial edema (see p. 263) are recognized chief complaints.
- With concurrent hypothyroidism, the patient may manifest lethargy, poor haircoat, or other signs of hypothyroidism (see p. 558).
- With concurrent hyperthyroidism, the patient may have polyphagia, polyuria and polydipsia, weight loss, restlessness, and tachypnea (see p. 558).
- With medullary carcinoma, the patient may manifest diarrhea and tetany (hypocalcemia).

PHYSICAL EXAM FINDINGS

- The normal paired thyroid glands lie lateral to the trachea and just caudal to the larynx. A thyroid carcinoma is generally palpable as a cervical mass that is subcutaneous and usually lateralized, firm, sessile/broad-based, asymmetric, irregular, and nonpainful; may be fixed or movable.
- With concurrent hyperthyroidism, tachycardia is possible.

ETIOLOGY AND PATHOPHYSIOLOGY

- Etiology is unknown.
- Metastasis to the lungs or regional lymph nodes is common: ≈30%-50% of affected animals have clinically detectable metastasis at the time of diagnosis.
- Local invasion of vital vascular and neurologic structures, including external carotid artery, external jugular vein, and

vagosympathetic trunk, are common. In these cases, full excision is impossible, contributing substantially to morbidity and mortality.
- Unilateral tumors are more common than bilateral tumors.
- Ectopic thyroid tissue can occur anywhere from the base of the tongue to the heart.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis of thyroid neoplasia involves confirming the abnormal tissue is of thyroid origin (cytologic/histopathologic evaluation and/or advanced imaging). This confirmation and appropriate staging allows the development of a comprehensive treatment plan.

DIFFERENTIAL DIAGNOSIS

Cervical mass:

- Other primary tumors: soft-tissue sarcoma, salivary gland adenocarcinoma, parathyroid neoplasia, lymphosarcoma
- Metastatic tumors: oral squamous cell carcinoma (SCC), oral melanoma
- Abscess or granuloma
- Salivary mucocele

INITIAL DATABASE

- CBC, serum biochemical profile, and urinalysis:
  - Usually normal
  - Mild anemia possible
  - If hypothyroidism: fasting hypercholesterolemia is common
  - If medullary carcinoma: hypocalcemia likely
- Serum total thyroxine (T4), free T4, and endogenous thyroid-stimulating hormone (TSH) concentrations: results depend on functional status of tumor (see p. 588 and 562)
- Thoracic radiographs (three views): possible metastasis
- Fine-needle aspirate (FNA) of regional lymph nodes: possible metastasis
- Cervical ultrasound: can help assess the extent of tissue invasion and vascularity

ADVANCED OR CONFIRMATORY TESTING

- FNA of the mass:
  - These are often difficult to assess cytologically because of heavy contamination with peripheral blood, and neoplastic cells may not exfoliate well. It is not possible to differentiate benign versus malignant thyroid tumors based on cell characteristics.
  - May help rule out nonthyroidal tumors such as lymphoma or metastasis from an oral tumor
  - Risk of persistent hemorrhage even with small-gauge needle
- Needle biopsy: greater diagnostic yield than an aspirate but high risk of hemorrhage. This biopsy should not be performed without ultrasound guidance, and even with such guidance, both the owner and animal should be prepared for immediate surgery if intractable bleeding occurs.
- Cervical exploratory surgery for incisional biopsy and histopathologic evaluation
- CT scan with contrast enhancement or MR imaging: helps differentiate thyroidal from nonthyroidal cervical masses; assesses tissue invasion and feasibility of surgical excision and can also be useful in planning radiation therapy.
- Thyroid scintigraphy (technetium-99m [^{99m}Tc]-pertechnetate scan): may identify ectopic or metastatic tissue, can help predict radioactive iodine (^{131}I) uptake, and can be used after surgery to identify residual disease.

TREATMENT

TREATMENT OVERVIEW

Surgical excision is the best treatment for freely movable tumors without deep tissue invasion. If complete surgical excision is not possible, halting/slowing tumor growth and metastasis become the primary goals. Any related thyroid dysfunction needs to be addressed with medications.

ACUTE GENERAL TREATMENT

- The best treatment option depends on tumor size, mobility, and functionality and whether metastasis is present.
- Nonfixed tumor without metastasis: thyroidectomy
- Fixed/locally invasive tumor without metastasis: surgical debulking (if debulking is not possible because of vascularity or extent of invasion, initial radiation therapy may shrink the tumor so that surgical debulking becomes possible), or radiation therapy can be used as definitive treatment.
- Fixed or nonfixed tumor with metastasis: surgical debulking, palliative or definitive radiation therapy
- Local residual disease: radiation therapy and/or chemotherapy (doxorubicin and/or cisplatin; consult a veterinary oncologist for treatment regimen details).
- Metastatic disease: chemotherapy as already described
- Use of ^{131}I: effectiveness in dogs controversial. Can be considered for residual and/or metastatic disease if the thyroid tissue is functional, but higher doses are required than those used for treating benign disease.

CHRONIC TREATMENT

- If hyperthyroidism is not present: T4 supplementation may be helpful insofar as T4 inhibits endogenous TSH secretion, and TSH may stimulate remaining tumor cells (see p. 588).
- If hyperthyroidism is present: methimazole, 2.5-5 mg PO q 8 h, to decrease systemic signs and treat thyrotoxicosis prior to definitive treatment.

POSSIBLE COMPLICATIONS

- Tumor alone: anemia, hypercalcemia (paraneoplastic—adenocarcinoma), hypocalcemia (paraneoplastic—medullary carcinoma), respiratory distress, disseminated intravascular coagulation
- Surgery: extensive hemorrhage, laryngeal paralysis, postoperative hypoparathyroidism and hypothyroidism (if bilateral excision)
- External beam radiation therapy: mucositis, dry to moist skin desquamation, and alopecia within the treatment field
- Chemotherapy: myelosuppression, cardiotoxicity (doxorubicin), nephrotoxicity (cisplatin)

RECOMMENDED MONITORING

- Bilateral thyroidectomy: monitor serum calcium concentrations for 7-10 days.
- Chemotherapy: monitoring dependent on protocol used
- General: physical examination, thoracic radiographs, and ± serum T4 concentrations every 3 to 4 months

PROGNOSIS AND OUTCOME

- Long-term prognosis usually guarded to poor because of tumor size, local invasion, and relatively high incidence of metastasis at the time of diagnosis; however, tumors with a volume <20 cm^3 are less likely to have metastasized, and surgery may be curative if the tumor is movable.
- Neither chemotherapy nor external beam radiation therapy is curative, but long-term progression-free intervals (>3 years) have been reported in some dogs treated with the latter.

TECHNICIAN TIP

Since prognosis and ease of excision improve with early detection, incidentally finding a mass in the cranial ventral neck can be very important and is always worth bringing to the attention of the attending veterinarian.

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Thymoma

BASIC INFORMATION

DEFINITION

A benign or malignant primary tumor originating from the thymic epithelium. Clinically, the presenting complaints for animals with thymoma are signs caused by the space-occupying nature of the mediastinal mass or by paraneoplastic syndromes such as myasthenia gravis, megaesophagus, and hypercalcemia.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dog: average age is 8-10 years.
- Cat: average age is 9-12 years.

GENETICS & BREED PREDISPOSITION: Dog: large-breed dogs (Labrador retriever, German shepherd) may be more commonly affected.

ASSOCIATED CONDITIONS & DISORDERS

- Paraneoplastic syndromes associated with thymoma:
  - Myasthenia gravis (20%-50% of dogs with thymoma)
  - Hypercalcemia
- Immune-mediated syndromes (less common):
  - Polymyositis, dermatitis (e.g. feline thymoma-associated exfoliative dermatitis), and myocarditis
- Megaesophagus
- Cardiac arrhythmias: rare
- Cranial vena cava syndrome (see p. 263): rare

DISEASE FORMS/SUBTYPES: Epithelial-dominant, lymphocyte-dominant, and mixed forms exist and can make diagnosis by fine-needle aspiration difficult.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Respiratory signs: very common chief complaints (dyspnea, coughing); signs may be surprisingly mild given size of thymoma.
- Anorexia and weight loss also common
- Weakness: associated with myasthenia or hypercalcemia
- Regurgitation: if megaesophagus is present

PHYSICAL EXAM FINDINGS

- Respiratory system: muffled or absent lung and heart sounds due to pleural effusion and/or space-occupying nature of mass:
  - Increased, harsh lung sounds: aspiration pneumonia
- Weakness: episodic or sustained; associated with loss of muscle tone, decreased spinal reflexes. Can be focal, associated with the pharyngeal, laryngeal, or facial muscles.
- Decreased chest wall compliance noted with manual compression of the cranial thorax:
  - Important physical finding in cats with medium to large thymomas

ETIOLOGY AND PATHOPHYSIOLOGY

- Neoplastic transformation of thymic epithelial cells
- Cranial mediastinal mass ± pleural effusion:
  - Clinical signs of respiratory compromise
- Paraneoplastic syndrome of myasthenia gravis:
  - Result of aberrant immune stimulation

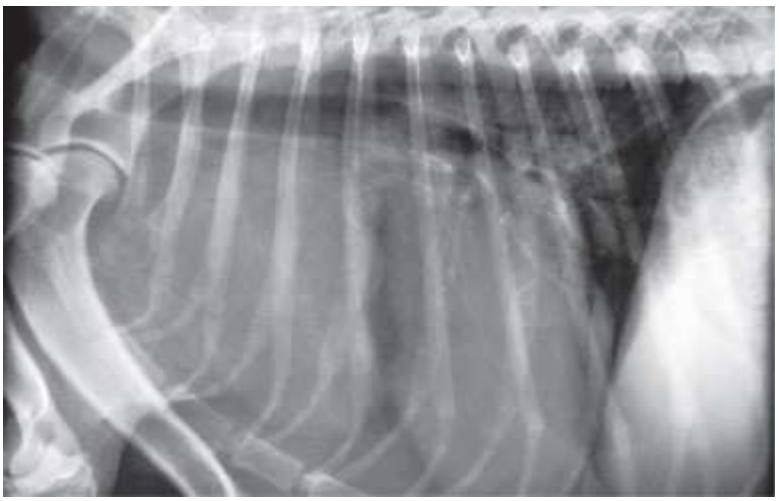
DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis of thymoma is suspected based on presenting history, physical examination findings, and the demonstration of a well-defined cranial mediastinal mass on thoracic radiographs. Ultrasound-guided fine-needle aspirates or needle biopsies are required to confirm the diagnosis and rule out other causes such as mediastinal lymphoma. CT scan helps determine whether the mass is surgically resectable.

DIFFERENTIAL DIAGNOSIS

- Thymic lymphoma
- Thymic hyperplasia
- Thymic hemorrhage
- Branchial cyst
- Ectopic thyroid or parathyroid neoplasia
- Neurogenic tumor
- Heart base tumor
- Mediastinal abscess or granuloma



THYMOMA Lateral thoracic radiograph. A large soft-tissue/fluid opacity mass occupies the entire cranial thorax of this dog, elevating the trachea.

(Courtesy Dr. Richard Walshaw.)

INITIAL DATABASE

- CBC, serum biochemical profile, and urinalysis:
  - Preoperative evaluation
- Feline leukemia virus (FeLV) and feline immunodeficiency (FIV) serologic testing in cats
- Survey thoracic radiographs (three views):
  - Extent of primary neoplasm
  - Evidence of metastasis
  - Evidence of megaesophagus and/or aspiration pneumonia (secondary to myasthenia gravis)
  - Pleural effusion
- Thoracic ultrasound:
  - Morphologic examination of mass, including association with/invasion of vascular structures, presence or absence of cysts
  - Fine-needle aspirate (FNA) cytologic examination/needle biopsy of mass:
    - Rule out lymphoma
  - Collection of pleural fluid (analysis, cytologic examination)
- Survey abdominal radiographs, ultrasound:
  - Rule out abdominal organ involvement:
    - Lymphoma

ADVANCED OR CONFIRMATORY TESTING

- MRI (see p. 1302) or CT (see p. 1233) scan: determine whether surgical excision is a viable treatment option. Evaluate compression, displacement, invasion, or incorporation of adjacent structures (e.g., vessels, esophagus, trachea) and metastasis. Evaluation of invasion of the cranial vena cava, however, is difficult. Contrast administration does not assist in determining cell type of mediastinal masses.
- Acetylcholine (ACh) receptor antibody titers: positive with thymoma-associated myasthenia gravis
- Flow cytometry of samples collected by fine-needle aspirate and stored in fetal bovine serum may be useful in differentiating thymoma from lymphoma. The test utilizes T-cell marker expression of CD4 and CD8 on T cells; >20% expression of CD4 and CD8 is consistent with thymoma, and lack of CD4 and CD8 expression rules out thymoma.

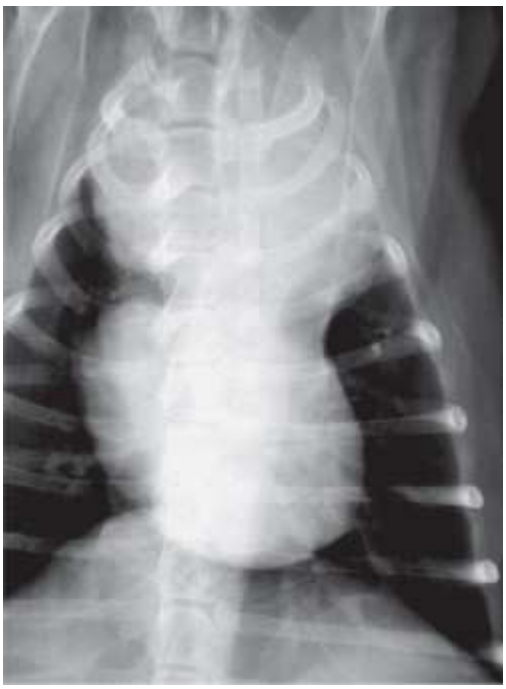
TREATMENT

TREATMENT OVERVIEW

Complete surgical resection is the recommended treatment for thymoma.

ACUTE GENERAL TREATMENT

- Complete surgical excision: often feasible with thymoma. May be carried out thoracoscopically (see p. 1340) for noninvasive thymoma.
- Incomplete surgical excision: more likely when thoracic ultrasonography reveals invasion into or attachment to local vessels. The size of thymoma is not necessarily predictive of complete versus incomplete resection
    - Chemotherapy:
        - Lymphoma protocol (see pp. 673 and 674)
    - Radiation therapy
- Nonresectable masses:
    - Radiation therapy ± chemotherapy
- Myasthenia gravis (see p. 736):
    - Resolution following complete resection of neoplasm
    - Prednisone, 2 mg/kg PO q 24 h for 4 weeks, then tapered
    - Hypercalcemia (see p. 553)
    - Aspiration pneumonia (see p. 1583):
        - Antibiotic therapy: based on culture and sensitivity (C&S) testing
    - Megaesophagus (see p. 709):
        - Consider tube gastrostomy for medical and nutritional support
- Therapeutic thoracocentesis (see p. 1338):
    - If respiratory compromise
    - Preanesthetic patient stabilization



THYMOMA Dorsoventral radiograph of same dog. Midline location suggests a mediastinal mass. Surgical excision and histopathologic analysis confirmed thymoma.

(Courtesy Dr. Richard Walshaw.)

CHRONIC TREATMENT

- Chemotherapy for nonresectable disease:
  - Lymphoma protocol (see pp. 673 and 674)

POSSIBLE COMPLICATIONS

- Inability to resolve the associated myasthenia gravis:
  - Persistent regurgitation
  - Recurring aspiration pneumonia
  - Intraoperative hemorrhage
- Regrowth of thymoma: occurs in some cases after complete surgical resection as well as cases with incomplete surgical resection. Monitoring is essential regardless of completeness of resection

RECOMMENDED MONITORING

- Following surgical resection (complete or incomplete):
  - Every 3 months (exam, thoracic radiographs) for 1 year, then every 6 months
- If patient is receiving chemotherapy:
  - As determined by protocol

PROGNOSIS AND OUTCOME

Dog:

- Resectable thymoma without megaesophagus: 70%-80% 1-year survival. 50% 3-year survival
- Nonresectable thymoma: poor
- Presence of myasthenia gravis or megaesophagus: guarded to poor; may resolve over a period of months

Cat:

- Resectable thymoma: 2-year median survival, 89% 1-year survival, 74% 3-year survival

PEARLS & CONSIDERATIONS

COMMENTS

- Adjuvant radiation therapy ± chemotherapy may benefit animals with nonresectable thymoma.
- Closely monitor animals for development of aspiration pneumonia and myasthenia gravis after surgery.

TECHNICIAN TIPS

- Knowledge of and experience in working with thoracostomy tubes is important in the postoperative management of patients who have undergone a thoracotomy.
- Patients with megaesophagus will require nutritional support (see p. 709):

SUGGESTED READING

Zitz JC, Birchard S, Couto GC, et al: Results of excision of thymoma in cats and dogs: 20 cases (1984-2005). J Am Vet Med Assoc 232:1186, 2008.

AUTHOR: MARYANN G. RADLINSKY

EDITOR: RICHARD WALSHAW

Thymic Hemorrhage

BASIC INFORMATION

DEFINITION

Accumulation of blood in the parenchyma of the thymus

SYNONYM

Thymic hematoma

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Generally an uncommon disease that occurs primarily in dogs; rare cases in cats have been reported.
- Thymic hemorrhage has been described predominantly in dogs <2 years of age, although it has been seen in older dogs.

GENETICS & BREED PREDISPOSITION: No sex or breed predilections have been identified, but in some reports, German shepherds have been overrepresented.

RISK FACTORS: Potential risk factors that have been identified include:

- Thoracic trauma or cervical stretching
- Exposure to anticoagulant rodenticides
- Thymic neoplasia (uncommon)

ASSOCIATED CONDITIONS & DISORDERS

- Hemothorax
- Hemomediastinum
- Hemopericardium (with heart base thymic remnants)

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Acute onset of lethargy, depression
- Tachypnea, respiratory distress
- Increased respiratory effort
- Sudden death

PHYSICAL EXAM FINDINGS

- Mucous membrane pallor
- Tachycardia
- Tachypnea
- Muffled heart sounds and decreased lung sounds ventrally are possible.
- Pain with compression of the cranial thorax

ETIOLOGY AND PATHOPHYSIOLOGY

- Intrathymic bleeding secondary to thymic trauma or a coagulation disorder, such as vitamin K rodenticide toxicity, will be the proximate cause identified in some cases.
- The initiating cause may not be identified in some animals.
- Another proposed cause includes bleeding from increased vessel fragility associated with normal thymic involution.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The initial key to the diagnosis of thymic hemorrhage is having suspicion for the disorder in young animals with unexplained anemia and respiratory distress.

DIFFERENTIAL DIAGNOSIS

- Other causes of hemothorax such as:
  - Trauma
  - Anticoagulant rodenticide toxicosis
  - Intrathoracic neoplasia
- Other causes of hemopericardium:
  - Heart base tumors
  - Right atrial hemangiosarcoma
  - Pericarditis
- Occult blood loss into other sites such as the gastrointestinal (GI) and urinary tracts.

INITIAL DATABASE

- CBC: anemia; thrombocytopenia has been described in some animals.
- Serum biochemical profile: hypoproteinemia (hypoalbuminemia and hypoglobulinemia)
- Thoracic radiographs/ultrasound: pleural effusion or a mediastinum widened by a soft-tissue density (hemorrhage)

ADVANCED OR CONFIRMATORY TESTING

- Thoracocentesis and fluid analysis will confirm hemothorax.
- Prolongations of one-step prothrombin time (PT) and activated partial thromboplastin time (APTT) will be expected in animals with anticoagulant rodenticide toxicity. These animals may also have increases in serum levels of proteins induced by vitamin K absence or antagonism (PIVKA); toxicologic analysis could reveal high concentrations of specific rodenticides identified in blood samples.
- Cardiac ultrasound and pericardiocentesis can rule out or document the presence of heart base masses/tumors and pericardial effusion (hemopericardium), respectively.

TREATMENT

TREATMENT OVERVIEW

Treatment goals are to identify an underlying cause whenever possible and provide hemodynamic support.

ACUTE GENERAL TREATMENT

- IV fluids (crystalloids, colloids)
- Blood products (whole blood, packed red blood cells [RBCs], plasma) or hemoglobin solutions (e.g., Oxyglobin).
- Vitamin K1 for animals with historic or laboratory features suggestive of anticoagulant rodenticide toxicity

POSSIBLE COMPLICATIONS

Complications of treatment or of the primary disease have not been described for those animals that survive.

RECOMMENDED MONITORING

- Clinical signs
- Packed cell volume (PCV), total protein
- PT, APTT, particularly as vitamin K1 therapy is discontinued

PROGNOSIS AND OUTCOME

- Most reported cases have been associated with fatal outcomes, possibly because of the low clinical suspicion of the disease and delay in diagnosis and treatment.
- Provision of timely, aggressive supportive care in the form of fluids and blood products and administration of vitamin K1 for animals with known or suspected rodenticide toxicosis have been associated with survival of some affected animals.

PEARLS & CONSIDERATIONS

COMMENTS

- Perform thoracic radiographs on young animals with an acute onset of respiratory distress and anemia of undetermined origin. Consider the diagnosis if there is evidence of a mass or density in the mediastinum or if the animal has pleural effusion (hemothorax).
- When hemorrhage is documented or suspected in the absence of a history of trauma, assess coagulation parameters to rule out coagulation disorders.

TECHNICIAN TIPS

- It may be difficult to place an IV catheter in patients with severe hemodynamic collapse; an intraosseous catheter (proximal humerus, proximal femur) is a viable substitute for initial fluid or blood component therapy.
- Patients that receive hemoglobin solutions will have discolored plasma and urine for a time after administration, and the free hemoglobin can interfere with a number of laboratory test results.

PREVENTION AND CLIENT EDUCATION

Avoid trauma and exposure to rodenticides.

SUGGESTED READING

Coolman BR, et al: Severe idiopathic thymic hemorrhage in two littermate dogs. J Am Vet Assoc 205:1152, 1994.

Liggett AD, et al: Thymic hematoma in juvenile dogs associated with anticoagulant rodenticide toxicosis. J Vet Diagn Invest 14:416, 2002.

Van der Linde-Sipman JS, van Dijk JE: Hematomas in the thymus in dogs. Vet Pathol 24:59, 1987.

AUTHOR & EDITOR: RANCE K. SELLON

Thrombocytopenia, Immune-Mediated

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Thrombocytopenia resulting from idiopathic destruction of platelets. A causative etiologic agent cannot be identified.

SYNONYM

Idiopathic thrombocytopenic purpura (ITP)

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs are far more frequently affected than cats; reported in male and female dogs from 8 months to 15 years of age, with middle-aged females predisposed.

GENETICS & BREED PREDISPOSITION: Cocker spaniels, Old English sheepdogs, German shepherds, and poodles are overrepresented.

ASSOCIATED CONDITIONS & DISORDERS: Immune-mediated diseases may affect multiple body systems; for example, immune-mediated thrombocytopenia (IMT) may be associated with polyarthritis or proteinuria. Anemia may be due to blood loss (especially gastrointestinal [GI]) or concurrent immune-mediated hemolytic anemia (Evans syndrome).

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Primary IMT remains idiopathic despite investigation. Secondary IMT occurs in association with infection, drug therapy, or neoplasia.

HISTORY, CHIEF COMPLAINT: Owners commonly notice bleeding in the skin, from the nose or mouth, or associated with minor trauma. Frank blood in the stool or melena may be detected. The patient may continue to eat and act normally, although some cases present with lethargy and weakness. Signs caused by bleeding into vital organs (brain, spinal cord) are an uncommon presentation.

PHYSICAL EXAM FINDINGS

- Petechiae, ecchymoses
- Ocular hemorrhage/hyphema
- GI bleeding, manifesting as melena or hematochezia noted after defecation, on rectal examination, or on a thermometer
- Pale mucous membranes
- Fever: present in <20% of cases

ETIOLOGY AND PATHOPHYSIOLOGY

- Occurs when a stimulus triggers a patient with the appropriate susceptibility genes
- The identification and inheritance of predisposing genes are unknown.
- Triggering factors may include vaccination, drug administration, stress, or infection.
- Bleeding does not occur until the platelet count is less than 25,000/µL, although bleeding may occur in the face of higher platelet counts if the platelets are dysfunctional (thrombocytopathia; see p. 881).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected in patients showing overt signs of bleeding in the history, physical exam, or both and is confirmed by demonstrating repeatable severe thrombocytopenia (<50,000/µL) in the absence of an identifiable cause.

DIFFERENTIAL DIAGNOSIS

- Breed-associated physiologic thrombocytopenia (greyhounds and Cavalier King Charles spaniels)
- Thrombocytopathia (drug-related, inherited, von Willebrand disease; see online chapter: Platelet Dysfunction)
- Tickborne disease (ehrlichiosis, anaplasmosis, Rocky Mountain spotted fever)
- Splenic disease (neoplasia, torsion, infarction)
- Drug administration (chemotherapy, antibiotics, estrogen, nonsteroidal antiinflammatory drugs [NSAIDs], albendazole, griseofulvin, propylthiouracil, ketoconazole)
- Recent vaccination
- Bacterial sepsis, vasculitis, disseminated intravascular coagulation
- Bone marrow disease (myelofibrosis, myelodysplasia, necrosis, myelophthisis)
- Severe hemorrhage (anticoagulant rodenticide, trauma)
- Cats: feline leukemia virus (FeLV), feline immunodeficiency virus (FIV) infections

INITIAL DATABASE

- CBC with manual differential: usually normal unless excess bleeding causes anemia
- Platelet count: low, usually <25,000 µL (severe thrombocytopenia)
- Biochemical profile: usually normal
- Urinalysis (voided):
  - Usually normal or may show hematuria
  - Avoid cystocentesis in any severely thrombocytopenic animal.
- Coagulation profile: usually normal
- Thoracic radiographs: usually normal
- Abdominal ultrasonography: usually normal or may show mild splenomegaly
- Titers for tickborne diseases in endemic

ADVANCED OR CONFIRMATORY TESTING

- Bone marrow cytologic examination is unnecessary in most cases (only necessary if the animal has concurrent leukopenia or nonregenerative anemia): may show increased (peripheral platelet destruction) or decreased (marrow-based destruction) megakaryocytes
- Testing for platelet-bound antibody is unnecessary in most cases.

TREATMENT

TREATMENT OVERVIEW

Severe bleeding may require transfusion (uncommon); cases with profound thrombocytopenia, signs of blood loss (e.g., lethargy, pallor), or owner inability to control activity require hospitalization. Stable patients may be treated as outpatients, with therapies aimed at raising the platelet count into the normal range and correcting the underlying cause if present. In some cases, it may be preferable to allow a low grade of thrombocytopenia to persist to decrease medications to tolerable levels.

ACUTE GENERAL TREATMENT

- Prednisone/prednisolone, 2.2 mg/kg PO q 24 h or divided q 12 h (alternative: dexamethasone, 0.2 mg/kg IV q 24 h or divided at q 12 h)
- Vincristine, 0.02 mg/kg (or 0.5 mg/m^2) IV once weekly
- Azathioprine, 2.2 mg/kg PO q 24 h
- Red blood cell (RBC) transfusions (fresh whole blood, packed cells) given as needed (see p. 1347)
- Platelet transfusions usually are impractical, since platelets are immediately destroyed.
- Human IV immunoglobulin (0.5 g/kg slowly IV q 24 h × 1-3 days) has been effective in refractory cases.

CHRONIC TREATMENT

- Discontinue vincristine once platelet count is >50,000 µL or if no response.
- Taper prednisone/prednisolone and azathioprine together once platelet count has normalized
- Decrease doses by half every month (in general) while monitoring platelet count.
- The minimum duration of therapy is 4-6 months.
- Increase to the previous dose, and attempt to taper more slowly if the platelet count falls during the drug tapering.

BEHAVIOR/EXERCISE

Activity and excitement should be minimized to avoid self-trauma until a normal, stable platelet count is achieved and all clinical signs

have resolved.

DRUG INTERACTIONS

- Extravasation of vincristine must be avoided because it causes severe skin necrosis; use an indwelling IV catheter.
- Avoid drugs such as aspirin or other NSAIDs.

POSSIBLE COMPLICATIONS

- Avoid the use of cyclophosphamide; hemorrhagic cystitis may be fatal.
- Prolonged administration of azathioprine may cause bone marrow suppression; monitor CBC and decrease dosage once platelet count returns to normal.
- Thrombosis has been rarely seen in patients after rapid rise of the platelet count. Patients with rapid (<3-5 days) rise of their platelet count to >200,000/ µL. may have their immunosuppressant medications tapered more quickly and/or antithrombotic medication administered (clopidogrel, 1 mg/kg PO q 24 h for 30 days).

RECOMMENDED MONITORING

- Platelet counts every other day until >50,000 µL, then weekly until normal
- CBC 1 week after starting azathioprine, then every 2 weeks while on daily dosing. Bone marrow suppression is unusual once azathioprine is tapered to 2.2 mg/kg every other day, so CBC need only be monitored every 2-3 months.

PROGNOSIS AND OUTCOME

- The prognosis is initially guarded, with fatal bleeding into the brain or spinal cord possible.
- Response often takes 3-10 days.
- Once the platelet count normalizes, the prognosis is fair to good.
- Many pets may be completely tapered from immunosuppressive medications, although relapse remains possible.

PEARLS & CONSIDERATIONS

COMMENTS

- The presence of severe thrombocytopenia (<25,000 µL in an otherwise healthy-appearing animal is most likely due to IMT.
- If bleeding is present when the platelet count >25,000 µL, an additional problem such as clotting factor deficiency, thrombocytopathia, or vasculitis must be present.
- Many animals are euthanized owing to adverse effects of glucocorticoids. Strategies to decrease glucocorticoid-induced adverse effects include avoidance of obesity, substituting prednisone with methylprednisolone or prednisolone, use of an additional immunosuppressive agent and lower glucocorticoid doses, and routine monitoring for infection of the skin and urinary tract.
- Combination immunosuppressive therapy with azathioprine is often more effective and has fewer adverse effects than prednisone or prednisolone alone.

PREVENTION

- Although a **link** has not been proven, future vaccinations should be limited to those considered absolutely essential.
- Stressful circumstances should be avoided if possible to avoid triggering relapse during remission and to reduce the risk of minimal but catastrophic self-trauma during severe thrombocytopenia.

TECHNICIAN TIPS

Venipuncture should be performed with the least possible trauma and pressure maintained over the vein for a full 60 seconds. Venipuncture from the jugular veins should be avoided to lessen the chance for cervical bleeding.

CLIENT EDUCATION

- Routine monitoring should be scheduled to detect relapse of disease and side effects of immunosuppressive medications.
- Weight must be carefully monitored and obesity avoided.

SUGGESTED READING

Bianco D, Armstrong PJ, Washabau RJ: Treatment of severe immune-mediated thrombocytopenia with human IV immunoglobulin in 5 dogs. J Vet Intern Med 21:694–699, 2007.

Lewis DC, Meyers KM: Canine idiopathic thrombocytopenic purpura. J Vet Internal Med 10:207, 1996.

Putsche JC, Kohn B: Primary immune-mediated thrombocytopenia in 30 dogs (1997-2003). J Am Anim Hosp Assoc 44(5):250–257, 2008.

AUTHOR: MICHAEL STONE

EDITOR: SUSAN M. COTTER

Third Eyelid Abnormalities/Protrusion

BASIC INFORMATION

DEFINITION

- Scrolled cartilage is an everted scrolllike malformation of the third eyelid.
- Third eyelid gland prolapse is a dorsal displacement of the gland from the base of the third eyelid.
- Protrusion of the third eyelid is a dor-solateral displacement of a normal third eyelid structure, typically as a result of alteration of ocular or orbital contents, orbital muscular tone, or globe position.
- Neoplasia of the third eyelid involves a smooth or irregular mass or diffuse thickening of the third eyelid; adenocarcinoma is reported to be most common; papilloma is second most common.

SYNONYMS

- Third eyelid: nictitating membrane, membrana nictitans
- Scrolled cartilage: everted cartilage, bent cartilage
- Third eyelid gland prolapse: cherry eye, Haws syndrome
- Third eyelid inflammatory disorders:
    - Plasma cell infiltration of the third eyelid: plasmoma, pannus, or chronic superficial keratitis of the third eyelid
    - Nodular granulomatous episclerokeratitis of the third eyelid: nodular episcleritis, nodular fasciitis (dogs)
    - Proliferative (eosinophilic) keratoconjunctivitis (cats)
    - Follicular conjunctivitis: lymphofollicular conjunctivitis
- Third eyelid protrusion: elevation of third eyelid

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Scrolled cartilage: congenital/early developmental disorder (dogs and cats)
- Third eyelid gland prolapse: generally occurs before 2 years of age (dogs and cats)

GENETICS & BREED PREDISPOSITION

- Scrolled cartilage: familial problem in large breeds including basset hound, bloodhound, English setter, German shepherd, Great Dane, Newfoundland, Rhodesian ridgeback, weimaraner; reported as simple recessive trait in Saint Bernard and German short-haired pointer dogs; uncommon in cats but reported in Burmese
- Third eyelid gland prolapse: predisposed breeds include American and English cocker spaniels, English bulldog, beagle, shihtzu (dogs); Burmese (cats)
- Third eyelid inflammatory disorders:
    - Breeds predisposed to plasma cell infiltration include German shepherds, Belgian sheepdog, Borzoi, Doberman pinscher, English springer spaniel.
    - Nodular granulomatous episclerokeratitis can involve the third eyelid of all dog breeds, with the collie apparently predisposed.
    - Follicular conjunctivitis: primarily large breeds, dogs typically <18 months of age.

ASSOCIATED CONDITIONS & DISORDERS: Third eyelid inflammation:

- Dogs:
    - Chronic superficial keratitis (see p. 825)
    - Nodular granulomatous episclerokeratitis (limbal lesions; see p. 356)
    - Follicular conjunctivitis (bulbar con-junctival lesions; see p. 239)
- Cats:
    - Proliferative (eosinophilic) keratoconjunctivitis (see p. 254)
    - Feline herpesvirus type 1 infection (see pp. 237 and 524)

Protrusion of the third eyelid:

- Conditions causing alteration of orbital contents: dehydration, loss of orbital fat from emaciation, temporal muscle atrophy,

orbital neoplasia, cystic disease in the orbit, and orbital cellu-litis, abscess, or hemorrhage (see p. 790)
- Conditions associated with alteration in globe size:
  - Microphthalmia (congenital smallness of the eye; see p. 778)
  - Chronic uveitis or glaucoma or ocular trauma causing phthisis bulbi (shrinkage of the eye; see pp. 448 and 1151)
- Conditions associated with alteration in orbital muscle tone: tetanus (see p. 1083), strychnine poisoning (see p. 1055), Horner's syndrome (see p. 543)
- Conditions associated with alteration in globe position:
  - Painful ocular disorders including: corneal ulceration (see p. 250), uveitis, and conjunctivitis
- In cats, also consider dysautonomia or a bilateral chronic idiopathic condition associated with gastrointestinal (GI) parasites, GI malfunction, or feline leukemia virus (FeLV) infection

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- “Membrane covering part of the eye” (layperson's description)
- Abnormal appearance of or position of third eyelid or gland of the third eyelid

PHYSICAL EXAM FINDINGS

- Scrolled cartilage: anterior (rostral) folding of the dorsal portion of the third eyelid
- Third eyelid gland prolapse appears as a smooth, moist (mucosa-covered) pink to red mass at the medial canthus, protruding over the free margin of the third eyelid; may be unilateral or bilateral.
- Third eyelid inflammatory disorders:
  - Plasma cell infiltration causes a thickened, pebbly, often depigmented, hyperemic third eyelid, especially along the free margin.
  - Nodular granulomatous episclerokeratitis lesions of the third eyelid are typically smooth, hyperemic subconjunctival tubular-like swellings along the palpebral surface of the third eyelid.
  - Animals with follicular conjunctivitis have an increased number of larger-than-usual follicles on the bulbar side of the third eyelid in addition to multiple small, pink follicles along the bulbar conjunctival surface.
- Neoplasia of the third eyelid: typically appears as a smooth to irregular, occasionally ulcerated, pink to red mass at the medial canthus, arising from the third eyelid; typically unilateral.

ETIOLOGY AND PATHOPHYSIOLOGY

- Scrolled cartilage: differential growth rate of the posterior (caudal) portion of the cartilage compared to that of the anterior (rostral) portion
- Third eyelid gland prolapse: may result from weakness of connective tissue attaching the base of the gland to the periorbital structures
- Third eyelid protrusion; movement of the third eyelid is passive and occurs with:
  - Changes in volume of globe or orbit
  - Secondary globe retraction via retractor bulbi muscle (e.g., ocular pain)
  - Changes in extraocular muscle tone (e.g., Horner's syndrome results in decreased sympathetic tone; tetanus produces increased extraocular muscle tone)
- Third eyelid inflammatory disorders:
  - Plasma cell infiltration is often associated with chronic superficial keratitis (see p. 825); the inflammatory infiltrate consists of plasma cells and lymphocytes.
  - Nodular granulomatous episclerokeratitis appears to be an immune-mediated disease; lesions are characterized by a chronic granulomatous inflammatory cell response.
  - Follicular conjunctivitis is thought to represent chronic antigenic stimulation.

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

The diagnosis of many disorders of the third eyelid rests on careful physical examination of the third eyelid lesions; confirmatory testing is needed in a minority of cases.

DIFFERENTIAL DIAGNOSIS

- Scrolled cartilage is diagnosed based on ophthalmic examination revealing a curled or bent third eyelid.
- The differential diagnosis for a smooth, fleshy mass at the medial canthus in a middle-aged or older dog is neoplasia, versus

glandular prolapse in a young (<2 year) dog.
- Third eyelid protrusion (as described above)

INITIAL DATABASE

- Characteristic clinical examination findings exist for most lesions involving the third eyelid, as described above.
- Definitive diagnosis of mass lesions may require excisional biopsy and histologic examination.
- Complete physical and ophthalmic examinations (see p. 1313) to determine cause of third eyelid protrusion, including:
  - Pupillary light reflexes (PLRs) (e.g., miotic pupil in Horner's syndrome and uveitis)
  - Fluorescein dye application (positive fluorescein stain retention in corneal ulceration)
  - Evaluate globe size (e.g., if small: microphthalmia versus phthisis bulbi)
  - Retropulsion of globe (may be reduced with orbital disease; see p. 790)
  - Hydration status
  - Body condition
  - Signs of systemic illness (fever, lethargy, etc.)

ADVANCED OR CONFIRMATORY TESTING

- Variable depending on underlying abnormality
- Imaging studies (ocular or orbital ultrasound, CT scan, MRI) for retrobulbar space-occupying lesions, possibly in conjunction with fine-needle aspirates (FNAs) and cytologic examination and/or biopsy and histologic examination of the orbital mass

TREATMENT 

TREATMENT OVERVIEW

Goals of treatment are to:

- Improve the appearance and function of third eyelid structures to as normal as possible to minimize chronic low-grade corneal and conjunctival irritation and associated ocular discharge (scrolled cartilage and third eyelid gland prolapse).
- Preserve vital tear production from the gland of the third eyelid (third eyelid gland prolapse).
- Formulate specific goals according to the nature of the abnormality.

ACUTE GENERAL TREATMENT

- Scrolled cartilage: treatment is surgical, requiring removal of the folded/ scrolled portion of the cartilage through the bulbar conjunctival surface of the third eyelid.
- Third eyelid gland prolapse requires surgical replacement of the third eyelid gland, which involves:
  - Anchoring the prolapsed gland to the orbital periosteum
  - Burying the prolapsed gland in a pocket created under the conjunctiva of the third eyelid
  - Fixation of the prolapsed gland to the cartilage of the third eyelid
  - Contraindicated: excision of the gland of the third eyelid. It is associated with significantly decreased tear production and a high incidence of keratoconjunctivitis sicca (KCS) months to years postoperatively.
- Third eyelid inflammatory disorders:
  - Treatment of plasma cell infiltrate typically consists of topical (q 6-12 h), subconjunctival (q 2-4 weeks initially), or (rarely) systemic corticosteroids; topical cyclosporine A (q 12 h) used for a long period of time (see p. 825)
  - Nodular granulomatous episclerokeratitis is generally controllable with the long-term use of topical and/or systemic corticosteroids and/or systemic azathioprine (see p. 356).
  - Follicular conjunctivitis is often self-limiting. In severe cases or those cases that feature unacceptable hyperemia or ocular discharge, irrigation of the conjunctival cul-de-sac with saline and judicious use of topical corticosteroids are helpful. Mechanical débridement with a gauze square/sponge following instillation of topical anesthesia (e.g., 0.5% proparacaine ophthalmic solution) is described but seldom necessary.
  - Neoplasia of the third eyelid may necessitate surgical removal of the entire third eyelid.

CHRONIC TREATMENT

If the third eyelid and gland are removed for neoplasia of the third eyelid, long-term use of topical artificial tear supplements (q 6-12 h) with or without topical cyclosporine A or tacrolimus (q 12 h) may be required, especially if KCS develops.

POSSIBLE COMPLICATIONS

- Third eyelid gland prolapse: if uncorrected, chronic exposure of the gland results in glandular hypertrophy, decreased tear

production, chronic KCS, and ocular discharge.
- Use caution with deep passage of suture needle in orbital “tie-down” procedures, because perforation of the globe may cause devastating consequences.

PROGNOSIS AND OUTCOME

- Scrolled cartilage: following surgery, most third eyelids return to normal function and appearance; in some cases, surgical removal of the scrolled section still does not produce complete flattening against the globe.
- Third eyelid gland prolapse: although surgical failure (up to 20%) can occur, subsequent repositioning is typically successful.
- Most inflammatory conditions of the third eyelid can be controlled medically; however, recurrence may arise, and maintenance therapy is often necessary.
- Prognosis of third eyelid protrusion depends on the underlying disease process and ranges from excellent (e.g., orbital cellulitis) to grave (malignant orbital neoplasia).
- Neoplasia of the third eyelid: adenocarcinoma is the most common condition and is associated with recurrence following excision; the second most common is papilloma, for which local excision is typically curative.

PEARLS & CONSIDERATIONS

COMMENTS

- The only indication for surgical removal of the third eyelid is neoplasia.
- Be suspicious of neoplasia of the third eyelid gland rather than third eyelid gland prolapse in a middle-aged or older dog. Do not surgically replace the gland in a suspicious case until confirmed (by FNA and Cytologic examination or wedge biopsy and histologic examination) that it is not neoplastic.
- Check the bulbar surface (i.e., underside) of the third eyelid in cases with third eyelid protrusion and cases in which concurrent corneal ulcers are not responding to treatment.

SUGGESTED READING

Barnett KC: Diseases of the nictitating membrane of the dog. J Small Anim Pract 19:101, 1978.

Plummer CE, et al: Intranictitans tacking for replacement of prolapsed gland of the third eyelid in dogs. Vet Ophthalmol 11:228, 2008.

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Thiamin (Vitamin B1) Deficiency

BASIC INFORMATION

DEFINITION

Inadequate intake of thiamin

SYNONYMS

Thiamine deficiency, Chastek paralysis (fox, mink)

EPIDEMIOLOGY

SPECIES, AGE, SEX: Cats and dogs of all ages. Thiamin requirement is higher in cats and increases during growth and reproduction. Thiamin is a heat-labile, water-soluble vitamin not synthesized in tissues of cats and dogs and therefore must be continually ingested in food.

RISK FACTORS

- Consumption of raw flesh and viscera of certain fish and shellfish containing thiaminases, which degrade thiamin. Thiaminases are inactivated by cooking.
- Feeding heat-processed foods without added thiamin or inadequately supplemented commercial diets. Pet food manufacturers overcome predictable losses by supplementation.
- Feeding sulfur dioxide- or sulfite-preserved cooked or raw meats. The U.S. Department of Agriculture (USDA) prohibits the use of sulfiting agents to preserve meats.

ASSOCIATED CONDITIONS & DISORDERS

- Feeding foods with active thiaminases or sulfiting agents at the same time with a thiamin source (e.g., commercial pet food) can inactivate thiamin and cause deficiency.
- Gastrointestinal disease causing malassimilation; inappetence or anorexia; polyuria/polydipsia; fluid diuresis.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Dietary history compatible with the risk factors listed above
- In dogs, nonspecific clinical signs include combinations of depression, inappetence, anorexia, weight loss, vomiting, reduced mentation, and failure to grow in puppies. Neuromuscular signs are progressive and consist of ataxia, circling, head tremor, thoracic limb hypermetria, stiff hind limb gait, increased muscle tone, paraparesis, tetraparesis, inability to walk, tonic-clonic convulsions, recumbency with opisthotonus, coma, and death.
- In cats, decreased food intake and salivation develop within 1-2 weeks of consumption of a deficient diet. Early clinical signs include combinations of inappetence, weight loss, vomiting, diarrhea, general weakness and mild ataxia. This stage may progress to spastic gate, spastic ventroflexion of the head and neck (so-called praying sign), and dilated unresponsive pupils. Severely affected cats may develop stupor, seizures, opisthotonos, and limb spasticity prior to death.

PHYSICAL EXAM FINDINGS

- In dogs, abnormalities may include tachypnea, tachycardia and weak femoral pulses. Neurologic examination (see p. 1311) may reveal reduced mentation, dilated and unresponsive pupils, positional horizontal or vertical nystagmus, deficits of postural reactions in all limbs, absence of deep and superficial pain in all limbs, hyperactive patellar and biceps reflexes, and hyperesthesia.
- In cats, sinus arrhythmia and bradycardia have been reported. Dilated unresponsive pupils, nystagmus, anisocoria or absence of menace responses may be present. Spastic ventroflexion of the head and neck is characteristic of disease. When suspended by the hind legs, affected cats keep their head ventroflexed instead of dorsiflexed. Cats may show abnormal behavior, abnormal postural reactions, hyperesthesia, or tetraparesis.

ETIOLOGY AND PATHOPHYSIOLOGY

- Thiamin plays essential roles in carbohydrate metabolism, energy production and neural function. Thiamin pyrophosphate (TPP) is a coenzyme in the conversion of pyruvate to acetyl coenzyme A, which enters the tricarboxylic acid (TCA) cycle to generate energy. It also catalyzes reactions in the oxidation of glucose by the hexose monophosphate shunt to produce NADPH for biosynthetic processes. Thiamin deficiency impairs the TCA cycle and generation of energy. Thiamin's role in neural function is unclear, but it is probably nonenzymatic, such as activation of ion channels.
- The mechanism by which thiamin deficiency results in observed clinical signs is unknown but may relate to dependence of neuronal and cardiac tissue on energy derived from glucose metabolism.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on the dietary history and consistent clinical signs. These findings justify prompt treatment with parenteral thiamin.

DIFFERENTIAL DIAGNOSIS

- Toxicity
- Inflammatory or infectious central nervous system diseases
- Multifocal neoplastic process
- Nutritional disease
- Metabolic disease

INITIAL DATABASE

- Review diet history to identify dietary risk factors.
- Question owners about possibility of toxin ingestion.
- CBC, serum biochemical profile, urinalysis, and CSF analysis are generally unremarkable.
- Neuroanatomic localization is consistent with multifocal central nervous system lesion.

ADVANCED OR CONFIRMATORY TESTING

- Treat with thiamin; expect rapid response within 12-48 hours.
- Erythrocyte transketolase activity assay (ETKA): limited availability
- MRI of the brain
- Analysis of the food for thiamin and sulfur dioxide concentration

TREATMENT

TREATMENT OVERVIEW

Clinical signs are rapidly progressive and fatal. Therefore treatment with parenteral thiamin must be initiated before results of advanced and confirmatory tests are obtained.

ACUTE GENERAL TREATMENT

- Supportive care (intravenous fluids)
- Control of seizures (anticonvulsant medications)
- Thiamin hydrochloride: recommended parenteral dose for cats and dogs varies from 5-250 mg IM or SQ q 12 h. Little clinical evidence exists other than case reports to identify an optimal dosage, so 5-20 mg per patient would likely be sufficient, as this is at least 4-30 times a patient's recommended daily allowance, depending on species and body weight. Follow-up oral treatment with 25-50 mg q 24 h is optional when enteric function is normal.

NUTRITION/DIET

- Nutritional support (enterally or parenterally) is indicated in all anorexic patients.
- Feeding a diet that is known to be nutritionally adequate for the life stage of the dog or cat. Diet change is preferred over thiamin supplementation of the inadequate diet.

PROGNOSIS AND OUTCOME

Excellent if recognized and treated before the animal reaches convulsive stage.

PEARLS & CONSIDERATIONS

COMMENTS

Response to treatment and improvement of clinical signs is rapid if deficiency of thiamin is the cause of the signs.

PREVENTION

Feed a properly formulated diet; avoid feeding foods that contain thiaminases and sulfiting agents.

CLIENT EDUCATION

Explain the dietary risk factors associated with thiamin deficiency and the importance of feeding a properly formulated complete and balanced diet.

SUGGESTED READING

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Garosi LS, Dennis R, et al: Thiamine deficiency in a dog: clinical, clinicopathologic, and magnetic resonance imaging findings. J Vet Intern Med 17:719, 2003.

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Tetraplegia/Tetraparesis

BASIC INFORMATION

DEFINITION

The suffix *-plegia* signifies complete paralysis; *-paresis* signifies incomplete paralysis. Either may manifest with upper motor neuron (UMN) or lower motor neuron (LMN) signs. *Tetraplegia* is complete paralysis of all limbs; *tetraparesis* is incomplete paralysis of all limbs.

SYNONYMS

Tetraplegia: quadriplegia. Tetraparesis: quadriparesis.

EPIDEMIOLOGY

GENETICS & BREED PREDISPOSITION

- Toy breed dogs: atlantoaxial instability
- Older Doberman pinschers, young Great Danes, and other large-breed dogs: cervical spondylomyelopathy
- Chondrodystrophic dog breeds: cervical intervertebral disk protrusion
- Burmese cats: hypokalemia
- Labrador retrievers: exercise-induced collapse
- Various dog breeds: breed-associated motor neuron diseases
- Various cat/dog breeds: breed-associated muscular dystrophies and myopathies

RISK FACTORS

- Exposure to carrion: botulism (dogs)
- Exposure to toxins (e.g., 2,4-D herbicide; organophosphates/carbamates)
- Penetrating wounds (tetanus)
- Areas endemic for coral snakes; black widow spiders *(Latrodectus* spp.); *Dermacentor* spp., *Amblyomma* spp., and *Ixodes* spp. of ticks (tickbite paralysis)

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Tetraplegia:

- Inability to bear weight, voluntarily move limbs, or ambulate

Tetraparesis:

- Impaired locomotion, ranging from mild weakness or spasticity (usually with ataxia) to recumbency
- Ability to voluntarily move limbs even if recumbent
- Tetraparetic/tetraplegic animals with diseases involving the cerebral cortex and/or brainstem will typically show other abnormal neurologic signs:
    - Abnormal mentation and/or seizures (cerebral cortex or diencephalon)
    - Dullness, stupor, or coma (brainstem)
    - Cranial nerve disturbances (brainstem)
    - Abnormal respiratory character (brain, cervical spinal cord)

PHYSICAL EXAM FINDINGS

- Variable (see specific diseases)
- It is important to neuroanatomically localize the lesion (see p. 1311).
- Tetraplegia or tetraparesis can be seen with UMN and/or LMN signs.
- Symmetry or asymmetry of paresis should be noted because this finding may help narrow the differential diagnosis.
- Animals may have UMN or LMN bladder depending upon the neuroanatomic location of the lesion(s).
- Animals with tetraplegia or tetraparesis have a disease involving one of the following regions:

- Tetraplegia or tetraparesis with UMN signs (e.g., increased muscle tone and hyperreflexia) to all four limbs
  - Bilateral cerebral cortex
  - Bilateral brainstem (midbrain)
  - Bilateral cervical spinal cord
- Tetraplegia or tetraparesis with hind limb UMN (as above) and forelimb LMN signs (decreased muscle tone, hyporeflexia)
  - Bilateral C6-T2 spinal cord involvement
- Tetraplegia or tetraparesis with LMN signs to all four limbs
- Disease affecting motor neurons of C6-T2 and L4-S2
  - Disease affecting peripheral nerves (motor component) of all four limbs
  - Disease affecting the neuromuscular junction
  - Disease affecting the skeletal muscle
  - If one particular region cannot be logically identified, disease process is likely multifocal.

ETIOLOGY AND PATHOPHYSIOLOGY

- UMNs are found in the brain and control LMNs.
- LMNs transmit information from the central nervous system (CNS) to an effector organ-like skeletal muscle.
- Conditions affecting UMNs and/or their axons result in UMN signs:
  - Paralysis or paresis
  - Normal to increased spinal reflexes
  - Later onset muscle atrophy (disuse atrophy)
  - Normal to increased muscle tone
- Conditions that affect LMNs, their axons, and the neuromuscular junction result in LMN signs:
  - Paralysis or paresis
  - Decreased or absent spinal reflexes
  - Rapid, severe muscle atrophy (neurogenic atrophy)
  - Decreased muscle tone
- Primary or systemic diseases affecting skeletal muscle cause impaired muscular function and can manifest as tetraplegia or tetraparesis.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Tetraparesis/tetraplegia implies a neurologic syndrome; severe systemic disturbances (see p. 235) must be ruled out with physical examination. A neurologic exam is pivotal in establishing an anatomic diagnosis, which narrows the differential diagnosis and allows the clinician to choose specific diagnostic tests.

DIFFERENTIAL DIAGNOSIS

- Intracranial:
  - Neoplasia
  - Trauma
  - Encephalitis (various causes, including infectious and immune-mediated granulomatous meningoencephalitis [GME] diseases)
  - Hydrocephalus
  - Postictal state
- Cervical spinal cord:
  - Intervertebral disk prolapse
  - Trauma
  - Cervical spondylopathy
  - Atlantoaxial instability
  - Myelitis (various causes, including infectious and immune-mediated [GME] diseases)
  - Osteochondromatosis
  - Synovial or arachnoid cysts
- Peripheral nerves or neuromuscular junction:
  - Tickbite paralysis
  - Idiopathic polyradiculoneuritis
  - Snake or spider envenomation
  - Myasthenia gravis
  - Botulism
  - Hypothyroidism

- Various toxins
- Muscle:
  - Immune-mediated polymyositis (primary or secondary to another disease, such as neoplasia)
  - Hypokalemia
  - Endocrine disease (hyperthyroidism [cats], hypothyroidism, hyperadrenocorticism)
  - Various breed-related muscular dystrophies and myopathies

INITIAL DATABASE

- Assess patient stability (some may present with impaired respiratory function and/or cardiac anhythmias)
- Complete physical and neurologic examinations (see p. 1311)
- CBC, serum chemistry profile, and urinalysis for assessment of systemic causes and preanesthetic evaluation

ADVANCED OR CONFIRMATORY TESTING

- Plain skull or spinal radiographs
- Cerebral spinal fluid (CSF) analysis (see p. 1228)
- Myelography (see p. 1306)
- MRI (see p. 1233) or CT (see p. 1302) scan
- Electrodiagnostic and histopathologic evaluation of affected muscle and nerves
- Detection of antibodies to acetylcholine receptors in cases of fulminant myasthenia gravis

TREATMENT

TREATMENT OVERVIEW

Treatment goals are to eliminate the inciting cause and provide adequate supportive nursing care.

ACUTE GENERAL TREATMENT

- Treat underlying condition if possible.
- Intensity of nursing care depends on the individual needs of the animal.
- Some supportive therapies to be considered:
  - Assisted pulmonary ventilation (see p. 1362): if inadequate spontaneous ventilation
  - Caloric intake: handfeeding (see p. 1377), feeding via esophagostomy/gastrostomy tube (see p. 1270), or parenteral nutrition (see p. 1322)
  - Hydration: appropriate fluid therapy
  - Muscle contracture: passive range-of-motion exercises
  - Pressure sores: turn animals frequently, and treat the lesions early and aggressively if they occur.
  - Urinary bladder (e.g., catheterization) and bowel management (e.g., stool softener)
  - Hygiene: regular cleaning of perineum; ensure animals are kept on clean, dry bedding.

CHRONIC TREATMENT

Long-term supportive therapy may be necessary.

POSSIBLE COMPLICATIONS

Complications associated with tetraplegia or severe tetraparesis include:

- Pressure sores
- Urinary tract infections (with chronic bladder catheterization)
- Fecal impaction
- Pneumonia

RECOMMENDED MONITORING

- Complete physical examinations two times per day to identify complications from recumbency
- Regularly scheduled and frequent neurologic assessments to monitor disease progression
- Severe or progressive CNS or neuromuscular disease: regular assessment of respiratory function

PROGNOSIS AND OUTCOME

Variable, depending on underlying cause

PEARLS & CONSIDERATIONS

COMMENTS

- Referral to an appropriate treatment center is often necessary.
- Nursing care is often times intensive, extensive, and expensive.

TECHNICIAN TIP

Technicians caring for these patients should be able to turn the patients regularly to minimize the risk for pressure sores, be familiar with precautions to be taken when moving patients that have spinal cord disease, be familiar with urinary catheter management, and be able to perform range-of-motion exercises.

CLIENT EDUCATION

Diseases resulting in tetraplegia or tetraparesis can be costly to diagnose and treat.

SUGGESTED READING

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Tetralogy of Fallot

BASIC INFORMATION

DEFINITION

A congenital heart malformation that consists of a large (unrestrictive) ventricular septal defect (VSD), pulmonic stenosis (PS), dextropositioned or overriding aorta, and secondary right ventricular hypertrophy. Ventricular outflow obstruction may be subvalvular or valvular.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs and cats; present at birth; some survive to maturity (occasionally >5 years).

GENETICS & BREED PREDISPOSITION: Keeshond, West Highland white terrier, English bulldog, and French bulldog are often affected. In the keeshond, three distinct gene loci contribute to conotruncal malformations, the embryologic basis for tetralogy of Fallot (TF).

ASSOCIATED CONDITIONS & DISORDERS: Patent ductus arteriosus (PDA) or atrial septal defect (ASD) may be cofindings.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Most cases of TF manifest overt clinical signs resulting from hypoxemia or polycythemia. Right-sided congestive heart failure (CHF) is very rare.

HISTORY, CHIEF COMPLAINT

- Cardiac murmur in an apparently healthy puppy or kitten
- Exercise intolerance, often with tachypnea
- Exertional syncope
- Stunted growth

PHYSICAL EXAM FINDINGS

- Systolic murmur over the pulmonic valve area with radiation dorsally and to the right. A softer murmur may be evident with severe PS, marked polycythemia, or pulmonary atresia.
- Generalized cyanosis may be observed, particularly after exertion.
- Palpable right precordial heave, indicating ventricular hypertrophy.

ETIOLOGY AND PATHOPHYSIOLOGY

- TF is a cardiac malformation that causes bidirectional shunting across a large VSD, leading to hypoxemia, cyanosis, secondary polycythemia, and impaired exercise capacity.
- Hyperviscosity syndrome may develop from polycythemia.
- Increased blood flow through bronchial artery collateral vessels increases venous admixture and further lowers the arterial Po2.
- Sudden cardiac death is the typical outcome in untreated cases.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected when a young dog or cat either is noted to have a systolic murmur on routine examination, or is presented for evaluation of exercise intolerance, cyanosis, or both.

DIFFERENTIAL DIAGNOSIS

- PS with ASD or VSD

- Pulmonary or tricuspid valve atresia (with associated ventricular or atrial septal defect), as well as other complex malformations such as transposition of the great arteries.
- Double-chambered right ventricle with VSD proximal to the midventricular obstruction
- Severe pulmonary hypertension (Eisenmenger's physiology)
- Other causes of polycythemia (polycythemia vera, renal mass lesions)
- Respiratory diseases

INITIAL DATABASE

- Chest radiographs show right ventricular prominence, straight left auricular border on the dorsoventral projection, and pulmonary hypoperfusion. Radiographs also exclude primary pulmonary causes of cyanosis and respiratory distress.
- The electrocardiogram (ECG) usually shows a right ventricular hypertrophy pattern (or a cranially directed axis).
- CBC may demonstrate polycythemia.
- Pulse oximetry (or arterial blood gas [ABG]) testing quantifies oxygen saturation and functional status.

ADVANCED OR CONFIRMATORY TESTING

- Echocardiography with Doppler studies (± contrast echocardiography) is confirmatory, demonstrating the four principal lesions and associated shunting across the VSD.
- Cardiac catheterization and angiography are rarely needed.

TREATMENT

TREATMENT OVERVIEW

- Definitive therapy requires open heart surgery with cardiopulmonary bypass and is rarely done.
- Palliation involves preventing arterial desaturation by surgically creating a left-to-right, systemic arterial-to-pulmonary shunt to enhance pulmonary blood flow and left ventricular volume.
- Control of the hematocrit to prevent severe polycythemia is critical. A slightly higher than normal packed cell volume (PCV) is beneficial for increasing oxygen-carrying capacity and raising systemic vascular resistance.
- Avoid drugs that are vasodilators and reduce systemic vascular resistance (increasing right-to-left shunting).

ACUTE GENERAL TREATMENT

For bouts of dyspnea:

- Enforce rest, providing a cool, well-ventilated or fanned space (prevent overheating).
- Although supplemental oxygen has minimal benefits for patients with right-to-left shunting, it should be provided, and the effect on oxygen saturation should be measured by pulse oximetry.
- Sedation with butorphanol may be helpful, but avoid acepromazine.
- Treat severe bradycardia with atropine if necessary.
- If necessary, increase systemic vascular resistance with an alpha-adrenergic agonist (phenylephrine) to reduce right-to-left shunting.
- Once the patient is stable for handling, measure the PCV; if >68%, perform a phlebotomy, replacing the removed volume with a balanced crystalloid (100%-150% of volume removed).

CHRONIC TREATMENT

- Assuming definitive repair is not possible, long-term benefits can be achieved by referral for extracardiac thoracic surgery. A palliative left-to-right shunt between a systemic artery and the pulmonary artery (e.g., modified Blalock-Taussig shunt) increases pulmonary blood flow and usually raises arterial oxygen saturation to >90%.
- Alternatively, “partial” balloon valvuloplasty of the stenotic right ventricular outlet can be considered, provided a residual pulmonary obstruction is maintained to prevent severe left-to-right shunting across the unrestrictive VSD. Theoretically, catheterization of the aorta (through the VSD) may permit identification of excessive collateral vessels that may be occluded by coil embolization.
- Periodic phlebotomy, maintaining PCV < 68% (target 62%-65%, although lower values may be well tolerated).
- The nonspecific beta-blocker, propranolol (0.5-1 mg/kg PO q 8 h; begin low and titrate upward), can mitigate dynamic right ventricular outflow tract obstruction from hypertrophy while preventing drug-induced vasodilation.
- Consider a trial course of hydroxyurea (30-50 mg/kg PO q 24-48 h; titrate based on PCV) to suppress the bone marrow when frequent phlebotomies are needed.
- Prescribe low-dose aspirin to animals with surgically created palliative shunts (to impede thrombosis).
- Limit exercise, and avoid high heat/ humidity conditions; prevent dehydration.

- Consider pentoxifylline to improve red blood cell (RBC) flexibility in the micro-circulation (however, use in animals with TF is completely empirical).

POSSIBLE COMPLICATIONS

- Adverse effects of the aforementioned drugs
- Gradual spontaneous closure or thrombosis of a surgically created palliative shunt
- Acute pulmonary edema from creation of a large palliative shunt or overzealous balloon valvuloplasty for relief of PS
- Paradoxical (right-to-left) thromboembolic episode following venipuncture, causing stroke or coronary embolus. In cats with TF, atrial thrombi may result in arterial thromboembolism.

RECOMMENDED MONITORING

- Clinical signs: exercise capacity and respiratory effort at home
- Mucous membrane color and arterial oxygen saturation (oximetry)
- Hematocrit or full CBC with platelet count if the patient is taking hydroxyurea
- Resting heart rate, as bradycardia (<60 in dogs or <120 in cats) may indicate overdosage of propranolol.
- Pulmonary blood flow in surgically created shunts (by auscultation and echo-Doppler studies of the pulmonary artery)

PROGNOSIS AND OUTCOME

Guarded; most affected dogs and cats will succumb to complications of hypoxia or polycythemia (or will have to be euthanized because of clinical signs). Common findings include:

- Bouts of exertional dyspnea or respiratory distress
- Stroke or other signs of hyperviscosity syndrome
- Sudden cardiac death

PEARLS & CONSIDERATIONS

COMMENTS

- Systemic vascular resistance and pulmonary blood flow impact clinical outcome.
- Vigorous exercise, anemia, thyrotoxicosis, and vasodilator drugs reduce systemic vascular resistance, increasing right-to-left shunting.
- Mild PS or concurrent PDA may reduce clinical signs, leading to a “pink” tetralogy of Fallot.
- The magnitude of polycythemia may not correlate with clinical signs.
- Palliative surgery for TF can significantly improve clinical outcome and permit a relatively long life. This surgery is challenging and should be performed only by a surgeon with experience in vascular surgery.

PREVENTION

Do not breed dogs that have TF.

CLIENT EDUCATION

- Observe exercise capacity, effort and rate of breathing, and general well-being.
- Avoid environmental and exercise extremes.
- Report progressive signs or syncope.
- Provide ventilation (a fan) and water during periods of respiratory distress.

SUGGESTED READING

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Tetanus

BASIC INFORMATION

DEFINITION

An infectious disease caused by a potent neurotoxin produced by the bacterium *Clostridium tetani,* resulting in a sustained tonic contraction of the muscles

SYNONYM

Lockjaw

EPIDEMIOLOGY

SPECIES, AGE, SEX: All domestic animals are susceptible; cats are more resistant than dogs.

RISK FACTORS: Open wounds; exposure to organism in feces or in the environment

GEOGRAPHY AND SEASONALITY: Ubiquitous in the environment; no seasonally

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Focal versus generalized dependent on inoculation site; the generalized form is more common.

HISTORY, CHIEF COMPLAINT

- Cutaneous/soft-tissue wound (cut, puncture, surgical [e.g., ovariohysterectomy])
- Progressively worsening gait stiffness

PHYSICAL EXAM FINDINGS

- Extreme sensitivity to tactile and auditory stimulation: mildly to extremely exaggerated reaction to sound or touch
- Characteristic facial expression due to facial muscle spasm: ears held erect, forehead wrinkled, lips drawn back (risus sardonicus)
- Trismus (teeth clenching)
- Protrusion of third eyelids, enophthalmos, strabismus, hypersalivation, laryngeal spasm, dysphagia
- Mild hyperthermia due to excessive muscular activity
- Dyspnea, coughing possible from aspiration pneumonia
- Progression to periodic generalized tonic muscle contraction possible
- Autonomic “storms”: cardiac arrhythmias, hypotension or hypertension
- Death can result from respiratory compromise.

ETIOLOGY AND PATHOPHYSIOLOGY

- *C. tetani* typically enters the body through wounds.
- A potent neurotoxin (tetanospasmin) is formed in the patient's body during vegetative growth of *C. tetani*
- Tetanospasmin enters the neuromuscular end plate of motor nerves and migrates to the neuronal cell body in the spinal cord or brainstem.
- Tetanospasmin blocks inhibitory neu-rotransmitter release (glycine, gamma-aminobutyric acid [GABA]), facilitating muscle contraction.
- Tetanospasmin's binding to presynaptic sites of inhibitory neurons is irreversible; recovery depends on sprouting of new axon terminals.
- Signs occur within 5-10 days of injury but can be delayed up to 3 weeks.
- Wounds close to the head are associated with a more rapid onset of signs than those in the extremities.

TETANUS Dog with fulminant tetanus. Contraction of facial muscles has drawn the ears dorsally, and a divergent strabismus is present. Canthi of the lips were drawn into a sardonic grin (not seen here); mouth could not be opened. Extreme rigidity of the limbs explains stiff, stilted posture.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Tetanus is diagnosed based on clinical signs and history of a recent wound; there is no practical clinical confirmatory test. The source of infection or wounds is not always immediately apparent.

DIFFERENTIAL DIAGNOSIS

Hypocalcemic tetany

TETANUS Same dog after having made a complete recovery.

(Courtesy John Sylvester.)

INITIAL DATABASE

All the following test results may be seen, but none is required for a diagnosis of tetanus:

- CBC: leukocytosis (neutrophilia with left shift)
- Serum biochemistry profile: elevated serum creatine phosphokinase (CPK)
- Cerebrospinal fluid (CSF) analysis: unremarkable
- Electrocardiogram (ECG): tachyarrhythmias or bradyarrhythmias (atrioventricular [AV] block, sinus arrest) possible
- Thoracic and abdominal imaging: megaesophagus with or without aspiration pneumonia possible; abdominal effusion possible if source of *C. tetani* is septic peritonitis (metritis, enteritis, ruptured abscess)
- Muscle biopsy: usually unremarkable
- Serum antibody titers to tetanus toxin may support the diagnosis (compared to control animals).
- Isolation of *C. tetani* from wounds is unrewarding.

TREATMENT

TREATMENT OVERVIEW

Treatment is mostly supportive and may be protracted: resolution of clinical signs may take days to weeks, depending on form (generalized or localized) and individual response.

ACUTE GENERAL TREATMENT

- As much as possible, keep the animal in a quiet, soundproof area with minimal stimulation.
- Wound débridement and resection of necrotic tissue; wounds are left open (avoid anaerobic conditions).
- Antitoxin: equine antitetanus serum (ATS) (given IM or IV) or human tetanus immunoglobulin (TIG) given IM. Equine ATS:
  - Give the initial test dose, 0.1-0.2 mL SQ or ID, 15-30 minutes before IV administration; monitor for anaphylaxis.
  - If no anaphylaxis, therapeutic dose is 2.5-25 IU/kg IV; continue to monitor for anaphylaxis during and immediately after administration.
  - Intralesional injection appears promising (experimental studies).
  - Antitoxin prevents further toxin binding to axons but does not eliminate currently bound toxin.
- Sedation (e.g., one of the following: diazepam [helps enhance GABA inhibition], phenobarbital, acepromazine,

chlorpromazine) is recommended.
- Antibacterial treatment *(C. tetani):* sodium or potassium penicillin, 20,000-50,000 IU/kg slow IV q 6 h for 10 days; and metronidazole, 10 mg/kg PO q 8 h for 10 days.

CHRONIC TREATMENT

- Physical rehabilitation (see p. 1329)
- Intensive nursing care to include IV fluids and nasogastric or percutaneous endoscopic gastrostomy (PEG) tube feedings (see p. 1269 and 1270)
- Prevention of decubital ulcers
- Indwelling urinary catheter

DRUG INTERACTIONS

- Narcotics can depress the respiratory center and may stimulate other areas of the central nervous system (CNS).
- Parasympatholytic drugs such as atropine should be avoided in routine cases.

POSSIBLE COMPLICATIONS

- Aspiration pneumonia
- Decubital ulcers
- Respiratory paralysis

RECOMMENDED MONITORING

- Heart and respiratory rates
- Temperature monitoring
- Seizure watch
- Urine output

PROGNOSIS AND OUTCOME

- Guarded; better with mild clinical signs and localized clinical signs
- In mildly affected animals, normal function usually returns within 3 weeks of the initial treatment.
- Survival rates have varied between 50% and 92% in the literature.

PEARLS & CONSIDERATIONS

PREVENTION

- Avoid exposure to potential sources of infection.
- Routine immunoprophylaxis (tetanus toxoid) not recommended in dogs and cats
- Appropriate (open) care of infected wounds and rational antibiotic therapy

TECHNICIAN TIP

These patients can be exquisitely sensitive to light and sound; any efforts to prevent stimulating them (e.g., signs to alert clinic staff, selection of an appropriate location in the hospital for housing and recovery) are important during convalescence.

CLIENT EDUCATION

- Treatment of the disease can take weeks, but a cure is possible.
- seek veterinary attention in cases of open wounds.

SUGGESTED READING

Burkitt JM, Sturges BK, Jandrey KE, et al: Risk factors associated with outcome in dogs with tetanus: 38 cases (1987-2005). J Am Vet Med Assoc 230(1):76–83, 2007.

Dewey CW, Cerda-Gonzalez S: Myopathies: disorders of muscle. In A practical guide to canine and feline neurology, ed 2, Ames, IA, 2008, Wiley-Blackwell, pp 469–515.

AUTHOR: KAREN L. KLINE

EDITOR: CURTIS W. DEWEY

Testicular Tumors

BASIC INFORMATION

DEFINITION

Neoplasia arising from testicular germ cells or sex-cord stromal cells; common in dogs, uncommon in cats

SYNONYMS

Germ cell: seminoma

Mixed tumors: germ cell/stromal tumors Sex-cord stromal: Leydig (interstitial) cell tumor, Sertoli (sustentacular) cell tumor

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs:

- Incidence: common (75% of all tumors affecting the male urogenital tract)
- Age: aged patients, most >7 years
- Equal incidence of seminoma, Leydig cell tumor, Sertoli cell tumor much less common

Cats: all tumor types are very rare.

GENETICS & BREED PREDISPOSITION

- Seminoma: all canine breeds; boxer is predisposed.
- Sertoli cell: miniature schnauzers with persistent Müllerian duct syndrome are predisposed.

RISK FACTORS

Dogs, cryptorchidism:

- Overall risk of testicular tumor development increased 13-14 times
- Risk of Sertoli cell tumor increased 20 times
- Approximately half of Sertoli cell tumors occur in cryptorchid testes.
- Approximately one-third of seminomas occur in cryptorchid testes.

Cats: none identified

ASSOCIATED CONDITIONS & DISORDERS: Sertoli cell tumor: hyperestrogenism occurs in approximately 20%-30% of affected dogs.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Primary: unilateral or bilateral, focal or multifocal
- Metastatic (rare)

HISTORY, CHIEF COMPLAINT

- Testicular enlargement ± atrophy of unaffected testis (most severe associated with Sertoli cell tumor but can occur with other neoplasms, especially larger tumors)
- Sertoli cell tumor: symmetric hair loss, feminization (gynecomastia, attractiveness to other male dogs, pendulous penile sheath, lethargy, loss of libido, redistribution of body fat)

PHYSICAL EXAM FINDINGS: Testicular enlargement ± atrophy of contralateral testis

- Seminoma: soft to slightly firm texture
- Sertoli cell tumor: very firm texture, discrete mass
- Leydig cell tumor: soft texture, discrete mass
- Mixed germ cell/stromal tumors: variable texture, generally discrete and focal
- Sertoli cell with hyperestrogenism: endocrine dermatopathy, gynecomastia, pendulous penile sheath, redistribution of body fat, marked contralateral testicular atrophy

ETIOLOGY AND PATHOPHYSIOLOGY

Cryptorchidism: altered testicular environment due to increased testicular temperature favors neoplastic transformation of Sertoli cells and (less commonly) germ cells.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

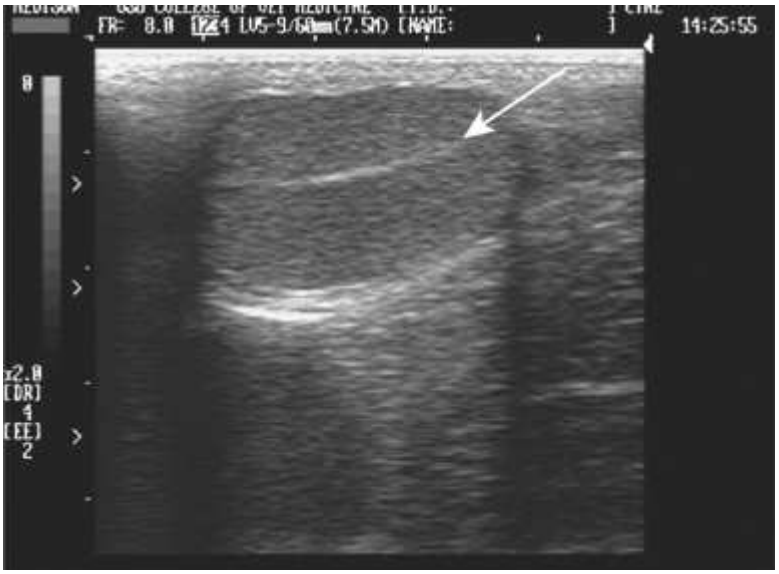
Diagnosis relies on palpation of an enlarged testis or abnormal firm area within a normal-sized testis. Ultrasound and cytologic evaluation may aid in diagnosis, but in most cases excision of the affected testis and submission for histopathologic evaluation will confirm neoplasia and allow classification of the tumor.

DIFFERENTIAL DIAGNOSIS

- Testicular torsion
- Abscess
- Cyst

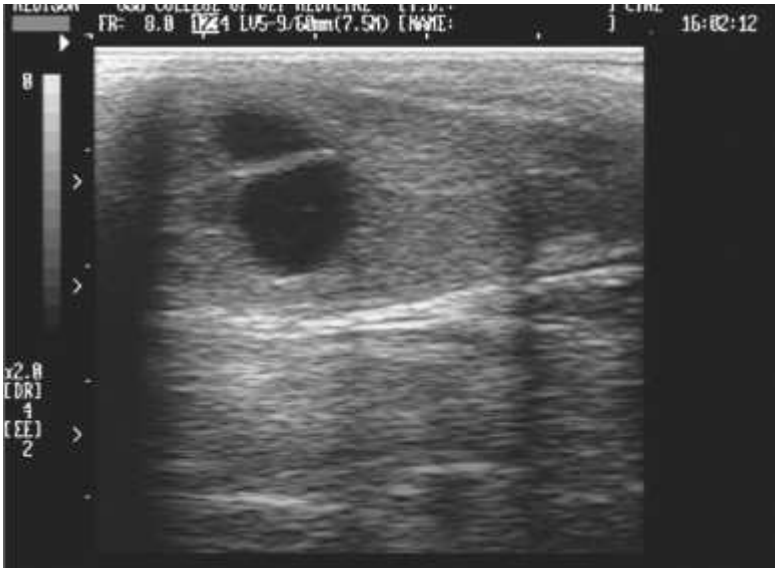
INITIAL DATABASE

- CBC: rule out bone marrow suppression due to Sertoli cell tumor-associated hyperestrogenism.
- Semen evaluation and/or testicular biopsy with histologic examination of unaffected testis will aid in decision for unilateral or bilateral castration in breeding dogs.



TESTICULAR TUMORS Transscrotal ultrasonogram of left testis of a normal fertile male dog. Echotexture of the parenchyma is homogeneous, with the exception of the hyperechoic mediastinum (rete testis; *arrow).*

(Courtesy Dr. Michelle A. Kutzler.)



TESTICULAR TUMORS Transscrotal ultrasonogram of left testis of an infertile male dog. Two anechoic cystic structures are present within the parenchyma on either side of the mediastinum. Differential diagnoses include cystic neoplasia or testicular cyst.

(Courtesy Dr. Michelle A. Kutzler.)

ADVANCED OR CONFIRMATORY TESTING

- Ultrasound, all tumortypes: hypoechoic or mixed echotexture
- Gross pathologic examination of excised testis:
    - Seminoma signs include soft to slightly firm testis, homogeneous gray/white glistening appearance, areas of discoloration due to hemorrhage or necrosis possible, focal to multifocal.
    - Sertoli cell tumor signs include very firm testis, discrete, white or gray in color, tan or yellow hemorrhagic areas possible, usually focal.
    - Leydig cell tumor signs include soft testis, discrete, yellow/brown in color, bulges on section, areas of hemorrhage or cystic change common, focal to multifocal.
    - Mixed germ cell/stromal tumors signs include variable texture, pale white or gray, generally discrete and focal.
- Bilateral tumors are common, and multiple tumor types are often present within the same testis.
- Histopathologic examination: include spermatic cord to evaluate for local invasion; multiple tumor types can occur in the same testis.

TREATMENT

TREATMENT OVERVIEW

Therapy consists of surgical removal of the affected testis.

ACUTE GENERAL TREATMENT

- Testicular removal: unilateral castration if contralateral testis is normal to small in size, and future breeding with the dog is desired
- Supportive care for dogs with Sertoli cell tumor-associated bone marrow suppression

CHRONIC TREATMENT

For metastatic seminoma, both chemotherapy and radiation therapy have been described. Methotrexate, vincristine, and cyclophosphamide; cisplatin; bleomycin: and radiation therapy have been reported to have some degree of efficacy.

BEHAVIOR/EXERCISE

Avoid estrous females and restrict physical activity for approximately 1 week following surgery.

POSSIBLE COMPLICATIONS

- Bone marrow suppression (hyperestrogenism) from Sertoli cell tumors
- Behavioral changes (hyperandrogenism) from Leydig cell tumors

RECOMMENDED MONITORING

- Seminoma, Leydig cell tumor, nonactive Sertoli cell tumor, mixed sex cord/ stromal tumor: yearly physical examination
- Sertoli cell tumor with bone marrow suppression: close follow-up for evidence of bacterial septicemia; yearly physical examination

PROGNOSIS AND OUTCOME

- Seminoma: excellent following testicular removal; metastasis is rare. Sertoli cell tumor: excellent following testicular removal; metastasis is rare, but risk of metastasis is increased for tumors >2 cm diameter.
- Leydig cell tumor: excellent following testicular removal; metastasis is not expected.
- Mixed sex cord/stromal tumor: excellent following testicular removal; metastasis is not expected.

PEARLS & CONSIDERATIONS

COMMENTS

- Histopathologic examination is needed for determination of tumor type.
- Unilateral castration may result in up to 50% hypertrophy of the remaining testis. Return to fertility following unilateral castration depends on the severity of testicular atrophy secondary to hormonal downregulation and presence of underlying disease (testicular degeneration with loss of spermatogo-nia).

PREVENTION

Testicular removal, especially of cryptorchid testes

CLIENT EDUCATION

- Regular examination of testes and evaluation of the semen in breeding animals
- Prompt presentation for veterinary examination if an abnormality is detected

SUGGESTED READING

MacLachlan NJ, Kennedy PC: Tumors of the genital systems. In Meuten DJ, editor: Tumors in domestic animals, ed 4, Ames, IA, 2002, Iowa State Press, pp 561–567.

AUTHOR: BETH A. VALENTINE

EDITOR: MICHELLE A. KUTZLER

Tenesmus

BASIC INFORMATION

DEFINITION

Ineffectual or painful straining to defecate due to obstruction or inflammatory lesions of distal colon, rectum, or anus

SYNONYM

Straining to defecate

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Frequent posturing to defecate/urinate without producing feces/urine
- Turning around/looking at hind end while attempting to defecate
- Excessive licking/chewing of perineal region
- Flattened, ribbon-like stools
- Vocalizing (cats most often)
- Inappropriate defecation in the house/ outside litter box or refusal to defecate owing to severe pain and secondary constipation
- Common error in cats: overdiagnosis of constipation by owner or veterinarian; careful history/observation reveals lower urinary tract signs

PHYSICAL EXAM FINDINGS

- Observe the animal defecate/urinate; assess if the animal's tail between the legs, low carriage of the tail, resentment of tail elevation (discomfort), presence of an arched back (abdominal or back pain).
- Examine anus/perianal area: erythema of anal/perineal region, perineal fistulas, perineal masses, pseudocoprostasis (anal obstruction due to severe matting of fur with feces).
- Abdominal palpation: mass, signs of discomfort despite gentle palpation
- Rectal palpation may require sedation/ general anesthesia if patients have very painful perineal conditions. Assess for presence of perineal hernia, mass, prostatomegaly, pelvic fractures, fecal consistency (constipation, foreign material), stricture, foreign bodies (e.g., bones, rocks, grass, fur, food wrappers)
- Cytologic analysis (infection, inflammation)
- If origin of clinical signs are unclear, catheterize urethra/urinary bladder
- Palpation of anal sacs (mass, impaction, infection, abscess, or rupture)

ETIOLOGY AND PATHOPHYSIOLOGY

- Perianal (specifically adjacent to anus) and perineal (whole region between tail and pubis) disorders may be due to anal sac impaction, anal sacculitis, anal sac abscess, perianal gland tumors, perineal hernia, perianal fistula, neoplasia (anal sac adenocarcinoma), pseudocoprostasis.
- Large bowel: acute diarrhea (see p. 303)
- Genitourinary (GU) tract: in general, GU abnormalities produce disorders of urination rather than tenesmus (careful history and examination for accurate diagnosis). Prostatomegaly (benign prostatic hyperplasia/hypertrophy [BPH], prostatitis, abscess, neoplasia), paraprostatic cyst, GU neoplasia
- Caudal abdominal cavity disorders include mass (organ compression), pelvic fractures (misaligned healing of old pelvic fractures), pelvic osteosarcoma

DIAGNOSIS

DIAGNOSTIC OVERVIEW

- Tenesmus is a clinical sign, not a disease; successful management requires identifying the underlying cause.
- Diagnostic test selection is highly dependent upon obtaining a clear history, observing the animal urinate and defecate, and

performing a thorough examination of the rectum, perineal, and perianal areas.

DIFFERENTIAL DIAGNOSIS

see Etiology and Pathophysiology, above.

INITIAL DATABASE

- Observe the animal defecating/ urinating.
- Proper examination of the perineal, perianal area, anus, and rectum (may require sedation if very painful)
- Urogenital system: vaginal examination to exclude impostors for tenesmus (see p. 1360)
- Neurologic exam (see p. 1311): perineal reflex, and tone, presence of lumbosacral/back pain
- CBC, serum biochemical profile, urinalysis: elucidate possible urinary tract or systemic abnormalities
- Radiographs (abdominal/pelvic): constipation, megacolon, prostatomegaly, pelvic fractures, malunion of pelvic fractures, foreign bodies, masses, or sublumbar lymphadenopathy

ADVANCED OR CONFIRMATORY TESTING

- Abdominal ultrasonography: gastrointestinal (GI)/pelvic mass, ± lymphadenopathy, urogenital tract, GI motility, distension/wall thickening
- Intrarectal ultrasonography: specific probes required
- Colonoscopy: rigid and/or flexible to biopsy polyp/mass(es), strictures or infiltrative lesions
- Urogenital system (to exclude impostors for tenesmus): vaginal examination, ultrasonography and/or urinary tract contrast radiography, urethroscopy/cystoscopy, culture and sensitivity of urine/prostatic fluid, cytologic examination, and/or biopsies of urinary tract/prostate.

TREATMENT

TREATMENT OVERVIEW

Treatment should address the underlying cause and relieve any discomfort the animal is experiencing.

ACUTE GENERAL TREATMENT

- Clip fur and gently wash perineal area if needed.
- Hydrotherapy to affected area multiple times per day if indicated
- Enemas: soften impacted feces if constipation
- Topical cutaneous glucocorticoids/ anesthetics (creams, ointments, suppositories): reduce inflammation/pain
- Corticosteroid enemas if severe, non-infectious colitis: budesonide (Entocort) 2 mg dissolvable tablet. Give 0.5-1 mg (¼-½ tablet dissolved in enema diluent) per rectum (dose is for most small animals). Budesonide does not tend to reach high concentrations outside the GI-hepatoportal system (high first-pass metabolism), which minimizes systemic glucocorticoid effects.
- Drain/flush anal gland abscesses.
- Cyclosporine (3-5 mg/kg PO q 12 h) or topical tacrolimus ointment (0.03%-0.1%) for perianal fistula; cyclosporine more effective
- Surgery: perineal hernias (repair), colonic or rectal polyps (excision), colonic/rectal/anal sac tumors (resection), rectal strictures (rectal “pull-through”)
- Adjunctive chemotherapy and/or palliative therapy with piroxicam (0.3 mg/ kg PO q 24-48 h) for anal sac adenocarcinomas

CHRONIC TREATMENT

Dependent on the underlying cause

DRUG INTERACTIONS/SIDE EFFECTS

- Immunosuppressive therapy (azathioprine, chlorambucil): myelosuppression
- 5-aminosalicylates: keratoconjunctivitis sicca
- Iatrogenic hyperadrenocorticism with chronic glucocorticoid use
- Nonsteroidal antiinflammatories (e.g., piroxicam) can cause GI ulceration, renal failure. Blood work prior to initiation recommended to assess liver and renal function.
- Do not use glucocorticoids and nonsteroidal antiinflammatories concurrently: increased risk of GI ulceration.

POSSIBLE COMPLICATIONS

- Recurrent tenesmus, a colonic/rectal obstruction causing obstipation, or a rectal prolapse (uncommon; usually young patients <6 months old)
- Surgery: risk of postoperative fecal incontinence

PROGNOSIS AND OUTCOME

- Colonic/rectal inflammatory lesions: often successful (medical therapy)
- Anal sac disease, perineal hernias, wounds within and sunounding the anorectal area: better prognosis than strictures or neoplasia
- Perineal fistulas: improved prognosis with cyclosporine, but costly. Tacrolimus is less expensive, but not as effective.

PEARLS & CONSIDERATIONS

COMMENTS

- Stranguria is a common impostor for tenesmus, especially in cats. Thorough questioning during history taking, and observation of the animal's elimination process, are essential for avoiding misdiagnosis.
- Tenesmus is a clinical sign, not a disease. Therefore, an underlying cause must be sought.
- Workup is highly dependent upon obtaining a clear history and observing the animal urinate/defecate.

SUGGESTED READING

Zoran DL: Rectoanal disease. In Ettinger SJ, Feldman EC, editors: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders Elsevier, pp 129–135.

AUTHOR: LISA CARIOTO

EDITOR: ETIENNE CÔTÉ

Temporomandibular Joint Luxation

BASIC INFORMATION

DEFINITION

Complete displacement of the mandibular condyle out of the corresponding mandibular fossa of the temporal bone. Subluxation of the temporomandibular joint (TMJ) occurs when the mandibular condyle is incompletely displaced.

EPIDEMIOLOGY

SPECIES, AGE, SEX: TMJ luxation can occur in dogs and cats of any age. TMJ luxation with regional fracture is more common in younger cats with head trauma. Cats have a higher incidence of TMJ luxation than dogs, owing to decreased mandibular symphyseal movement and shorter jaw length. GENETICS & BREED PREDISPOSITION: Any breed affected when associated with trauma. Breeds predisposed to TMJ dysplasia (shallow to flat mandibular fossa with flattening of mandibular condyle) are at risk for TMJ subluxation and luxation and open-mouth jaw locking (Basset hound, dachshund, Irish setter; Persian cats).

RISK FACTORS: Trauma, TMJ dysplasia, increased mandibular symphyseal laxity

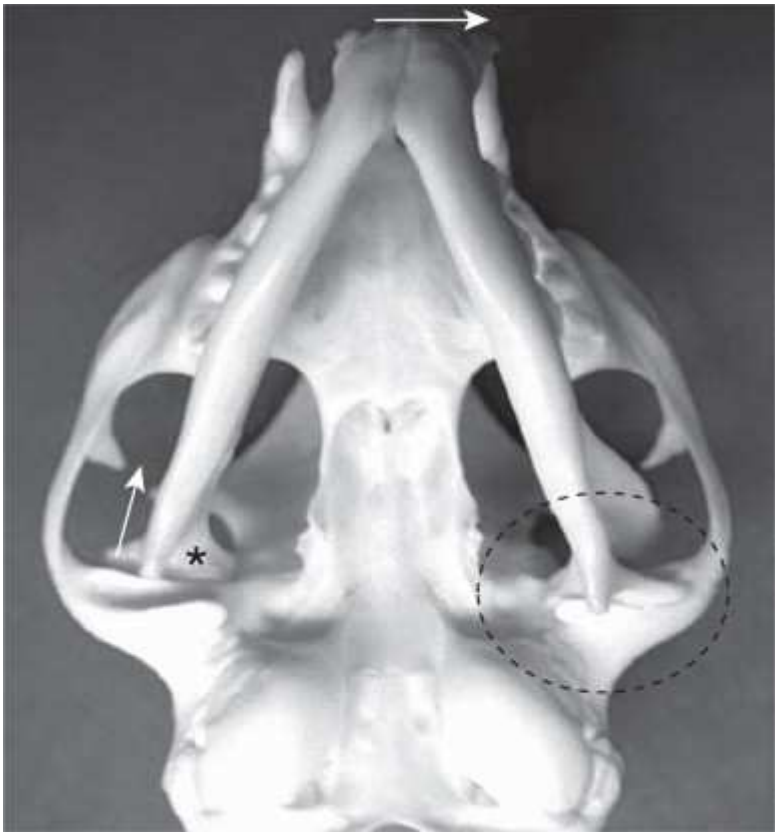
CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Subluxation: minimal displacement of the mandibular condyle, which is still situated in its corresponding mandibular fossa of the temporal bone
- Luxation:
  - Rostrodorsal: most common and usually unilateral
  - Caudoventral: rarely noted; usually associated with fracture of the retroarticular process of the temporal bone
- Open-mouth jaw locking (see Etiology and Pathophysiology, below)

HISTORY, CHIEF COMPLAINT: Owners present animals for head trauma or inability to close the mouth fully, pain on chewing/yawning, reluctance to play or chew on toys, inappetence, and/or an audible click when opening or closing the mouth. Depending on etiology, progression may be peracute, acute, or chronic.

PHYSICAL EXAM FINDINGS: In rostrodorsal luxation, the lower jaw is shifted and tilted ventrally to the unaffected side. This malocclusion results in abnormal upper and lower tooth contact, leading to inability to close the mouth fully. Other findings may include decreased range of lower jaw motion, decreased eye globe retropulsion on the affected side, swelling and discoloration of the ipsilateral glossopalatine region, swelling, crepitation and pain with affected TMJ palpation, dehydration, and hypersalivation.



TEMPOROMANDIBULAR JOINT LUXATION Skull of a cat, ventral view. Right mandibular condyle *(asterisk)* is luxated rostrally and dorsally, causing lower jaw to shift towards the left side *(arrows).* For comparison, note normal left temporomandibular joint *(dotted oval),* with mandibular condyle articulating with mandibular fossa of temporal bone.

ETIOLOGY AND PATHOPHYSIOLOGY

Relevant anatomy:

- Mandibular ramus: vertical part of mandible that lies medial to the zygomatic arch, caudolateral to the orbit
- Mandibular condyle: articular process of the mandible; articulates with mandibular fossa of the temporal bone to form temporomandibular joint
- Retroarticular process: process of the temporal bone preventing caudal dislocation of the mandibular condyle
- Coronoid process: dorsal protuberance of the mandibular ramus providing insertion for the temporal muscle

Luxation with/without regional fracture:

- Trauma is the most common inciting cause; TMJ dysplasia may predispose the animal to subluxation/luxation without obvious outside force.
- Luxation in a rostrodorsal direction is most common because the prominent retroarticular process prevents caudoventral movement of the mandibular condyle.
- More tightly seated mandibular condyle in the mandibular fossa of the temporal bone makes luxation in cats more common when there is an associated regional fracture. Dogs have a more loosely seated mandibular condyle, and luxations usually occur without regional fracture.
- In rostrodorsal luxation, the lower jaw will be shifted rostrally and laterally to the unaffected side.
- With complete luxation, the joint capsule is damaged; serious injury to the articular disk may be present.

TMJ dysplasia with/without coronoid process displacement:

- Rare congenital or acquired malformation: shallow mandibular fossa, underdeveloped/misshapen retroarticular process, flattened mandibular condyle, and periarticular osteophytosis; abnormal laxity in mandibular symphysis also reported as inciting cause of open-mouth jaw locking
- Open-mouth jaw locking: TMJ subluxation/luxation, rotational movement of the mandibular body and locking of the coronoid process ventrolateral to the zygomatic arch; mouth is locked wide open, and compared to TMJ luxation, there is no tooth-

to-tooth contact.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Clinical presentation and head radiographs (under general anesthesia) will provide conclusive diagnosis. If subluxation/luxation due to TMJ dysplasia is suspected, then CT scan with 3-D reconstruction or fluoroscopic imaging may be necessary for diagnosis. General anesthesia for diagnostic imaging also provides an opportunity for esophagostomy tube placement if prehension and chewing functions are unlikely to be reestablished immediately.

DIFFERENTIAL DIAGNOSIS

- TMJ luxation with/without regional fracture
- TMJ dysplasia with/without coronoid process displacement
- Mandibular neurapraxia (dysfunction of mandibular branch of cranial nerve V)
- Neurogenic atrophy of temporal, masseter, and digastricus muscles
- Mandibular ramus/zygomatic arch fracture
- Masticatory myositis
- Dental/skeletal malocclusion
- Periorbital/caudal mandibular/caudal maxillary neoplasia
- Foreign body

INITIAL DATABASE

- CBC and serum biochemistry panel: generally unremarkable; preanesthetic
- Head radiographs under general anesthesia: dorsoventral (ventrodorsal), right and left lateral oblique, and open-mouth views that show displacement of the mandibular condyle or coronoid process with/without fracture of associated bone structures

ADVANCED OR CONFIRMATORY TESTING

CT scan (see p. 1233):

- Excellent imaging modality for assessing TMJ disease
- Subtle abnormalities not identified on radiographs easily demonstrated on CT scan
- Three-dimensional (3-D) reconstruction beneficial for diagnosis and treatment planning and owner education

TREATMENT

TREATMENT OVERVIEW

Treatment goals are to alleviate discomfort and obtain functional lower jaw movement and occlusion.

ACUTE GENERAL TREATMENT

Acute TMJ luxation:

- Manual reduction of rostrodorsal luxation:
  - Chemical restraint (sedation or anesthesia)
  - Place a wooden dowel (pencil in small pets) between carnassial teeth of affected side only, and gently force the mouth closed until the joint is reduced. Remove the dowel/ pencil, but keep the mouth closed to maintain joint reduction.
  - Apply a slightly snug tape muzzle for 1-3 weeks. The muzzle should be sufficiently loose to allow the animal to lap up water and liquefied food.
  - Recovery from sedation/anesthesia, with particular attention to aspiration (e.g., remove muzzle immediately if vomiting appears imminent).
- Regional fractures (condylar process of mandible; mandibular fossa/retroarticular process of temporal bone) are usually treated conservatively without surgical intervention. Owners must be warned of possible complications such as TMJ ankylosis, which may become apparent 6-8 weeks after traumatic incident. Muzzling is contraindicated.

CHRONIC TREATMENT

Chronic TMJ luxation:

- Maxillomandibular fixation (applying a muzzle using white medical tape or inserting a composite bridge between upper and lower canines) for 4-6 weeks
- Condylectomy and bone fragment resection indicated for severe regional fractures resulting in TMJ ankylosis and arthrosis

NUTRITION/DIET

If normal prehension of food is not possible (e.g., complex jaw fractures, severe swelling), placement of an esophagostomy tube may be needed for nutritional support (see p. 1267).

PROGNOSIS AND OUTCOME

Excellent if no regional fracture; fair to poor if regional fracture ± ankylosis, particularly in immature/adolescent animals

PEARLS & CONSIDERATIONS

COMMENTS

- The most common form, rostrocaudal TMJ luxation, is usually unilateral.
- Do not force the mouth closed in patients presenting with the mouth wide open. Manual correction of open-mouth jaw locking is achieved by opening the mouth a little further, pressing the coronoid process medially, and closing the mouth. Definitive surgical treatment of open-mouth jaw locking is achieved with unilateral or bilateral partial zygomectomy, partial coronoidectomy, or a combination of both procedures.

TECHNICIAN TIPS

- Patients with tape muzzles may have compromised thermoregulation and should not be outdoors on warm or hot days. Restriction in mouth opening also bears the risk of aspiration in the regurgitating or vomiting patient, requiring extra vigilance during patient monitoring.
- To reduce the possibility of local pyoderma from a soiled muzzle, tape muzzles may be removed during drinking and eating and put back in place once feeding is completed.

SUGGESTED READING

Reiter AM: Symphysiotomy, symphysiectomy, and intermandibular arthrodesis in a cat with open-mouth jaw locking: case report and literature review. J Vet Dent 21:147, 2004.

Schwarz T, et al: Imaging of the canine and feline temporomandibular joint: a review. Vet Radiol Ultrasound 43:85, 2002.

AUTHOR: JENNIFER E. RAWLINSON

EDITOR: ALEXANDER M. REITER

Tear Film Abnormalities (Excluding KCS)

BASIC INFORMATION

DEFINITION

A relatively common ophthalmic condition characterized by abnormal mucin (produced by goblet cells of the conjunctiva) and/or lipid (produced by meibomian [tarsal] glands) component(s) of tears. Keratoconjunctivitis (KCS) is discussed separately on .

SYNONYMS

Qualitative tear deficiencies or abnormalities

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs and cats, any age, either sex

GENETICS & BREED PREDISPOSITION

- Cats predisposed to corneal sequestration (e.g., brachycephalic breeds) may be predisposed to tear film abnormalities (TFAs).
- Dogs predisposed to chronic eyelid and/or conjunctival irritation (e.g., breeds with inherited entropion and/or ectropion) are predisposed to developing qualitative tear deficiencies (see p. 348).

RISK FACTORS

- Disorders affecting the meibomian glands (e.g., alkali burns of the eye)
- Patients with diseases resulting in primary (e.g., feline herpesvirus-1 infection) or secondary keratoconjunctival (e.g., entropion/ectropion, keratoconjunctivitis sicca [KCS]) disorders

ASSOCIATED CONDITIONS & DISORDERS

- Conjunctivitis and TFAs commonly coexist (unclear which is causative).
- Superficial keratitis (nonulcerative or ulcerative)
- Eyelid disorders:
  - Entropion (common)
  - Ectropion (common)
  - Eyelid agenesis (rare)
  - Autoimmune disorders (rare)
  - Infectious marginal blepharitis (occasional)
- Chemical ocular burns (occasional)
- Primary or secondary skin disease involving eyelid mucocutaneous junctions (common)
- Keratoconjunctivitis sicca (common; see p. 628)
- Diabetes mellitus in dogs (common)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Mucin tear deficiency, lipid tear deficiency

HISTORY, CHIEF COMPLAINT

- Swollen eyelids
- 'Red' eye
- Serous or mucoid to mucopurulent ocular discharge
- Previous bout(s) of conjunctivitis responsive to standard topical medication(s) but recurrent
- Squinting
- Corneal cloudiness (see p. 245)

PHYSICAL EXAM FINDINGS

- Systemic: generally unremarkable except in those cases where systemic disease is present (e.g., diabetes mellitus; generalized seborrhea)
- Ophthalmic:
  - Serous or mucoid to mucopurulent ocular discharge
  - Conjunctival hyperemia ± chemosis
  - ± Blepharospasm
  - ± Protrusion of the third eyelid
  - Signs of keratitis with chronicity:
    - Corneal vascularization (see p. 254)
    - Corneal pigmentation (see p. 246)
    - Corneal ulceration (see p. 250)
    - Blepharitis, usually marginal with associated meibomianitis with or without overt lipogranulomas/chalazia

ETIOLOGY AND PATHOPHYSIOLOGY

- Mucin tear deficiency:
  - Primary/spontaneous of unknown cause
  - Secondary to conjunctivitis; loss of the conjunctival goblet cells, diminished mucin production with unstable tear film
- Lipid tear deficiency:
  - Inflammation of the meibomian glands (which produce the lipid component of the tear film) directly or by extension from margins of the eyelids (marginal blepharitis):
    - Diseased meibomian glands produce highly polar lipids which destabilize the nonpolar lipid layer of the tear film, allowing rapid evaporation of the aqueous component of tears.
    - Dried lipid plugs meibomian gland ducts
    - Chronic meibomianitis can cause rupture and lipid release into palpebral tissue.
    - With eyelid agenesis: lack of meibomian glands

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is suspected on presenting complaint and physical exam (e.g., recurrent conjunctivitis, “red” eye, ocular discharge) and confirmed with identification of abnormal meibomian glands (lipid tear deficiency) and/or abnormal tear film breakup time (TFBUT).

DIFFERENTIAL DIAGNOSIS

- Other keratoconjunctival disorders, including:
  - Keratoconjunctivitis sicca (see p.628), conjunctivitis (see pp. 237 and 239), chronic superficial keratitis (CSK/pannus, dogs; see p. 825), feline herpesviral keratitis (see p. 524), proliferative (eosinophilic) keratoconjunctivitis (cats), and corneal exposure/ineffectual blinking (e.g., lagophthalmos)
- Blepharitis

INITIAL DATABASE

- History ± bouts of conjunctivitis that were temporarily responsive to routine topical medications
- Complete ophthalmic examination () including:
  - Schirmer tear test (STT): normal or elevated STT values; normal STT value ≥ 15 mm/min in dogs; variable in cats.
  - Fluorescein dye application: secondary corneal ulceration is possible.
  - Intraocular pressures: normal IOP values; normal IOPs range from 15-25 mm Hg (dogs and cats).

ADVANCED OR CONFIRMATORY TESTING

- Meibomian gland examination using magnification lipid tear abnormalities: slight protrusions of meibomian gland ductal openings; swollen, rounded, hyperemic eyelid margins; yellowish subconjunctival masses [lipogranulomas/chalazia] possible)
- Evaluation of TFBUT: mean normal TFBUT = 19.6 seconds in dogs and 16.7 seconds in cats; TFBUT is rapid/ accelerated with mucin tear deficiency (i.e., TFBUT < 5-10 seconds):
  - Prior to instillation of topical solutions on the surface of the eye or a few hours following ophthalmic examination
  - Evaluates stability of the tear film
  - Performed by instilling one drop of fluorescein stain onto the eye, closing the eyelids to distribute the stain, and then opening them, using a cobalt-blue filter, and immediately commencing timing until the appearance of the first black/dark spot within the green fluorescein-stained corneal tear film
- Palpebral conjunctival biopsy and staining with periodic acid-Schiff (PAS) for quantification of epithelial goblet cells

(diminished to absent with mucin tear deficiency)

TREATMENT

TREATMENT OVERVIEW

The treatment goals are to stabilize the tear film and eliminate ocular pain. Identifying and treating the underlying cause of the TFA is essential.

ACUTE AND CHRONIC TREATMENT

- Variable depending on the underlying cause
- Lacrimomimetics (tear substitutes and stabilizers) q 4-8 h (e.g., viscous mucinomimetic [e.g., hyaluronic acid 0.4%]) for mucin tear deficiency; emollient/ oil-based tear supplement (e.g., Lacri-Lube ointment) for lipid tear deficiency) may be used for initial 3-4 weeks without concurrent lacrimostimulant if rapid improvement in clinical signs noted and no concurrent KCS.
- ± Lacrimostimulants:
  - Cyclosporine A (CsA) 0.2% ointment or 0.5%-2% solution q 8-12 h usually required for at least 4 weeks and possibly lifelong. May increase to q 8 h if TFBUT < 10 seconds after 3-4 weeks of treatment; some advocate increasing concentration of solution (e.g., 0.2%-2%). May decrease to q 24 h if TFBUT ≥ 10 sec and clinical signs improve/resolve.
  - Tacrolimus 0.02%-0.03% ointment or aqueous suspension q 12 h if no response to CsA after 3-6 weeks (unproven long-term safety).
- Antimicrobials if secondary bacterial conjunctivitis and/or corneal ulceration:
  - Topical broad-spectrum antibiotic (e.g., bacitracin-neomycin-polymyxin solution q 6-8 h for 7-14 days or until the corneal ulcer has healed)
- Antiinflammatories if severe conjunctivitis and/or corneal vascularization/ pigmentation:
  - Prednisolone acetate 1% suspension q 6-8 h if corneal ulceration is ruled out

NUTRITION/DIET

Consider L-lysine supplementation for feline herpesvirus 1 infection (see p. 524).

POSSIBLE COMPLICATIONS

- Corneal ulceration
- Vision impairment from progressive corneal vascularization/pigmentation (chronic uncontrolled qualitative tear deficiency)

RECOMMENDED MONITORING

- Complete ophthalmic examination with STT, TFBUT, and corneal fluorescein staining performed every 3-4 weeks initially
- Rechecks performed every 4-6 weeks until qualitative tear deficiency and associated disorder(s) (e.g., marginal blepharitis and meibomianitis) is/are controlled, then every 3-4 months

PROGNOSIS AND OUTCOME

- Variable depending on underlying cause
- Delayed diagnosis and treatment may result in permanent quantitative and qualitative changes in meibomian glands and/or goblet cell function.

PEARLS & CONSIDERATIONS

COMMENTS

- Response to lacrimomimetics may occur following 3-4 weeks; if not, instituting concurrent topical lacrimostimulants is advised and may be required lifelong.
- May take weeks to months of therapy before determining if favorable response to lacrimostimulants

PREVENTION

Breeds predisposed to eyelid disorders associated with qualitative tear deficiencies: avoid breeding affected or closely related dogs.

SUGGESTED READING

Cullen CL, Lim C, Sykes J: Tear film breakup times in young healthy cats before and after anesthesia. Vet Ophthalmol 8:159–165, 2005.

AUTHOR & EDITOR: CHERYL L. CULLEN

Taurine Deficiency

BASIC INFORMATION

DEFINITION

Inadequate intake or availability of dietary taurine

EPIDEMIOLOGY

SPECIES, AGE, SEX: Taurine is an essential nutrient for cats but not for dogs under most circumstances. Deficiency can occur in cats that cannot meet metabolic needs from dietary sources and occasionally in dogs, particularly if on restricted diets.

GENETICS & BREED PREDISPOSITION

- None reported in cats
- In dogs, isolated occurrences of taurine-deficient dilated cardiomyopathy have been identified in a variety of breeds, including American cocker spaniels, golden retrievers, and Newfoundlands.

RISK FACTORS

- Cats: inadequately supplemented commercial or home-prepared diets
- Dogs: breed predisposition, inadequate protein and sulfur-containing amino acid intake (restricted diets), possible impact of diet composition on intestinal availability

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Cats: central retinal degeneration (CRD), reproductive failure, growth retardation, and dilated cardiomyopathy (DCM)
- Dogs: DCM in susceptible breeds or individuals

HISTORY, CHIEF COMPLAINT

- Cats: compatible diet history (poorly formulated commercial or home-prepared diet) is suggestive but not pathognomonic; dyspnea, respiratory distress.
- Dogs: exercise intolerance and weight loss progressing to cough, respiratory distress, and eventually ascites; possible diet history of restricted diet (very low-protein diets, vegan diets, dry dog food with lamb meal, rice, or both as the primary ingredient)

PHYSICAL EXAM FINDINGS

- Cats: variable combinations of tachypnea, dyspnea, tachycardia, lethargy, dehydration, and hypothermia. Systolic murmur at the apex on the left side, with gallop rhythm in severe cases. Peripheral vasoconstriction may result in cold extremities.
- Dogs: similar to cats; tachyarrhythmia

ETIOLOGY AND PATHOPHYSIOLOGY

- Taurine is synthesized from methionine and cysteine. It does not occur in proteins but is required for a variety of cellular homeostatic functions. Synthesis occurs in cats too slowly to maintain taurine balance in the absence of adequate intake. Dogs have a greater ability to synthesize taurine than cats but occasionally develop taurine deficiency as well. Obligatory loss also occurs in cats and dogs, because only taurine can combine with cholesterol during bile salt synthesis, whereas most other species can substitute glycine for taurine.
- In cats, excessive taurine-conjugated bile salt loss in feces occurs secondary to variable combinations of type of diet processing, protein source, changes in location and/or numbers of intestinal microflora, and/or increased secretion of bile salts due to changes in the release of cholecystokinin.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The possibility of taurine deficiency should be considered in cats and dogs with a compatible diet history and signs of cardiac dysfunction (dogs, cats) or blindness (cats).

DIFFERENTIAL DIAGNOSIS

- Idiopathic DCM
- Other causes of myocardial failure

INITIAL DATABASE

- Cats: radiography to determine presence of heart failure (cardiomegaly plus pleural effusion, pulmonary edema, or both). Do not attempt to obtain radiographs of severely dyspneic, struggling patients, because the stress of the procedure may result in the death of the cat.
- Dogs: radiography, as for cats; electrocardiographic (ECG) signs include variable combinations of left-sided enlargement, sinus tachycardia, atrial fibrillation, and ventricular tachyarrhythmias.

ADVANCED OR CONFIRMATORY TESTING

- Echocardiography is the test of choice for diagnosis of DCM: dyskinesis (reduced systolic motion) of the left ventricular walls, increased end-diastolic diameter, and reduced shortening fraction.
- Blood and/or plasma taurine concentration (draw sample into heparin [green top] tube):
    - Animals with low taurine concentrations (whole blood: <200 nmol/mL in cats, <150 nmol/mL in dogs; plasma <40 nmol/mL in cats and dogs) should be switched to diets known to result in higher plasma concentrations or supplemented with taurine. Plasma taurine concentrations fluctuate with food intake, whereas whole blood taurine reflects long-term (weeks to months) intake.

TREATMENT

TREATMENT OVERVIEW

The goals of treatment are to restore taurine homeostasis and improve cardiac function.

ACUTE GENERAL TREATMENT

- Supportive care for congestive heart failure (CHF; see p. 470), inotropic support (digoxin, pimobendan) and arrhythmias
- Taurine supplementation pending confirmation of diagnosis

CHRONIC TREATMENT

- Cats: recommend switching the cat to a satisfactory diet and supplementing with taurine at 250-500 mg PO or in food q 12 h for 3-6 months or until echocardiographic parameters return to normal.
- Dogs: recommend 1000 mg taurine/ day PO (divided, or once a day). Change to a diet containing more protein and sulfur-containing amino acids and less fiber if possible.

RECOMMENDED MONITORING

- Clinical condition
- Taurine levels should be reevaluated in 1-2 months.
- Radiography, echocardiography

PROGNOSIS AND OUTCOME

- The prognosis is better when deficiency is identified and treated appropriately before extensive permanent change exists in the myocardium. Clinical signs of advanced heart failure, such as hypothermia or thromboembolism, suggest a poorer

prognosis.
- Dogs that improve in conjunction with taurine supplementation become more energetic after a few weeks; they then also show reduction in cardiomegaly, and improvement in echocardiographic parameters should be observed in 3-6 months.

PEARLS & CONSIDERATIONS

COMMENTS

Recovery of function and appetite occur within days to weeks after provision of taurine if deficiency of this amino acid is the cause of the signs. When they occur, reduction in cardiomegaly and improvement in echocardiographic parameters may require 3-6 months of supplementation; improvement may permit reduction or discontinuation of cardiac medications.

PREVENTION

Feeding a properly formulated diet

CLIENT EDUCATION

Explain the importance of feeding pets a properly formulated diet.

SUGGESTED READING

Buffington CAT: Nutritional diseases and nutritional therapy. In Sherding RG, editor: The cat: diseases and clinical management, New York, 1994, Churchill Livingstone, pp 161–190.

Meurs KM: Primary myocardial disease in the dog. In Ettinger SJ, Feldman EC, editors: Textbook of veterinary internal medicine, St Louis, 2005, Elsevier Saunders, pp 1077–1082.

Pion PD: Traditional and nontraditional effective and noneffective therapies for cardiac disease in dogs and cats. Vet Clin North Am Small Anim Pract 34:187, 2004.

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Tarsal Trauma

BASIC INFORMATION

DEFINITION

Includes ligament damage, luxation/subluxation of individual tarsal bones, fractures, or shearing injuries

SYNONYM

Tarsal breakdown

EPIDEMIOLOGY

GENETICS & BREED PREDISPOSITION: Racing greyhounds: central tarsal bone fractures. Border collies: central tarsal bone fracture with luxation. Shelties and collies: luxation of superficial digital flexor tendon.

RISK FACTORS: Racing or agility activities; distal hind limb trauma

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Sprains, fractures, and shearing or degloving wounds; coaptation-related injuries, including pressure sores from casts or splints, dermatitis from soiled bandages, and wound infection or dehiscence from contaminated dressings

HISTORY, CHIEF COMPLAINT: Hind limb trauma; lameness after competition or exercise

PHYSICAL EXAM FINDINGS

- Lameness
- Swelling
- Open wounds around the tarsus
- Pain or crepitation on palpation of the tarsus
- Gross instability characterized by a plantigrade stance
- Tarsal deformity

ETIOLOGY AND PATHOPHYSIOLOGY

- Racing animals on counterclockwise tracks are predisposed to right-sided injuries.
- In racing greyhounds, there is a classic triad of fractures involving the central tarsal bone, calcaneus, and base of metatarsal V.
- In border collies, unknown etiology for exercise induced subluxation with central tarsal bone fracture
- In pets, fractures often occur in the calcaneus.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Tarsal injuries are best diagnosed by physical and radiographic examinations.

DIFFERENTIAL DIAGNOSIS

- Autoimmune polyarthropathy (systemic lupus erythematosus [SLE], rheumatoid arthritis)
- Infectious (Lyme borreliosis, rickettsial disease)

INITIAL DATABASE

- Mediolateral and dorsopalmar radiographic projections of the tarsus

- CBC, chemistry panel, and urinalysis based on the animal's stability and the American Society of Anesthesiologists (ASA) classification (see p. 1372)
- Thoracic/abdominal radiographs, abdominal ultrasound, electrocardiogram (ECG) for animals that have undergone severe trauma

ADVANCED OR CONFIRMATORY TESTING

- Oblique radiography (nondisplaced fractures); skyline views (trochlea of the talus)
- Stress-film radiography (mediolateral radiograph with tarsus manually forced into dorsal and plantar extension and a dorsoplantar radiograph with a medial to lateral stress applied) to identify location of joint instability

TREATMENT

TREATMENT OVERVIEW

The goal of therapy is anatomic and functional restoration of tarsal functions:

- Fractures: stabilization and anatomic reduction
  - Buttress repair of comminuted tarsal bone fractures to prevent joint collapse
- Ligamentous injuries: reestablishment of joint support by repairing collateral ligaments or arthrodesis/ankylosis
- Shearing injuries: wound management

ACUTE GENERAL TREATMENT

- Minimally displaced, nonarticular fractures and grade I and most grade II sprains can be stabilized for 6-8 weeks with an external splint (see p. 1336):
  - Luxated joints, intraarticular fractures, and grade III sprains are supported in a modified Robert-Jones bandage until surgery.
- Shearing injuries require initial wound-management treatment (see p. 1016):
  - Gentle lavage of open wounds using warm saline, lactated Ringer's solution, and dilute chlorhexidine solutions to reduce gross contamination. (Animals are sedated and given analgesics.)
  - Coverage of tissues with moistened (above solutions) gauze sponges useful in débridement (wet-to-dry-bandages) as they are changed daily.
  - Alternatively, direct application of sugar or honey has been used for reducing infection and promoting healing for highly contaminated, traumatic open wounds, but the role of such treatment in the joint is unclear.
  - Final surgical débridement and joint lavage can be performed during orthopedic stabilization surgery.
  - Wounds with healthy granulation tissue, reduced contamination, and early epithelialization can be closed with sutures or covered with a non-adherent dressing and allowed to heal via second intention.

CHRONIC TREATMENT

- Surgical repairs to the tarsus require 6-12 weeks of external coaptation (splints or external fixatures) and exercise restriction.
- Collateral ligament disruption requires stabilization with tension-band principle (malleolar fractures) or replacement with prosthetic suture.
- Instability of the tarsocrural joint or complete (grade III) plantar tarsal disruption necessitates pantarsal arthrodesis.
- Individual tarsal bone fractures require lag screw fixation, except for lesions of the calcaneus (tension-band principle).
- Plantar intertarsal and plantar tarso-metatarsal subluxations are unstable in weight-bearing animals and require partial tarsal arthrodesis with pins or small plates (tension-band principle).
- Dorsal intertarsal and dorsal tarso-metatarsal subluxations are rare and stable (compressed) in weight-bearing animals:
  - Establishing the diagnosis requires stress film radiography.
  - Primary ligament repair or partial tarsal arthrodesis is performed.
- Luxation of the superficial digital flexor tendon is treated by suturing of torn retinacular tissues.

POSSIBLE COMPLICATIONS

- Reduction/implant failure
- Delayed or failed arthrodesis
- Plantar necrosis (vascular injury)
- Wound infection
- Coaptation-related morbidity
- Degenerative joint disease

RECOMMENDED MONITORING

- Lameness evaluation 1-3 months following injury and treatment
- Serial radiographic studies to evaluate fracture healing or progression of arthrodesis

PROGNOSIS AND OUTCOME

- Good to excellent for noncompeting dogs
- Variable for return to preinjury status for competing dogs
- Severe shearing injuries with neurovascular compromise may necessitate limb amputation.

PEARLS & CONSIDERATIONS

COMMENTS

- When conservatively managed, intraarticular fractures rarely heal with osseous bridging, thus leading to degenerative joint disease. Surgical treatment is recommended to reduce the risk of such adverse consequences.
- Severe shearing injuries are commonly due to motor vehicle trauma. Despite significant damage, acceptable function is possible with various reconstructive efforts.
- In noncompeting animals, solitary intertarsal joint fusion/ankylosis (i.e., calcaneotarsal, calcaneoquartal, quartalmetatarsal) can lead to near normal function.

SUGGESTED READING

Dee JF: Tarsal injuries. In Bloomberg MS, Dee JF, Taylor RA, editors: Canine sports medicine and surgery, Philadelphia, 1998, WB Saunders, pp 120–137.

Piermattei DL, Flo GL, DeCamp CE: Fractures and other orthopedic injuries of the tarsus. In Brinker, Piermattei, and Flo' s handbook of small animal orthopedics and fracture repair, ed 4, St Louis, 2006, Elsevier, pp 661–713.

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EDITOR: JOSEPH HARARI

Tail Paralysis

BASIC INFORMATION

DEFINITION

Severe impairment or loss of tail motor function

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dependent on underlying cause

GENETICS & BREED PREDISPOSITION

- Pugs, bulldogs (spina bifida, sacrocaudal dysgenesis)
- Chondrodystrophic breeds (disk herniation)

RISK FACTORS

- Outdoor cats (trauma)
- Free-roaming dogs
- Cardiomyopathies in cats (aortic thromboembolism)
- Type I disk herniation with severe paraparesis
- Degenerative lumbosacral stenosis (cauda equina syndrome)

ASSOCIATED CONDITIONS & DISORDERS

- Cutaneous wounds of the tail:
  - Self-inflicted if sensation altered by neurologic disease
  - Secondary to external trauma (hit by car, falls, etc.)
- Tail fracture

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Trauma involving the hind quarters (hit by car, falls, stepped on, etc.)
- Trauma involving traction injury on the tail (exercise-related, malicious, caught in door, etc.)
- Unwillingness to jump up (e.g., lumbosacral diseases)
- Acute-onset vocalization and hind limb paresis/paralysis (aortic thromboembolism)

PHYSICAL EXAM FINDINGS

- Impaired tail motility with or without hind limb paresis
- Skin wounds (limbs, trunk, abdomen and/or tail)
- Concurrent fractures of the axial skeleton, pelvis, pelvic limbs, and/or thoracic limbs
- Urinary and/or fecal incontinence, urine- or feces-soiled tail
- Pain originating from the pelvic area
- Weakness, pale mucous membranes, dyspnea (if cat with thromboembolic disease)
- Shock if massive trauma
- Tachycardia, heart murmur, gallop, weak or absent pulses, cyanosis of the pelvic limbs (if feline cardiomyopathy)
- Transverse myelopathy (T3-L3 or L4-S3 or Cd1-Cd5 only)
- Large, distended bladder:
  - Easy to empty if spinal lesion involves lumbar intumescence (“lower motor neuron bladder”)
  - Difficult to empty if spinal lesion is cranial to lumbar intumescence (“upper motor neuron bladder”)
- Rectal exam: painful and might induce sacrocaudal instability if associated with trauma

ETIOLOGY AND PATHOPHYSIOLOGY

- Orthopedic:
  - Spinal/coccygeal fracture
  - Degenerative lumbosacral stenosis
- Neurologic:
  - Spinal malformations
  - Spinal fracture
  - Nerve root avulsion (lumbar intumescence/coccygeal)
  - Disk herniation (with or without paraparesis)
  - Tumor of the spine/spinal canal/cord
- Cardiac/vascular:
  - Feline thromboembolic disease
  - Vascular compromise secondary to trauma (arterial avulsion or thrombosis)
  - Fibrocartilaginous embolism

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Tail paralysis is apparent on physical exam. A complete neurologic exam helps identify the extent of the causative lesion, which in turn contributes to determining the prognosis, and whether or not treatment is likely to require tail amputation.

DIFFERENTIAL DIAGNOSIS

- Anomalous (spina bifida, hemivertebra, sacrocaudal dysgenesis, dermoid sinus)
- Degenerative lumbosacral stenosis (stenosis of vertebral canal, type II disk at L7-S1 space, sacral osteochondrosis, instability and misalignment of L7-S1, articular facet arthritis)
- Intervertebral disk disease (type I or type II)
- Spinal trauma/fracture/avulsion
- Vascular (feline thromboembolism, fibrocartilaginous embolism)
- Neoplasia
- Diskospondylitis

INITIAL DATABASE

- Rectal exam to document pain, swelling, instability, mass effect
- Complete neurologic examination to localize the lesion (see p. 1311)
- Radiographs of the spine, including sacrocaudal region (malformations, fracture/trauma/avulsion, diskospondylitis, osteolytic/osteoproliferative tumor, intervertebral disk disease)
- CBC, serum biochemistry panel, urinalysis depending on patient stability and systemic involvement
- Thoracic radiographs:
  - To evaluate the presence of thoracic lesions secondary to trauma
  - To assess for metastases if neoplasia is suspected
- Ultrasound:
  - Thoracic (for feline cardiomyopathy)
  - Abdominal if suspected pelvic canal tumor

ADVANCED OR CONFIRMATORY TESTING

- Advanced imaging modalities: myelography (see p. 1306), CT (see p. 1233), MRI (see p. 1302)
  - May be indicated for assessing underlying spinal abnormalities
- Electromyography (rare instances of neuromuscular disease)
- Fine-needle aspiration if possible for cytologic evaluation (masses, diskospondylitis)
- Ultrasound-guided biopsy (masses)

TREATMENT

TREATMENT OVERVIEW

- Orthopedic or neurologic:
  - Treatment limited to addressing underlying cause if no vascular compromise

    - Medical management of fractures, using pain management, bandages for immobilization
    - Amputate tail if vascular compromise:
        - Leave 3-4 coccygeal vertebrae if well vascularized.
        - Amputate to the level of the skin if tail is devascularized.
- Cardiac/vascular:
    - Tail amputation if tail is soiled by urine and/or feces or if tail has not revascularized well
    - Address underlying cardiac disease.
- Neoplasia:
    - Wide surgical excision if possible
    - Radiation therapy or chemotherapy if indicated and if possible
- Skin wound of the tail (see p. 1016):
    - With vascular compromise, amputate tail at appropriate level.
    - Without vascular compromise, treat accordingly by local débridement (wet-to-dry bandaging or surgical débridement).
    - Use second-intention healing (bandages with hydrogel).
    - If wound closure impossible via second-intention healing, use secondary closure (local skin flaps, free skin grafts).

ACUTE GENERAL TREATMENT

- Treat shock if present.
- Treat underlying cardiac cause.
- Administer corticosteroids if tail paralysis is secondary to spinal cord/nerve compression (controversial; see p.1039).
- Once patient is stable, treatment depends on underlying cause.

CHRONIC TREATMENT

- Hygiene and topical care to prevent urine/fecal contact dermatitis:
    - Bathing, keeping area dry and clean, clipping perianal region, and protective ointment if necessary
- Bladder catheterization if necessary
- Physical therapy for paraparetic patients
- As indicated by underlying cardiac disease

POSSIBLE COMPLICATIONS

- Dependent on therapeutic options
- Beware of corticosteroid administration:
    - Associated with gastrointestinal ulceration, colonic perforation

RECOMMENDED MONITORING

Dependent on primary cause and therapeutic options

PROGNOSIS AND OUTCOME

- Trauma:
    - Intact deep pain perception and normal vascularization: guarded. Generally these patients will regain enough motor activity to avoid lack of hygiene.
    - Absence of deep pain for more than 48 hours: poor prognosis for return of motor activity, but good if tau amputated and normal voluntary hind limb activity and bladder control
- Guarded to poor if feline thromboembolic disease (recurrence risk)

PEARLS & CONSIDERATIONS

COMMENTS

- The most common causes of tail paralysis are trauma and degenerative lumbosacral stenosis:
    - Prognosis depends on deep pain perception and vascular supply.
- In dogs and cats, the tail is not essential to life:
    - Tail amputation in patients with normal limb function and bladder control provides excellent quality of life.
- Beware: pain originating from the pelvic canal (e.g., prostatic abscess, degenerative lumbosacral stenosis) can mimic tail paralysis.

CLIENT EDUCATION

Variable: depends on primary cause of tail paralysis

SUGGESTED READING

De Lahunta A, Glass EC: Veterinary neuroanatomy and clinical neurology, ed 3, St Louis, 2009, Saunders Elsevier.

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EDITOR: ETIENNE CÔTÉ

Uveitis

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Inflammation of part or all of the uveal tract, including the iris, ciliary body, and choroid. May be associated with inflammation of adjacent structures such as the retina, vitreous, sclera, lens, and cornea.

SYNONYMS

Anterior uveitis: iridocyclitis, cyclitis, panuveitis (inflammation of the entire uveal tract)

Posterior uveitis: choroiditis, chorioretinitis, retinochoroiditis

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs and cats; any age or sex

GENETICS & BREED PREDISPOSITION: Many forms of uveitis have a significant immune-mediated component and thus may have a genetic/breed predisposition:

- Uveodermatologic syndrome/Vogt-Koyanagi-Harada (VKH) syndrome: causes granulomatous uveitis and depigmenting dermatitis in dogs, especially Akitas, Samoyeds, and Siberian huskies
- Pigmentary uveitis: associated with pigment dispersion in the anterior chamber in the golden retriever:
  - Uveal cysts (see p. 1149) are often seen in conjunction with pigmentary uveitis.

CONTAGION & ZOONOSIS: A few selected forms of uveitis associated with certain infectious diseases may have contagion and zoonotic potential: *Brucella* uveitis (dogs): both contagious and zoonotic implications (see p. 162); feline leukemia virus (FeLV, see p. 385), feline infectious peritonitis (FIP; see p. 383), and feline immunodeficiency virus (FIV; see) infections are contagious between cats; and toxoplasmosis could have zoonotic potential, but the majority of cats are not passing oocysts during clinical ocular disease (see p. 1105).

GEOGRAPHY AND SEASONALITY: Certain infectious disease etiologies may exhibit seasonality and/or geographic incidence.

ASSOCIATED CONDITIONS & DISORDERS

- Uveitis associated with infectious diseases frequently, but not invariably, may have associated systemic signs.
- Immune-mediated causes of uveitis may also have nonocular signs (e.g., dermatologic signs as noted in uveodermatologic syndrome/VKH).

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Portion of the uvea involved (anterior: iris and/or ciliary body; posterior: choroid; panuveitis: entire uveal tract)
- Acute versus chronic
- Type of inflammation (i.e., nongranulomatous versus granulomatous; nonsuppurative versus suppurative)
- Cause of the uveitis

HISTORY, CHIEF COMPLAINT

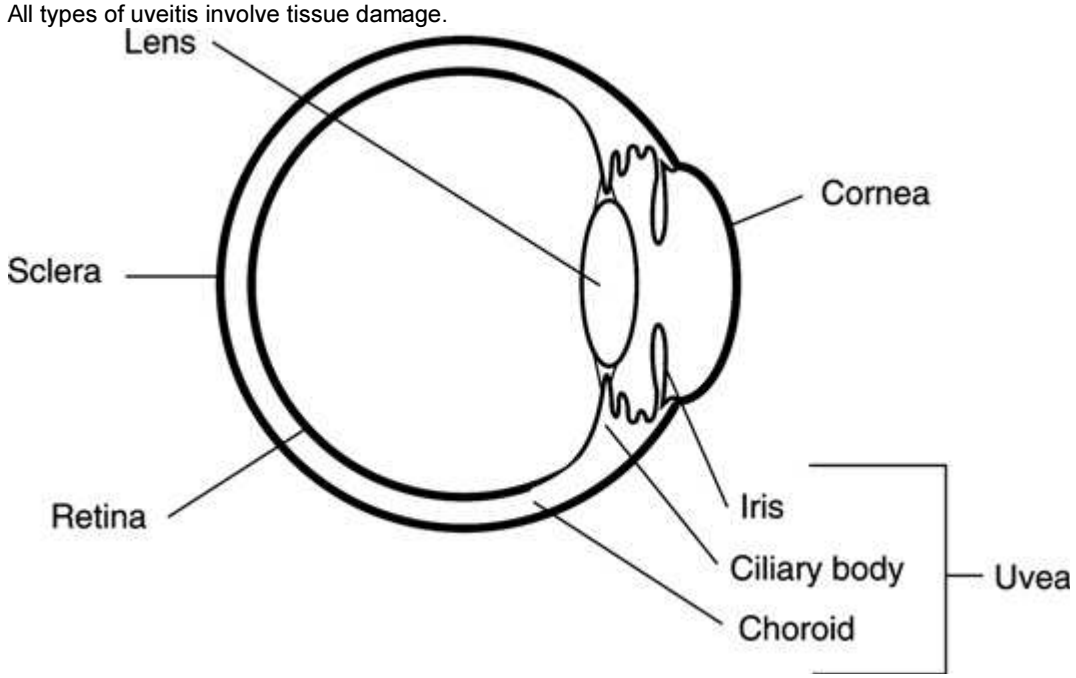
- Variable systemic complaints if caused by systemic disease
- “Red eye”
- Vision problem
- Photophobia
- Blepharospasm
- Color changes in interior of eye

PHYSICAL EXAM FINDINGS

- Conjunctiva and episclera:
  - Congestion/hyperemia of blood vessels
- Cornea:
  - Corneal edema of varying degrees
  - Corneal vascularization (deep) if more chronic
  - +/− Keratic precipitates (forms of white blood cell [WBC] aggregates in which multiple round to ovoid, gray to yellowish opacities are noted on the posterior cornea)
- Anterior chamber:
  - Aqueous flare (cloudiness of the aqueous humor caused by increased protein levels)
  - +/− Fibrin clots
  - +/− Hyphema
  - +/− Hypopyon
- Iris:
  - Color changes (e.g., blue iris becomes brown, brown iris becomes darker or depigmented).
  - Texture changes (e.g., thickened iris with possible visible neovascularization, such as in rubeosis iridis)
- Pupil:
  - Acute, often miotic; chronic, mid-range in size
  - Slow to dilate in response to or lack of response to mydriatics, such as to topical 1% tropicamide
  - Focal or diffuse posterior synechiae (adhesions of iris to lens; e.g., iris bombé, 360° pupillary synechia impairing aqueous drainage and causing iris to balloon forward)
  - Lack of consensual pupillary light reflex in opposite eye if involved eye is blind
- Lens:
  - +/− Varying degrees of cataract; if inflammation is secondary to cataract, the cataract is relatively diffuse; if the cataract is secondary to uveitis, the opacity is usually incomplete and on the capsule/anterior cortex.
- Intraocular pressure (IOP): low unless complicated by secondary glaucoma
- Posterior segment:
  - Posterior uveitis may be accompanied by effusive retinal detachments of varying degrees
  - +/− Vitreal haze due to inflammation in vitreous humor
  - +/− Diffuse or (more likely) multifocal color changes in the fundus, associated with inflammatory infiltrates
  - Optic nerve swelling and hyperemia in some cases

ETIOLOGY AND PATHOPHYSIOLOGY

- All types of uveitis involve tissue damage.



UVEITIS Sagittal section of the globe, showing the anatomic relationships of the uvea to the other parts of the eye.

- Clinical signs are attributed to disruption of the blood-ocular barrier (physiologic mechanism that prevents exchange of large molecular materials between the blood and chambers of the eye) and release of numerous chemical mediators following tissue damage.

Etiology:

- Primary ocular:
  - Blunt and perforating trauma (see p. 249), including surgical trauma
  - Corneal ulceration (see p. 250)
  - Lens-induced:
    - Rapidly developing or hypermature cataracts leaking soluble lens proteins into eye, causing uveitis
    - Lens capsule rupture, causing phacoclastic uveitis; often also have bacterial contamination if due to perforating injury such as cat claw
    - Lens luxation (see p. 644) o Scleritis (see p. 356)
  - Uveal cysts (see p. 356)
  - Primary intraocular neoplasia, such as uveal melanoma (see p. 1149)
  - Retinal detachment (see p. 985)
- Systemic:
  - Infectious diseases that are often species-specific:
    - Cats: toxoplasmosis, FIP, FeLV, FIV, systemic mycoses, bartonellosis, tuberculosis, herpesvirus
    - Dogs: infectious canine hepatitis, ehrlichiosis, Rocky Mountain spotted fever, toxoplasmosis, protothecosis, brucellosis, borreliosis, leptospirosis, leishmaniasis, systemic mycoses
  - Aberrant metazoan parasites: *Dirofilaria immitis,* ascarids, fly larvae
  - Secondary intraocular neoplasia (e.g., lymphoma most common)
  - Immune-mediated: uveodermatologic syndrome/VKH
  - Pigmentary uveitis in golden retrievers
  - Idiopathic: In the dog, roughly 50%-60% of uveitis workups fail to identify a definite cause and are probably immune mediated; in the cat, lymphocytic-plasmacytic uveitis of undetermined cause is common.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A complete ocular examination of both eyes is warranted to help determine whether or not the uveitis affects the anterior segment (i.e., anterior uveitis), posterior segment (i.e., posterior uveitis), or both segments of the eye(s) (i.e., panuveitis), as this will help determine the possible underlying causes for the uveitis and an appropriate treatment protocol.

DIFFERENTIAL DIAGNOSIS

Other causes for ”red eye”:

- Glaucoma
- Conjunctivitis
- Episcleritis/scleritis
- Keratitis
- Orbital disease

INITIAL DATABASE

- Complete ophthalmic examination (p. 1313) of both eyes:
  - A patient may have anterior lesions in one eye and posterior lesions in the contralateral eye.
- IOP: glaucoma is a frequent complication of uveitis (see p. 448):
  - Normal range is 10-25 mm Hg.
  - A measurement of <10 mm Hg is consistent with uveitis; >30 mm Hg is consistent with glaucoma.
- Thorough general physical examination and history: systemic causes for uveitis are common.
- Ocular ultrasound is indicated when opaque ocular media preclude thorough examination.
- Unless the cause is obvious, a systemic workup beginning with CBC, serum biochemistry profile, and urinalysis is indicated.

ADVANCED OR CONFIRMATORY TESTING

- Selected infectious disease titers based on species, geography, and systemic signs
- Chest radiographs for neoplasia and systemic mycoses
- Fine-needle aspirate (FNA)/biopsy of enlarged lymph nodes, abnormal organs
- Anterior chamber/aqueous centesis in selective cases for culture, cytologic examination, and titers (referable procedure)

TREATMENT

TREATMENT OVERVIEW

Goals of treatment are to reduce the inflammation before inflammatory sequelae produce blindness, alleviate ocular pain, and eliminate the initiating cause if possible.

ACUTE GENERAL TREATMENT

- In general, topical therapies are used for anterior uveitis, whereas systemic therapies are required for effective treatment of posterior uveitis.
- Reduce ocular inflammation with anti-inflammatory drugs:
  - Corticosteroids:
    - Topical and/or systemic depending on severity and location of uveitis
    - Contraindicated with many infectious etiologies (i.e., systemic mycoses; acute bacterial) and corneal ulceration
    - Start with frequent dose q 4-6 h for topical (e.g., prednisolone acetate 1%, dexamethasone 0.1%) and antiinflammatory doses of systemic drug (e.g., prednisone 1 mg/kg PO q 24 h).
  - Nonsteroidal antiinflammatory drugs (NSAIDs):
    - Topical and/or systemic depending on severity and location of uveitis
    - Topical (flurbiprofen or diclofenac q 4-6 h, depending on severity of disease) and/or systemic (dog: meloxicam, 0.2 mg/kg SQ loading dose and 0.1 mg/kg PO q 24 h; cat: ketoprofen, 2 mg/kg SQ loading dose and 1 mg/kg PO q 24 h for 4 days).
  - Do not use systemic glucocorticoids and systemic NSAIDs concurrently (gastrointestinal [GI] ulceration).
  - Miscellaneous immunosuppressive drugs: severe recalcitrant forms of inflammation may necessitate systemic drugs such as azathioprine and cyclosporine.
- Control ocular pain and prevent synechiae:
  - Topical atropine 1% q 6-8 h to dilate the pupil (i.e., mydriatic) in acute cases to minimize posterior synechiae and prevent spasms of the ciliary body muscle (i.e., cycloplegic) that contribute to pain.
- Other therapies:
  - Specific therapies:
    - If an infectious agent is the initiating cause, specific antiinfective therapy, such as antibiotics, is indicated.
    - Usually administered by both topical and systemic routes
    - Broad-spectrum, bactericidal drugs are preferred until sensitivity is known.
  - Tissue plasminogen activator (tPA) injected into the anterior chamber (referable procedure): 25 mcg of tPA may release a posterior synechia and dramatically dissolve fibrin clots of anterior chamber in animals with acute uveitis.

CHRONIC TREATMENT

- After 7-10 days, antiinflammatory therapy is usually reduced in frequency if the uveitis is significantly reduced, but is continued for several weeks at a lower frequency and/or systemic dose.
- Some immune-mediated diseases (e.g., uveodermatologic syndrome/VKH) are treated indefinitely.
- Most infectious causes are treated for 3-4 weeks with antibiotics; some, such as those caused by *Brucella* spp. and *Leishmania,* may require prolonged therapy.

DRUG INTERACTIONS

Topical NSAIDs may elevate IOP and, if secondary glaucoma develops, may need reevaluation.

POSSIBLE COMPLICATIONS

Blindness (see p. 141), glaucoma (see p. 448), cataracts (see p. 181), synechiae resulting in pupil immobility, retinal detachment (see p. 985), corneal opacity (see p. 245), prolonged ocular hypotony (low IOP), phthisis bulbi (shrinkage of the eye)

RECOMMENDED MONITORING

- Animals with acute severe forms should be monitored daily until inflammation begins to subside, then weekly and biweekly.
- IOPs should be monitored:
  - At a frequency dependent on progress
  - As the uveitis subsides and aqueous production normalizes, any outflow restrictions from adhesions/synechiae may become manifest and require therapy (see Acute General Treatment, above).
- Certain infectious diseases may be monitored by repeat titers.

PROGNOSIS AND OUTCOME

- The prognosis is highly variable depending on severity of inflammation, stage at presentation, and underlying cause.
- Any significant inflammation of the interior of the eye should have a guarded prognosis for maintenance of ocular function.

PEARLS & CONSIDERATIONS

COMMENTS

- Despite extensive medical workups, more than 50% of cases of uveitis in the dog are idiopathic and, by default, thought to be immune-mediated conditions.
- In the younger cat, systemic infectious diseases are often implicated; in the older cat, uveitis is often idiopathic (i.e., lymphocytic-plasmacytic).
- Infectious etiologies *(Brucella,* systemic mycoses) may be difficult to clear from the eye despite specific therapy.
- Many of the infectious disease tests are antibody titers and are often only presumptive of exposure unless serial tests demonstrate rising titers.

PREVENTION

- Minimize infectious diseases through vaccination and restriction of environment.
- Surgical removal of primary cataracts (referable procedure) before the cataracts become mature to hypermature
- Removal of injured or displaced lenses in eyes with vision potential:
    - Perforating injuries that have created lens rupture (specifically, capsular tears of greater than 2 mm)
    - Lens luxation

CLIENT EDUCATION

- Any inflammation of the interior of the eye is potentially serious and can threaten vision.
- Causes of uveitis are multiple and often difficult to pinpoint; nevertheless, it is important to perform laboratory diagnostics in hopes of formulating a specific therapy and to determine the systemic prognosis.

SUGGESTED READING

Martin CL: Anterior uvea and anterior chamber. In Ophthalmic disease in veterinary medicine. London, 2005, Manson Publishing, pp 298–336.

Massa KL, et al: Causes of uveitis in dogs: 102 cases (1989-2000). Vet Ophthalmol 5:93, 2002.

AUTHOR: CHARLES L. MARTIN

EDITOR: CHERYL L. CULLEN

Uveal Cysts

BASIC INFORMATION

DEFINITION

Generally benign/incidental, round to ovoid, pigmented intraocular structures arising from the iris or ciliary body. They may be seen attached at the pupillary margin and/or posterior iris, free-floating in the anterior chamber, and (rarely) in the vitreous.

SYNONYMS

Anterior chamber cysts, ciliary cysts, iridociliary cysts, iris cysts, pupillary cysts

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs, cats, and other domestic species; in dogs, mean age is 6.8-9.1 years.

GENETICS & BREED PREDISPOSITION

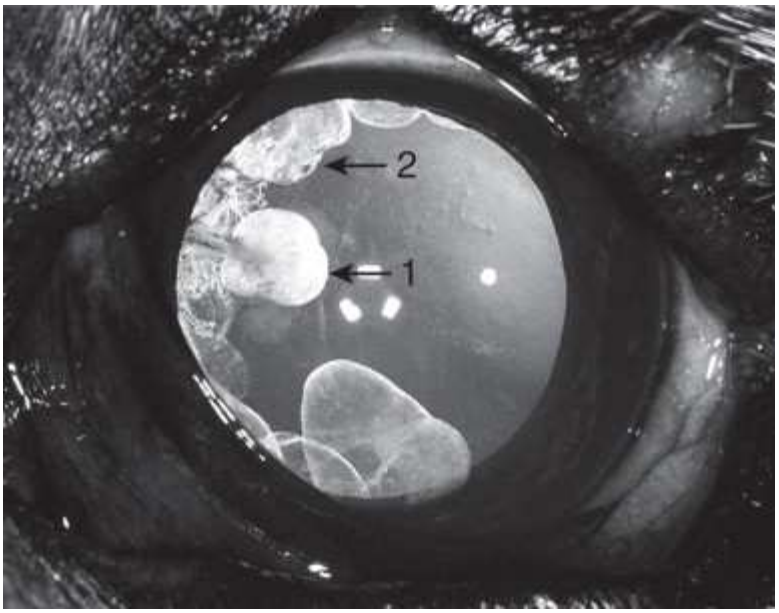
- Dogs: golden retrievers, Labrador retrievers, Boston terriers, Great Danes, rottweilers
- Cats: Siamese (one report)

RISK FACTORS

- Trauma
- Uveitis, especially lens-induced uveitis; uveal cysts may arise as a consequence of uveitis, or uveitis may result as a consequence of the cysts (see p. 1151)

ASSOCIATED CONDITIONS & DISORDERS

- Dogs: uveitis and secondary glaucoma (i.e., glaucoma results as a complication of the cysts) associated with iridociliary cysts in golden retrievers and Great Danes
- Cats: cysts may be associated with trauma or uveitis.



UVEAL CYSTS Dog with multiple uveal cysts in the anterior chamber *(1)* and posterior to the iris *(2)*.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Free-floating cysts within the anterior chamber
- Cysts attached to the pupillary margin
- Iridociliary cysts
- Rarely, cysts in the vitreous

HISTORY, CHIEF COMPLAINT

- Usually incidental findings
- Pigmented intraocular mass
- Signs of uveitis (see p. 1151) and glaucoma (see p. 448) in golden retrievers and Great Danes
- Intraocular bleeding (rare)
- Vision impairment

PHYSICAL EXAM FINDINGS

- Single or multiple pigmented masses in anterior chamber, along pupillary margin, posterior to the iris, or rarely in the vitreous
- Canine uveal cysts are often translucent such that they can be transilluminated (i.e., it is possible to see through them using a strong light source, such as a Finnoff transilluminator), whereas feline uveal cysts may be very dark and difficult to transilluminate.

ETIOLOGY AND PATHOPHYSIOLOGY

- Most are spontaneous in nature but may be associated with previous trauma or anterior uveitis.
- Generally arise from the pigmented epithelial layer of iris or ciliary body

DIAGNOSIS

DIAGNOSTIC OVERVIEW

An intraocular mass (noted by the owner or encountered incidentally on physical exam) raises the possibility of a uveal cyst. Definitive confirmation is possible in some cases with simple transillumination or with ocular ultrasound evaluation.

DIFFERENTIAL DIAGNOSIS

- Iridal or anterior uveal melanomas
- To differentiate uveal cysts (often translucent and thus can be transilluminated) from neoplastic tissue (more dense/opaque and cannot be transilluminated), a strong light source such as a Finnoff transilluminator is advised.

INITIAL DATABASE

- Neuro-ophthalmic examination (see p. 1311)
- Schirmer tear test, intraocular pressure measurement, and fluorescein staining
- Full ocular examination (see p. 1313) performed with and without mydriasis (topical tropicamide 1%)

ADVANCED OR CONFIRMATORY TESTING

- Ocular ultrasonography may confirm the diagnosis by revealing a cyst's anechoic (fluid-filled) center.
- Biopsy of cyst and its contents can be performed, but this is usually not necessary.

TREATMENT

TREATMENT OVERVIEW

- A true cyst is a benign structure that poses a risk only by its physical presence. Removal can be contemplated if the cysts are very large, obstruct the pupillary axis, cause corneal edema, or are associated with iris plateauing and glaucoma.

ACUTE GENERAL TREATMENT

- Laser ablation of cysts with Nd: YAG or diode laser
- Aspiration of the cyst with a 25-G to 27-G needle through a limbal paracentesis

CHRONIC TREATMENT

- Usually not necessary unless chronic uveitis or glaucoma is present. Therapy may entail topical steroidal ophthalmic preparations (prednisolone acetate 1% or dexamethasone 0.1%), topical nonsteroidal agents (diclofenac 0.1% or flurbiprofen 0.03%), as well as topical and oral antiglaucoma medications.

POSSIBLE COMPLICATIONS

- Cyst rupture, with adhesion to the corneal endothelium or anterior lens capsule
- Mechanical interference with iris function
- Aqueous outflow obstruction:
    - Secondary glaucoma

RECOMMENDED MONITORING

- For most cases diagnosed incidentally, monitor every 6-12 months.
- If the condition is associated with uveitis or glaucoma, recheck every 2-4 months or sooner.

PROGNOSIS AND OUTCOME

Generally benign condition; of concern in the golden retriever and Great Dane breeds. According to one report, 46% of affected eyes studied in golden retrievers became blind as a result of glaucoma.

PEARLS & CONSIDERATIONS

COMMENTS

A strong light source is advised for ocular examination and transillumination (Finnoff transilluminator) to differentiate uveal cysts (often translucent) from neoplastic tissue (more dense/opaque and cannot be transilluminated).

PREVENTION

- Breeds of dogs predisposed to uveal cysts: avoid breeding affected or closely related individuals.
- If associated with uveitis, topical anti-inflammatory medications are advised.

CLIENT EDUCATION

- Uveal cysts are typically a benign condition requiring no therapy. Periodic recheck evaluations are advised every 6-8 months.
- If the cysts become large, impair vision, or are associated with glaucoma, laser ablation can be considered.

SUGGESTED READING

Gemensky-Metzler AJ, Wilkie DA, Cook CS: The use of semiconductor diode laser for deflation and coagulation of anterior uveal cysts in dogs, cats, and horses: a report of 20 cases. Vet Ophthalmol 7:360–368, 2004.

Sapienza JS, et al: Golden retriever uveitis: 75 cases (1994-1999). Vet Ophthalmol 3:241–246, 2000.

AUTHOR: JOHN S. SAPIENZA

EDITOR: CHERYL L. CULLEN

Uterine Neoplasia

BASIC INFORMATION

DEFINITION

Benign or malignant cellular proliferations involving the uterus. Uncommon in dogs and cats.

SYNONYMS

Uterine mass, nodule, or polyp

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Most common in bitches >10 years of age and queens between 5 and 10 years of age
- Accounts for 1%-19% of all reproductive tumors in dogs and l%-2% of all reproductive tumors in cats

GENETICS & BREED PREDISPOSITION: Boxers may be overrepresented.

RISK FACTORS: Older age, intact reproductive tract

CONTAGION & ZOONOSIS: Transmissible venereal tumor (TVT) uterine metastases can result in TVT dysgerminoma.

ASSOCIATED CONDITIONS & DISORDERS: Uterine torsion and/or rupture may occur as a result of uterine neoplasia.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: May involve the endometrium (polyp); myometrium (leiomyoma, fibroma, fibroleiomyoma, fibroadenoma, adenoma, leiomyosarcoma, adenocarcinoma, fibrocarcinoma); lipoma; or metastatic disease (lymphoma; transmissible venereal tumor dysgerminoma).

HISTORY, CHIEF COMPLAINT

- Bloody, mucoid, mucopurulent or mucohemorrhagic vulvar discharge
- Abdominal distension
- Ascites
- Depression or lethargy
- Vomiting
- Anorexia
- Dysuria
- Constipation
- Chronic low-grade fever: uncommon

PHYSICAL EXAM FINDINGS

- Bloody vulvar discharge
- Abdominal distension with palpable midcaudal abdominal mass
- Weight loss
- Depression
- Lymph node enlargement (especially inguinal): uncommon

ETIOLOGY AND PATHOPHYSIOLOGY

- Uterine tumors may be of endometrial, myometrial, serosal origin; may be primary or metastatic.
- Leiomyoma is the most common tumor and may be found incidentally or concurrent with pregnancy.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is typically suspected with a history of bloody vulvar discharge with supportive cytologic findings and/or ultrasound evidence of a uterine mass. Histopathologic examination of a specimen from the mass is the confirmatory test of choice.

DIFFERENTIAL DIAGNOSIS

- Pyometra
- Segmental endometrial hyperplasia
- Uterine lithiasis
- Pregnancy
- Mummified fetus
- Subinvolution of placental sites (SIPS)
- Adenomyosis
- Granuloma
- Mural abscess
- Decidual reaction
- Remnant of the mesonephric duct
- Serosal inclusion cysts

INITIAL DATABASE

- CBC, serum biochemistry profile, urinalysis (avoid unguided cystocentesis): results may be normal with benign tumors to abnormal with metastatic disease, depending on metastatic location.
- Cytologic examination of vulvar discharge may demonstrate neoplastic cells.
- Radiographs may reveal an enlarged caudal abdominal viscus.
- Abdominal ultrasound examination reveals a mass in the uterine, cervical, or vaginal lumen:
    - If mass appears solid (homogeneous, minimally vascularized), fineneedle aspiration for cytologic examination is appropriate.
- Thoracic radiographs for evidence of metastasis

ADVANCED OR CONFIRMATORY TESTING

- Hysteroscopy may reveal a luminal or mural mass.
- Biopsy may be taken via transcervical endoscopic collection technique (TECT).
- MRI may better delineate the mass and provide further evidence of metastasis (rarely necessary).

TREATMENT

TREATMENT OVERVIEW

Ovariohysterectomy (OHE): either partial or complete

ACUTE GENERAL TREATMENT

- Typically, complete OHE is recommended to ensure that any small masses not palpable or visible are removed at the time of initial surgery.
- Abdominal inguinal lymph nodes may be submitted for assessment of metastasis.
- If the tumor is long-standing, necrosis of the uterine wall is possible, or adhesions to other abdominal tissues may require resection.

CHRONIC TREATMENT

Depending on tumor type and presence of metastasis, chemotherapy, immune modulators, or radiation therapy may be appropriate. Consultation with an oncologist is recommended.

POSSIBLE COMPLICATIONS

If malignancy is present, complications associated with tumor metastasis in other locations may occur.

RECOMMENDED MONITORING

If malignant, monitoring of other organ systems for metastasis may be required.

PROGNOSIS AND OUTCOME

Good for benign tumors; guarded to poor for metastatic or malignant tumors

PEARLS & CONSIDERATIONS

PREVENTION

Ovariohysterectomy will prevent uterine disorders from developing.

CLIENT EDUCATION

Brood bitches, regardless of their age, should be spayed after the last litter to prevent tumors from developing.

SUGGESTED READING

Johnston SD, Root Kustritz MV, Olson PN: Disorders of the canine uterus and uterine tubes. In Canine and feline theriogenology. Philadelphia, 2001, WB Saunders, p 206.

AUTHOR: CHERYL LOPATE

EDITOR: MICHELLE KUTZLER

Uterine Disorders, Non-Neoplastic

BASIC INFORMATION

DEFINITION

- Uterine torsion: an uncommon condition involving twisting of one or both uterine horns or the uterine body on its own axis
- Uterine prolapse: a rare condition where the uterus everts through the cervix and vagina (one or both horns may be involved)

EPIDEMIOLOGY

SPECIES, AGE, SEX: Either condition may occur at any age or parity. Uterine torsion may occur unrelated to pregnancy.

RISK FACTORS

- Large litter size may predispose to torsion.
- Any condition causing excessive straining may predispose to prolapse (dystocia, necrotic vaginitis, severe cystitis, diarrhea, constipation).

ASSOCIATED CONDITIONS & DISORDERS: Both uterine torsion and uterine prolapse may be associated with shock, sepsis, disseminated intravascular coagulation (DIC), multiple organ dysfunction syndrome (MODS), and systemic inflammatory response syndrome (SIRS).

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Torsion may involve one or both horns or the uterine body and may be from 90○ to 2160○ (6 complete turns described in one case).
- Prolapse occurs in the puerperal period and may involve one or both horns, be partial or complete, and occurs rarely prior to delivery of all fetuses.

HISTORY, CHIEF COMPLAINT

Torsion:

- History of no progression from stage 1 to stage 2 of labor, or cessation of ongoing stage 2 labor
- Acute abdominal pain
- Shock

Prolapse:

- History of prolonged straining (labor, other)
- Tissue protrudes from the vulvar lips.
- Queens may present up to 48 hours after delivery of last kitten.

PHYSICAL EXAM FINDINGS

- Acute abdominal pain and splinting
- Crying
- Hemorrhagic vulvar discharge
- Excessively vulvar licking
- Abdominal distension
- Tachycardia and tachypnea
- Pale mucous membranes with increased capillary refill time
- +/− Collapse
- +/− Devitalized prolapsed tissue

ETIOLOGY AND PATHOPHYSIOLOGY

- Torsion: unknown etiology; may be due to fetal or bitch activity or abnormal uterine motility (inertia) with continued fetal activity
- Prolapse: eversion of the tip of a uterine horn followed by excessive straining (due to any cause) during uterine involution or eversion of the tip of a horn due to uterine inertia followed by normal uterine contraction patterns

DIAGNOSIS

DIAGNOSTIC OVERVIEW

- Torsion: diagnosis is based on cessation of labor or acute abdominal pain. Ultrasound may be supportive, but the diagnosis is conclusively made on exploratory laparotomy.
- Prolapse: diagnosis is based on physical exam findings of prolapsed tissue from the vulvar lips following parturition. Inability to locate the uterus on ultrasound of the abdomen is confirmatory.

DIFFERENTIAL DIAGNOSIS

Uterine torsion:

- Pyometra
- Uterine rupture
- Uterine inertia (primary or secondary)
- Acute gastrointestinal disorders (bloat, gastric or mesenteric torsion), other causes of the acute abdomen

Uterine prolapse:

- Bladder or vaginal prolapse
- Vaginal, cervical, or uterine neoplasia

INITIAL DATABASE

- CBC: +/− leukocytosis +/− toxic neutrophils, evidence of dehydration
- Serum biochemistry profile: normal to increased renal and hepatic values and electrolyte disturbance depending on duration.
- Abdominal ultrasonography:
    - Hemorrhage into the uterine lumen and edema (hypoechogenicity) of the uterine wall adjacent to the torsion
    - Fetuses may be viable or dead.
    - Intraluminal gas may be present.

ADVANCED OR CONFIRMATORY TESTING

TREATMENT

TREATMENT OVERVIEW

Treatment goals are:

- Patient stabilization (IV fluid resuscitation, pain control)
- Exploratory laparotomy for correction of torsion, Caesarian section to deliver remaining fetuses if still viable, or ovariohysterectomy (OHE) if tissue is devitalized.
- Prolapsed tissue is cleaned and replaced with combination of manual manipulation externally +/− abdominal approach. OHE may be necessary if tissue devitalized.

ACUTE GENERAL TREATMENT

Torsion:

- Broad-spectrum antibiotics (ampicillin, 10-20 mg/kg IV q 6-8 h + enrofloxacin, 2.5-5 mg/kg IM q 12 h; maximum 5 mg/kg q 24 h in cats) as soon as the diagnosis is confirmed and when devitalized tissue is present.
- Do not detorse the affected horn(s), as this may result in reperfusion injury and allow systemic circulation of bacteria and

toxin.
- If only one horn is affected, a partial OHE may be performed, oversewing the uterine body at the level of the bifurcation.

Prolapse:

- Initially, digital pressure and inversion of the horn into itself starting distally and working towards the tip
- Care should be taken to invert the entire horn to its tip (ultrasound may be used to confimi this).
- Oxytocin may be administered after complete inversion.
- If manual reduction is impossible, uterine amputation is indicated.

CHRONIC TREATMENT

Long-term antibiotics (2 weeks) should be administered.

BEHAVIOR/EXERCISE

If the dam is stable, she may be allowed to nurse the neonates.

RECOMMENDED MONITORING

CBC, serum biochemistry profile

PROGNOSIS AND OUTCOME

- With early diagnosis, the prognosis is good for survival.
- With systemic illness, the prognosis for survival may be guarded to poor.
- Recurrence is unlikely.

PEARLS & CONSIDERATIONS

COMMENTS

- Caution should be taken when handling either condition, as the uterine wall may be friable.
- Do not administer calcium or oxytocin to patients suspected of torsion or prolapse.

PREVENTION

Ovariohysterectomy will prevent uterine disorders from developing.

CLIENT EDUCATION

- Failure of an animal to continue to progress through labor should instigate a veterinary examination.
- Bloody discharge or abdominal pain during or after delivery is abnormal.

SUGGESTED READING

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http://www.vetmed.lsu.edu/eiltslotus/theriogenology-5361/canine_surgery.htm

AUTHOR: CHERYL LOPATE

EDITOR: MICHELLE KUTZLER

Urolithiasis, Urate/Biurate

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Organized concretions within the urinary tract, composed of uric acid and its salts; these comprise approximately 5%-10% of uroliths in dogs (except dalmatians, which form mostly urate uroliths) and cats.

SYNONYMS

Biurate urolithiasis, purine urolithiasis, ammonium urate urolithiasis, uric acid urolithiasis, urate calculi/stones

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Urate uroliths account for ~6% of canine uroliths and 5% of feline uroliths.
- Urate uroliths are the most common urolith of dalmatian dogs (prevalence ~35%) and occur predominantly in middle-aged males.
- Most often seen in young to middle-aged adult dogs and young adult cats

GENETICS & BREED PREDISPOSITION

- All dalmatians are unique in their excretion of uric acid instead of allantoin as an end product of purine metabolism, but only a subset develop urate urolithiasis. The tendency to form uroliths is heritable, although genetics are incompletely understood.
- Predisposed non-dalmatian breeds include English bulldog and Russian black terrier. Miniature schnauzer, shih tzu, and Yorkshire terriers are over-represented (likely due to congenital portosystemic shunts).

RISK FACTORS

- Portosystemic shunt (PSS; see p. 905)
- Hepatic microvascular dysplasia
- Hepatic cirrhosis
- Acidic urine and/or urinary infection with urease producing bacteria

ASSOCIATED CONDITIONS & DISORDERS

- Urinary tract infection
- Ureteral or urethral obstruction

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Clinical signs often absent. When apparent, signs may include:

- Hematuria
- Pollakiuria
- Inappropriate elimination (penuria)
- Dysuria
- Stranguria
- If congenital hepatic disease is present, growth retardation
- If hepatic dysfunction is present, encephalopathy and/or hypoglycemia (e.g., altered mentation, seizures)
- Rarely, systemic illness due to urinary obstruction

PHYSICAL EXAM FINDINGS: Physical exam is usually unremarkable. Abnormalities may include:

- Hematuria (stains on prepuce, vulva, hocks)
- Palpable cystic calculi
- Palpable urethral calculi (via digital rectal exam in dogs)

- Enlarged, turgid bladder if urethral obstruction present
- Renomegaly related to PSS or hydronephrosis
- Small body size if PSS present
- Neurologic deficits related to encephalopathy and/or hypoglycemia if due to congenital hepatic disease

ETIOLOGY AND PATHOPHYSIOLOGY

- Dalmatians:
  - During protein catabolism in non-dalmatian dogs, purine metabolism leads to uric acid oxidation by hepatic uricase, with resultant allantoin production.
  - Despite normal uricase activity, dalmatians convert uric acid to allantoin inadequately, resulting in increased urinary excretion of poorly soluble uric acid.
  - Contributing mechanisms may include decreased tubular resorption of uric acid and less activity of urinary crystal-inhibiting proteins.
- Dogs with hepatic dysfunction: reduced uricase production and increased renal excretion of uric acid and ammonia, resulting from reduced hepatic conversion/urea synthesis
- Non-dalmatian dogs and cats without hepatic dysfunction: unknown

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is suspected in dogs with radiolucent uroliths and either a breed predisposition (dalmatian, English bulldog) or hepatic dysfunction. Diagnosis in cats and healthy dogs of other breeds is usually based on quantitative stone analysis.

DIFFERENTIAL DIAGNOSIS

- Urinary tract infection
- Other types of uroliths
- Urinary tract neoplasia

INITIAL DATABASE

- CBC: often unremarkable, but PSS is associated with microcytosis.
- Serum biochemical profile: often unremarkable, but may suggest hepatic dysfunction (low blood urea nitrogen [BUN], hypoglycemia, hypocholesterolemia, hypoalbuminemia; hyperbilirubinemia if cirrhosis present). Urinary obstruction leads to azotemia, hyperkalemia, and metabolic acidosis.
- Urinalysis: frequently aciduria; urate crystals sometime identified; physical irritation and/or secondary infection sometimes leads to hematuria, pyuria, or bacteruria
- Urine culture and sensitivity to rule out secondary infection
- Abdominal radiographs: urate uroliths are often radiolucent (radiopacity: struvite = oxalate = $CaPO_4$ = silica > cystine > urate).
  - If visible, often few smooth round uroliths identified
- Microhepatica is suggestive of PSS, cirrhosis
- Abdominal ultrasound: confirm urolithiasis, which may be missed on abdominal radiographs. Confirms location of uroliths within the urinary tract; may identify PSS, hepatic abnormalities.

ADVANCED OR CONFIRMATORY TESTING

- In non-dalmatian dogs or when appropriate: serum bile acids or other tests to rule out hepatic disease
- Contrast cystography/urethrography: alternative to ultrasound for confirmation/localization of radiolucent stones (see pp. 1237 and 1357)
- Urolith analysis: retrieved stones submitted for quantitative analysis (crystallography, x-ray diffraction, infrared spectroscopy) to determine urolith type
- Cystoscopy may facilitate urolith removal for analysis and therapy (see p. 1239).

TREATMENT

TREATMENT OVERVIEW

Although uncommon, urinary tract obstruction requires immediate removal of uroliths. In the absence of urinary obstruction, treatment consists of either medical stone dissolution or manual removal of stones, as well as treatment of underlying disorders (e.g., PSS) or preventive therapy.

ACUTE GENERAL TREATMENT

- Relieve urinary tract obstruction (see pp. 1353 and 1355).
- If present, treat hepatic encephalopathy (see p. 501).
- If present, treat urinary infection (see p. 276).
- Choose between medical dissolution (see Chronic Treatment, below) and mechanical removal:
    - Urinary tract obstruction should be relieved mechanically.
    - Mechanical removal allows for urolith analysis, culture.
    - Cats are poorly amenable to medical dissolution of urate uroliths.
- Mechanical removal of calculi:
    - Urohydropropulsion (voiding, retrograde; see pp. 1353 and 1355)
    - Avoid performing voiding urohydropropulsion in male cats.
    - Catheter-assisted retrieval
    - Cystoscopic-assisted retrieval (see p. 1239)
    - Cystotomy/urethrotomy/urethrostomy/pyelotomy/nephrotomy
    - Lithotripsy (see p. 1297; intracorporeal or extracorporeal shock wave lithotripsy)

CHRONIC TREATMENT

- Animals with hepatic disease:
    - Surgical correction of PSS prevents recurrence; cystotomy may be used to remove uroliths during surgical correction of hepatic shunt.
    - If hepatic disease cannot be corrected, institute medical management (including restricted protein diet), and monitor for recurrence.
- Promote water consumption to avoid concentrated urine (e.g., canned food, wetting dry food, use of cat water fountains).
- Feed low-purine calculolytic diet (see Nutrition/Diet, below).
- If urine remains acidic after diet change, consider adding sodium bicarbonate (25-50 mg/kg PO q 12 h) or potassium citrate (50-150 mg/kg PO q 12 h), with dose adjustment to maintain urine pH of 7.0 to 7.5.
- Allopurinol 10-15 mg/kg q 12 h PO, with dose reduction for azotemic dogs

NUTRITION/DIET

Reduced protein (therefore reduced purine) diet:

- Dogs: for example, Hills u/d, Royal Canin Urinary UC Low Purine, Royal Canin Vegetarian Formula. For English bulldogs, a renal diet may be preferred, as ultra low-protein diets have been associated with cardiomyopathy.
- Cats: for example, Hills l/d or k/d

POSSIBLE COMPLICATIONS

- Chronic use of low purine diets may result in cardiomyopathy, perhaps related to carnitine or taurine deficiency (esp. English bulldogs).
- Severely protein-restricted diets are inappropriate for growing, pregnant, or lactating animals.
- Xanthine urolith formation with allopurinol administration

RECOMMENDED MONITORING

- Serum biochemical profile and urinalysis 2 weeks after diet change. Goal is urine pH 7.0 to 7.5, specific gravity < 1.020, and absent crystals. Assuming adequate renal function and diet adherence, BUN should be < 10 mg/dL. Monitor urinalysis q 2-4 weeks until uroliths resolved and q 3-6 months thereafter.
- Monitor dissolution of uroliths q 2-4 weeks via lower urinary tract contrast studies or ultrasound. Monitor for recurrence in like manner q 3-6 months for a year, then q 6-12 months.

PROGNOSIS AND OUTCOME

- Prognosis for dissolution is good in dogs.
- Recurrence is common unless cause resolved (e.g., PSS corrected).

PEARLS & CONSIDERATIONS

COMMENTS

- Non-dalmatian dogs with urate uroliths should be evaluated for hepatic disease, even when showing no overt clinical signs of hepatopathy.
- Cats with urate urolithiasis have underlying hepatic disease less commonly than non-dalmatian dogs.

PREVENTION

- Avoid high-protein diets in at-risk dogs (e.g., dalmatian), but severely protein-restricted diets or allopurinol prior to a first episode of urate urolithiasis is not recommended.
- Heritability of tendency to form urate uroliths suggests breeding affected dalmatians should be avoided.
- Long-term dietary +/− allopurinol therapy is indicated for dalmatians after first episode of urolithiasis.

CLIENT EDUCATION

- Urethral obstruction is life threatening. Stranguria should prompt immediate veterinary attention.
- Adherence to dietary therapy must be strict.
- Implications for heritability in dalmatians should be addressed.
- Once dalmatians have formed urate uroliths, preventive therapy should continue lifelong.

SUGGESTED READING

Albasan H, et al: Evaluation of the association between sex and risk of forming urate uroliths in dalmatians. J Am Vet Med Assoc 227:565, 2005.

Bannasch DL, et al: Inheritance of urinary calculi in the dalmatian. J Vet Intern Med 18:483, 2004.

Bartges JW, et al: Canine urate urolithiasis. Etiopathogenesis, diagnosis, and management. Vet Clin North Am Small Anim Pract 29:161, 1999.

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Urolithiasis, Struvite

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Organized concretions within the urinary tract composed of magnesium ammonium phosphate; struvite uroliths occur commonly in both dogs and cats.

SYNONYMS

Magnesium ammonium phosphate stones, struvite calculi/struvite stones, triple phosphate calculi/stones, urease calculi/stones

EPIDEMIOLOGY

SPECIES, AGE, SEX

Dogs:

- The most common urolith of dogs, canine struvite uroliths are usually associated with urinary tract infections (UTI) involving urease-producing bacteria.
- Sterile struvite urolithiasis is rare in dogs.
- Found at any age, they occur nearly twice as often in females as in males, as females are more likely to have UTIs.

Cats:

- The second most common urolith of cats, struvite uroliths are typically found in sterile, alkaline urine.
- Male cats may be at increased risk.
- Compared to calcium oxalate uroliths (most common in cats), cats with struvite uroliths are generally younger (4-7 years of age) and are more likely to be neutered.

GENETICS & BREED PREDISPOSITION

- Dogs: any breed can be affected, but miniature Schnauzers, shih tzus, bichon frises, miniature poodles, cocker spaniels, and Lhasa apsos are overrepresented. Cocker spaniels may form sterile struvite uroliths.
- Cats: commonly affected breeds include the domestic shorthair, foreign shorthair, ragdoll, Chartreux, Oriental shorthair, and Himalayan.

RISK FACTORS

Dogs:

- UTI
- Highly concentrated urine
- Infrequent urination

Cats:

- Highly concentrated urine
- Alkaline urine
- Diets high in magnesium

ASSOCIATED CONDITIONS & DISORDERS

- Dogs: UTI
- Cats: feline lower urinary tract signs/disease (FLUTS/D), urethral obstruction

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Clinical signs often absent. When signs are apparent, they may include:

- Hematuria
- Pollakiuria
- Dysuria
- Stranguria
- Inappropriate elimination (penuria)
- Rarely, systemic illness due to urinary obstruction or to ascending infection causing pyelonephritis

PHYSICAL EXAM FINDINGS: Physical exam is usually unremarkable. Abnormalities may include:

- Hematuria (stains on prepuce, vulva, or hocks)
- Painful urinary bladder
- Palpable cystic calculi
- Palpable urethral calculi (via digital rectal exam in dogs)
- Enlarged turgid bladder, if urethral obstruction
- Renomegaly, if secondary hydronephrosis

ETIOLOGY AND PATHOPHYSIOLOGY

- Infection-associated struvite urolithiasis (mainly dogs):
  - Bacterial urease converts urea to ammonia and bicarbonate
    - The most common urease-producing pathogens are *Staphylococcus* and *Proteus* spp.
    - Other urease-producing pathogens include *Pseudomonas. Klebsiella,* and *Ureaplasma* (urease-producing *Mycoplasmd)* spp.
  - Ammonium binds to phosphorus and magnesium, forming struvite crystals.
  - Bicarbonate increases urine pH.
  - Alkalinity decreases solubility of magnesium ammonium phosphate crystals.
  - Crystals aggregate with organic material (including viable bacteria) and combine to form uroliths.
  - Decreased presence of glycosaminoglycans suggested as a cause in some cases of FLUTS/D.
- Sterile struvite urolithiasis (mainly cats): there appears to be a complex relationship between diet, water intake, individual predisposition and subsequent urine pH and relative supersaturation.
  - Diets high in magnesium, phosphorus, calcium, chloride, and fiber, with moderate protein content may predispose to struvite crystal formation.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is suspected in dogs with radiopaque bladder stones, alkaline urine, and/or urinary infection. The diagnosis is suspected in cats with radiopaque bladder stones, alkaline urine, and/or struvite crystalluria. Quantitative stone analysis is necessary to confirm the diagnosis and provide an optimal treatment/prevention plan.

DIFFERENTIAL DIAGNOSIS

- Urinary tract infection
- Other types of uroliths
- Urinary neoplasia

INITIAL DATABASE

- CBC: unremarkable
- Serum biochemistry profile (including electrolytes): unremarkable unless urinary tract obstruction present (see p. 1131)
- Complete urinalysis: neutral or alkaline (common) urine pH, bacteria (especially likely in dogs), pyuria (especially likely in dogs), hematuria (inconsistent), and crystalluria (inconsistent) are possible.
  - Storage of urine may lead to precipitation of struvite crystals; therefore, urine sediment should be examined within 1 hour of collection.
- Urine culture (identify uropathogen) and susceptibility (influence antimicrobial therapy)
- Abdominal radiographs:
  - Struvite calculi are generally radiopaque (radiopacity: struvite = oxalate = $CaPO_4$ = silica > cystine > urate). o Often smooth or round in shape
  - Most commonly located in bladder, sometimes urethra, ureter, or kidney.

ADVANCED OR CONFIRMATORY TESTING

- Abdominal ultrasound: little benefit beyond abdominal radiography but will confirm location of stones, assess kidneys for evidence of pyelonephritis or hydronephrosis
- Urolith analysis: retrieved stones should be submitted for quantitative analysis (crystallography, x-ray diffraction, infrared spectroscopy) to determine urolith type.
- Urolith culture: retrieved stones can be cultured if urine culture obtained by cystocentesis is negative.

TREATMENT 

TREATMENT OVERVIEW

Although uncommon, urinary tract obstruction requires immediate removal of uroliths. In the absence of urinary obstruction, treatment consists of either a stone-dissolution diet or manual removal of stones as well as treatment of UTI.

ACUTE GENERAL TREATMENT

- Relieve urinary tract obstruction if present (see pp. 1353 and 1355).
- Antibiotics for urinary tract infection, based on culture and susceptibility results (dogs > cats; see see p. 276). Generally, antimicrobial therapy is continued until struvite urolith has dissolved or been removed.
- Choose between medial dissolution and mechanical calculi removal:
    - Urethral obstruction should be relieved mechanically.
    - Mechanical removal allows for urolith analysis, culture.
    - Even large struvite uroliths can be amenable to medical dissolution.
    - Provided urethral obstruction is absent, trial of medical dissolution prior to mechanical removal is reasonable; potential drawbacks include risk of obstruction prior to complete dissolution and ineffective dissolution.
- For medical dissolution, calculolytic diets (see Nutrition/Diet, below) and appropriate antimicrobials are required:
    - Mean time to dissolution is 3 months (less for sterile uroliths, longer time for nephroliths than for cystoliths).
    - Urinalysis and urine culture should be repeated 5-7 days after initiating medical therapy. Goals are urine pH < 7.0, urine specific gravity 1.010-1.020, and negative culture.
    - Medical therapy is continued 1 month beyond radiographic disappearance of uroliths.
    - Small urolith may become lodged in the urethra (especially males) during urolith dissolution.
- Mechanical removal of uroliths:
    - Urohydropropulsion (voiding, retrograde; see pp. 1353 and 1355)
    - Avoid performing voiding urohydropropulsion in male cats.
    - Catheter-assisted retrieval
    - Cystoscopic-assisted retrieval (see p. 1239)
    - Cystotomy/urethrotomy/urethrostomy/pyelotomy/nephrotomy
    - Lithotripsy (intracorporeal or extracorporeal shock wave lithotripsy)

CHRONIC TREATMENT

- Predisposing causes of UTI should be addressed (e.g., control glucosuria in diabetic animals, treat hyperadrenocorticism).
- For animals in which UTI is a recurrent problem, chronic prophylactic therapy may be considered after appropriate therapy of recognized infection (see p. 276).
- Promote water consumption to avoid concentrated urine (e.g., canned food, wetting dry food, use of cat water fountains; see p. 387).
- Dietary therapy is crucial; see Nutrition/Diet, below.
- Urinary acidifiers are seldom required if the pet is eating an appropriate diet and urinary tract infection is eliminated.

NUTRITION/DIET

- Many commercially diets designed to aid in struvite urolith dissolution (e.g., Hill's prescription diet s/d, Innovative Veterinary Diets dissolution formula, Royal Canin SO).
- Monitor urolith size periodically via radiographs (see monitoring).
- Some dissolution diets provide inadequate nutrition for long-term feeding. Calculolytic diet is continued 1 month past radiographic disappearance of uroliths.
- Other diets aid in the prevention of recurrent struvite urolithiasis and can be fed long-term (e.g., Hills Pet nutrition c/d and w/d, Royal Canin SO, Eukanuba Low pH/S/Feline)

POSSIBLE COMPLICATIONS

- Risk of urethral obstruction either from small stones or during medical dissolution as the stones become small enough to pass into the urethra (males):
  - Urinary tract obstruction
  - Hydronephrosis
  - Hydroureter
- Urinary tract infection
- Urinary polyp formation
- Uroliths inadvertently may be left behind during surgery (up to 20% of stones are not removed).
- Some diets appropriate for treatment/prevention of struvite urolithiasis may predispose to calcium oxalate urolithiasis.
- Malnutrition due to long-term feeding of certain dissolution diets

RECOMMENDED MONITORING

- Repeat radiographs every 2-4 weeks during medical dissolution to evaluate the size and number of uroliths.
- If no improvement is seen on radiographs after 4-8 weeks, mechanical removal is indicated.
- Repeat urinalysis 5-7 days after initiating medical dissolution therapy to ensure pH between 6.5 and 7, specific gravity between 1.010 and 1.020, absent struvite crystals, and absent bacteruria.
- Ideally, urine culture is repeated 5-7 days after initiating medical dissolution therapy to ensure sterile urine.
- Repeat urine culture 5-7 days after stopping antibiotics to evaluate for recurrence of infection, then again 3-4 weeks later.
- If predisposing causes of bacterial cystitis cannot be corrected, or in animals with sterile struvite urolithiasis, repeat urinalysis every 4-6 months.
- If predisposing causes of bacterial cystitis cannot be corrected, or in animals with sterile struvite urolithiasis, repeat abdominal radiographs initially every 3-6 months for 1 year, then every 6 months thereafter.

PROGNOSIS AND OUTCOME

- Prognosis for dissolution of uroliths is good.
- Recurrence of struvite urolithiasis is common.

PEARLS & CONSIDERATIONS

COMMENTS

- Struvite urolithiasis in dogs is routinely associated with a UTI. Elimination of infection is crucial for dissolution of stones with a calculolytic diet.
- Struvite urolithiasis in cats is rarely associated with UTI; long-term diet modification is often necessary to prevent recurrence.
- If uroliths fail to resolve with medical therapy, consider:
  - Inadequate infection control
  - Failure to comply with diet restrictions
  - Mixed or alternative urolith composition
- Struvite crystalluria can be found in normal urine and does not reliably predict struvite urolithiasis.

PREVENTION

- Dogs: if urinary infection can be eliminated, long-term diet change is usually not necessary.
- Cats: long-term use of canned struvite-management diets (e.g., Waltham SO or Hills Pet Nutrition c/d or w/d) is best if recurrence noted.
- The merit of supplementing with glycosaminoglycans is unknown.

TECHNICIAN TIPS

Any voided urinary stone should be saved for analysis.

CLIENT EDUCATION

- Adherence to dietary therapy must be strict.
- Urinary tract obstruction is life threatening. Stranguria should prompt immediate veterinary attention.

SUGGESTED READING

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Urolithiasis, Oxalate

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Organized concretions within the urinary tract composed of calcium oxalate; oxalate uroliths occur commonly in both dogs and cats.

SYNONYMS

Jackstones. Calcium oxalate dihydrate crystals: weddellite.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs:

- The relative frequency of calcium oxalate urolithiasis has increased over the last 20 years. Since 2004, they have become the most common canine urolith analyzed at the Minnesota Urolith Center.
- Incidence is greatest in middle-aged to older castrated male dogs. Calcium oxalate uroliths tend to occur at a younger age in bichon frise dogs.

Cats:

- In recent years, calcium oxalate uroliths have become the second most common feline urolith analyzed at the Minnesota Urolith Center.
- Incidence is greatest between 7 and 10 years of age, with males accounting for ~60% of affected cats.

GENETICS & BREED PREDISPOSITION

- Dog breeds at increased risk for developing calcium oxalate stones include the miniature schnauzer, Lhasa apso, Yorkshire terrier, bichon frise, Pomeranian, shih tzu, and miniature poodle.
- Cat breeds at increased risk for forming calcium oxalate stones include the ragdoll, British shorthair, foreign short-hair, Himalayan, Havana brown, Scottish fold, Persian, and exotic shorthair.

RISK FACTORS

- Hypercalcemia
- Acidic urine
- Highly concentrated urine
- Infrequent urination
- Primary hyperparathyroidism
- Hyperadrenocorticism
- Chronic metabolic acidosis
- Obesity
- Diets designed to minimize struvite formation in cats

ASSOCIATED CONDITIONS & DISORDERS: Feline lower urinary tract signs/disease (FLUTS/D), urethral obstruction, chronic kidney disease, urinary tract infection

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Clinical signs are often absent. When clinical signs are apparent, they may include:

- Hematuria
- Pollakiuria
- Dysuria
- Stranguria
- Inappropriate elimination (penuria)
- Rarely, systemic illness due to urinary obstruction

- Polyuria/polydipsia if concurrent hypercalcemia or renal failure

PHYSICAL EXAM FINDINGS: Physical exam is usually unremarkable. Abnormalities may include:

- Hematuria (stains on prepuce, vulva, or hocks)
- Painful urinary bladder
- Palpable cystic calculi
- Palpable urethral calculi (via digital rectal exam in dogs)
- Enlarged, turgid bladder if urethral obstruction
- Renomegaly if secondary hydronephrosis
- Findings associated with predisposing factors (e.g., hyperadrenocorticism: pot-bellied appearance, alopecia, hepatomegaly)

ETIOLOGY AND PATHOPHYSIOLOGY

- Hypercalciuria and/or hyperoxaluria promote formation of calcium oxalate urolithiasis.
- Hypercalciuria may result from increased intestinal absorption of calcium, increased renal excretion of calcium, or increased resorption of calcium from bone with or without hypercalcemia.
- Hypercalcemia is identified in ~35% of cats and ~4% of dogs with calcium oxalate urolithiasis.
- Hyperoxaluria in cats may be related to dietary sources, inadequate vitamin B6, and hepatic enzyme deficiencies.
- Urolith formation is potentiated by diminished concentrations of urinary crystallization inhibitors (e.g., citrate, pyrophosphate, glycosaminoglycans, Tamm-Horsfall mucoprotein).
- Diets with moderate fat and carbohydrate levels are associated with an increased risk of calcium oxalate stone formation, while diets high in moisture with a moderate magnesium, phosphorus, and calcium content result in a diminished risk.

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

Diagnosis is suspected in animals with radiopaque bladder stones and acidic urine, or in animals with radiopaque nephroliths. Quantitative stone analysis is necessary to confirm the diagnosis and identify an optimal treatment/prevention plan.

DIFFERENTIAL DIAGNOSIS

- Urinary tract infection
- Other types of uroliths
- Urinary neoplasia

INITIAL DATABASE

- CBC: unremarkable
- Serum biochemistry profile (including electrolytes) typically unremarkable:
  - Hypercalcemia or evidence of endocrinopathy detected uncommonly
  - Urinary tract obstruction leads to azotemia, hyperkalemia, and metabolic acidosis.
- Urinalysis: acidic to neutral pH unless secondary bacterial infection present; crystalluria (inconsistent); hematuria and/or pyuria (occasional):
  - Storage of urine may lead to precipitation of oxalate crystals (artifact); urine sediment should be examined within 1 hour of collection.
  - Urine culture and sensitivity to rule out secondary infection
- Abdominal/pelvic radiographs: radiopaque calculi most commonly located in bladder, sometimes urethra, ureter, or renal pelvis:
  - Relative radiopacity of uroliths: struvite = oxalate = $CaPO_4$ = silica > cystine > urate
  - Shape varies from spiculated (dihydrate) to smooth (monohydrate), sometimes jackstone.
  - The perineum must be included in the radiographic field in order to see uroliths located in the urethra.

ADVANCED OR CONFIRMATORY TESTING

- Abdominal ultrasound: little benefit beyond abdominal radiography but will confirm location of stones, assess kidneys for evidence of pyelonephritis or hydronephrosis.
- Urolith (stone) analysis: retrieved stones should be submitted for quantitative analysis (crystallography, x-ray diffraction, infrared spectroscopy) to determine urolith type.
- Urolith culture: retrieved stones can be cultured if urine culture obtained by cystocentesis is negative.
- Cystoscopy may facilitate stone removal for analysis and therapy (see p. 1239).

- Specific diagnostic tests may be indicated to identify predisposing conditions (e.g., parathyroid hormone assay).

TREATMENT

TREATMENT OVERVIEW

Although uncommon, urinary obstruction requires immediate removal of uroliths. Oxalate stones cannot be dissolved through medical therapy, so uroliths in the bladder or urethra should be removed mechanically if they are causing clinical signs. Recurrence is common (up to 50% in 3 years in dogs).

ACUTE GENERAL TREATMENT

- Relieve urinary tract obstruction (see pp. 1353 and 1355).
- Antibiotics (choice based on culture and susceptibility) if secondary urinary tract infection is identified
- If uroliths are found incidentally in the absence of clinical signs, it is reasonable to institute preventive measures to minimize growth of uroliths and adopt a program of regular follow-up, including periodic urinalysis, urine culture, and radiography.
- Mechanical removal of bladder/urethral calculi producing clinical signs. Radiographs should be repeated afterwards to ensure complete removal:
  - Urohydropropulsion (voiding, retrograde; see pp. 1353 and 1355)
  - Avoid performing voiding urohydropropulsion in male cats.
  - Catheter-assisted retrieval
  - Cystoscopic-assisted retrieval (see p. 1239)
  - Cystotomy/urethrotomy/urethrostomy/pyelotomy/nephrotomy
  - Lithotripsy (see p. 1297; intracorporeal or extracorporeal shock wave lithotripsy)
- Calcium oxalate is the most common type of nephrolith/ureterolith. Because surgical removal of nephroliths may be associated with loss of renal function (see p. 760), it is not uniformly indicated.

CHRONIC TREATMENT

- Determine whether underlying disorder (e.g., hyperadrenocorticism, hyperparathyroidism) is present, and treat appropriately.
- For cats with idiopathic hypercalcemia, a diet high in fiber may be beneficial. To simultaneously alkalinize the urine, add potassium citrate (75 mg/kg PO q 12 h, adjusted to increase urine pH to 6.5-7.0).
- Initiate measures to prevent recurrence, as described (see Prevention, below).

NUTRITION/DIET

- Avoid calcium supplements.
- Avoid foods high in oxalate.
- Feed reduced protein diets which promote diuresis and formation of alkaline urine. For example, Hill's Pet Nutrition u/d or w/d, Royal Canine Urinary SO, CNM NF-Formula (dogs) or Hill's Pet Nutrition Feline c/d Multicare, Royal Canine Urinary SO, CNM NF-Formula (cats)
- Feed canned food when possible.

POSSIBLE COMPLICATIONS

- Urinary tract obstruction
- Hydronephrosis
- Hydroureter
- Chronic kidney disease (nephrolithiasis)
- Urinary tract infection
- Some diets appropriate for prevention of calcium oxalate urolithiasis may predispose to struvite urolithiasis.

RECOMMENDED MONITORING

- Repeat urinalysis q 2 weeks, starting 2 weeks after removal of stones and initiation of dietary changes until pH is between 6.5 and 7.0, specific gravity is between 1.010 and 1.020, and no calcium oxalate crystals are found. If goals are not met, consider adding supplementary therapies (see Prevention, below).
- Repeat abdominal radiographs and a urinalysis every 3-6 months for the first year, then every 6-12 months thereafter to evaluate for recurrence of uroliths.
- Monitor and treat any concurrent conditions such as hypercalcemia.

PROGNOSIS AND OUTCOME

- Recurrence is common; therefore, long-term monitoring and care are required.
- Nephrolithiasis may be associated with diminished renal function.

PEARLS & CONSIDERATIONS

COMMENTS

- Calcium oxalate urolithiasis frequently recurs. Therefore, long-term management and observation are necessary.
- Calcium oxalate crystalluria does not necessarily correlate with the presence of calcium oxalate uroliths.
- Calcium oxalate dihydrate crystals (square envelope or Maltese cross shape) are more commonly associated with nutritional or artifactual causes, whereas calcium oxalate monohydrate crystals (picket fence board or flattened hexagon shape) are sometimes associated with ethylene glycol intoxication. Calcium oxalate dihydrate crystalluria can be found in normal urine and does not reliably predict oxalate urolithiasis.
- Large quantities of calcium oxalate dihydrate crystals or large crystal aggregates should prompt evaluation of hyperoxaluric or hypercalciuric conditions.
- The appearance of calcium oxalate monohydrate crystals in a dog presenting with acute renal failure is strongly suggestive of ethylene glycol intoxication (see p. 369). Because it is an acute intoxication, ethylene glycol does not lead to oxalate urolithiasis.

PREVENTION

- Treat any identified cause of hypercalcemia/hypercalciuria.
- Initiate measures to prevent recurrence in a stepwise manner, adding the next measure when the first one is found to be insufficient to produce urine with a pH between 6.5 and 7.0, a urine specific gravity between 1.010 and 1.020, or prevent calcium oxalate crystal formation:
    - Promote water consumption (e.g., canned diet, wetted food, water fountains for cats).
    - Provide diet with restricted oxalate, sodium, and protein and which does not acidify the urine (see Nutrition/Diet, above). Potassium citrate can be added if the urinary pH remains acidic. Initial dose of 50-75 mg/kg PO q 12 h is adjusted to maintain urine pH 6.5-7.0.
    - If calcium oxalate crystalluria persists despite prior measures, hydrochlorothiazide (2-4 mg/kg PO q 12 h) or vitamin B6 (2 mg/kg PO q 12 h) can be added.
    - Avoid supplementation of vitamins C and D.
- For male cats with recurrent history of urethral obstruction, consider perineal urethrostomy.

CLIENT EDUCATION

- Adherence to dietary therapy must be strict.
- Urinary tract obstruction is life threatening. Stranguria should prompt immediate veterinary attention.

SUGGESTED READING

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Urolithiasis, Other

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Organized concretions within the urinary tract composed of cystine, calcium phosphate (CaPO4), or silica; these are uncommon to rare in dogs and cats.

SYNONYMS

CaPO4: apatite uroliths. Cystine: cysteine

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Cystine: uncommon in dogs, rare in cats. Onset in middle age; occurs predominantly in males.
- CaPO4: uncommon in dogs, rare in cats. Middle-aged to older. Gender prevalence varies: brushite—mostly males; hydroxyapatite—either sex; carbonate apatite—female. Silica: very rare in dogs. Onset in middle age; males predominate.

GENETICS & BREED PREDISPOSITION: Several breeds are overrepresented for each urolith type:

- Cystine: many dog breeds, including Newfoundland and Labrador (autosomal recessive trait), English bulldog, Siamese cats. Prevalence greater in Europe than in the United States.
- CaPO4: Yorkshire terrier, miniature schnauzer, bichon frise, shih tzu, pug, springer spaniel, Pomeranian, miniature poodle, and cocker spaniel
- Silica: German shepherds, Labrador, boxer, Old English sheepdogs, rottweiler, miniature schnauzer, shih tzu, Lhasa apso, bichon frise, and Yorkshire terrier

RISK FACTORS

- Cystine: renal tubular transport defect
- CaPO4: primary hyperparathyroidism, distal renal tubular acidosis, hypercalcemia

ASSOCIATED CONDITIONS & DISORDERS

- Urethral obstruction
- Urinary tract infection
- Renal dystrophic mineralization
- A link between cystinuria and taurine-deficient dilated cardiomyopathy has been proposed in the Newfoundland dog but remains unproven (cystine is a precursor for taurine synthesis).

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Clinical signs may be absent. If present, they may include:

- Hematuria
- Pollakiuria
- Dysuria
- Stranguria
- Inappropriate elimination (periuria)
- Rarely, systemic illness due to urinary obstruction

PHYSICAL EXAM FINDINGS: Examination is often unremarkable. Abnormalities, if present, may include:

- Hematuria (stains on prepuce, vulva, if present, or hocks)
- Painful urinary bladder
- Palpable cystic calculi

- Palpable urethral calculi (via digital rectal exam)
- Enlarged turgid bladder, if urethral obstruction
- Renomegaly, if secondary hydronephrosis

ETIOLOGY AND PATHOPHYSIOLOGY

- Cystine:
  - Inborn error of metabolism leads to defective renal tubular transport of cystine (± other amino acids) resulting in cystinuria, but not all animals with cystinuria form uroliths.
  - Cystine becomes insoluble in acidic urine.
- CaPO4:
  - Hypercalcemia is contributory but not necessary.
  - Hypercalciuria may occur without hypercalcemia.
  - Factors decreasing the solubility of calcium salts (e.g., urine pH) or promoting crystallization (e.g., deficient inhibitor substances, epitaxy [concentric layered formation of a stone of mixed composition]) also contribute.
- Silica:
  - Poorly understood. May be associated with ingestion of silica-rich feedstuffs such as rice or soybean hulls.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Radiolucent uroliths can be missed by routine abdominal radiography but are often identified via ultrasonography. Confirmation of the specific urolith type, which dictates optimal treatment and prevention, ultimately depends upon analysis of uroliths after removal.

DIFFERENTIAL DIAGNOSIS

- Other types of uroliths (struvite, calcium oxalate uroliths most common)
- Urinary neoplasia
- Urinary tract infection (UTI)

INITIAL DATABASE

- CBC: unremarkable
- Serum biochemical profile: hypercalcemia in some animals with CaPO4 uroliths. If urinary obstruction present, azotemia and electrolyte abnormalities (see p. 1131)
- Complete urinalysis: hematuria, bacteruria, pyuria are found inconsistently.
  - Cystine: aciduria to neutral urine pH; sometimes flat, hexagonal crystals
  - CaPO4: alkaluria (apatite/hydroxyapatite) to neutral to aciduria (brushite); sometimes amorphous or long, thin prism-like crystals
  - Silica: pH variable (solubility not linked to pH)
- Urine culture and susceptibility to rule out UTI
- Abdominal radiographs:
  - Cystine uroliths: radiolucent to slightly radiopaque, round to oval, typically smooth
  - CaPO4 uroliths: radiopaque, round or faceted, smooth
  - Silica uroliths: radiopaque, jackstone (radial spokes from round center)
  - Relative radiopacity: struvite ≥ oxalate = CaPO4 = silica > cystine > urate
- Abdominal ultrasound: confirm/identify radiopaque/radiolucent uroliths, assess kidneys for pyelonephritis, hydronephrosis.
- If urethral obstruction is suspected, catheterization to identify or rule out obstruction.

ADVANCED OR CONFIRMATORY TESTING

- Contrast cystography/urethrography for radiolucent uroliths
- Urolith analysis: retrieved stones should be submitted for quantitative analysis (crystallography, x-ray diffraction, infrared spectroscopy) to determine urolith type
- Cystoscopy may facilitate stone removal for analysis and therapy.
- Screening tests for cystinuria (Metabolic Screening Laboratory, Veterinary Hospital, University of Pennsylvania: www.vet.upenn.edu/penngen)
- Assay of urine calcium excretion rarely used to document hypercalciuria
- Specific tests to identify cause of hypercalcemia, if present (see p. 553)

TREATMENT

TREATMENT OVERVIEW

Although uncommon, urinary obstruction requires immediate removal of uroliths. Appropriate treatment depends upon identification; mechanical removal facilitates identification of these uncommon uroliths. Silica and CaPO4 uroliths are not amenable to medical dissolution.

ACUTE GENERAL TREATMENT

- Relieve urinary tract obstruction if present (see pp. 1353 and 1355)
- Antibiotics for documented urinary tract infection; selection based on culture and susceptibility
- Choose between medical dissolution and mechanical calculi removal:
    - Urinary obstruction should be relieved mechanically.
    - Mechanical removal allows for urolith analysis, culture.
    - Cystine uroliths are amenable to medial dissolution; CaPO4 and silica uroliths are not.
    - Medical dissolution: see Chronic Treatment, below.
- Mechanical removal of calculi:
- Urohydropropulsion (voiding, retrograde; see and)
- Avoid performing voiding urohydropropulsion in male cats.
- Catheter-assisted retrieval
- Cystoscopic-assisted retrieval (see p. 1239)
- Cystotomy/urethrotomy/urethrostomy/pyelotomy/nephrotomy
- Lithotripsy (see p. 1297; intracorporeal or extracorporeal shock wave lithotripsy)

CHRONIC TREATMENT

- Promote water consumption to avoid concentrated urine (e.g., canned food, wetting dry food, use of cat water fountains). Precipitation/concretion of minerals less likely in dilute urine.
- Cystine uroliths: dissolution may require 1-6 months
    - Limit dietary cystine with a restricted protein diet low in methionine (e.g., Hill's u/d). See Nutrition/Diet, below.
    - If urine remains acidic, add potassium citrate (50-150 mg/kg PO q 12 h; dose adjusted to maintain urine pH of 7.0-7.5). Avoid sodium bicarbonate.
    - Solubility of cystine in dogs is increased by administration of *N*-(2-mercaptopropionyl)-glycine (2-MPG)
    - A higher dose (15-20 mg/kg PO q 12 h) promotes urolith dissolution.
    - A lower dose (10-15 mg/kg PO q 12 h) is used to prevent recurrence.
- CaPO4: medical dissolution not possible. After mechanical removal, address conditions causing hypercalcemia when present.
- Silica: medical dissolution not possible. After mechanical removal, decrease consumption of vegetable materials and soil (see Nutrition/Diet, below).

NUTRITION/DIET

-
    - Cystine: Calculolytic diet with restricted protein and low in methionine (e.g., Hills Prescription Diet u/d) fed at least 1 month past dissolution.
    - If an ultra low-protein diet is not appropriate, consider a renal diet (e.g., Hill's k/d) with the addition of potassium citrate to keep the urine pH > 7.2.
    - Low purine diets (e.g., Royal Canine Urinary UC Low Purine, Hill's k/d) can be fed to reduce cystine recurrence.
    - Silica: although dissolution not possible, feeding a diet low in vegetable materials and soil may reduce recurrence (e.g., avoid rice, soybean hulls).

POSSIBLE COMPLICATIONS

- Risk of urethral obstruction (small stones or during medical dissolution of cystine uroliths)
    - Urinary tract obstruction
    - Hydronephrosis
    - Hydroureter
- Urinary tract infection
- Urinary polyp formation
- Uroliths may be left behind during surgery (up to 20% of stones are not removed).
- Cystinuric dogs (especially English bulldogs) fed ultra low-protein diets may be at risk of dilated cardiomyopathy.
- Although uncommon, 2-MPG can lead to aggression, dermatopathy, myopathy, proteinuria, spherocytic anemia,

thrombocytopenia, or increased hepatic enzymes.

RECOMMENDED MONITORING

- Repeat urinalysis 2 weeks after initiation of medical therapy or diet changes, and again every 2-4 weeks thereafter to assess for pH, crystals, specific gravity, or evidence of infection. When pH and specific gravity have met goals (specific gravity < 1.020, pH as appropriate for urolith type), monitoring frequency can be extended to q 3-6 months for a year, then q 6-12 months.
- Imaging (radiographs for $CaPO_4$ and silica; contrast or ultrasound for cystine) should be repeated after mechanical removal or q 2-4 weeks during dissolution (cystine). Thereafter, imaging should be repeated q 6-12 months.
- Urine should be cultured if signs/uroliths recur or an active urine sediment is identified on urinalysis.

PROGNOSIS AND OUTCOME

Because cystinuria is due to a persistent renal tubular defect, recurrence of cysteine urolithiasis is likely without dietary modification ± 2-MPG

PEARLS & CONSIDERATIONS

COMMENTS

All of these uroliths are rare, and only the cystine urolith can be medically dissolved.

PREVENTION

- Promote water consumption (e.g., canned food, wetted food, water fountains).
- Cystine: restricted protein diet, urine alkalinization as necessary, ± long-term use of 2-MPG. Avoid breeding carrier dogs.
- $CaPO_4$: address hypercalcemic disorders directly (e.g., surgical correction of hyperparathyroidism). Avoid low-calcium diets (paradoxic hypercalciuria). Other therapies (e.g., thiazide diuretics, dietary modifications, acidification of urine) may be warranted in cases with multiple recurrences.
- Silica: avoid feedstuffs high in silica (e.g., rice, soybean hulls).

CLIENT EDUCATION

- Adherence to dietary therapy must be strict for urolith dissolution.
- Animals with metabolic defects should not be bred. Genetic tests are available for cystinuria in Newfoundlands and Labradors (University of Pennsylvania).
- Urinary tract obstruction is life threatening. Stranguria should prompt immediate veterinary attention.

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Uroabdomen

BASIC INFORMATION

DEFINITION

A condition characterized by accumulation of urine within the peritoneal and/or retroperitoneal spaces; caused by leakage of urine from the kidneys, ureters, bladder, or proximal urethra

SYNONYMS

Urinary tract rupture, uroperitoneum

EPIDEMIOLOGY

SPECIES, AGE, SEX: May affect all species and ages and both sexes; males may be slightly more predisposed due to anatomic characteristics.

RISK FACTORS: Preexisting compromise of the urinary tract owing to urinary obstruction (urolith[s], neoplasia, other), iatrogenic causes (urethral catheterization, aggressive bladder palpation, surgical complication [laceration or ligation of urinary tract]), or abdominal or pelvic trauma (hit by car, pelvic fractures of any cause, penetrating abdominal wounds)

ASSOCIATED CONDITIONS & DISORDERS

- Hyperkalemia
- Metabolic acidosis
- Septic abdomen (if urine was infected)
- Postrenal azotemia

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Nonspecific lethargy, anorexia, discomfort, vomiting
- Signs identifying or suggesting the underlying cause (e.g., witnessed being hit by a car; worsening pollakiuria due to obstruction)
- Urination: ability to pass urine does not rule out urinary tract rupture or uroabdomen; patient may or may not be hematuric.

PHYSICAL EXAM FINDINGS

- Dehydration
- Abdominal pain:
  - Lack of signs of abdominal pain does not rule out uroabdomen, but because of chemical peritonitis, most are painful.
- Lack of a palpable bladder:
  - Palpable bladder does not rule out urinary tract rupture/uroabdomen (small rupture, but still potentially life threatening).
- Bruising (perineum, ventral abdomen, and inguinal region)
- Depression
- Inappropriate bradycardia (from hyperkalemia):
  - Unlike dogs, cats may have severe hyperkalemia and maintain a normal or elevated heart rate.

ETIOLOGY AND PATHOPHYSIOLOGY

Accumulation of urine in the abdominal cavity results in the following consequences:

- Translocation of solutes that are normally higher in urine concentration (urea, creatinine, potassium, hydrogen) across the peritoneal lining into the extracellular fluid spaces and systemic circulation
- Postrenal azotemia
- Metabolic acidosis
- Hyperkalemia

- Chemical peritonitis

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Definitive diagnosis is based on demonstration of urine in the abdomen. Plasma-to-abdominal fluid gradients of creatinine and potassium are helpful to differentiate uroabdomen from other causes of azotemia and ascites.

DIFFERENTIAL DIAGNOSIS

- Acute abdomen
- Ascites of other causes (e.g., hypoalbuminemic, cardiogenic, hemorrhagic)
- Acute (oliguric/anuric) renal failure

INITIAL DATABASE

- CBC: generally unremarkable
- Serum biochemistry profile: moderate or marked blood urea nitrogen (BUN), creatinine, and potassium elevations as well as low $Hco3^{-}$ are common.
- Urinalysis: cystocentesis not feasible if bladder has collapsed; catheter acceptable if no urethral resistance. Hematuria is most common finding.
- Abdominal radiographs: loss of serosal detail
- Abdominal ultrasound: free abdominal fluid (anechoic); ultrasound contrast cystography may confirm bladder rupture (e.g., bladder bubble study).
- Abdominocentesis, with increased creatinine and potassium of fluid compared with serum

ADVANCED OR CONFIRMATORY TESTING

Positive contrast radiography (cystourethrography [bladder, urethra; see and] or IV excretory urography [kidneys, ureters; see]). The most sensitive method to confirm urine leakage and localize the site of leakage.

TREATMENT

TREATMENT OVERVIEW

The mainstay of treatment is normalization of perfusion and correction of hyperkalemia if present. Once the animal is stable, surgical exploration is usually required for definitive repair. Urethral and ureteral surgery is technically demanding, and transfer of the patient to a center with advanced surgical facilities should be considered.

ACUTE GENERAL TREATMENT

- Intensive fluid therapy to treat shock if present and correct severe dehydration:
  - Fluid without potassium is recommended as an initial choice (e.g., 0.9% NaCl)
  - High fluid rates are often necessary for dehydration correction or for management of postobstructive diuresis.
  - Fluid type and rate are continually reassessed based on physical monitoring and serial electrolyte levels.
- If the patient's potassium > 7-8 mEq/L and/or there are clinical (e.g., bradycardia) or electrocardiographic (ECG) (e.g., no P waves in all ECG leads) changes due to hyperkalemia, immediate medical therapy and stabilization is required (see p. 556).
- For animals with lower urinary tract injury and urine accumulation in the peritoneal space:
  - Placement of peritoneal drainage catheter (see p. 1192; simple and life-saving!).
  - Placement of urethral catheter (bladder decompression and prevention of further urine leakage)
  - Placement of prepubic tube cystostomy in animals with severe urethral trauma
  - Analgesia and sedation as indicated, nonsteroidal antiinflammatory drugs should be avoided until azotemia has resolved and renal function has normalized.
  - If urinary tract infection is suspected, broad spectrum antimicrobial drugs are indicated. Every effort should be made to collect urine for culture, and ongoing antimicrobial usage should be guided by culture and sensitivity.

CHRONIC TREATMENT

- Fluid therapy to replace ongoing losses, including the presence of postobstructive diuresis

- Surgical correction of the site of leakage

NUTRITION/DIET

All animals with uroabdomen, but especially cats, can have a long recovery from surgery. Consideration should be given to the placement of a feeding tube (nasoesophageal or esophageal; see and) at the time of surgery.

DRUG INTERACTIONS

Do not add potassium chloride (KC1) to IV fluids until serum potassium level is known to be normal or low.

POSSIBLE COMPLICATIONS

- Obstruction of the peritoneal drainage catheter with omentum
- Injury to other intraabdominal structures during placement of peritoneal drainage catheter
- Urethral stricture formation and urinary incontinence
- Persistent renal insufficiency

RECOMMENDED MONITORING

- Frequent monitoring of vital signs, including blood pressure (BP)
- ECG monitoring if hyperkalemia
- Fluid input and urine output from both peritoneal drainage and urethral catheters q 2-4 h
- Serum chemistry, venous blood gas (VBG), packed cell volume (PCV) q 8-12 h during initial stabilization
- Patient's weight q 12 h

PROGNOSIS AND OUTCOME 

- Prognosis is good with early diagnosis, aggressive emergency management, and definitive repair.
- The mortality rate is increased in animals with concurrent injuries or underlying neoplasia.

PEARLS & CONSIDERATIONS 

COMMENTS

- Consider uroabdomen in animals with a history of abdominal or pelvic trauma, urinary obstruction, or urethral catheterization.
- A palpable bladder and the ability to void urine do not rule out uroabdomen, because animals with urinary tract disruption may continue to urinate.
- The abdominal fluid obtained is serosanguineous and may not look like urine; creatinine and potassium concentrations of the fluid are diagnostic when compared to serum levels.
- Asepsis (urethral and peritoneal drainage catheters, sterile collection system) is essential for preventing complications secondary to infection.
- In dogs and cats, lower urinary tract injuries are more common than renal/ureteral injuries. Therefore, contrast cystography and retrograde urethrography take precedence over intravenous excretory urography.
- Surgical repair should not be attempted until the animal has been stabilized with fluid therapy and abdominal drainage.

TECHNICIAN TIPS

Fluid therapy is a challenge in these patients, and accurate recording of fluid administration and fluid output are crucial. Patients with uroabdomen often have concurrent disease or injuries and may have a long recovery period; adequate attention to analgesia and nutrition can be of huge benefit to their recovery.

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1ST EDITION AUTHOR: KRISTI GANNON

Urinary Bladder and Urethral Rupture

BASIC INFORMATION

DEFINITION

Traumatic rupture of the urinary bladder and/or urethra.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Urethral trauma more common in males

RISK FACTORS

- Ability to roam freely
- Blunt trauma (e.g., vehicular accident, kicks, falls)
- Penetrating injury (e.g., gunshot wound, cystocentesis)
- Pelvic fracture
- Fracture of the os penis
- Urolithiasis
- Lower urinary tract obstruction
- Urethral catheterization
- Urogenital surgery

ASSOCIATED CONDITIONS & DISORDERS

- Azotemia/uremia
- Hyperkalemia

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Precipitating event (e.g., trauma, penetrating injury)
- Dysuria or anuria (common); ability to produce urine stream does not rule out urinary bladder rupture.
- Hematuria (common)
- Vomiting (common)
- Depression (common)
- Anorexia (common)
- Abdominal pain (may not be noticed by owners)
- Urethrocutaneous fistula (uncommon; chronic)

PHYSICAL EXAM FINDINGS

- Abdominal effusion (especially with bladder rupture)
- Caudal abdominal pain (especially common with bladder rupture)
- Dehydration (common)
- Depression (common)
- Dysuria (especially common with urethral rupture)
- Halitosis (with uremia)
- Hematuria (especially common with urethral rupture)
- Hypovolemia secondary to urine peritonitis/uroabdomen
- Inability to palpate bladder (especially common with bladder rupture)
- Pelvic fracture (sometimes present when trauma causes urinary tract rupture)
- Stranguria (especially common with urethral rupture)
- Uremic oral ulcers +/−
- Ventral abdominal wall or perineal bruising +/−

ETIOLOGY AND PATHOPHYSIOLOGY

- Blunt external trauma, penetrating projectiles, perforation by fracture fragments
- Iatrogenic: secondary to catheterization, cystocentesis, or other diagnostic procedure errors; forceful bladder expression
- Intraperitoneal accumulation of urine results in chemical peritonitis, azotemia, hyperkalemia, and acidemia; death may occur in 3-5 days if animal is left untreated.
- Extraperitoneal accumulation of urine results in cellulitis and tissue death acutely and may result in formation of urethrocutaneous fistulas if the rupture is not treated.
- See Uroabdomen, .

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Urinary tract rupture should be suspected in animals with uremia and dysuria/oliguria, especially after either abdominal trauma or suspected urethral obstruction. Whereas animals with simple urethral obstruction often have large bladders, the bladder may be small or nonpalpable in animals with urinary bladder rupture.

DIFFERENTIAL DIAGNOSIS

- Bladder rupture:
  - Urinary tract infection
  - Urine leakage from upper urinary tract
  - Other causes of peritonitis
- Urethral rupture:
  - Urinary tract obstruction due to urolithiasis, neoplasia, granulomatous urethritis, or prostatic disease
  - Periurethral hematoma or abscess

INITIAL DATABASE

- CBC:
  - Initially unremarkable, progressing to neutrophilic leukocytosis, often with left shift as urinary peritonitis develops
- Serum biochemical profile:
  - Azotemia common
  - Hyperkalemia worsens with time (may be life threatening; i.e., >8 mEq/L)
  - Metabolic acidemia common
- Abdominal/pelvic radiographs:
  - Loss of serosal detail as urine accumulates in peritoneal space
  - Pelvic or os penis fracture occasionally identified
- Abdominocentesis (see p. 1193) or peritoneal lavage (see online chapter: Diagnostic Peritoneal Lavage) with fluid analysis:
  - Compare fluid and serum creatinine; fluid creatinine 2× greater than serum creatine is strongly supportive of urinary tract rupture.
  - Abdominal fluid potassium 4× greater than serum potassium also strongly supportive.
- Urethral catheterization should normally encounter no friction/resistance.

ADVANCED OR CONFIRMATORY TESTING

- Positive-contrast urethrocystogram (see pp. 1357 and 1237)
- Ultrasonography

TREATMENT

TREATMENT OVERVIEW

Rupture of the bladder or urethra represents an urgent problem. Immediate therapy is aimed at stabilization of fluid, electrolyte and acid-base disturbances, with a goal of restoring urinary tract integrity via surgical intervention or temporary urinary diversion while smaller tears in the urinary tract heal on their own.

ACUTE GENERAL TREATMENT

- Temporary urinary diversion by transurethral catheter or cystostomy tube
- Correct electrolyte and acid-base disturbances:

    - If potassium >7 mEq/L, consider one or more of the following (see p. 556):
        - Regular crystalline insulin (¼ unit/kg IV bolus) with IV dextrose (2 g dextrose/unit insulin over 6 hours IV; 50% dextrose is 0.5 g/mL, 5% dextrose is 0.05 g/mL. Generally administered as 5% dextrose infusion; dextrose concentrations >10% can cause phlebitis).
        - Sodium bicarbonate: 1 mEq/kg IV bolus
        - Calcium gluconate (10% solution): 1 mL/kg slow IV bolus (cardio-protective)
            - Monitor electrocardiogram (ECG) and stop infusion if new arrhythmia occurs.
    - If pH < 7.1, institute sodium bicarbonate therapy:
        - Calculate bicarbonate deficit: [(0.3) × (BW in kilograms) × (base deficit)]. Base deficit is (24 -patient's $Hco3^-$) in milliequivalents per liter.
        - Administer half of deficit in IV fluids over 6 hours.
- Provide crystalloid fluids at an adequate rate:
    - Rehydration: % dehydration* × body weight (kilograms) = deficit (liters); the asterisk sign* for this equation refers to dehydration entered as a decimal, so 10% is 0.1, 7% is 0.07, and so on.
    - Maintenance: 60 mL/kg per day
    - Ongoing loss: estimate loss from vomiting, third-space loss, and other such losses.
- Abdominocentesis (see p. 1193) or peritoneal lavage to decrease the effects of uroabdomen
- Primary repair of rupture or conservative management by urine diversion until adequate healing occurs:
    - Primary repair:
        - Bladder ruptures due to blunt trauma; complete abdominal exploration
        - Complete urethral transections
    - Conservative management by urine diversion:
        - Small bladder perforations (e.g., from catheter trauma)
        - Incomplete urethral lacerations
        - Bladder rupture: urethral catheter ± peritoneal lavage catheter
        - Urethral rupture: urethral catheter or cystostomy tube

CHRONIC TREATMENT

- Antimicrobial therapy for bacterial cystitis may be necessary after urinary diversion catheter is removed.
- Stricture formation or urethral dehiscence postoperatively may necessitate antepubic urethrostomy.

POSSIBLE COMPLICATIONS

- Cardiac bradyarrhythmia due to hyperkalemia
- Urinary tract infection as a result of urinary catheterization
- Continued leakage after surgical correction

URETHRAL STRICTURE RECOMMENDED MONITORING

- Positive-contrast urethrocystography after conservative management to assess adequacy of healing and identify formation of any strictures
- Observation of animal for dysuria or stranguria
- Urinalysis and/or urine culture after removing urinary diversion catheter

PROGNOSIS AND OUTCOME

- Good to excellent for bladder rupture and incomplete urethral transection
- Guarded to good with complete urethral transection, especially if complicated by urethrocutaneous fistula formation

PEARLS & CONSIDERATIONS

COMMENTS

- Emergency surgery to repair bladder or urethral rupture is rarely necessary if urinary diversion can be established.
- Address life-threatening shock and metabolic disorders prior to surgery.

PREVENTION

Avoid excessive force during bladder expression or catheterization.

TECHNICIAN TIPS

Urinary bladder rupture is possible with aggressive manipulation, especially when urinary obstruction is present. Do not attempt manual bladder expression against firm resistance.

CLIENT EDUCATION

- Do not allow pets to roam.
- Dysuria/stranguria can indicate a life-threatening problem and warrant rapid veterinary evaluation.
- Dysuria and/or stranguria after treatment of urinary tract rupture could indicate stricture formation.

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Urethral Sphincter Mechanism Incompetence

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Urethral sphincter mechanism incompetence is a common cause of involuntary voiding of urine (urinary incontinence). It is most frequently identified in ovariohysterectomized bitches.

SYNONYMS

Estrogen-responsive or hormone-responsive incontinence, hormone-responsive urethral incompetence

EPIDEMIOLOGY

SPECIES, AGE, SEX: Middle-aged female dogs predominantly affected, although hormone-responsive incontinence can occur in bitches of any age and occurs rarely in neutered males. Onset of incontinence may be months to years after ovariohysterectomy (OHE).

GENETICS & BREED PREDISPOSITION: Usually medium- to large-breed dogs. A positive association between tail docking and hormone-responsive incontinence has been demonstrated. Over-represented breeds include boxer, Doberman pinscher, German shepherd, Old English sheepdog, rottweiler, springer spaniel, weimaraner

RISK FACTORS: Intrapelvic bladder, short urethra, and obesity. Often occurs in association with ectopic ureter. Any cause of polyuria may initiate or exacerbate clinical signs.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Urinary incontinence, often most evident during rest (i.e., patients leave “puddles” after sleeping)
- Excessive licking of perineum
- Dogs retain ability to produce normal voluntary urine stream.

PHYSICAL EXAM FINDINGS

- Usually unremarkable. Complete neurologic examination should be conducted, including evaluation of tail and anal tone.
- Observed episode of urination is normal; bladder will empty nearly completely after voluntary voiding.
- Perineal urine staining or perivulvar dermatitis sometimes observed.

ETIOLOGY AND PATHOPHYSIOLOGY

- The vast majority of neutered dogs remain continent. It is unclear why only a minority of neutered bitches develop urethral sphincter mechanism incompetence.
- Sex hormones apparently sensitize the internal urethral sphincter to the effects of α-adrenergic stimulation.
- The bladder may be positioned in a relatively caudal position in neutered bitches, lessening the intraabdominal pressures on the urethra that help maintain urethral closure.
- Urethral sphincter mechanism incompetence is commonly found in intact dogs with ectopic ureter, and may account for continued incontinence after surgical correction of ectopia.

DIAGNOSIS

DIAGNOSTIC OVERVEIW

The diagnosis is suspected when an otherwise healthy neutered bitch develops urinary leakage, especially during sleep. Ruling out other causes of incontinence and response to therapy are usually used to confirm the diagnosis.

DIFFERENTIAL DIAGNOSIS

- For inappropriate urination, distinguish between urinary incontinence and pollakiuria, polyuria, or behavioral disorders.
- Differentials for urinary incontinence: lower motor neuron disease/peripheral neuropathy; upper motor neuron disease; dysautonomia; urge incontinence; partial urethral obstruction; and congenital and acquired urinary tract structural defects (ectopic ureter[s], vaginal stricture/stenosis, urethrovaginal fistula).

INITIAL DATABASE

- Complete neurologic examination (see p. 1311): normal
- CBC and serum biochemistry profile: unremarkable
- Complete urinalysis: occasionally reveals evidence of secondary urinary tract infection
- Urine culture: to rule out urinary tract infection
- Abdominal radiographs or ultrasound of urinary structures: unremarkable, or bladder may display intrapelvic positioning.

ADVANCED OR CONFIRMATORY TESTING

- Contrast studies (see p. 1357) and/or cystoscopy (see p. 1239): not routinely required, but can rule out structural causes of urinary incontinence.
- Urethral pressure profile (UPP) and/or leak point pressure (requires specialized equipment/expertise): not routinely employed for clinical diagnosis but can objectively identify urethral sphincter incompetence. May have prognostic utility in animals with ectopic ureter to predict resolution of incontinence after surgical correction.
- Positive response to therapy is often used for supporting the diagnosis, but interpretation of result should be cautious because optimal response may require dosage adjustment over weeks.

TREATMENT

TREATMENT OVERVIEW

Medical treatment with either phenylpropanolamine or hormone therapy usually results in control of incontinence. Endoscopic and surgical therapies are also options.

ACUTE GENERAL TREATMENT

- If polyuria is identified, the cause should be sought and treatment instituted (underlying cause is likely not hormone-responsive incontinence alone or at all).
- Medical therapy with phenylpropanolamine or estrogen compounds
- Treatment of secondary urinary tract infection with appropriate antimicrobials

CHRONIC TREATMENT

- Phenylpropanolamine is an α-agonist sympathomimetic used for increasing internal urethral sphincter tone. Available as chewable tablets or oral solution (1-1.5 mg/kg PO q 8-12 h) or as time-released 75-mg capsules (<40 lb: ½ capsule daily; dogs 40-100 lb: 1 capsule daily; >100 lb: 1.5 capsules daily). Discontinue if anxiety, hyperactivity, or tachycardia.
- Diethylstilbestrol (DES) is a synthetic estrogen that increases sensitivity of internal urethral sphincter to catecholamines. Dosage is empirical, with reduction in frequency and dose to least possible that controls clinical signs. Starting dose: 0.1 mg (small dog), 0.3 mg (medium dog), or 0.7 mg (large dog) total daily dose PO q 24 h for 3-5 days. Then the same dose is given q 5-8 days as needed to control incontinence.
- Conjugated estrogens (e.g., Premarin, 20 mcg/kg PO q 4 days) have been used in place of DES.
- Testosterone cypionate (2.2 mg/kg IM q 30 days) can be used in castrated males (but phenylpropanolamine is preferred).
- Gonadotropin releasing hormone (GnRH) analog can be used in place of DES but is less effective than phenylpropanolamine.
- Hormones may be administered concurrently with phenylpropanolamine when incontinence persists despite therapy (synergistic actions).
- Surgical therapies are usually reserved for refractory patients:
    - Cystoscopically administered periurethral injections of collagen or Teflon; may need to be repeated
    - Adjustable hydraulic urethral sphincter placed at surgery
    - Colposuspension, cystourethropexy, urethroplasty, or urethral intussusception

DRUG INTERACTIONS/CONTRAINDICATIONS

- Hormone therapy may cause adverse reactions: estrogen compounds (e.g., bone marrow suppression), testosterone (e.g., prostatomegaly, behavioral changes)
- AVOID estradiol cypionate because of increased risk of marrow suppression.

- Phenylpropanolamine may cause adverse reactions (e.g., lethargy, decreased appetite, GI upset, hyperactivity, hypertension). Use with caution or avoid if there is systemic hypertension, heart disease, cardiac arrhythmias, central nervous system disease, or if monoamine oxidase inhibitors or other sympathomimetic agents are used.

POSSIBLE COMPLICATIONS

Secondary urinary tract infection

RECOMMENDED MONITORING

- Periodic urinalysis with Gram stain of sediment and/or bacterial culture and sensitivity if incontinence persists
- Periodic monitoring of blood pressure in dogs treated with phenylpropanolamine
- Periodic monitoring of CBC in dogs treated with estrogen drugs

PROGNOSIS AND OUTCOME

Most dogs respond to medical therapy with improvement or resolution of clinical signs. Some dogs require more than a single type of medication, and ancillary surgical procedures may be required in some cases.

PEARLS & CONSIDERATIONS

COMMENTS

- Hormone-responsive urinary incontinence is a common cause of urinary incontinence.
- Diagnosis usually based on clinical presentation, ruling out other common causes of incontinence, and response to therapy.
- Minimal evaluation includes neurologic examination, observation of urination and palpation of bladder afterwards, urinalysis and urine culture, and imaging of the urinary tract with radiographs or ultrasound.

PREVENTION

Hormone-responsive incontinence occurs in only a small percentage of ovariohysterectomized bitches. There is little evidence that early neutering increases likelihood of developing incontinence.

SUGGESTED READING

Barth A, et al: Evaluation of long-term effects of endoscopic injection of collagen into the urethral submucosa for treatment of urethral sphincter incompetence in female dogs: 40 cases (1993-2000). J Am Vet Med Assoc 226:73–76, 2005.

Byron JK: Effect of phenylpropanolamine and pseudoephedrine on the urethral pressure profile and continence scores of incontinent female dogs. J Vet Intern Med 21:47–53, 2007.

Rose SA, et al: Long-term efficacy of a percutaneously adjustable hydraulic urethral sphincter for treatment of urinary incontinence in four dogs. Vet Surg 38:747–753, 2009.

AUTHOR & EDITOR: LEAH A. COHN

Urethral Prolapse

BASIC INFORMATION

DEFINITION

Prolapse of urethral mucosa from urethral orifice

EPIDEMIOLOGY

SPECIES, AGE, SEX: Young, intact male dogs

GENETICS & BREED PREDISPOSITION: English bulldog

RISK FACTORS

- Intact male dog
- Brachycephalic breed

ASSOCIATED CONDITIONS & DISORDERS: Brachycephalic airway syndrome

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Excessive licking of prepuce or penis
- Blood from preputial opening
- Stranguria

PHYSICAL EXAM FINDINGS

- Hemorrhagic discharge from prepuce
- Red or purple mass protruding from urethral orifice
- A prolapsed urethra typically appears as a small red bulb of smooth, congested (red) mucosa at the tip of the penis surrounding the urethral opening.

ETIOLOGY AND PATHOPHYSIOLOGY

Possible causes include:

- Excessive sexual excitement
- Masturbation
- Genitourinary infection
- Urolithiasis

Secondary swelling of the prolapsed segment prevents spontaneous reduction.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is based on patient signalment, presenting history, and physical examination findings.

DIFFERENTIAL DIAGNOSIS

- Penile trauma
- Urethritis
- Neoplasia (transmissible venereal tumor [TVT])

INITIAL DATABASE

- Presurgical CBC, serum chemistry profile: generally unremarkable
- Urinalysis (cystocentesis) ± microbiologic culture:
    - Rule out associated urinary tract infection (UTI), prostatic disease.

ADVANCED OR CONFIRMATORY TESTING

- Impression smear of prolapsed tissue for cytologic examination:
    - Rule out TVT
- Abdominal ultrasound examination:
    - Rule out prostatic disease

TREATMENT

TREATMENT OVERVIEW

The prolapsed urethral mucosa requires surgical correction. Postoperatively appropriate measures should be taken to prevent recurrence of the problem.

ACUTE GENERAL TREATMENT

Surgical correction of prolapsed urethra:

- Urethropexy technique: inversion of urethral mucosa using several mattress sutures

CHRONIC TREATMENT

- Prevent masturbation in the immediate postoperative period.
- Treat UTI, prostatic disease, and urolithiasis if present.
- Consider castration to reduce sexual arousal:
    - Dog should not be used for breeding purposes because of genetic predisposition.

POSSIBLE COMPLICATIONS

Recurrence of prolapse after surgical correction

RECOMMENDED MONITORING

Observe animals for recurrence of bleeding from prepuce; the signs may indicate recurrence of prolapse.

PROGNOSIS AND OUTCOME

Excellent prognosis with appropriate surgical technique

PEARLS & CONSIDERATIONS

COMMENTS

The hallmark of diagnosis is the physical finding of a red bulb-like mass at the tip of the penis in a patient with stranguria or penile self-trauma.

PREVENTION

- Recognize genetic predisposition for the problem: English bulldog.
- Early castration to reduce sexual activity or excitement
- Prevention of masturbation
- Prevention of obesity

TECHNICIAN TIPS

Perioperative in-hospital care consists of:

- Preoperative prevention of additional trauma to prolapsed urethra
- Sedation, Elizabethan collar
- Postoperative prevention of trauma to surgical site (see above)
- Ensuring that adequate analgesia is provided in the postoperative period

CLIENT EDUCATION

- Early castration in predisposed breeds to reduce sexual activity or excitement
- Prevention of masturbation and self-trauma to penis
- Avoid circumstances that would exacerbate respiratory problems in brachycephalic dogs:
  - Obesity
  - Stress
  - Heat, humidity

SUGGESTED READING

Kirsch JA, Hauptman JG, Walshaw R: A urethropexy technique for surgical treatment of urethral prolapse in the male dog. J Am Anim Hosp Assoc 38:381–384, 2002.

AUTHOR & EDITOR: RICHARD WALSHAW

Urethral Obstruction

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

A common condition that involves obstruction of the lower urinary tract, usually due to urolith or matrix formation. Other causes (e.g., neoplasia, stricture, infections) are less common.

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Cats and less commonly dogs of any age
- Males are anatomically predisposed to obstruction.

GENETICS & BREED PREDISPOSITION

- Certain breeds predisposed to specific urolith formation (e.g., Dalmatians: urate uroliths)
- Other breed predisposed to urethral neoplasia (e.g., Scottish terrier)

RISK FACTORS

- Feline lower urinary tract signs/disease (FLUTS/D)
- Neoplasia
- Urinary tract infection
- Risk factors associated with urolithiasis (see pp. 1138, 1141, 1143, and 1145)

ASSOCIATED CONDITIONS & DISORDERS

- Hydronephrosis
- Azotemia/uremia
- Hyperkalemic cardiac dysrhythmia
- Urinary bladder rupture
- Bladder atonia/hypotonia
- Urinary tract infection
- Post obstructive diuresis

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Stranguria
- Anuria/oliguria
- Hematuria
- Lethargy
- Anorexia
- Vocalization
- Restlessness
- Dribbling urine
- Licking prepuce/vulva (urethral discharge)
- Dyschezia
- History of urinary infection or urolithiasis

PHYSICAL EXAM FINDINGS

- Enlarged, turgid urinary bladder (characteristic)
- Abdominal discomfort (common)
- Dribbling urine (occasionally)

- Bloody preputial/vulvar discharge (occasionally)
- Palpable urethral urolith or tumor (digital rectal exam in dogs) (occasionally)
- Bradycardia if severe hyperkalemia (in very advanced cases)

ETIOLOGY AND PATHOPHYSIOLOGY

- Urine supersaturation, urinary tract infection, certain disease states, and breed predisposition contribute to urolithiasis.
- In cats especially, urethral plugs may be composed of matrix (cellular debris, virus-like particles, +/− bacteria, urinary crystals).
- Uroliths or plugs can obstruct the urethra; urethral anatomy favors obstruction in males.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis of urethral obstruction is suspected in any patient that is straining to urinate and has an enlarged, firm urinary bladder present on abdominal palpation.

DIFFERENTIAL DIAGNOSIS

- Detrusor atony
- FLUTS/D
- Fungal granulomas
- Reflex dyssynergia
- Trauma (pelvic fracture) with urethral damage, bladder entrapment hernia, penile fracture
- Urethral neoplasia
- Urethral stricture
- Urethral tissue valve/flap
- Urethritis
- Urolithiasis

INITIAL DATABASE

- CBC: unremarkable
- Serum biochemical profile: possible azotemia, hyperkalemia, findings consistent with predisposing conditions
- Urethral catheterization: distinguish functional from structural urethral obstruction, localize structural obstruction, may relieve obstruction and provide urine for analysis
- Urinalysis: possible hematuria, crystalluria, pyuria, epithelial cells, dilute urine, bacteruria. Rarely, fungal hyphae or neoplastic cells
- Urine culture: if sample is obtained by catheterization, quantitative culture to distinguish contamination ($<10^3$ colony-forming units/mL) from infection
- Abdominal/pelvic radiographs: distended urinary bladder, possible radiopaque uroliths, renomegaly, ascites
- Abdominal ultrasound: possible uroliths, urinary bladder debris, pyelectasia, ascites
- Electrocardiogram: hyperkalemia signs (absent P waves, wide QRS complexes, bradycardia)

ADVANCED OR CONFIRMATORY TESTING

- Voiding cystourethrogram: determine location of urethral obstruction
- Retrieved uroliths: quantitative analysis, culture
- Other testing for conditions predisposing to urolith formation (e.g., bile acids as screen for portosystemic shunt)

TREATMENT

TREATMENT OVERVIEW

Treatment consists of relieving the urinary obstruction. This is generally done by passing a urinary catheter into the urinary bladder and draining the urine.

ACUTE GENERAL TREATMENT

- Intravenous catheter for crystalloid fluid therapy, correcting electrolyte disorders, and administering sedation/anesthesia:
  - Crystalloid fluids: 5-10 mL/kg/h during sedation/anesthesia
  - Thereafter, rate should provide maintenance (60 mL/kg q 24 h), correct dehydration, and match postobstructive diuresis losses.
    - Closed urine collection system to identify profound postobstructive diuresis, maintain sterility, and allow "ins-and-outs" fluid treatment plan
  - If serum potassium >7 mEq/L, consider calcium gluconate, sodium bicarbonate, or insulin/dextrose therapy (see pp. 31 and 556).
- Small plug/urolith at the tip of the penis: remove via gentle massage (cats)
- Urethral catheterization can be attempted without sedation in male dogs; in cats, bitches, or dogs resistant to catheterization, sedation/anesthesia is usually required (see pp. 1266, 1353, and 1355).
- Insert a sterile red rubber catheter or open-ended polypropylene catheter into the urethra to the point of obstruction. Once encountered, retropulse the urolith/debris into the urinary bladder using sterile saline or a 75% sterile saline and 25% sterile water-based lubricant mixture.
  - In male cats, a sterile 22-G, 1-inch intravenous catheter (without stylet) may be used to dislodge urethral plug.
  - The urinary bladder is emptied; if debris is identified, lavage with sterile saline.
- An indwelling urinary catheter attached to a sterile, closed urine collection system is often indicated (e.g., pending correction of anatomic or functional obstruction, in cats with FLUTS/D, or to prevent urolith movement back into urethra following retropulsion and pending cystotomy).
  - For indwelling purposes, polypropylene catheters should be replaced with red rubber or Foley catheters.
  - Ideally, radiographs are obtained to identify remaining radiopaque urethral/bladder uroliths and to evaluate appropriate catheter placement. The catheter should just enter the trigone.
- If a urinary catheter cannot be passed, periodic cystocentesis can be performed to temporarily empty the urinary bladder pending definitive treatment.
- See Urethral Obstruction (Canine): Medical Management, ; Urethral Obstruction (Feline): Medical Management, .

CHRONIC TREATMENT

- Maintain indwelling urinary catheter appropriately (sterile, closed collection system):
  - Typically for 24-72 hours in cats with crystalluria or FLUTS/D
- Phenoxybenzamine (dog: 0.25 mg/kg PO q 12 h; cat: 2.5 mg/cat PO q 12-24 h) may decrease urethral spasm.
- Antibiotic therapy based on urine culture/sensitivity; obtain culture when removing catheter.
- Address urolithiasis:
  - Diet/medical dissolution possible for some types, but risk of repeated obstruction
  - Consider cystotomy, urohydropulsion (voiding, retrograde), cystoscopic-assisted retrieval.
- Perineal urethrostomy considered for male cats (or dogs) with recurrent obstruction
- Tube cystostomy for urethral neoplasia while waiting for chemotherapy to work

POSSIBLE COMPLICATIONS

- Urethral tear
- Urinary bladder rupture
- Urethritis
- Iatrogenic urinary tract infection
- Urethral stricture
- Recurrent urinary tract infections with perineal urethrostomy and tube cystostomy

RECOMMENDED MONITORING

- Daily bladder palpation during hospitalization after removing urinary catheter
- Repeat urinalysis and urine culture when urinary catheter is removed and again 1 week later.
- Monitor as appropriate for urolith type or FLUTS/D (see p. 1555).

PROGNOSIS AND OUTCOME

- Urethral obstruction is rapidly life threatening.
- If obstruction is alleviated and electrolyte disorders are addressed, prognosis is good (exception: neoplasia).
- Risk for recurrence is present regardless of cause.

PEARLS & CONSIDERATIONS

PREVENTION

Dietary/medical therapy are indicated when uroliths are identified. Predisposing factors for urolith formation should be addressed directly whenever possible.

TECHNICIAN TIPS

- Overly aggressive attempts at manual expression of the bladder must be avoided because bladder rupture can result.
- Straining to urinate without producing a urine stream is highly suggestive of urethral obstruction.

CLIENT EDUCATION

- Urinary tract obstruction is life threatening. Stranguria or dysuria should prompt immediate veterinary attention.
- Adherence to dietary therapy for urolith dissolution must be strict.

SUGGESTED READING

Bartges JW, et al: Pathophysiology of urethral obstruction. Vet Clin North Am Small Anim Pract 26:255, 1996.

Lekcharoensuk C, et al: Evaluation of trends in frequency of urethrostomy for treatment of urethral obstruction in cats. J Am Vet Med Assoc 221:502, 2002.

Osborne CA, et al: Medical management of feline urethral obstruction. Vet Clin North Am Small Anim Pract 26:483, 1996.

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Ureteral Obstruction

BASIC INFORMATION

DEFINITION

Obstruction of urine flow through one or both ureters. Ureteral obstruction is recognized with increasing frequency, especially in cats.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs or cats of any age or sex

RISK FACTORS

- Intraluminal obstruction (e.g., urolith, trauma, inflammation, fibrosis/stricture, congenital stenosis, blood clots)
- Intramural obstruction (e.g., fibrosis/stenosis, ureterocele, fibroepithelial polyps, proliferative ureteritis, neoplasia)
- Extramural obstruction (e.g., retroperitoneal or pelvic masses, prostatic/bladder neoplasia, inadvertent ligation or fibrotic entrapment of ureter)

ASSOCIATED CONDITIONS & DISORDERS

- Renal failure +/− uremia
- Hydronephrosis/hydroureter
- Pyelonephritis
- Uroabdomen (associated with ruptured ureter)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Partial or complete
- Unilateral or bilateral

HISTORY, CHIEF COMPLAINT: Clinical signs are often absent, especially with unilateral obstruction. When signs are present, they may be related to acute renal failure or to overt chronic kidney disease. Any of these may be seen:

- Lethargy/depression (due to uremia or renal pain)
- Anorexia/vomiting (due to uremia or renal pain)
- Polyuria and polydipsia (with chronic kidney disease)
- Dysuria, stranguria, pollakiuria, or hematuria
- Oliguria or anuria (bilateral obstruction)

PHYSICAL EXAM FINDINGS: Physical examination is often normal; abnormalities can include:

- Dehydration
- Poor body condition
- Enlarged kidney(s) (due to hydronephrosis)
- Abdominal mass
- Abdominal discomfort (severity related to rate of onset of obstruction rather than degree of obstruction)
- Halitosis and/or oral ulceration (due to uremia)
- Abdominal fluid wave (if rupture and uroabdomen)

ETIOLOGY AND PATHOPHYSIOLOGY

Urolithiasis is an especially common cause of ureteral obstruction. However, there are many other potential causes (see above).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Ureteral obstruction may be discovered incidentally during imaging studies or (less often) may be identified as the cause of acute renal failure due to bilateral obstruction. Animals with subclinical or overt chronic kidney disease may be identified as having ureteral obstruction during imaging examinations.

DIFFERENTIAL DIAGNOSIS

Other causes of renomegaly (see p. 979), other causes of acute renal failure (see p. 31)

INITIAL DATABASE

- CBC generally unremarkable:
  - Normocytic, normochromic, nonregenerative anemia (if chronic kidney disease or chronic inflammation)
  - Leukocytosis with left shift possible if concurrent pyelonephritis
- Serum biochemical profile; abnormalities depend on degree of obstruction and/or nephron loss:
  - Azotemia
  - Hyperphosphatemia
  - Hyperkalemia
  - Metabolic acidosis
- Urinalysis may be normal or may reveal:
  - Isosthenuria
  - Hematuria
  - Pyuria
- Urine culture and sensitivity (C&S) indicated even if sediment is inactive (occult infection)
- Blood pressure (BP) to rule out hypertension (see p. 1209)
- Abdominal radiographs; renomegaly common; may identify:
  - Urolithiasis
  - Prostatomegaly
  - Abdominal mass
  - Loss of retroperitoneal/abdominal contrast
  - Distended ureter
  - Mass associated with ureter or bladder

ADVANCED OR CONFIRMATORY TESTING

- Abdominal ultrasound (sensitive and specific):
  - Pyelectasia (dilation of renal pelvis) common
  - Hydronephrosis common
  - Hydroureter common
  - Often allows identification of a cause of ureteral obstruction (e.g., urolithiasis, mass)
- Excretory urography (intravenous pyelography [IVP]; see), percutaneous nephropyelography:
  - Pyelectasia
  - Ureteral dilatation or lack of filling (IVP only)
- Renal scintigraphy or CT:
  - Affected kidney contributes little to overall glomerular filtration rate (GFR).
- Quantitative analysis and culture of uroliths

TREATMENT

TREATMENT OVERVIEW

When unilateral obstruction is believed to be long-standing, specific therapy may not be necessary. Acute bilateral ureteral obstruction requires intervention both to relieve obstruction and address consequences such as uremia, electrolyte, and acid-base disorders. Whenever possible, attempts should be made to prevent further obstruction (e.g., prophylaxis of urolithiasis, correction of anatomic defects, removal of obstructive masses).

ACUTE GENERAL TREATMENT

- Correct hydration, acid-base, and electrolyte disorders if present:
  - Crystalloid fluid therapy for azotemia, dehydration (see p. 31):
    - Initial rate of 120 mL/kg per day unless diuresis contraindicated

        - Postobstructive diuresis may require the “ins-and-outs” method of adjustment (rate based on measured urine output).
        - Diuresis may flush out ureterolith.
    - Address electrolyte disorders and acidosis (see pp. 1131 and).
    - Consider hemodialysis or peritoneal dialysis for stabilization.
- Percutaneous nephrostomy tubes may be used for preventing further renal damage while assessing renal function prior to surgical intervention:
    - Only possible if renal pelvis dilated
    - Placed with ultrasound guidance or via laparotomy
- Analgesia for abdominal pain (e.g., buprenorphine, 0.01 mg/kg IM, IV, or SQ q 6-8 h)
- Address uremic signs (see pp. 31 and 207).

CHRONIC TREATMENT

- Intervention is not always required if obstruction is partial, there is adequate renal function, and infection is absent.
- Ureteral surgery or stenting is indicated for bilateral obstruction or when function of contralateral kidney is impaired; major complication is postoperative ureteral stricture formation. Nuclear scintigraphy or CT provides quantitative assessment of each kidney's contribution to glomerular filtration rate:
    - Ureterotomy: for intraluminal or intramural obstruction in the proximal third of the ureter
    - Ureteroneocystostomy: for resection of distal ureter
    - Ureteroureterostomy: to repair ureter after resection or transection (anastomosis of proximal ureter to distal portion of ureter on ipsilateral side), usually when proximal third cannot be implanted directly into bladder neck
        - Highest incidence of postoperative obstruction
- Ureteral stent placed via interventional endoscopy or surgery should be considered, but has limited availability. Surgery is more widely available, especially if the patient is unstable to transfer to referral centers equipped to perform this noninterventional method.
- Nephrectomy: reserved for animals with unilateral obstruction, adequate function in contralateral kidney, and infection or loss of function in the affected kidney.
- Antibiotics if appropriate (e.g., pyelonephritis, bacterial cystitis) based on C&S.
- Therapeutic or prophylactic measures for urolithiasis if present (see pp. 1141, 1143, and 1138)
- Therapeutic measures for other identified causes of obstruction (e.g., removal of tumors obstructing urine flow)

POSSIBLE COMPLICATIONS

- Renal failure
- Postoperative ureteral stenosis
- Urinary rupture and uroabdomen

RECOMMENDED MONITORING

- Repeat ultrasound 10-12 weeks after initial evaluation. Remaining renal parenchymal changes are likely permanent.
- Animals with permanent hydroureter/hydronephrosis are monitored as for chronic kidney disease (see pp. 205 and 207). Azotemic animals are monitored more intensively than nonazotemic animals.

PROGNOSIS AND OUTCOME

- Dependent on underlying cause, duration of obstruction, extent of renal parenchymal damage, presence of concurrent infection, and ability to resolve underlying cause.
- Structural renal changes persisting 14-45 days or more after relief of ureteral obstruction are generally permanent.
- Complete bilateral obstruction of more than 3 days is fatal without appropriate treatment.

PEARLS & CONSIDERATIONS

COMMENTS

- Ureteral obstruction should be considered in the differential diagnosis for renal failure, especially in patients with evidence of nephrolithiasis or pyelonephritis.
- Bilateral ureteral obstruction is rare compared to unilateral obstruction but is life threatening.
- Ureteral obstruction can recur, especially in the presence of existing nephroliths.

PREVENTION

Strategies that limit the formation of urolithiasis (see pp. 1141, 1143, and 1138)

TECHNICIAN TIPS

Animals in acute renal failure should have urine output carefully quantified. One possible correctible cause of oliguria/anuria is bilateral ureteral obstruction.

CLIENT EDUCATION

Strict adherence to dietary recommendations can minimize the risk of ureteral or urethral obstruction due to urolithiasis.

SUGGESTED READING

Hardie EM, et al: Management of ureteral obstruction. Vet Clin North Am Small Anim Pract 34:989, 2004.

Kyles AE, et al: Clinical, clinicopathologic, radiographic, and ultrasonographic abnormalities in cats with ureteral calculi: 163 cases. J Am Vet Med Assoc 226:932–936, 2005.

Kyles AE, et al: Management and outcome of cats with ureteral calculi: 153 cases (1984-2002). J Am Vet Med Assoc 226:937–944, 2005.

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Urachal Diverticulum

BASIC INFORMATION

DEFINITION

Embryonic remnant at the apex of the urinary bladder; although diverticula occur commonly, they seldom result in clinical problems.

SYNONYM

Vesicourachal diverticulum

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs and cats

RISK FACTORS: Microscopic diverticula in cats may create risk for developing macroscopic diverticula following urinary tract obstruction from any cause.

ASSOCIATED CONDITIONS & DISORDERS

- Urinary tract infection (UTI)/bacterial cystitis
- Urolithiasis (especially struvite)
- Feline lower urinary tract signs/disease (FLUTS/D)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Macroscopic: intramural and extramural
- Microscopic
- Acquired macroscopic

HISTORY, CHIEF COMPLAINT: Clinical signs are often absent. When clinical signs are apparent, they may include any of the following:

- Hematuria
- Pollakiuria
- Dysuria
- Stranguria
- Inappropriate elimination
- Systemic illness due to urinary tract obstruction (rare)

PHYSICAL EXAM FINDINGS: Physical exam is usually unremarkable. When present, abnormalities are nonspecific and may include:

- Hematuria (stains on prepuce, vulva, or hocks)
- Painful urinary bladder
- Enlarged, turgid bladder with urethral obstruction

ETIOLOGY AND PATHOPHYSIOLOGY

The urachus is a canal connecting the fetal bladder with the allantois. The urachal lumen normally becomes obliterated during development, but on occasion the lumen remains patent (patent urachus) or the obliteration is incomplete, leaving a remnant diverticulum. Cause of incomplete urachal atrophy is unknown.

- Macroscopic:
  - Most common form in dogs
  - May not be associated with clinical signs

    - May be associated with or predispose the animal to chronic/recurrent UTI and urolithiasis
- Microscopic:
    - Most common form in cats
    - Remnants of urachus at bladder apex that can extend from the level of the submucosa to the subserosa
    - Not associated with clinical signs
- Acquired macroscopic:
    - Microscopic diverticula may become macroscopic secondary to sustained increase in bladder intraluminal pressure.
    - May spontaneously regress if the cause of increased bladder pressure is removed

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis of urachal diverticulum is based on imaging of the urinary tract through ultrasonography, contrast radiography, or visual inspection at surgery. Often, diverticula are incidental findings.

DIFFERENTIAL DIAGNOSIS

- Neoplasia
- Polyps
- Urolithiasis
- Blood clots

INITIAL DATABASE

- CBC: unremarkable
- Serum chemistry profile: unremarkable unless urinary obstruction exists; in these rare instances, azotemia, hyperkalemia, or acidemia are identified.
- Urinalysis: often unremarkable; sometimes shows pyuria, hematuria, bacteruria, or struvite crystalluria
- Urine culture and sensitivity (C&S) is used for identifying urinary tract infection.
- Abdominal radiographs to rule out radiopaque uroliths

ADVANCED OR CONFIRMATORY TESTING

- Contrast cystography:
    - Positive-contrast cystography
    - Double-contrast cystography
- Ultrasonography
- Cystoscopy
- Exploratory celiotomy and cystotomy

TREATMENT

TREATMENT OVERVIEW

Incidentally discovered urachal diverticula may not require therapy. Those associated with recurrent urinary tract infection or urolithiasis are surgically addressed.

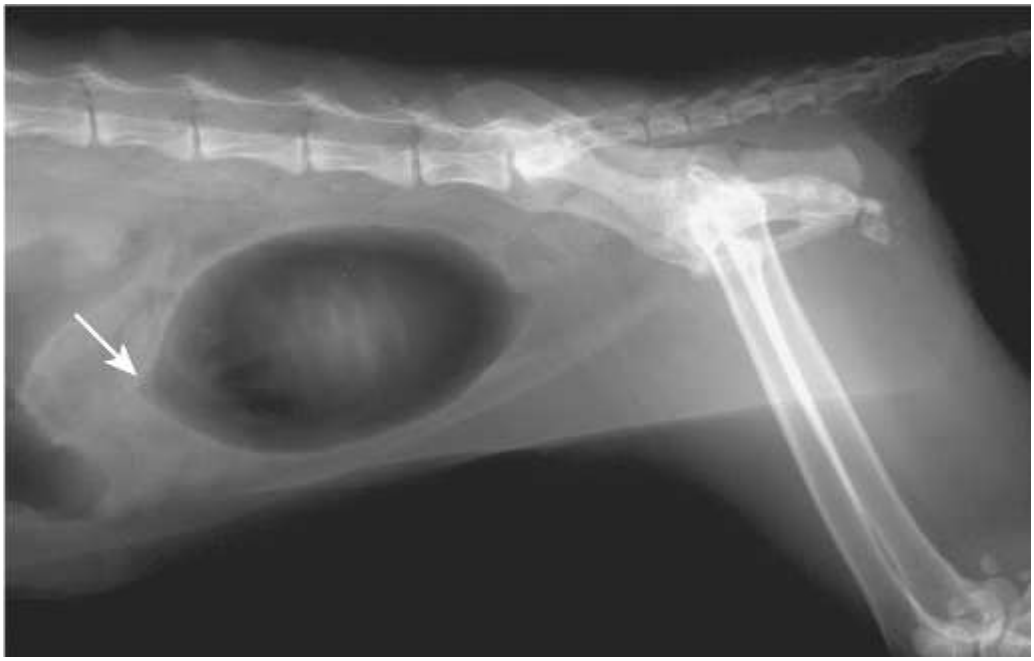
ACUTE GENERAL TREATMENT

- Relieve urethral obstruction if present (see 1353)
- Fluid therapy and correction of electrolyte disturbances if present (see pp. 1353 and 1555)
- Antimicrobial therapy for bacterial cystitis if present (see 276)

CHRONIC TREATMENT

- Animals with clinical signs or a urinary tract infection related to either congenital macroscopic diverticula or nonresolving acquired macroscopic diverticula should undergo surgical resection of the diverticulum:
    - Exploratory celiotomy
    - Ventral midline cystotomy

    - Identification of diverticulum at apex of bladder
    - Excision of diverticulum with elliptical incision
    - Routine closure
- Address chronic feline lower urinary tract signs/disease (see 387).
- Address urolithiasis (see 1143).



URACHAL DIVERTICULUM Lateral radiographic projection of a double-contrast cystogram performed on a 4-year-old male domestic shorthaired cat with a history of chronic urinary tract infections. A small "out-pouching" of the bladder wall is present at the apex *(white arrow)*. Diagnosis: bladder diverticulum predisposing the animal to chronic cystitis.

(Courtesy Dr. Stephanie Essman, University of Missouri.)

NUTRITION/DIET

Animals with urinary tract infection may develop struvite urolithiasis. Diets low in ash designed to acidify the urine may be used in conjunction with appropriate antimicrobial therapy to aid in dissolution of struvite calculi (see 1143).

POSSIBLE COMPLICATIONS

- Obstruction of the urinary tract as a result of struvite urolithiasis is a possible complication of urinary tract infection associated with urachal diverticula.
- Suture-line leakage with peritonitis is a possible complication following surgical excision of diverticula.

RECOMMENDED MONITORING

- Monitor cats with acquired macroscopic diverticula for regression of diverticulum by contrast cystography 2-3 weeks after treatment of obstruction and resolution of clinical signs.
- Monitor for recurrence of signs of FLUTS/D (see 387).

PROGNOSIS AND OUTCOME

- Surgical excision for congenital macroscopic diverticula is curative.
- Acquired macroscopic lesions that spontaneously resolve may recur with repeated episodes of lower urinary tract obstruction.

PEARLS & CONSIDERATIONS

COMMENTS

Patent urachus causes umbilical urine dribbling in neonates and should be corrected surgically.

PREVENTION

Prevention of lower urinary tract obstruction will prevent acquired diverticula formation.

CLIENT EDUCATION

- Recurrent UTI may be a sequela to uncorrected congenital macroscopic diverticula.
- Recurrent or persistent UTI may lead to struvite urolithiasis.

SUGGESTED READING

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Groesslinger K, et al: Prevalence and radiologic and histologic appearance of vesicourachal diverticula in dogs without clinical signs of urinary tract disease. J Am Vet Med Assoc 226:383–386, 2005.

EDITOR: LEAH A. COHN

1ST EDITION AUTHOR: ERIC POPE

Upper Respiratory Infection, Cat

BASIC INFORMATION

DEFINITION

A complex of viral and bacterial agents can cause upper respiratory tract signs such as sneezing, nasal congestion, and nasal discharge in cats. Etiologies include feline herpesvirus (FHV), feline calicivirus (FCV), *Bordetella bronchiseptica. Chlamydophila felts,* and (less commonly) feline reovirus, cowpox virus, and mycoplasmas.

SYNONYMS

Feline infectious respiratory disease, feline respiratory disease complex

C. felts previously known as *Chlamydia psittaci*

Feline herpesvirus: feline rhinotracheitis

EPIDEMIOLOGY

SPECIES, AGE, SEX: The main causative infectious agents (herpesvirus and calicivirus) are confined to the family of Felidae and are typically found in young animals. Mycoplasmas are often found as normal flora in the upper respiratory tract of many species.

RISK FACTORS

- Poor husbandry and overcrowding in catteries or rescue shelters
- Exposure to free-roaming cats in high-density feral populations

CONTAGION & ZOONOSIS

- FHV and FCV are shed in ocular, nasal, and oral secretions and are passed via direct cat-to-cat contact. Both viruses spread easily through susceptible populations and are perpetuated by carrier animals not showing overt signs. Disease can be spread via fomites such as contaminated cages, bowls, and clothing. FCV can persist in the environment for up to 1 month.
- Direct aerosol transmission is actually an unlikely cause of respiratory disease spread, owing to the small feline tidal lung volume and lower numbers of pathogenic organisms in the respiratory volume. Sneezing of nasal/oral secretions, however, may disseminate a virus more readily over a radius of several feet (>1 m).

GEOGRAPHY AND SEASONALITY: Worldwide and no true seasonally; more cases may be noted in late spring and summer when many susceptible kittens are added to the population.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Herpesvirus: in young animals, usually acute, severe upper respiratory signs; in chronic adult cases, often manifests as a chronic conjunctivitis/keratitis without respiratory signs.
- Calicivirus: typical upper respiratory signs; isolated highly virulent strains that cause severe systemic disease and death have been noted.

HISTORY, CHIEF COMPLAINT

- General signs of respiratory disease complex include anorexia, lethargy, ocular and nasal discharges, sneezing, epiphora, blepharospasm.
- Specific to calicivirus (see p. 172), herpesvirus (see p. 524), and *C. felts* (see p. 193)

PHYSICAL EXAM FINDINGS: Respiratory disease complex:

- Serous to mucopurulent nasal and ocular discharge
- Epiphora, blepharospasm, chemosis, conjunctival hyperemia

- Fever
- Dyspnea, increased airway sounds, wheezes, cough

In addition:

- Herpesvirus: conjunctivitis, ± dendritic corneal ulcers
- Calicivirus: oral, nasal, lip ulcers, or generalized stomatitis and gingivitis
- Rare severe cases of very virulent calicivirus strains: facial/limb edema, dermal necrosis, vomiting, diarrhea, icterus, petechiae and ecchymoses from disseminated intravascular coagulation, or sudden death
- *B. bronchiseptica:* fever, submandibular lymphadenopathy, and cyanosis/dyspnea in cases of severe bronchopneumonia

ETIOLOGY AND PATHOPHYSIOLOGY

Feline herpesvirus:

- A double-stranded DNA alpha-herpes-virus specific to Felidae. It attacks mucosal epithelial cells of the soft palate, tonsils, turbinates, cornea, and conjunctiva, leading to multifocal epithelial necrosis and secondary clinical signs. Pulmonary involvement is rare.
- Incubation period is 2-6 days; disease usually runs its course in 10-20 days.
- Turbinate destruction due to herpesvirus infection may be permanent and can predispose the cat to chronic rhinitis, even in the absence of active infection.
- Chronic conjunctivitis/keratitis can lead to symblepharon (adhesion of bulbar conjunctiva to palpebral conjunctiva), corneal scarring, or keratoconjunctivitis sicca (KCS).
- Essentially all cats infected with FHV become chronic carriers; the virus remains latent in the trigeminal ganglia. However, a smaller proportion of cats are truly susceptible to recrudescence, and these animals act as the FHV reservoir for the feline population. Recrudescence and viral shedding often occur 1-3 weeks after a stressful event. Not all recrudescence is accompanied by obvious clinical signs.

Feline calicivirus: see p. 172

B. bronchiseptica: see

C. felis: see

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Usually the diagnosis is based on clinical presentation: a cat with signs of conjunctivitis, anterior uveitis, ocular or nasal discharge, gingivitis, faucitis, stomatitis, glossitis, fever, and lymphadenomegaly has an upper respiratory infection. Specific identification of a causative agent is not always necessary, but ruling out non-viral causes is important for treatment considerations.

DIFFERENTIAL DIAGNOSIS

- Nasal signs: nasal neoplasia, nasopharyngeal polyps, periodontal disease, foreign body, fungal infection, structural malformation of nasal passages/sinuses, esophageal motility dysfunction
- Ocular signs: corneal and/or conjunctival trauma, corneal foreign body, eosinophilic keratoconjunctivitis, neoplasia, KCS, uveitis, glaucoma
- Cough or dyspnea: feline asthma, intrathoracic neoplasia (pulmonary, lymphoid, mediastinal, or pleural), congestive heart failure (CHF), pleural effusion of other causes, feline heartworm disease

INITIAL DATABASE

- CBC: neutrophilia with left shift if secondary bacterial infection is severe. Stress leukogram is possible. Results are often normal.
- Serum biochemistry profile and urinalysis: may reflect dehydration but typically unremarkable. With virulent calicivirus infections, increases in alanine aminotransferase (ALT), creatine kinase (CK), and bilirubin levels; and decreased albumin level possible.
- Thoracic radiographs: assessing for signs of pneumonia in cats with lower respiratory tract signs
- CT scan of the skull, with rhinoscopy and nasal biopsy/culture can help rule out neoplasia, fungal infection, dental disease, nasopharyngeal polyps, and structural deformities as causes of chronic respiratory signs.

ADVANCED OR CONFIRMATORY TESTING

- Serologic testing for herpesvirus and calicivirus is unrewarding because of widespread vaccination.
- Virus isolation from nasal, conjunctival, or oropharyngeal swabs is the best diagnostic assay for FHV and FCV. Requires special swabs or media for transport; however, FCV is commonly isolated from the oral/respiratory mucosa of healthy cats, so positive viral culture should be supported by appropriate clinical presentation.
    - Feline upper respiratory disease panel: www.idexx.com or www.antechonline.net; requires swab samples depending on location of predominant clinical signs.
- Conjunctival scrapes may demonstrate basophilic intracytoplasmic inclusions indicative of *C. felis* infection.
- Culture or PCR on conjunctival swabs can also be used to rule out *C. felis.* Special transport medium is required for culture. Serologic testing may also be helpful in the unvaccinated cat, because affected animals typically have high titers.
- Transtracheal or bronchoalveolar washes with cytologic examination and culture and sensitivity (C&S) are helpful in isolating *B. bronchiseptica, C. felis,* or secondary bacteria as causative agents of pneumonia.
- Cryptococcal antigen titer to rule out cryptococcosis.

TREATMENT

TREATMENT OVERVIEW

Treatment is typically supportive, with the goal of controlling secondary bacterial infections and maintaining comfort and appetite.

ACUTE GENERAL TREATMENT

Most cats with upper respiratory infections can and should be managed at home by the owner to decrease pathogen dissemination in the hospital setting. Animals that are febrile, dehydrated, severely depressed, or compromised should be treated in the hospital until they are stable and can be sent home; they should be isolated from other cats. Acute treatment includes:

- IV crystalloids and colloids if patients are febrile and/or dehydrated or have evidence of hypovolemia
- Broad-spectrum antibiotics (one of the following):
    - Amoxicillin-clavulanate, 13.75 mg/kg PO q 12 h
    - Cefadroxil, 10-30 mg/kg PO q 8-12 h
    - Cephalexin, 22-30 mg/kg PO q 8-12 h
    - Enrofloxacin, 5 mg/kg PO q 24 h
- Antibiotics most effective against specific bacteria (see pp. 144 and 193):
    - Doxycycline, 5 mg/kg PO q 12 h; or tetracycline, 20 mg/kg PO q 8 h
- Topical ophthalmic preparations:
    - Artificial tears q 2-6 h
    - Tetracycline ophthalmic preparations are the treatment of choice for *C. felis* and *Mycoplasma* spp. conjunctivitis and in FHV cats to prevent secondary bacterial infections. Topical tetracyclines can be irritating. Chloramphenicol, erythromycin, or fluoroquinolone topicals are alternative options.
    - Topical or systemic corticosteroids should not be used in suspected FHV keratitis.
    - Most “triple-antibiotic” ophthalmic preparations (neomycin, polymyxin, and bacitracin/gramicidin) are typically ineffective against *C. felis, Mycoplasma* spp., and FHV-1.
- Topical and systemic antiviral drugs for FHV keratitis/conjunctivitis (see p. 524)
- Treatment duration with antibiotics and antivirals should be determined on an individual case basis, but typically 1-2 weeks is required while the viral disease runs its course.

CHRONIC TREATMENT

- Home nebulization (putting the cat on a dry surface in a steamy bathroom) may help ease nasal or airway congestion.
- Owners should be instructed to cleanse the face, mouth, and nares regularly to minimize accumulation of discharges or saliva.
- Herpesvirus carriers that have bouts of recrudescence can be treated on as-needed basis with L-lysine (250-500 mg PO q 12 h for life) to decrease severity of outbreaks.

NUTRITION/DIET

- Appetite stimulants may be necessary:
    - Cyproheptadine, 2 mg/cat PO q 12-24 h; *or*
    - Diazepam, 0.05-0.15 mg/kg IV q 24 h; may cause extreme sedation soon after administration. Paradoxically in some cats, may lead to hyperexcitability and fractiousness.
- Feed animals very pungent, highly palatable foods to overcome a decreased sense of smell from nasal infection (see p.

1377).
- Tube feeding may be necessary in chronic cases with prolonged anorexia.

POSSIBLE COMPLICATIONS

FHV keratoconjunctivitis can predispose the animal to KCS.

PROGNOSIS AND OUTCOME

Except in very young or compromised animals or in cases of virulent calicivirus, prognosis is usually good for recovery from acute bouts of respiratory disease. Some animals develop chronic rhinitis and/or keratoconjunctivitis and will have recurrent bouts of disease that may require lifelong management.

PEARLS & CONSIDERATIONS

PREVENTION

- Several modified live or killed vaccines are available for protection against herpesvirus and calicivirus. They offer good to moderate protection against clinical disease but are not guaranteed to prevent infection or development of a carrier state.
  - Modified live vaccines (MLV) may induce a mild form of respiratory disease.
- Vaccines are available for *B. bronchiseptica* and *C. felis,* but because these diseases are relatively benign and easy to treat, the benefit of immunization in most pet cats is questionable. Vaccination may be warranted in cattery or shelter situations.
- Dilute bleach (1 part bleach to 32 parts water) is the best disinfectant for preventing FHV and FCV spread in the hospital environment. FCV has shown resistance to common disinfectants such as quaternary ammonium compounds and chlorhexidine.

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1ST EDITION AUTHOR: SHANNON STROUP

Upper Airway Obstruction

BASIC INFORMATION

DEFINITION

Inability to move air effectively through trachea, larynx, pharynx, or nose and mouth

SYNONYMS

Choking, occlusion of the upper airway

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Airway foreign body more likely in young dogs; neoplasia, laryngeal paralysis more likely in adult older dogs
- Young cats may have nasopharyngeal polyps.

GENETICS & BREED PREDISPOSITION: Short-nosed (brachycephalic) animals are predisposed to airway obstruction (see p. 151).

RISK FACTORS: Environmental factors: excitement, heat, and exercise, especially in animals with physical predisposition (e.g., elongated soft palate, laryngeal paresis)

GEOGRAPHY AND SEASONALITY: More common in warmer climates (heat stress)

ASSOCIATED CONDITIONS & DISORDERS: Brachycephalic upper airway syndrome, laryngeal paralysis, neoplasia

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Supraglottic structures: brachycephalic upper airway syndrome (see p. 151), laryngeal paralysis (unilateral/bilateral), foreign bodies (pharyngeal), laryngeal collapse, laryngeal edema, and nasopharyngeal polyps (cats)
- Subglottic structures: tracheal neoplasia, tracheal hypoplasia, tracheal collapse, foreign body aspiration, trauma

HISTORY, CHIEF COMPLAINT

- Owners often report that their pet appears anxious or agitated, that he or she is having difficulty breathing, and that they can hear loud respiratory noises or a honking cough.
- Clinical signs can occur more commonly after exercise, excitement, or on a warm day.
- Animals may have been witnessed aspirating a foreign object (e.g., ball/marble/acorn), although the mistaken belief that a foreign body has been aspirated is a common error that some clients believe passionately ("something stuck in the throat") even when the problem is clearly different (e.g., pulmonary edema, pleural effusion).

PHYSICAL EXAM FINDINGS

- Noisy and/or stridorous breathing
- Hyperthermia possible (excessive muscle activity from inspiratory effort)
- Conformation changes (e.g., short nose) raise the suspicion of associated malformations as the underlying cause.
- Loud sounds may be ausculted over the trachea and may be referred to the lower airways.

ETIOLOGY AND PATHOPHYSIOLOGY

- Most of the resistance to airflow occurs in the upper airways. Any fixed or dynamic obstruction in the upper airways will increase the resistance to breathing and, subsequently, the work of breathing.
- Inspiration against a partially or completely closed upper airway may cause flooding of pulmonary alveoli with plasma (i.e., noncardiogenic pulmonary edema due to negative pressure generated in the air space).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis is based on physical exam findings, including difficulty breathing and/or stridorous breathing. Specifically, inspiratory dyspnea, often with the point of stridor audibly in the upper airway (making the site of obstruction manifestly clear on distant physical exam alone) helps localize the anatomic lesion. Oral examination, diagnostic imaging, and endoscopy are cornerstones for confirming the site (and sometimes nature) of the obstruction, and are selected based on suspected location of the obstruction, available means, and patient stability.

DIFFERENTIAL DIAGNOSIS

Occasionally, pleural effusion in cats will mimic upper respiratory obstruction.

INITIAL DATABASE

- Oral examination under sedation is the most important diagnostic test (see p. 1295). The clinician should be prepared for an emergent tracheostomy (and possibly positive-pressure ventilation, if noncardiogenic pulmonary edema is present; see and) if needed. Doxapram may be used for stimulating ventilation during oral examination in sedated dogs and cats.
- Other ancillary testing includes radiographs (thoracic and neck), ultrasound, CBC/serum biochemistry profile, and evaluation of oxygenation (pulse oximetry or arterial blood gas [ABG] analysis).

ADVANCED OR CONFIRMATORY TESTING

Bronchoscopy, fluoroscopy, or CT scan may be useful for evaluating focal lesions or obtaining biopsies or cytologic specimens.

TREATMENT

TREATMENT OVERVIEW

Minimize stress and address the clinical signs until a definitive diagnosis is made; sometimes the diagnosis and treatment occur simultaneously (e.g., foreign body is identified and removed).

ACUTE GENERAL TREATMENT

- Tranquilizers or analgesics, corticosteroids at antiinflammatory doses, and oxygen supplementation. Secure airway if necessary (see pp. 1292 and 1318).
- If hyperthermia is due to exertion or anxiety (i.e., muscle activity, not true fever), it can respond to physical cooling measures but not to antiinflammatory drugs (see p. 1564).

CHRONIC TREATMENT

Either medical or surgical management of the underlying problem:

- Medical: anxiolytics, antitussives, and environmental control
- Surgical: stenotic nares repair; soft palate resection; everted laryngeal saccule resection; abscess drainage; tracheal ring implants/stent placement; removal of foreign body, tumor, or polyp; permanent tracheostomy; or temporary tracheotomy

BEHAVIOR/EXERCISE

Ideally, pets that are at risk should be kept calm and in an air-conditioned area. At the least, exercise or exertion should be avoided in those animals that are predisposed.

POSSIBLE COMPLICATIONS

Postsurgical complications include the recurrence of clinical signs, aspiration pneumonia, noncardiogenic pulmonary edema, and/or respiratory arrest.

RECOMMENDED MONITORING

Monitor respiratory rate/effort and mucous membrane color.

PROGNOSIS AND OUTCOME

Depend on the actual underlying problem and the severity of clinical signs. For example, presence of noncardiogenic pulmonary edema substantially worsens prognosis.

PEARLS & CONSIDERATIONS

COMMENTS

- Up to half the diameter of the airway can be compromised without obvious clinical signs.
- Major errors in the initial treatment include underestimation of the patient's distress, overzealous examination, and performance of diagnostics that are detrimental to the condition of the patient at that time.
- A common radiographic misdiagnosis is the interpretation of a prominent or mineralized (but normal) larynx as a foreign body, especially if the neck is radiographed obliquely.
- Thoracic radiography and positive-pressure ventilation should be planned in case dyspnea and/or hypoxemia persist after relief of upper airway obstruction, as can occur when noncardiogenic pulmonary edema is also present.

PREVENTION

Avoid overexertion, prevent heat stress, and know the medical options that are available to help break the cycle of distress and resultant respiratory difficulty.

TECHNICIAN TIPS

When administering treatments to these pets, stress should be minimized (minimal restraint) and treatments should be conducted in a stepwise manner.

CLIENT EDUCATION

Explain to owners that a brachycephalic animal is predisposed to developing upper airway problems

SUGGESTED READING

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AUTHOR: MEGAN WHELAN

EDITOR: ELIZABETH ROZANSKI

Unerupted Teeth

BASIC INFORMATION

DEFINITION

Teeth that have not emerged into the mouth are unerupted. Clinically, the tooth appears to be missing. Radiographic diagnosis is required.

SYNONYMS

- Embedded teeth (teeth exhibiting a lack of eruptive force without physical obstruction)
- Impacted teeth (teeth not erupting owing to a physical barrier)

EPIDEMIOLOGY

SPECIES, AGE, SEX: Unerupted teeth occur more commonly in the younger dog and less commonly in cats. They may not be recognized until animals have reached adulthood.

GENETICS & BREED PREDISPOSITION: Familial delayed eruption does occur in Tibetan and Wheaten terriers, and toy breeds can have overall slower eruption times. Because erupting teeth can be influenced by internal and external causes, a genetic link is suspected but difficult to prove. Symmetrically unerupted or missing teeth are usually genetic in origin. Brachycephalic and toy dog breeds appear to be predisposed to unerupted and missing premolar and molar teeth.

RISK FACTORS

- Persistent deciduous teeth (see 282)
- Regional trauma
- Certain endocrine disorders
- Malnutrition
- Canine distemper

ASSOCIATED CONDITIONS & DISORDERS: Dentigerous (tooth-containing) cyst (also called follicular cyst)

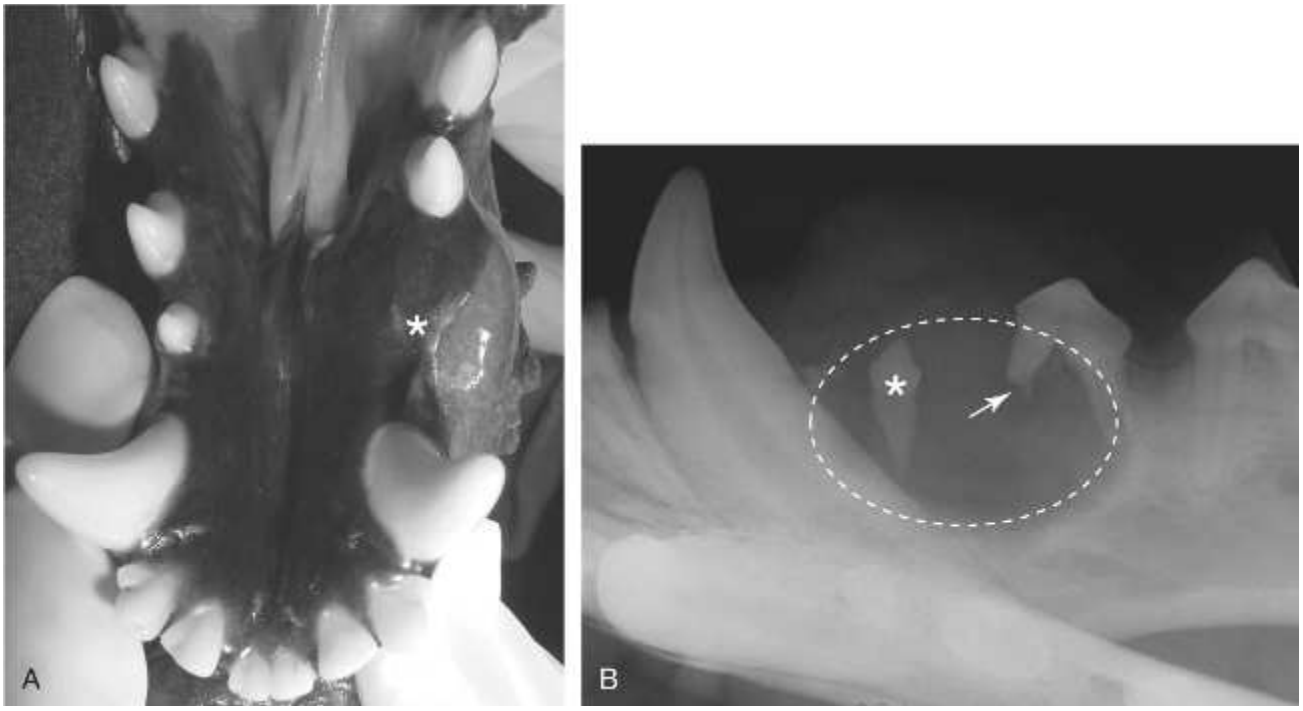
CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Animals are sometimes presented for evaluation of missing teeth, but the majority of unerupted teeth are found incidentally on routine physical examination.

PHYSICAL EXAM FINDINGS: Most animals are in good health. Oral examination reveals an edentulous (toothless) region. Permanent premolars are the most common unerupted teeth, but any tooth can be affected. If a dentigerous cyst is present, a fluctuant soft-tissue swelling may be located in the edentulous region.

ETIOLOGY AND PATHOPHYSIOLOGY

- Complications leading to abnormal tooth eruption are many and varied: primary defects in the eruptive process, genetic/traumatic displacement of the tooth bud or surrounding bone, mechanical obstruction from adjacent structures, regional odontogenic and nonodontogenic neoplasia.
- The most commonly unerupted teeth in the dog are the mandibular first premolar and third molar teeth.
- Endocrine abnormalities (hypothyroidism, cretinism, hypogonadism, mongolism, hypopituitarism, hyperparathyroidism) can prevent or slow the eruption of teeth.
- Unerupted teeth can incite dentigerous cyst formation: an epithelial-lined soft tissue is attached to the cementoenamel junction of an unerupted tooth, with the crown protruding into the fluid-filled cyst, causing pressure resorption of alveolar bone, displacement of adjacent teeth, abscess, and fistulation.



UNERUPTED TEETH A, Clinical photograph of rostral lower jaw of an adult dog. Note swelling in the area of a missing left mandibular first premolar tooth *(asterisk)* and distally displaced left mandibular second premolar tooth. **B,** Radiograph of left rostral mandible of same patient arranged in labial mounting (rostral toward the left, caudal toward the right of image). Note that left mandibular first premolar tooth *(asterisk)* is unerupted, and a dentigerous cyst *(dotted oval)* has developed around the unerupted tooth, causing pressure resorption of the roots of the caudally displaced left mandibular second premolar tooth *(arrow)*. (Copyright 2010 Dr. Alexander M. Reiter.)

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Dental radiography is necessary to differentiate unerupted teeth from missing teeth.

DIFFERENTIAL DIAGNOSIS

Edentulous region:

- Partially erupted, ankylosed, embedded, and impacted teeth
- Presence of an operculum (tough gingival covering preventing tooth eruption)
- Anodontia and hypodontia resulting from a large variety of causes
- Fractured tooth ± retained tooth roots
- Previously extracted tooth

Edentulous region associated with soft-tissue swelling:

- Odontogenic tumor (e.g., compound or complex odontoma)
- Cyst (e.g., radicular, dentigerous)
- Abscess
- Neoplasia

INITIAL DATABASE

- CBC, serum biochemistry panel, urinalysis (preanesthetic): generally unremarkable
- Full-mouth (intraoral) dental radiography

ADVANCED OR CONFIRMATORY TESTING

CT scan (see): if associated cystic structure is large and to define surgical margins and/or regions for débridement

TREATMENT

TREATMENT OVERVIEW

Treatment goals are to preserve normal anatomic arrangement and structure, encourage complete tooth eruption or extract tooth if eruption impossible or impractical, and prevent cyst/abscess formation.

ACUTE AND CHRONIC TREATMENT

- No treatment if entire tooth is missing on radiographs
- Some unerupted teeth can be orthodontically coaxed into position if tooth, patient, and owner are willing.
- If an operculum is present, dissect gingiva to allow for tooth eruption (operculectomy).
- To prevent dentigerous cyst development, surgically extract unerupted teeth without eruption potential. Curettage of the extraction site is recommended to remove remnant odontogenic tissue. Postoperative radiographs ensure complete removal of all tooth structures.
- If a dentigerous cyst is present, the tooth and cyst are removed en bloc. If this is not possible, extensive curettage to remove all epithelial cyst lining is mandatory because small islands of remaining epithelium can lead to cyst reoccurrence or malignant transformation. The débrided cyst cavity need not be filled with osteopromotive materials; natural bone remodeling will likely be clinically adequate.
- Flaps should be closed with synthetic absorbable suture material.
- Administration of antibiotics is not usually necessary after the extraction procedure unless another medical condition or extensive tissue trauma at the extraction site is present.
- Pain management: regional nerve block (0.5% bupivacaine) intraoperatively, followed by nonsteroidal antiinflammatory drugs (e.g., carprofen, 2 mg/kg PO q 12 h in dogs) ± opioid medications (butorphanol, 0.2-0.4 mg/kg PO q 4-6 h) given postoperatively for 2-3 days.

POSSIBLE COMPLICATIONS

- Inability to locate the unerupted tooth
- Extraction of a healthy erupting permanent tooth
- Cyst recurrence
- Regional trauma due to improper extraction technique
- Infection

RECOMMENDED MONITORING

- Examination 1-2 weeks postoperatively to evaluate extraction sites
- Cyst: examination with radiographs in 6 months

PROGNOSIS AND OUTCOME

- Unerupted teeth with operculectomy: fair for tooth eruption (depends on tooth eruption potential)
- Extracted unerupted teeth: excellent for extraction site healing
- Dentigerous cyst: excellent if all cystic lining is removed

PEARLS & CONSIDERATIONS

COMMENTS

- No tooth should be considered “missing” without radiographic diagnosis.
- Extraction of unerupted teeth may be unnecessary in older pets (>8-9 years) if there is no radiographic evidence of associated lesions. The odds a dentigerous cyst will form at this age are low.

PREVENTION

- Removal of persistent deciduous teeth
- Early recognition of “missing” teeth in young animals
- Selective breeding

TECHNICIAN TIPS

Technicians are at the frontline for identifying unerupted teeth during professional dental cleanings and pointing them out to the veterinarian if they were not noted previously.

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Umbilical Hernia

BASIC INFORMATION

DEFINITION

Full-thickness congenital abdominal wall defect at the umbilicus

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs and cats
- Greater incidence in females of predisposed breeds

GENETICS & BREED PREDISPOSITION

- Breed predisposition in dogs:
  - Airedale terrier, basenji, Pekingese, pointer, and weimaraner
- Could be an inherited defect:
  - Polygenic inheritance possible

ASSOCIATED CONDITIONS & DISORDERS

- Fucosidosis, an inherited lysosomal storage disease reported in English springer spaniels
- Cryptorchidism
- Incomplete caudal sternal fusion
- Peritoneopericardial diaphragmatic hernia
- Exstrophy of the bladder
- Hypospadias
- Imperforate anus

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Uncomplicated:
  - Single umbilical hernia without incarceration or strangulation of abdominal contents, concurrent anatomic abnormalities, or multiple hernias
- Complicated:
  - Presence of multiple hernias; other associated anatomic abnormalities, defects, or diseases; or strangulation or contamination of abdominal contents
- Omphalocele:
  - Large midline umbilical hernia and skin defect that allow abdominal organs to protrude externally. The umbilical sac is merely a thin transparent membrane (amniotic sac). The membrane is attached to the hernia edges and may rupture easily. Most affected puppies die or are euthanized before treatment is sought.
- Gastroschisis:
  - Grossly similar to omphalocele, but the defect is paramedian.

HISTORY, CHIEF COMPLAINT

- None; incidental finding (most common)
- Soft swelling at umbilicus may be noticed by some owners.
- Systemic signs of illness (anorexia, vomiting, lethargy) are possible if abdominal contents are strangulated (least common).

PHYSICAL EXAM FINDINGS

- Protruding mass at the umbilicus:
  - Soft, fluctuant, and reducible, especially if animal is placed in dorsal recumbency

- Large, firm, and irreducible if contents are incarcerated
- Acute intestinal incarceration or strangulation:
  - Firm, painful mass; vomiting, abdominal pain, signs of sepsis are possible.

ETIOLOGY AND PATHOPHYSIOLOGY

- Abdominal wall of the embryo normally is formed by migration of cephalic, caudal, and lateral folds.
- Umbilical aperture remains after normal migration and fusion of the folds.
- Umbilical hernia results when the lateral folds, principally the rectus abdominis muscle and fascia, fail to fuse or have delayed fusion after the midgut relocates in the sixth week of gestation.

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

The diagnosis is made entirely on physical examination. In complex cases with entrapped viscera, the identity of herniated organs is confirmed at surgery.

DIFFERENTIAL DIAGNOSIS

Traumatic umbilical hernia: peripartum insult caused by traction on umbilical cord or cutting cord too close to abdominal wall

INITIAL DATABASE

Survey abdominal and thoracic radiographs: only needed if hernia is very large and if other anomalies (diaphragmatic hernia, incomplete sternal fusion, strangulation/incarceration) are present.

ADVANCED OR CONFIRMATORY TESTING

Ultrasound examination (uncommonly used): only considered with large and/or incarcerated hernia contents to determine contents of hernia.

TREATMENT 

TREATMENT OVERVIEW

- Resolve any existing visceral entrapment.
- Reduce or eliminate risk of herniation of abdominal viscera.

ACUTE GENERAL TREATMENT

- Conservative treatment:
  - Small hernia (less than the size of the intestine; i.e., the size of a fingertip)
  - Spontaneous closure may occur as late as 6 months of age.
- Surgical correction:
  - Large hernia but no associated clinical problems (incarceration of abdominal contents):
    - Elective surgical correction; also repaired when another elective surgical procedure (ovariohysterectomy, orchiectomy) is performed
- Large hernia with evidence of incarcerated or strangulated viscera:
  - Immediate surgical correction
- Omphalocele:
  - Immediate surgical correction to prevent further organ damage or contamination

POSSIBLE COMPLICATIONS

- Dehiscence of repair:
  - Large defect
  - Excess tension on repair
  - Friability of abdominal wall
- Gastroschisis and omphalocele may be associated with early neonatal death:

- Contamination of abdominal contents
- Inability to correct defect

RECOMMENDED MONITORING

Counsel owners to watch for enlargement of hernia or acute gastrointestinal (GI) signs in animals that are managed conservatively; onset warrants immediate evaluation and consideration of surgical correction.

PROGNOSIS AND OUTCOME

- Excellent with uncomplicated umbilical hernia and successful closure
- Guarded to poor with complicated or open hernia
- Status of animal at presentation and health of herniated contents determine prognosis

PEARLS & CONSIDERATIONS

COMMENTS

- There are usually no clinical signs associated with umbilical hernias. Correction is usually an elective procedure.
- Entrapment of abdominal contents can occur with larger hernias.
- Always examine animals with umbilical hernias for additional congenital abnormalities.

PREVENTION

- Consideration should be given to avoiding breeding affected dogs or cats, because this condition is usually an inherited defect.
- At the time of the animal's birth, carefully ligate and transect the umbilical cord—without excessive traction—at least 1-2 cm from the neonate's body wall.

CLIENT EDUCATION

- Treatment may be conservative, or a herniorrhaphy may be required to prevent complications.
- Veterinarians should train breeders in proper neonatal care.

SUGGESTED READING

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AUTHOR: JOSEPH G. HAUPTMAN

EDITOR: RICHARD WALSHAW

1ST EDITION AUTHOR: ELLEN B. DAVIDSON DOMNICK

Ulcers, Oral Mucosal

BASIC INFORMATION

DEFINITION

Focal or multifocal loss of superficial epithelial integrity affecting the oral mucosa

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs and cats of either gender and all ages can be affected.

GENETICS & BREED PREDISPOSITION: Maltese, Cavalier King Charles spaniel, cocker spaniel, and Bouvier des Flandres dogs are predisposed to chronic ulcerative periodontal stomatitis (CUPS). Abyssinian and Somali cats are predisposed to lymphocytic/plasmacytic stomatitis (LPS).

CONTAGION & ZOONOSIS: Feline leukemia virus (FeLV), feline immunodeficiency virus (FIV), feline herpesvirus (FHV), and feline calicivirus (FCV) in cats are transmissible to other cats. Leptospirosis is transmissible to other animals and human beings.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Lethargy
- Anorexia
- Behavior change due to oral pain
- Halitosis
- Hypersalivation

PHYSICAL EXAM FINDINGS

- Gingivitis
- Faucitis (inflammation of the archway between the pharyngeal and oral cavities [formed by the tongue, anterior and posterior tonsillar pillars, and soft palate])
- Pharyngitis
- Dental plaque accumulation
- Oral mass
- Buccitis/buccal mucosal ulceration
- Lingual ulceration
- Kissing ulcers: mucosal ulceration (common in CUPS)
- Scar tissue formation on lateral margins of tongue (CUPS)

ETIOLOGY AND PATHOPHYSIOLOGY

- Metabolic causes: renal failure (uremia; common), diabetes mellitus, hypothyroidism, hypoparathyroidism
- Immune-mediated disease: oral ulcers occur with pemphigus vulgaris (90% of cases), bullous pemphigoid (80% of cases), systemic lupus erythematosus (SLE) (50% of cases), and discoid lupus erythematosus and can also be drug-induced (toxic epidermal necrolysis)
- Infectious: FeLV, FIV, FCV, FHV, leptospirosis (dogs), periodontal disease (dogs and cats)
- Neoplastic: melanoma, squamous cell carcinoma (SCC), fibrosarcoma
- Traumatic: foreign body, electric cord shock, malocclusion, “gum chewer's disease“ (chronic chewing of cheek)
- Idiopathic: eosinophilic granuloma (cats, Siberian huskies, Samoyeds), LPS, CUPS
- Miscellaneous: caustic burns (acids), thallium toxicity, protein-calorie malnutrition, riboflavin deficiency

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Oral mucosal ulcers may be easily noted on physical exam or may be subtle. A heightened index of suspicion is warranted with hypersalivating or anorexic patients. Features of the history and physical exam should guide the selection of diagnostic tests once ulcers have been observed.

DIFFERENTIAL DIAGNOSIS

- History, physical, and oral exam can differentiate foreign bodies, malocclusions, toxin/chemical exposure, and electrical burns.
- Breed predispositions and response to therapy can help identify idiopathic disorders.

INITIAL DATABASE

- Thorough oral examination (may require sedation or general anesthesia)
- CBC: inflammatory leukogram may be present with infectious or immunemediated diseases.
- Serum biochemical profile: evidence for metabolic disease (e.g., renal failure)
- Urinalysis: urine specific gravity may support a diagnosis of renal failure. Proteinuria may be present if immune-mediated, neoplastic, or infectious disorders cause secondary glomerular damage.

ADVANCED OR CONFIRMATORY TESTING

- Serologic titers or other tests (e.g., PCR for infectious agents such as FeLV, herpesvirus) or systemic immune-mediated disease (e.g., antinuclear antibody titer for SLE)
- Thyroid hormone assays
- Thoracic radiographs: evaluation for metastatic disease
- Oral radiographs: evaluation for concurrent osteomyelitis secondary to severe periodontal disease or bony involvement from malignant neoplasia
- Mucosal or gingival biopsy: support for diagnosis of idiopathic, immune-mediated, chronic inflammatory, and neoplastic diseases

TREATMENT

TREATMENT OVERVIEW

Correct underlying cause if possible.

ACUTE GENERAL TREATMENT

Supportive therapy:

- Soft diets
- Fluid support (SQ or IV) if the patient is dehydrated
- Nutrition: esophagostomy or gastrostomy feeding tubes (see pp. 1269 and 1270) may be required if oral disease or pain is resulting in steadfast and prolonged anorexia.

CHRONIC TREATMENT

- For idiopathic conditions (i.e., CUPS, LPS), meticulous dental care to prevent plaque accumulation is necessary. In addition, dental extractions (partial, caudal, or full mouth) may be necessary to remove the source of inflammation.
- Treat metabolic conditions if present.
- Immunosuppressive drug therapy (e.g., corticosteroids, azathioprine) may be required for immune-mediated diseases.
- Antimicrobial therapy may be required to treat secondary periodontal or oral infections.
- Topical solutions (e.g., chlorhexidine solution) to inhibit bacterial growth or promote improved dental health may be beneficial.

POSSIBLE COMPLICATIONS

Side effects from corticosteroid (e.g., polyuria and polydipsia [PU/PD]) or immunosuppressive medications (e.g., myelosuppression)

RECOMMENDED MONITORING

Dependent on cause and therapies employed

PROGNOSIS AND OUTCOME

- Dependent on underlying cause
- The idiopathic conditions (CUPS, LPS) can be difficult to treat and require considerable client commitment and compliance.

PEARLS & CONSIDERATIONS

CLIENT EDUCATION

For idiopathic conditions, clients should be encouraged to keep their pets' teeth as free from plaque as possible using both at-home (brushing, cleansing solutions; see) and veterinary (dental cleaning) therapies.

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Smith MM: Oral and salivary gland disorders. In Ettinger SJ, Feldman EC, editors: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Elsevier Saunders, pp 1290–1297.

AUTHOR: DARCY H. SHAW

EDITOR: ETIENNE CÔTÉ

Ulcerative and Erosive Skin Disorders

BASIC INFORMATION

DEFINITION

A cutaneous erosion is a shallow epidermal defect that does not penetrate the basal membrane. Erosions are usually associated with self-trauma or mild epidermal affections. A cutaneous ulcer is produced by a break in the continuity of the epidermis, with exposure of the underlying dermis. Ulcers are usually a consequence of a deep and serious pathologic process. Healing ulcers typically result in scarring.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Vary according to the underlying pathologic process:

- Some dermatoses are seen more frequently or strictly in one species rather than another (e.g., eosinophilic granuloma in cats).
- Young animals are predisposed to genetic defects or infectious diseases, whereas older animals are predisposed to immune-mediated diseases or neoplasia.

GENETICS & BREED PREDISPOSITION: Some diseases tend to have a genetic basis or are related to anatomic defects (e.g., intertrigo in such breeds as the Chinese shar-pei).

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: A thorough history of the animal is important, considering the extensive list of differential diagnoses. Some essential clues help define the condition:

- Travel history (e.g., leishmaniasis in dogs traveling to Europe), grooming and boarding (contagion risk; e.g., herpesvirus infection in cats), and similar environmental information may affect a patient's risk of developing a certain condition.
- Dietary history (e.g., food allergy)
- Presence of signs of systemic illness (e.g., lethargy, anorexia, lameness, etc.) may narrow the differential diagnosis, and diagnostic methods will be oriented differently (e.g., toward systemic lupus erythematosus [SLE], leishmaniasis, systemic mycoses).
- Prior treatments: response to prior therapy or therapy administered prior to onset of clinical signs allows the inclusion or exclusion of some dermatoses (e.g., drug eruption).

PHYSICAL EXAM FINDINGS

- Dermatologic examination for identifying erosive and ulcerative lesions, and general physical examination to detect signs of underlying systemic diseases.
- The clinician should take note of primary lesions such as vesicles, bullae, and pustules and the distribution of the lesions (e.g., involvement of the mucosa). This information can suggest a specific group of diseases.
- Secondary lesions such as crusts are common.
- Exact description of the lesions varies according to the underlying disease.

ETIOLOGY AND PATHOPHYSIOLOGY

Variable, depending on underlying cause.

- Congenital, hereditary, and conformational defects: for example, ulcerations can result from skin friction (e.g., intertrigo) or can be secondary to abnormal fragility of the dermoepidermal junction (e.g., epidermolysis bullosa).
- Infectious diseases (bacterial, viral, parasitic, fungal, rickettsial): some organisms infect and lyse keratinocytes (e.g., herpesvirus) or can cause epidermal necrosis secondary to either vasculitis (e.g., canine Rocky Mountain spotted fever) or a substantial inflammatory reaction, leading to ulcerative dermatitis.
- Immune-mediated disorders: ulcers may follow the rupture of vesicles and bullae caused by the action of antibodies.
- Drug-induced conditions
- Self-induced lesions
- Environmental injuries (e.g., coagulation necrosis of the epidermis/dermis associated with thermal or chemical burns results in ulcerations)

- Secondary to systemic diseases (e.g., uremia resulting from renal failure may cause oral ulceration).
- Ischemic disorders: any dermatopathy that interferes with vascular supply of the skin can potentially cause ulcers secondary to skin necrosis.
- Neoplasia: ulcerations noticed in skin tumors, such as cutaneous epitheliotropic lymphoma or squamous cell carcinoma (SCC), are usually secondary to the infiltration of the skin by neoplastic cells and often correlate with the aggressiveness of the tumor.
- Idiopathic condition

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A definitive diagnosis is required in order to institute the appropriate treatment regimen.

DIFFERENTIAL DIAGNOSIS

- Congenital and hereditary: idiopathic facial dermatitis of Persian and Himalayan cats, aplasia cutis, epidermolysis bullosa (EB), familial canine dermatomyositis
- Infectious diseases: demodicosis, flea bite hypersensitivity, feline mosquito bite hypersensitivity, fly dermatitis; systemic mycoses, sporotrichosis, phaeohyphomycosis, zygomycosis, candidiasis, dermatophyte granuloma, pseudomycetoma, protothecosis, pythiosis, aspergillosis; deep pyoderma, mucocutaneous pyoderma, pyotraumatic dermatitis; feline leukemia virus (FeLV), feline cowpox, feline calicivirus (FCV), feline herpesvirus (FHV); canine Rocky Mountain spotted fever, leishmaniasis
- Immune-mediated disorders: pemphigus, bullous pemphigoid, erythema multiforme, toxic epidermal necrolysis, vasculitis, lupus erythematosus, EB acquisita, cold-agglutinin disease, cutaneous drug eruption
- Self-induced lesions: pruritic dermatoses, psychogenic dermatoses, neuropathies
- Environmental injuries: burns, frostbites
- Systemic diseases: superficial necrolytic dermatitis (hepatocutaneous syndrome), calcinosis cutis, uremia
- Neoplasia: SCC, cutaneous epitheliotropic lymphoma, mast cell tumor, paraneoplastic alopecia
- Conformational dermatoses: intertrigo, pressure sores
- Iatrogenic: radiation therapy, thermal or tissue injury
- Miscellaneous: feline indolent ulcer, feline eosinophilic plaque, feline plasma cell pododermatitis, feline ulcerative dermatitis with linear sub-epidermal fibrosis, snakebite

INITIAL DATABASE

- Patient history and physical examination are very important in the diagnostic process.
- Cytologic examination of any exudate contents: bacteria, inflammatory cells, acantholytic keratinocytes (pemphigus), fungal organisms
- CBC, serum biochemistry panel, and urinalysis if systemic signs are observed

ADVANCED OR CONFIRMATORY TESTING

- Skin biopsies for histopathologic examination are indicated in most cases of ulcerative dermatoses.
- Endocrine tests and serologic examination depend on suspected disease.
- Coombs' test: cold-agglutinin disease
- Antinuclear antibody (ANA) test: positive in virtually all animals with SLE
- Imaging, if relevant, to confirm systemic disease or stage tumors

TREATMENT

TREATMENT OVERVIEW

Varies considerably according to the disease. It must address the primary cause of the erosions or ulcers.

ACUTE AND CHRONIC TREATMENT

- Immunosuppressive treatments are required in immune-mediated diseases, whereas infectious diseases require proper antimicrobial treatment.
- Antiparasitic treatments as required

- Neoplastic diseases should be addressed according to the type of tumor.
- Some patients with conformational dermatoses may need surgery to correct the skin defect.
- Supportive care may be required, especially in animals with severe lesions or systemic illness.

PROGNOSIS AND OUTCOME

Ranges widely from good to poor, depending of the primary cause

PEARLS & CONSIDERATIONS

COMMENTS

- Considering the wide range of treatments, make a definitive diagnosis to correctly address the disease and prevent adverse effects of an improper treatment trial.
- Primary lesions (e.g., vesicles, bullae, and pustules) or skin surrounding erosion/ulcer should be sampled when skin biopsy is performed.
- Some of these diseases are life threatening.
- Be aware of the zoonotic potential of some of these diseases (e.g., sporotrichosis).

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Scott DW, Miller WH, Griffin CE, eds: Muller and Kirk' s small animal dermatology, ed 6, Philadelphia, 2001, WB Saunders.

AUTHOR: FRÉDÉRIC SAUVÉ

EDITOR: MANON PARADIS

Vulvar Discharge

Additional Images Available on Website

BASIC INFORMATION

DEFINITION

Discharge of substance from the urogenital tract (most likely vagina or uterus). May be abnormal or physiologically appropriate. Very common in the bitch during the normal estrous cycle and periparturient period

EPIDEMIOLOGY

SPECIES, AGE, SEX: More common in dogs (spayed or intact)

RISK FACTORS

- Sexually intact bitch
- Post partum bitch or queen
- Vaginal stricture or septum, vaginal foreign body, vaginal neoplasia
- Ovarian remnant syndrome
- Urethral neoplasia, ectopic ureters, redundant lateral/dorsal vulvar fold
- Mibolerone treatment

CONTAGION & ZOONOSIS

- *Bruceila canis*
- Transmissible venereal tumor (TVT)

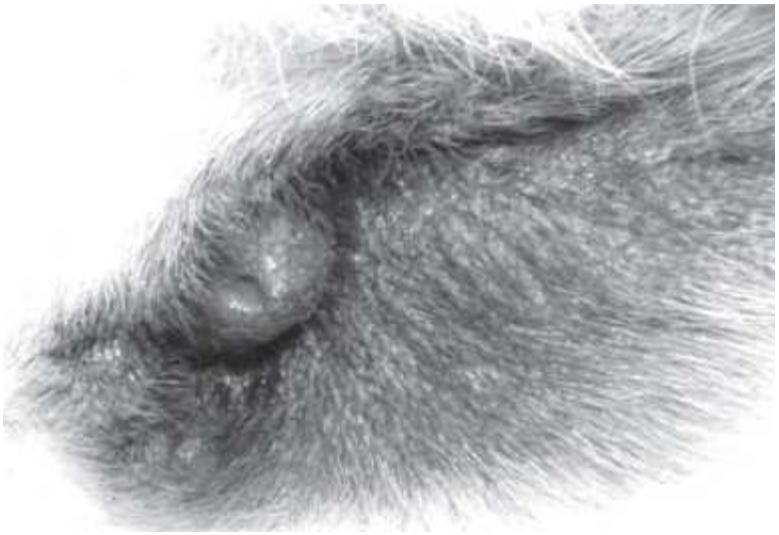
ASSOCIATED CONDITIONS & DISORDERS

- Frequently associated with pyometra
- Not uncommon in association with abortion/premature labor, metritis, or endometritis
- Rarely noted secondary to subinvolution of placental sites (SIPS) in the bitch
- Others: vulvar fold pyoderma, urinary tract infection (UTI), urinary incontinence, urethritis, pseudohermaphroditism, hermaphroditism

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Visible vulvar discharge
- Malodor
- Increased genital grooming
- Staining of carpet/bedding
- “Scooting” (rubbing perineum on floor)
- Pollakiuria
- Attracting males
- Hair staining in perineal area



VULVAR DISCHARGE Ulcerative perivulvar pyoderma typically seen in association with chronic vulvar discharge in dogs.

- Lethargy, inappetence in cases of sepsis or hypovolemic shock (e.g., pyometra)
- Polyuria and polydipsia with pyometra

PHYSICAL EXAM FINDINGS

- Generally, physical abnormalities are restricted to genital tract; exceptions: pyometra with sepsis, or coagulopathy
- Inflamed, moist, red perivulvar skin ± moist or ulcerative pyoderma
- Red ± ulcerated vulvar mucosa; clitoral enlargement
- Classification of discharge type assists diagnostic approach:
  - Color (colorless, brown, green, red, purulent)
  - Smell (malodorous or not)
  - Volume (mild, moderate, copious)
- Discharge associated with bacterial infection is typically purulent/mucosanguineous and malodorous with moderate to copious volume.
- Discharge due to inflammation is typically mucoid, white or clear, mild to moderate volume, and not malodorous.
- Rectal palpation may reveal foreign body or mass in the posterior vaginal vault and/or pelvic urethra.
- Digital vaginal examination (see p. 1360) may reveal discharge; small mucosal nodules (reactive lymphoid tissue) may be palpable with any inflammation and are not pathognomonic for any one cause.
- Most vaginal strictures are palpable at the level of the urethral papilla because of embryologic fusion of müllerian ducts and urogenital sinus.
- Fever, signs of septic shock, distended uterine horns, and/or abdominal discomfort: possible if pyometra
- Petechiae and bleeding of other mucous membranes (nose, gums) may be present when coagulopathy is the cause of vaginal discharge; may also be noted in association with sepsis.

ETIOLOGY AND PATHOPHYSIOLOGY

- Purulent vaginal discharge in adult intact animal (diestrous): commonly due to pyometra (see p. 954)
- Vaginal discharge in adult animals: commonly from secondary bacterial vaginitis due to anatomic abnormalities (lateral/dorsal vulvar fold dermatitis, vaginal stricture, septum), foreign body, urinary tract infection with urethritis/vestibulitis, or neoplasia
- Lymphoplasmacytic vaginitis and juvenile-onset “puppy” vaginitis: unknown etiology
- Strictures are associated with adult-onset vaginitis due to a change in vaginal mucus drainage.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

- Purulent vaginal discharge requires immediate evaluation for pyometra (or metritis/endometritis in the periparturient period).
- Hemorrhagic vaginal discharge warrants evaluation for systemic bleeding disorders (see p. 493).
- More chronic discharges should be initially evaluated with a thorough physical examination, including rectal and vaginal palpations, cytologic exam of the discharge, and routine database for detection of urinary tract infection, vulvar abnormalities, vaginal strictures, foreign body, and palpable neoplastic change.
- Additional imaging, culture, and biopsy sample acquisition for detection of uterine stump abnormalities, ovarian remnants,

urinary tract abnormalities, and vaginitis should be guided by preliminary findings and may require referral.

DIFFERENTIAL DIAGNOSIS

- Normal vaginal discharge; none should be malodorous:
  - Estrus: hemorrhagic, low volume
  - Parturition: moderate to large volume, hemorrhagic, green or brown
  - Postpartum: low to moderate volume for up to 4-6 weeks, green initially then brown
- Endometritis/metritis: purulent, mucosanguineous, malodorous, moderate volume in association with a febrile post partum bitch
- Subinvolution of placental sites (see p. 1060): hemorrhagic, moderate volume in association with periparturient period
- Juvenile-onset vaginitis: white, mucoid, moderate in volume
- Secondary bacterial vaginitis due to stricture, foreign body: mucoid, blood-tinged discharge; may be malodorous; scant to moderate in volume
- Herpesvirus, *Brucella canis* infection (abortion): abortion-associated discharge is typically brown, moderate in volume.
- Urogenital neoplasia: variable; may be hemorrhagic, serous, or mucoid; scant to moderate in volume
- Bleeding disorder: hemorrhagic; volume depends on degree of coagulation impairment
- Lymphoplasmacytic vaginitis: typically low volume, scant, and serous initially; may become mucoid with secondary bacterial infection; occasionally serosanguineous
- Primary bacterial vaginitis (uncommon)
- Urinary tract infection/urethritis
- Vulvar fold pyoderma: malodor is typically noted from the vulvar area; discharge may be mild to moderate in volume; mucoid and occasionally blood tinged
- TVT: vulvar mass typically noted; associated discharge is typically serosanguineous (see p. 1114).

INITIAL DATABASE

- Physical examination, including evaluation of vulvar lip conformation, mucosa, and digital rectal and vaginal examination
- Vaginal cytologic examination
- CBC: leukocytosis with left shift, toxic changes: common with pyometra; leukopenia possible with endometritis; anemia may be noted postpartum or in association with SIPS.
- Serum biochemical analysis: generally unremarkable unless systemic involvement
- Urinalysis, sediment examination, and culture: assess for concurrent UTI. Avoid cystocentesis if there is a possibility of pyometra or coagulopathy.
- Ultrasonographic evaluation of genitourinary tract: diagnostic test of choice for pyometra

ADVANCED OR CONFIRMATORY TESTING

- Guarded cranial vaginal aerobic/mycoplasma bacterial culture to evaluate bacterial population
- Retrograde double-contrast vaginocystourethrogram
- Cystoscopy and vaginoscopy, including examination of cervix if present: foreign body, congenital malformation, mass
- Vaginal biopsy ± mass biopsy
- Coagulation profile
- Urethral pressure profile

TREATMENT

TREATMENT OVERVIEW

Treatment goals are to restore patient's comfort, correct underlying cause, and prevent recurrence.

ACUTE AND CHRONIC TREATMENT

The nature and extent of treatment is determined by the underlying cause; vaginal discharge is simply a clue of underlying disease.

BEHAVIOR/EXERCISE

If discharge is associated with an infectious disease (e.g., *Brucella canis,* TVT), then bitch should be quarantined from other dogs to prevent transmission.

POSSIBLE COMPLICATIONS

Chronic estrogen supplementation may cause myelotoxicity.

RECOMMENDED MONITORING

- When diethylstilbestrol (DES) is used in high doses or for chronic therapy, regular evaluation of patient's CBC is advised (myelotoxicity).
- Patients with diminished renal function receiving cephalosporins may require more frequent renal monitoring.
- Baseline CBC, complete serum biochemistry, and urinalysis should be obtained prior to commencement of carprofen and rechecked on an ongoing basis during therapy.
- Nonsteroidal antiinflammatory drug (NSAID) use may be associated with hepatotoxicity, renal toxicity, and gastrointestinal disturbance.
- Clinical response for uncomplicated bacterial vaginitis
- Reexamination and reevaluation if complete resolution is not achieved after 14 days of therapy

PROGNOSIS AND OUTCOME

- Good prognosis for secondary bacterial vaginitis if underlying cause is identified and corrected.
- Idiopathic lymphoplasmacytic vaginitis is often recurrent but responsive to steroid therapy.

PEARLS & CONSIDERATIONS

COMMENTS

- Always rule out pyometra in an intact animal with vaginal discharge.
- Always perform digital vaginal and rectal palpation when initially evaluating a patient with vaginal discharge.
- Normal vaginal flora is mixed *(Escherichia coli, Pasteurella multocida,* β-hemolytic *Streptococcus* group G most common). Abnormal flora is typically a single isolate and/or heavy growth.
- Vaginal cytologic examination is always helpful to detect discharge due to estrus in the bitch and the presence of estrogen influence.
- Surgical correction of strictures is not advised; clitorectomy is advised in cases of clitoral hypertrophy.

PREVENTION

Pyometra may be avoided by ovariectomy/ovariohysterectomy.

TECHNICIAN TIPS

When taking a medical history, always ask owners when their bitch's last estrous cycle occurred or confirm previous ovariohysterectomy.

CLIENT EDUCATION

- Positive bacterial culture does not indicate disease is present.
- Prebreeding antibiotics do not prevent vaginitis or pyometra.
- Puppy vaginitis is usually self-limiting and does not require antimicrobial treatment; antimicrobial treatment of puppy vaginitis may prolong resolution of the problem.

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AUTHOR: SOPHIE GRUNDY

EDITOR: MICHELLE A. KUTZLER

von Willebrand Disease

BASIC INFORMATION

DEFINITION

Hereditary primary hemostatic defect caused by a quantitative or functional deficiency of von Willebrand factor (VWF). VWF is an adhesive protein required for normal platelet-collagen binding at sites of small vessel injury. Clinical expression varies in severity from a mild bleeding tendency manifesting primarily after injury to more severe forms characterized by recurrent mucosal hemorrhage and prolonged bleeding from normal processes, such as deciduous tooth loss.

SYNONYMS

Factor-VIII related antigen (old terminology; protein is now referred to as *VWF),* VWD

EPIDEMIOLOGY

SPECIES, AGE, SEX

- von Willebrand disease (VWD) is the most common hereditary bleeding disorder of dogs. It is a rare hemostatic defect of cats.
- Severe forms typically manifest by 1 year of age, and milder forms may be inapparent unless the patient undergoes surgery or trauma.

GENETICS & BREED PREDISPOSITION

- Autosomal trait with three type classifications:
  - Type 1 VWD: mild to moderate; recessive or incomplete dominant inheritance
  - Types 2 and 3 VWD: severe; recessive inheritance
- Males and females express and transmit VWD with equal frequency.
- In recessive forms, affected pups inherit a VWF mutation from both dam and sire.
- Affected breeds:
  - Type 1 VWD: Airedale, Akita, Bernese mountain dog, dachshund, Doberman pinscher, German shepherd, golden retriever, greyhound, Irish wolfhound, Kerry blue terrier, Manchester terrier, miniature pinscher, Papillon, Pembroke Welsh corgi, poodle, schnauzer, and sporadic cases in any breed
  - Type 2 VWD: German short-haired pointer, German wirehaired pointer
  - Type 3 VWD: Chesapeake Bay retriever, Dutch kooiker, Scottish terrier, Shetland sheepdog, and sporadic cases (recent cases in Australian shepherd, border collie, cocker spaniel, Labrador retriever, Maltese)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Type 1 VWD: quantitative protein deficiency. Low plasma concentration of VWF (von Willebrand factor antigen [VWF:Ag]) with proportionate reduction in VWF function; the VWF protein has a full distribution of multimeric forms.
- Type 2 VWD: both quantitative and functional protein deficiency; low plasma VWF:Ag has a disproportionate decrease in VWF function measured by collagen binding or support of platelet agglutination. VWF protein lacks the high molecular weight multimers.
- Type 3 VWD: severe VWF deficiency, no detectable plasma VWF

HISTORY, CHIEF COMPLAINT

- Severe forms: recurrent mucosal bleeds, prolonged bleeding from loss of deciduous teeth or minor wounds, blood loss anemia after surgery or trauma
- Mild forms: few spontaneous or severe bleeds; abnormal bleeding typically observed after surgical or traumatic injury

PHYSICAL EXAM FINDINGS

- Abnormal hemorrhage:
  - Mucosal bleeding

- Abnormal bleeding from traumatic/surgical wounds
- Pallor due to blood loss anemia

ETIOLOGY AND PATHOPHYSIOLOGY

- Distinct VWF mutations causative for type 3 VWD have been described in Scottish terriers and Dutch kooiker dogs.
- Homozygosity for a mutation located at a splice site of the VWF gene has been associated with low VWF protein in type 1 VWD.
- Types 2 and 3 VWD cause a moderate to severe bleeding tendency.
- The clinical severity of type 1 VWD generally correlates with decrease in VWF concentration.
- VWF is an adhesive protein required for normal platelet-collagen binding at sites of small vessel injury under high shear.
- A lack of VWF impairs platelet plug formation and causes bleeding despite normal in vitro platelet numbers, normal platelet aggregation, and normal coagulation cascade parameters (normal coagulation profile).

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

Von Willebrand disease typically causes signs of mucosal hemorrhage and prolonged postsurgical/traumatic hemorrhage. Platelet count and coagulation screening tests are normal in dogs (or cats) with VWD.

DIFFERENTIAL DIAGNOSIS

- Primary hemostatic defects:
  - Thrombocytopenia
  - Acquired or hereditary platelet dysfunction (thrombocytopathias; e.g., patient taking aspirin)
- Coagulation factor deficiency
- Vasculopathy or erosive/infiltrative vessel defect causing mucosal hemorrhage

INITIAL DATABASE

- Thorough physical exam to define single versus multiple sites of hemorrhage
- Baseline hematocrit and plasma protein: normal or decreased if bleeding is severe and chronic
- Platelet count or platelet estimate from blood smear: usually normal
- Point-of-care coagulation screening tests: usually normal:
  - Activated clotting time (ACT)
  - Activated partial thromboplastin time (APTT)
  - Prothrombin time (PT)
- Bleeding time (buccal mucosal bleeding time): increased (see p. 1222)

ADVANCED OR CONFIRMATORY TESTING

Clinical diagnosis is based on specific measurement of plasma VWF concentration:

- VWF concentration (VWF:Ag):
  - VWF:Ag < 50% is evidence of VWF deficiency, but clinical bleeding tendency is usually seen in animals having more severe deficiency (<25%).
  - Types 1 and 2 VWD in dogs are characterized by the presence of low protein concentration, whereas type 3 VWD is characterized by a complete absence of VWF (VWF:Ag < 0.1%).
- Differentiation of types 1 and 2 VWD is based on the presence of dysfunctional and structurally abnormal protein in the type 2 form. Abnormal protein is identified based on the following tests:
  - VWF:CB = VWF collagen binding activity (functional assay)
  - VWF multimer analyses = Western blot to visualize VWF subunit structure
- Hereditary type 2 VWD has been identified only in two breeds: German wirehaired and short-haired pointers.
- An acquired type 2 VWD occurs in human beings with aortic stenosis. A recent study of mitral valve disease in Cavalier King Charles spaniels revealed abnormal VWF multimer distribution, compatible with classification of type 2 VWD.

TREATMENT 

TREATMENT OVERVIEW

- Control active bleeding with transfusion therapy and local wound care.
- Minimize frequency of induced bleeds by avoiding surgery, trauma, and any drug therapy that inhibits platelet function or coagulation factor activity.
- Correct any underlying medical conditions that might impair hemostasis.

ACUTE GENERAL TREATMENT

A patient that had a normal preoperative platelet count but bleeds persistently during a surgical procedure, shows no physical evidence of severe systemic illness (vasculitis), and is not known to have been exposed to anticoagulant (e.g., rodenticide) or antiplatelet (e.g., aspirin) substances should be suspected of having VWD and may be treated as follows pending the results of confirmatory tests (see Advanced or Confirmatory Testing above):

- Transfusion to supply hemostatic levels of VWF is the best strategy to control active hemorrhage refractory to local wound care. Patients with severe VWD (typically types 2 and 3 VWD) may require a second or third transfusion within the first 24 hours of presentation to sustain hemostasis after an initial response.
- Transfusion of plasma components reduces risk of volume overload or red cell sensitization while maximizing VWF replacement.
- Fresh frozen plasma (10-15 mL/kg IV):
  - Transfuse at the high end of dosage range for the initial transfusion.
  - Severely deficient patients may require repeated transfusions at q 8-12 h intervals.
- Cryoprecipitate (unit dosage varies for different suppliers):
  - Cryoprecipitate is prepared from fresh frozen plasma and contains a fivefold to tenfold concentration of VWF in approximately one-tenth the volume of the starting plasma.
  - Cryoprecipitate's low volume eliminates the risk of volume overload if repeated transfusion is needed for high-dose VWF replacement.
- Fresh whole blood (12-20 mL/kg) can be used as a source of VWF replacement if plasma components are unavailable or if replacement of red blood cells (RBCs) and VWF is desired to treat ongoing blood-loss anemia:
  - Risk of volume overload generally limits whole blood transfusion to q-24-h intervals (see p. 1347).
- Packed RBC transfusion (6-12 mL/kg) is indicated to treat severe blood-loss anemia.
- Use local wound care (suture, pressure wrap, tissue glue) to help control bleeding from cutaneous or superficial sites.

CHRONIC TREATMENT

- Intermittent transfusion may be needed to control hemorrhagic events in patients with severe (types 2 and 3) VWD.
- Preoperative transfusion to patients with type 2 or 3 VWD or severe expression of type 1 VWD to replace VWF before surgical procedures:
  - Fresh frozen plasma and cryoprecipitate are the best products for preoperative prophylaxis: same dose as described previously.
  - Transfusion is administered just before the surgical procedure. Peak VWF is obtained immediately post transfusion, and values fall to baseline by 24 hours.
  - Close monitoring is required during the first 24 hours after the operation. Repeat transfusion (at q 8-12 h) may be required during this period for severe VWD.
- Desmopressin acetate (DDAVP; deamino-8-D-arginine vasopressin) is a synthetic vasopressin analog that can be used preoperatively to enhance surgical hemostasis in patients with mild to moderate VWD (type 1 VWD); dosage is 1 mcg/kg SQ, given 30 minutes preoperatively.
  - The response to DDAVP varies, and transfusion should be available if hemorrhage develops despite DDAVP therapy.
- The development of endocrinopathy (e.g., hypothyroidism, hypoadrenocorticism) or thrombocytopenia may exacerbate the bleeding tendency of VWF-deficient patients. Identification and correction of these disorders are indicated to help reduce risk of clinical signs.

BEHAVIOR/EXERCISE

Von Willebrand disease, unlike hemophilia and other hereditary coagulopathies, does not cause hemarthrosis. Exercise restrictions are unwarranted, but sharp sticks or chew toys should be avoided to prevent oral mucosal injuries.

DRUG INTERACTIONS

Avoid drugs with anticoagulant or antiplatelet effects in animals with VWD:

- Nonsteroidal antiinflammatory drugs (NSAIDs)
- Sulfonamide antibiotics
- Heparin, warfarin (Coumadin)
- Plasma expanders
- Estrogens

- Cytotoxic drugs

POSSIBLE COMPLICATIONS

RBC sensitization causing transfusion reactions:

- Transfuse plasma components when possible.
- Dogs with severe VWD should be blood typed because repeated transfusion may be required. Choose type-matched donors for RBC or whole blood transfusions.
- Canine transfusion: after a first RBC transfusion, perform a cross-match before subsequent transfusions.

RECOMMENDED MONITORING

Adequate VWF replacement is demonstrated by:

- Cessation of active bleeding
- Stabilization of hematocrit/plasma protein

PROGNOSIS AND OUTCOME 

- Most dogs clinically affected with VWD have a good quality of life and require transfusions intermittently or rarely:
  - Animals with severe VWD (types 2 and 3 VWD) are most likely to develop spontaneous bleeds or require repeated transfusion. All dogs affected with types 2 and 3 VWD should receive a preoperative transfusion before surgical procedures.
  - Many dogs with type 1 VWD have mild disease expression. Clinical signs of abnormal bleeding are most likely to develop in dogs with VWF:Ag < 25%.
- Acute bleeding crises may require aggressive transfusion support to rapidly provide hemostatic levels of VWF protein. High-dose component therapy (fresh frozen plasma or cryoprecipitate) may be needed to control severe bleeds.

PEARLS & CONSIDERATIONS 

COMMENTS

- Specific diagnosis of VWD requires measurement of plasma VWF concentration (VWF:Ag):
  - The findings of normal coagulation panel and platelet count do not rule out VWD.
- Signs of mucosal hemorrhage (rather than petechiae) are typical manifestations of VWD.

PREVENTION

- Screen animals preoperatively to determine baseline VWF:Ag for breeds or lines with a high prevalence of VWD. The risk of abnormal bleeding is greatest for dogs with VWF:Ag that is <25%.
- Clinically affected dogs should not be used for breeding. Carriers of the VWD trait can be identified based on low VWF:Ag (<50%). The VWF protein assay is relatively fast and inexpensive and does not require knowledge of mutation type; however, values for carrier and clear dogs may overlap at the low end of the normal range (50%-70% VWF:Ag). A direct mutation detection strategy is offered for several breed variants of VWD (Vetgen), using DNA isolated from cheek swabs. Using this method, dogs are classified as “VWD affected” if they are homozygous for a mutation, or “VWD carrier” if they are heterozygous. DNA analyses provide unambiguous information on the presence, absence, and copy number of a specific mutation type.
- Selective breeding practices can reduce the prevalence or eliminate VWD from an affected pedigree. Breeding two clear parents is ideal and is expected to produce entire litters of clear pups. Breeding one carrier parent to a clear mate may be acceptable, and the clear pups produced from these matings can be used for subsequent generations. Carrier-to-carrier matings may produce affected pups and therefore should be avoided.

TECHNICIAN TIPS

Sample quality is important for obtaining valid VWF:Ag assay results. To avoid activation and depletion of VWF, blood samples should be drawn directly into tubes or syringes containing anticoagulant and centrifuged to separate plasma as soon as possible after collection.

CLIENT EDUCATION

Owners and breeders should be aware of VWD and be advised to screen their pets to prevent propagation of the trait.

SUGGESTED READING

Brooks MB, Catalfamo JL: Platelet disorders and von Willebrand disease. In Ettinger S, Feldman E, editors: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Elsevier, pp 1918–1929.

AUTHOR: MARJORY B. BROOKS

EDITOR: SUSAN M. COTTER

Vomiting, Chronic

BASIC INFORMATION

DEFINITION

- Active expulsion of stomach and sometimes duodenal content preceded by nausea and retching
- Either intermittent course or persistent vomiting for more than 7 days
- Chronic vomiting is a very common clinical sign and can be associated with a variety of disorders.

SYNONYM

Chronic emesis

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Any animal can be affected; epidemiology depends on the underlying cause.
- Young animals are more likely to ingest foreign bodies.

GENETICS & BREED PREDISPOSITION

- Brachycephalic breeds: pyloric stenosis
- Airedale terrier: pancreatic carcinoma
- Shar-pei, rottweiler, German shepherd: inflammatory bowel disease (IBD)

RISK FACTORS

- Use of drugs such as nonsteroidal anti-inflammatory drugs (NSAIDs) and glucocorticoids, chemotherapy
- Numerous systemic diseases other than gastrointestinal (GI) disease can cause vomiting.

CONTAGION & ZOONOSIS: Zoonotic potential of *Helicobacter heilmanii* and *H. felis* unclear.

ASSOCIATED CONDITIONS & DISORDERS: Hypochloremic metabolic alkalosis initially; progression leads to dehydration and hypovolemia, and metabolic acidosis may emerge.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Owners may present animals that look healthy with no obvious signs of systemic disease.
- Owners may present animals that have signs of systemic disease (e.g., dehydration, icterus).

HISTORY, CHIEF COMPLAINT

- It is important to differentiate vomiting from dysphagia and regurgitation:
  - Vomiting involves forceful retching and abdominal contraction and may produce bile-stained contents.
- Administration of potentially ulcerogenic drugs such as NSAIDs or glucocorticoids
- The possibility of ingestion of a foreign body
- Dietary history, a description of the vomitus (e.g., possible hematemesis), and its time relation to food intake
- If vomiting of undigested or partially digested food occurs >7-10 hours after ingestion, a gastric outflow obstruction or gastric hypomotility is likely.

PHYSICAL EXAM FINDINGS

- A thorough physical examination is mandatory.
- Extra attention is warranted regarding:
  - Hydration status
  - Mouth inspection (sublingual linear foreign body in cats, ulcerations)

- Abdominal palpation (abdominal mass, thickened bowel loops)
- Rectal examination (presence of melena or hematochezia)

- In cats older than 6 years, palpation of the neck region for thyroid nodules is essential.

ETIOLOGY AND PATHOPHYSIOLOGY

- Stimulation of humoral (bloodborne substances) or neural (especially via receptors located throughout the GI tract) pathways can lead to activation of the vomiting center located in the brain (medulla oblongata).
- Certain drugs (e.g., apomorphine, xylazine), uremic toxins, and electrolyte, osmolar, or acid-base disorders can activate the chemoreceptor trigger zone (CRTZ), which is also in the medulla oblongata, and cause vomiting.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Differentiation of systemic causes from primary GI causes begins with history and physical exam; routine blood and urine tests and abdominal radiographs are warranted. If a cause is not found, abdominal sonography and specific tests (e.g., adrenocorticotropic hormone [ACTH] stimulation/resting cortisol in dogs, serum T4 in adult cats) should be considered. Prophylactic broad-spectrum deworming and diet trial are indicated at any time. Ultimately, failing a conclusive diagnosis from these measures, the structure of the proximal GI tract is assessed endoscopically and histologically.

DIFFERENTIAL DIAGNOSIS

Extra-GI causes:

- Extraabdominal disorders:
  - Azotemia/uremia
  - Hypoadrenocorticism
  - Especially in cats: hyperthyroidism, heartworm disease
  - Intoxications
  - Drugs o Neurologic disorders (especially vestibular)
- Intraabdominal disorders:
  - Hepatic disease
  - Pancreatitis
  - Peritonitis

GI causes:

- Gastritis (lymphocytic-plasmacytic, eosinophilic)
- Food intolerance/food allergy
- Foreign body
- Parasites *(Physaloptera* spp., *Ollulanus tricuspis)*
- Neoplasia
- Inflammatory bowel disease
- Bilious vomiting syndrome
- Motility disorders
- Colitis (up to 30% of dogs with colitis may vomit).
- Hiatal hernia

INITIAL DATABASE

- CBC, serum biochemistry profile (including sodium and potassium)
- Urinalysis
- Fecal examination
- Total thyroxine (older cats)
- Medical imaging: abdominal radiographs and/or abdominal ultrasound
- With hematemesis: check drug history, platelet count, coagulation profile, ACTH stimulation, and possibly serum gastriti concentration (gastrinoma); gastroduodenoscopy may be indicated.

ADVANCED OR CONFIRMATORY TESTING

- If clinically relevant, based on history, exam, and minimum database: liver function tests, ACTH stimulation test to rule out

hypoadrenocorticism, toxicologic testing, neurologic examination, canine or feline pancreatic lipase immunoreactivity, feline heartworm antibody testing.
- In some cases, especially to evaluate motility disorders or gastric outflow obstruction, GI contrast studies may be indicated.
- If all previous tests fail to identify a non-GI cause for chronic vomiting, gastroduodenoscopy or an exploratory laparotomy with GI and hepatic biopsies is indicated.

TREATMENT

TREATMENT OVERVIEW

Goals are supportive treatment if needed and elimination/treatment of the underlying cause.

CHRONIC TREATMENT

- Causative treatment is warranted, especially if the patient shows systemic clinical signs. If the patient seems otherwise healthy, dietary therapy alone can be tried if the initial database fails to identify abnormalities. If the response to this treatment is insufficient, further diagnostics are necessary, followed by specific treatment based on results.
- Antiemetics (e.g., maropitant [dogs only], 1 mg/kg SQ or 2 mg/kg PO q24 h; or metoclopramide, 0.2-0.4 mg/ kg SQ q 8 h) can be used empirically after the presence of a foreign body is ruled out. Maropitant should only been given 5 days maximum. Metoclopramide can cause lethargy and restlessness, especially in cats.
- Dietary manipulations (often low-fat, hypoallergenic diets containing a single and novel source of protein)
- Specific treatments (see specific information for individual disorders):
    - Foreign-body removal
    - Inflammatory bowel disease: diet, glucocorticoids, azathioprine
    - Antiparasitic treatments
    - Hypoadrenocorticism: mineralocorticoid and glucocorticoid replacement

DRUG INTERACTIONS

Cimetidine and ranitidine can interfere with hepatic metabolism of other drugs.

POSSIBLE COMPLICATIONS

- Weight loss due to malnutrition
- Dehydration
- Hypokalemia
- Sometimes metabolic alkalosis with hypochloremia if a pyloric (sub) obstruction is present

PROGNOSIS AND OUTCOME

Dependent on etiology

PEARLS & CONSIDERATIONS

COMMENTS

- Numerous causes of chronic vomiting exist. A first step is to rule out extra-GI causes with initial (imaging and laboratory-based) workup. If these results are not significantly abnormal, gastroduodenoscopy or exploratory laparotomy with hepatic and GI biopsies is recommended for animals that chronically vomit.
- Caution is warranted: often, concentrating only on the GI tract too early can lead to misdiagnosis and erroneous treatment.
- Some dogs or cats with vomiting due to IBD show no abnormalities on gastric endoscopy and biopsies. Therefore, endoscopy of the small intestine is important even with a history of chronic vomiting without diarrhea.
- The area under the tongue must be examined in every cat with a chronic vomiting condition; this area is most easily visualized by pressing dorsally on the skin of the underside (ventral surface) of the mandible, between the bodies of the mandible, while the mouth is open. This pressure elevates the sublingual tissues and tongue, exposing the region of interest.

SUGGESTED READING

Tams TR: Gastrointestinal symptoms. In Tams TR, editor: Handbook of small animal gastroenterology. Philadelphia, 2003, WB Saunders, pp 1–50.

AUTHOR: SYLVIE DAMINET

EDITOR: ETIENNE CÔTÉ

Vomiting, Acute

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Active expulsion of stomach and sometimes duodenal contents preceded by nausea and retching; duration is less than 7 days.

SYNONYM

Acute emesis

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Any animal can be affected; patient demographics depend on the underlying cause.
- Young animals are more likely to ingest foreign bodies or acquire infectious diseases (viral and parasitic).

RISK FACTORS: Use of drugs such as nonsteroidal antiinflammatory drugs (NSAIDs) and chemotherapy

GEOGRAPHY AND SEASONALITY: Infectious causes often are more prevalent in specific geographic regions.

ASSOCIATED CONDITIONS & DISORDERS: The most common cause of acute vomiting is dietary indiscretion; however, numerous gastrointestinal (GI) or systemic diseases can also cause vomiting.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Patients can be presented looking healthy with no concurrent signs of systemic involvement. These are classified as “nonserious cases.”
- Patients can be presented with concurrent systemic clinical signs (e.g., lethargy, dehydration, abdominal distension, icterus, fever). These are classified as “serious cases.”

HISTORY, CHIEF COMPLAINT: It is important to differentiate vomiting (active expulsion of GI contents) from dysphagia (difficulty swallowing) and regurgitation (passive movement of ingesta from the esophagus out the mouth). Important components of the history:

- Vaccination status (parvoviral enteritis and canine distemper are more likely in unvaccinated than vaccinated dogs).
- Administration or ingestion of potentially ulcerogenic drugs such as NSAIDs or glucocorticoids
- Possibility of ingestion of a foreign body (e.g., exposure to objects that could be ingested; individual propensity to such ingestions)
- Dietary history (e.g., recent changes; content and volume of recent and typical meals)
- Description of the vomitus (e.g., hematemesis) and productiveness (e.g., nonproductive with gastric dilatation/volvulus [GDV])
- Time relation of vomiting to food intake (if vomiting of undigested or partially digested food occurs >7-10 hours after ingestion, a gastric outflow obstruction or gastric hypomotility is likely).

PHYSICAL EXAM FINDINGS: A thorough physical examination is mandatory. Specific points requiring extra attention include:

- Hydration status
- Mouth inspection (e.g., linear foreign body in cats, ulcerations suggesting intoxication or uremia)
- Abdominal palpation (e.g., abdominal pain, abdominal distension, foreign body, mass, organomegaly)
- Rectal examination (e.g., presence of melena, foreign material)

ETIOLOGY AND PATHOPHYSIOLOGY

- Stimulation of humoral (bloodborne substances) or neural (especially via receptors located throughout the GI tract) pathways can lead to activation of the vomiting center located in the medulla oblongata.

- Certain drugs (e.g., apomorphine [dogs], xylazine [cats]), uremic toxins, and electrolyte, osmolar, or acid-base disorders can also activate the chemoreceptor trigger zone (CRTZ), which in turn triggers the vomiting center, causing vomiting.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A large proportion of patients presenting with this disorder have benign, self-resolving illness. Therefore, the extent of diagnostic testing is determined from presence or absence or signs of systemic illness; known inciting causes (e.g., overeating might prompt minimal investigation, whereas intoxication could warrant tests to evaluate body systems likely to be affected); and the wishes of the pet's owner.

DIFFERENTIAL DIAGNOSIS

GI causes:

- Adverse food reactions (dietary indiscretion, intolerance)
- Gastritis: viral (parvovirus, coronavirus, distemper), bacterial
- Foreign body
- Parasites *(Physaloptera* spp., *Ollulanus tricuspis;* see online chapter: Gastric Parasites)
- Motility disorders
- GDV

Extra-GI causes:

- Extraabdominal disorders:
  - Azotemia/uremia
  - Hypoadrenocorticism
  - Diabetic ketoacidosis
  - Intoxications
  - Drugs (NSAIDs, chemotherapy, glucocorticoids)
  - Neurologic disorders (especially vestibular)
- Intraabdominal disorders:
  - Hepatic failure
  - Pancreatitis
  - Peritonitis
  - Pyometra

INITIAL DATABASE

- If the animal is classified as a nonserious case: history and thorough physical examination are most important; further workup is determined by status and response to treatment.
- If the animal is classified as a serious case and/or if vomiting was nonproductive: further diagnostic workup is always warranted:
  - CBC, serum chemistry profile (including sodium and potassium)
  - Urinalysis
  - Fecal examination
  - Medical imaging:
    - Abdominal radiographs: radiopaque foreign bodies, signs of intestinal obstruction, ileus, GDV, or loss of abdominal detail, suggesting pancreatitis or peritonitis
    - Abdominal ultrasound: changes associated with organomegaly, identification of origin and extent of masses and other such findings
- With hematemesis: review medication/drug exposure history, coagulation profile, adrenocorticotropic hormone (ACTH) stimulation, gastroduodenoscopy

ADVANCED OR CONFIRMATORY TESTING

- If clinically relevant: liver function tests, ACTH stimulation test to rule out hypoadrenocorticism, toxicologic testing, neurologic examination, canine or feline pancreatic lipase immunoreactivity.
- In some cases, especially to evaluate motility disorders or gastric outflow obstruction, GI contrast studies can be performed.
- If vomiting persists (for more than 3-4 days) or worsens, approach the animal as a chronic vomiting case (see p. 1175); endoscopy is warranted if previous tests fail to identify the cause.

TREATMENT

TREATMENT OVERVIEW

- Rehydrate the animal if needed.
- Implement treatment for acutely life-threatening cases (e.g., GDV, intoxications)
- Otherwise, allow the GI tract to "rest" by giving nothing per os (NPO).

ACUTE GENERAL TREATMENT

Nonserious cases (animals generally treated as outpatients):

- NPO for 12-24 hours. If vomiting resolves, initiate a small amount of water or ice cubes. Thereafter, initiate feeding with small quantities of a highly digestible, low-fat diet for several days. Gradually transition to using the regular food.

Serious cases: hospitalize the animal and perform further diagnostic steps as described above (Initial Database and Advanced or Confirmatory Testing).

- NPO, water, and food identical to non-serious cases
- IV fluid therapy (crystalloids)
- Antiemetics:
  - Indications: when vomiting is severe and animal is at risk for dehydration or developing electrolyte/acid-base imbalances or reflux esophagitis
  - Should only be used if the possibility of GI obstruction has been ruled out
  - Maropitant, 1 mg/kg SQ or 2-8 mg/kg PO q 24 h (selective neurokinin[1] receptor antagonist). Dogs only; not labeled for use in cats; *or*
  - Metoclopramide, 0.2-0.5 mg/kg IM or SQ q 8 h (dopamine antagonist; central and peripheral antiemetic agent); *or*
  - Chlorpromazine, 0.1-0.5 mg/kg IM or SQ q 8-24 h, based on response (phenothiazine derivate with central antiemetic activity, α-antagonist, can cause hypotension, especially in dehydrated animals). Avoid chlorpromazine in epileptic animals (may lower seizure threshold).

POSSIBLE COMPLICATIONS

- Dehydration
- Reflux esophagitis
- Aspiration pneumonia
- Electrolyte and acid-base imbalances (especially hypokalemia and sometimes metabolic acidosis)

RECOMMENDED MONITORING

- Signs of dehydration
- Abdominal pain
- Frequency of the vomiting

PROGNOSIS AND OUTCOME

Very good with dietary indiscretion; otherwise, depends on underlying etiology

PEARLS & CONSIDERATIONS

COMMENTS

- Most cases of acute vomiting are self-limiting and do not require further diagnostics, but it is important to not miss the more seriously sick animals and to recommend further workup and treatment if the vomiting does not subside within a few days.
- Use antiemetics carefully because they can mask progressive disease and response to primary therapy.

CLIENT EDUCATION

Avoid dietary indiscretion (whenever possible).

SUGGESTED READING

Tams TR: Gastrointestinal symptoms. In Tams TR, editor: Handbook of small animal gastroenterology. Philadelphia, 2003, WB Saunders, pp 1–50.

AUTHOR: SYLVIE DAMINET

EDITOR: ETIENNE CÔTÉ

Voice Change

BASIC INFORMATION

DEFINITION

Condition characterized by reduced vocalization and/or change in pitch of vocalization

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Canine and feline
- Apparent male predisposition (3:1) for idiopathic laryngeal paralysis

GENETICS & BREED PREDISPOSITION

- Hereditary laryngeal paralysis (Bouvier des Flandres, Siberian husky, pit bull terrier)
- Generalized polyneuropathy (dalmatian)
- Acquired laryngeal paralysis (giant and large breeds have been reported to be overrepresented)
- Laryngeal edema/eversion of laryngeal saccules (brachycephalic breeds)

CONTAGION & ZOONOSIS: If secondary to infectious diseases (e.g., infectious tracheobronchitis [kennel cough]), potential but rare zoonosis (e.g., immunocompromised persons) with *Bordetella bronchiseptica*

ASSOCIATED CONDITIONS & DISORDERS Dogs:

- Infectious tracheobronchitis (kennel cough)
- Laryngeal paralysis
- Brachycephalic airway syndrome Cats:
- Lymphoma
- Squamous cell carcinoma (SCC)
- Secondary to thyroidectomy
- Laryngeal paralysis

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Voice change may be described as a change in pitch of bark or meow (dog/cat, respectively) or a persistent hoarseness.

- Variable voice change depending on condition:
  - Peracute if traumatic
  - Acute if infectious
  - Subclinical and subtle if associated with neoplasia or with laryngeal paralysis
- May be associated with:
  - Exercise intolerance if mild upper airway obstruction (structural or functional)
  - Inspiratory stridor and respiratory distress (dyspnea, cyanosis, syncope) if substantial upper airway obstruction (structural or functional)

PHYSICAL EXAM FINDINGS: Variable: dependent on primary cause

ETIOLOGY AND PATHOPHYSIOLOGY

- Anatomic cause: structure of the larynx affected
- Functional cause: innervation of the larynx affected

DIAGNOSIS

DIAGNOSTIC OVERVIEW

While most causes of voice change originate from a laryngeal/pharyngeal lesion (warranting a sedated laryngeal exam), systemic disturbances such as myasthenia gravis should be ruled out first, particularly if the history and physical exam are consistent with such disorders.

DIFFERENTIAL DIAGNOSIS

- Anatomic cause:
  - Laryngeal distortion:
    - Blunt trauma (e.g., choke chain, hit by car, kicked by horse)
    - Penetrating trauma (e.g., stick, gunshot, dog/snake bite)
  - Laryngeal edema (elongated soft palate, insect bite, chronic barking)
  - Eversion of the laryngeal saccules
  - Laryngeal/pharyngeal foreign body
  - Laryngeal inflammation (polyp, traumatic, infectious [viral, bacterial], granulomatous, immune mediated)
  - Laryngeal neoplasia (mast cell tumor, SCC, leiomyoma/sarcoma, rhabdomyoma/sarcoma, fibroma/fibrosarcoma, lymphoma)
- Functional cause:
  - Dysfunction of the recurrent laryngeal nerve:
    - Congenital/idiopathic laryngeal paralysis
    - Trauma to the nerve (direct or indirect):
      - Occurs after thyroidectomy in cats
    - Nerve compression (hematoma, abscess, tumor [thyroid carcinoma, lymphosarcoma])
    - Neuropathy, polyneuritis
  - Myopathy (including cricoarytenoid dorsalis muscle)
  - Neuromuscular disease (myasthenia gravis)

INITIAL DATABASE

- CBC, serum biochemistry panel, and urinalysis
- Cervical/thoracic imaging:
  - Radiographs: The normal larynx, especially if mineralized, should not be mistaken for a foreign body.
  - Ultrasound (mass lesions, laryngeal paralysis)
- Oral/laryngeal/pharyngeal examination (visual ± endoscopy); see require sedation depending on whether severe inspiratory dyspnea is present (with severe dyspnea, the laryngeal exam often may be performed while the patient is awake, because the patient is breathing with mouth and oropharynx maximally opened). In a study comparing three techniques for the diagnosis of laryngeal paralysis, direct per os laryngoscopy combined with the knowledge of the clinical history and physical examination was preferred over echolaryngoscopy and transnasal endoscopy (Radlinsky et al.).

ADVANCED OR CONFIRMATORY TESTING

- CT scan or MRI of larynx
- Serum acetylcholine receptor antibodies titer (myasthenia gravis)
- Electromyography (myopathies)
- Exploratory surgery ± biopsy and histopathologic examination

TREATMENT

TREATMENT OVERVIEW

- Stabilize the patient if upper airway obstruction/dyspnea.
- Determine cause of voice change.
- Address primary cause of the condition.

ACUTE GENERAL TREATMENT

- Stabilization of the patient:
  - If associated with mild inspiratory stridor:
    - Sedation of the patient, oxygen supplementation (see p. 1318)
  - If associated with severe inspiratory stridor and dyspnea:
    - Sedation of the patient, oxygen supplementation, intubation/ventilation if necessary, emergency tracheostomy

(see p. 1344) if indicated

- Addressing the primary cause:
  - If secondary to anatomic cause:
    - see Tracheobronchitis (Infectious): Dogs, p. 1109
    - Local trauma/inflammation: foreign-body removal, antiinflammatory drugs (e.g., carprofen, 2 mg/kg PO q 12 h; or meloxicam, 0.1 mg/kg PO q 24 h), antibiotics if indicated (penetrating wound; consider amoxicillin-clavulanate, 12.5 mg/kg PO q 12 h, then base the decision on aerobic and anaerobic culture and sensitivity [C&S]), soft palate resection
    - Eversion of laryngeal saccules: resection
    - Laryngeal mass: resection (ventriculocordectomy/partial laryngectomy), radiation therapy, or chemotherapy
    - If mass resection impossible: total laryngectomy with permanent tracheostomy
  - If secondary to functional cause:
    - Laryngeal paralysis: unilateral cricoarytenoid lateralization
    - Surgical decompression of recurrent laryngeal nerve (hematoma, abscess drainage, mass excision)
    - Acquired neuropathy/neuromuscular disease: treat according to primary cause

CHRONIC TREATMENT

Variable, dependent on primary cause

POSSIBLE COMPLICATIONS

Variable, dependent on primary cause:

- Laryngeal paralysis: aspiration pneumonia
- Tumor: recurrence, progression of disease (local, regional, systemic)
- Inflammation, infection, or foreign body: recurrence possible
- Trauma: potential irreversible nerve damage

RECOMMENDED MONITORING

Variable, dependent on primary cause

PROGNOSIS AND OUTCOME

Variable, depending on condition:

- Infectious tracheobronchitis: excellent
- Trauma, inflammation, or foreign body: good to guarded
- Laryngeal paralysis: good to guarded with surgery
- Resectable laryngeal mass: good if benign and clean resection; poor if malignant, nonresectable, and/or not responsive to chemotherapy or radiation therapy

PEARLS & CONSIDERATIONS

COMMENTS

A very common underlying dogs is laryngeal paralysis.

CLIENT EDUCATION

If the cause is infectious tracheobronchitis, the affected dog should avoid contact with other dogs, especially those that are unvaccinated.

SUGGESTED READING

Monnet E: Laryngeal paralysis and devocalization. In Slatter D, editor: Textbook of small animal surgery, ed 3, Philadelphia, 2003, WB Saunders, pp 837–845.

Radlinsky MG, Williams J, Frank PM, et al: Comparison of three clinical techniques for the diagnosis of laryngeal paralysis in dogs. Vet Surg 38:434–438, 2009.

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Vitamin A Toxicosis

BASIC INFORMATION

DEFINITION

Usually a chronic toxicosis seen in dogs and cats after repeated ingestion of high doses of vitamin A. Characterized by lethargy, anorexia, weight loss, cervical neck pain, skin conditions, and possibly reproductive problems. Acute intoxication may present as vomiting, diarrhea, abdominal pain, and rarely hepatitis.

SYNONYMS

Retinoids are vitamin A derivatives.

EPIDEMIOLOGY

SPECIES, AGE, SEX: All mammals are susceptible, but vitamin A intoxication clinically occurs mainly in the cat.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Acute: very rare
- Chronic: after months of high levels of vitamin A ingestion

HISTORY, CHIEF COMPLAINT

- History of chronic exposure to excesses of a high vitamin A–containing product (capsules) or diet (mainly or exclusively raw liver diet: most common):
  - Intoxication is more likely with repeated exposures than with a single acute exposure.
  - Toxicosis can occur in cats 2-9 years of age that are fed a diet high in raw liver (e.g., 4 days per week).
- Acute (rare): self-limiting mild vomiting, diarrhea, anorexia, depression
- Chronic: lethargy, anorexia, weight loss, gingivitis, matted haircoat, irritability, resentment of handling; signs typically develop over several months.
- Pregnant animals: teratogenicity (cleft palate, hydrocephalus, microencephaly), reproductive failure

PHYSICAL EXAM FINDINGS

- Neck and limb rigidity due to exostosis (proliferation from bone)
- Tense musculature
- Neck ventroflexion possible:
  - In contrast to neck ventroflexion from hypokalemia or thiamine deficiency (characterized by a flaccid neck), in patients with vitamin A intoxication, the ventroflexion is stiff (caused by bony exostoses).
  - Exfoliation, matted coat

ETIOLOGY AND PATHOPHYSIOLOGY

Source:

- Vitamin A and its congeners are not produced endogenously and must be supplied exogenously through different sources (dietary or oral supplementation); beta-carotene is a plant pigment found in a number of foods. It is converted to retinal in the intestine and is further oxidized to retinoic acid and retinol.
- Acidic forms of vitamin A (*cis*- or *trans*-retinoic acid), vitamin A derivatives (retinol, *trans*-retinyl palmitate, retinyl stearate), synthetic retinoids (tretinoin, isotretinoin, etretinate), and vitamin A capsules, tablets, and injections all represent potential pharmaceutical sources of vitamin A.
- Liver (typically from chicken, beef, seal, or fish) is a common nutritional source of vitamin A.

Mechanism of Toxicosis:

- Vitamin A plays an essential role in normal night vision, reproductive processes, maintenance of epithelial and membrane structure, normal cellular growth, and immune functions.
- Hypervitaminosis A can inhibit keratinization of epithelial cells, which can lead to skin problems.
- High concentrations of vitamin A induce chondrocytes to produce more extracellular matrix, which forms a framework for mineralization (exostoses: abnormal bone growth, cervical spondylosis).
- In humans, neurotoxicosis is due to increased intracranial pressure.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Clinical diagnosis is based almost entirely on unusual nutritional/dietary supplement history and characteristic exostotic bony changes on radiographs (especially cervicothoracic vertebrae) and is confirmed by elevated serum levels of retinol.

DIFFERENTIAL DIAGNOSIS

Other causes of acute gastrointestinal (GI) signs (vomiting, diarrhea) or liver damage (rare because acute vitamin A toxicosis [hepatotoxicosis] is very uncommon)

INITIAL DATABASE

- CBC: nonspecific changes or no significant changes expected
- Serum chemistry profile: liver enzymes elevated with acute intoxication
- Urinalysis: generally unremarkable
- Cervical radiograph: may show bone-density cervical mass ventral to C1-C2 intervertebral space

ADVANCED OR CONFIRMATORY TESTING

- Cats: serum/plasma retinol level > 3145 mcg/L is considered toxic (normal: 200-1600).
- Toxic levels in feline liver (postmortem): 8590-39,570 mcg/g
- In dogs, serum/plasma retinol > 20,000 mcg/L is considered toxic (normal: 300-1000 mcg/L)

TREATMENT

TREATMENT OVERVIEW

With acute intoxication, general decontamination procedures (induction of vomiting and administrations of activated charcoal) are indicated, whereas with chronic toxicosis, treatment simply consists of removing the source of excess vitamin A and providing supportive care. There is no antidote.

ACUTE GENERAL TREATMENT

- Decontamination of patient:
  - Induction of vomiting (see 1364)
  - Activated charcoal: 1-2 g/kg PO if recent large ingestion (within few hours)
- Remove source (excess vitamin A).
- Supportive care:
  - IV fluids
  - Vomiting may be controlled with metoclopramide at 0.1-0.4 mg/kg body weight PO, SQ, or IM q 8 h; or maropitant, 1 mg/kg SQ q 24 h.
  - Management of liver damage (rare) as needed (see 503)

DRUG INTERACTIONS

Hypervitaminosis A can interfere with the action of other fat-soluble vitamins.

RECOMMENDED MONITORING

- Serum biochemistry profile
- Body weight

PROGNOSIS AND OUTCOME

- Excellent in acute cases
- Chronic: guarded prognosis; bony changes are permanent, and some cats that were fed only liver may refuse to eat anything else.

PEARLS & CONSIDERATIONS

COMMENTS

- Vitamin A deficiency far more common than intoxication
- Dogs can convert beta-carotene into vitamin A, but cats cannot.
- The amount of vitamin A needed to cause toxic effects is usually 10-1000 times the dietary requirements for most species.
- The vitamin A requirement for cats is 10,000 IU/kg of diet fed, with levels up to 100,000 IU/kg of diet tolerated.
- For dogs, the requirement is 3333 IU/kg of diet fed, with up to 33,330 IU/kg of diet tolerated.
- Vitamin A is fat soluble; 90% is stored in the liver and 10% in adipose tissue.

TECHNICIAN TIP

An owner may mention that a cat eats a diet composed mainly of raw liver, and this information is worth relaying to the attending veterinarian because of the possibility of vitamin A toxicosis.

PREVENTION

Do not overfeed raw beef liver to cats.

CLIENT EDUCATION

Teach owners the value of a balanced diet.

SUGGESTED READING

Doireau V, et al: Vitamin A poisoning revealed by hypercalcemia in a child with kidney failure. Arch Pediatr 3(9):888–890, 1996.

Puls R: Vitamin A in dogs, vitamin A in cats. In Vitamin levels in animal health. Clearbrook, British Columbia, 1994, Sherpa International, pp 14, 20.

Rader JD: Vitamin A. In Plumlee K, editor: Clinical veterinary toxicology. St Louis, 2003, Mosby, p 330.

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Vestibular Disease

BASIC INFORMATION

DEFINITION

Category of disorders affecting the central or peripheral vestibular system of dogs and cats; usually cause clinical signs of head tilt, nystagmus, and/or loss of balance

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Occurs in both dogs and cats
- Idiopathic vestibular disease occurs in older dogs (usually >8 years) but in cats of any age.

ASSOCIATED CONDITIONS & DISORDERS: Nausea, vomiting

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Peripheral vestibular disease (PVD): vestibular nerve lesion in inner ear
- Central vestibular disease (CVD): brainstem lesion (medulla)

HISTORY, CHIEF COMPLAINT

- Regardless of the underlying cause, most animals present with a peracute to subacute onset of clinical signs.
- The most common chief complaints are head tilt, nystagmus, and ataxia.
- Acute-onset vestibular disorders may produce such profound dysequilibrium and ataxia that owners are concerned about the animal's having “had a stroke.”

PHYSICAL EXAM FINDINGS

- Head tilt, nystagmus, and vestibular ataxia (possibly to the extent of causing recumbency and whole-body rolling) are the hallmarks of both peripheral and central vestibular disorders.
- The most important aspect in localization of a lesion to the central vestibular system is identification of neurologic signs that cannot be attributed to PVD.
- Mental status:
  - Central: often altered (depression, stupor, or coma)
  - Peripheral: animal should be alert and responsive and can often appear disoriented.
- Gait: vestibular ataxia (falling, veering, leaning, rolling, circling), usually toward the side of the lesion; seen with both CVD and PVD. Hypermetria, intention tremors, and truncal sway may be observed if the cerebellum is affected (central).
- Head tilt: usually toward the side of the lesion; seen with both CVD and PVD.
- Spontaneous nystagmus: occurs with both CVD and PVD. Vertical nystagmus occurs only in animals with CVD, while horizontal or rotary nystagmus can be seen with either PVD or CVD. The fast phase of the nystagmus is usually away from the side of the lesion. Change in direction of the fast phase with altered head positions suggests CVD.
- Cranial nerve deficits: cranial nerve VII (facial nerve) paresis is sometimes seen in animals with PVD, owing to its proximity to peripheral vestibular structures. Cranial nerves V, VI, IX, and XII ipsilateral to lesion may be affected in animals with CVD but not PVD.
- Horner's syndrome: possible with PVD but rare with CVD ipsilateral to lesion
- Postural reaction deficits are commonly seen with CVD but should not be observed with PVD.
- Paradoxical CVD: lesion location as suggested by clinical signs related to the head (head tilt, nystagmus, etc.) does not match the lesion location suggested by the postural reaction deficits; the latter indicate the true side of the lesion (same side as hopping/proprioceptive deficit).
- Bilateral PVD: head tilt and nystagmus may not be present; animals may walk with a crouched gait.
- Clinical signs related to disease in other central nervous system (CNS) locations, such as seizures, behavioral changes, hypermetria, intention tremors, and truncal sway, suggest multifocal central neurologic disease.

ETIOLOGY AND PATHOPHYSIOLOGY

- Basic neuroanatomy of the vestibular system:
  - Peripheral: vestibular receptors (semicircular canals, saccule, utricle) located within the petrous temporal bone and cranial nerve VIII (vestibulocochlear nerve)
  - Central: vestibular nuclei in the dorsal portion of the medulla oblongata, vestibular pathways of the brainstem and spinal cord (medial longitudinal fasciculus, vestibulospinal tracts), vestibular components in the cerebellum, and vestibular pathways through the caudal cerebellar peduncle
- Etiology for idiopathic vestibular disease in dogs and cats is unknown; an immune-mediated mechanism is suspected, but immunosuppressive drugs such as glucocorticoids have not been shown to help.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Clinical signs of vestibular disease are usually distinctive (see above). The diagnostic challenge consists of identifying peripheral versus central disease, which can be done on physical exam in most cases. The underlying cause is found using specific diagnostic tests ranging from hormonal assays (hypothyroidism) to advanced imaging (structural brain lesion).

DIFFERENTIAL DIAGNOSIS

Peripheral vestibular diseases:

- Otitis media/interna
- Idiopathic vestibular disease
- Nasopharyngeal polyps: cats >> dogs
- Hypothyroidism: dogs
- Neoplasia: squamous cell carcinoma (SCC), ceruminous gland adenocarcinoma, and other related conditions
- Ototoxicity: topical chlorhexidine or iodine; systemic aminoglycosides and other drugs

Central vestibular diseases:

- Canine distemper virus (CDV) encephalomyelitis
- Feline infectious peritonitis (FIP)
- Rickettsial encephalitis: Rocky Mountain spotted fever (RMSF), ehrlichiosis
- Fungal encephalitis: *Cryptococcus neoformans* most common; blastomycosis or coccidioidomycosis in certain regions of North America
- Granulomatous meningoencephalomyelitis (GME)
- Protozoal encephalitis: *Toxoplasma gondii, Neospora caninum*
- Neoplasia: meningioma, choroid plexus tumor, lymphoma, metastatic neoplasia
- Metronidazole toxicosis
- Cerebrovascular accident (infarct)

INITIAL DATABASE

- CBC, serum biochemical analysis, urinalysis: results often normal
- Thyroid hormone analysis: low total T^4 and free T^4 and elevated thyroid-stimulating hormone (TSH) in dogs with hypothyroidism
- Otoscopic examination: evaluate tympanic membranes for integrity.

ADVANCED OR CONFIRMATORY TESTING

- Bulla radiographs: dorsoventral, oblique lateral, and rostroventral-caudodorsal open-mouthed views. Abnormalities include soft-tissue or fluid opacity within the bulla and sclerosis of the tympanic bulla.
- Oropharyngeal and otoscopic examination under general anesthesia to identify nasopharyngeal polyps and otitis media. Abnormalities include soft-tissue or fluid opacity within and sclerosis of the affected tympanic bulla (see p. 1316).
- Brainstem auditory evoked response (BAER) test may be useful for distinguishing PVD from CVD (see p. 1216).
- CT scan (see p. 1233): useful for examination of the middle ear in patients with PVD. CT scans can also be used for CVD; however, beam-hardening artifacts in the caudal brain may preclude evaluation of the brainstem, and small lesions may not be visualized (MRI preferable for this location).
- MRI (see p. 1302): useful for examination of both the peripheral and central vestibular structures. It provides superior resolution of brain parenchyma.

- Cerebrospinal fluid (CSF) analysis (see p. 1228): used as an adjunct to advanced imaging, primarily to rule out encephalitis.
- Infectious disease titers may be required in certain cases to rule out infectious encephalitis. CSF is the preferred sample for CDV, FIP, and cryptococcosis. Serum titers are performed for *Toxoplasma* and *Neospora* spp.
- CSF culture and sensitivity (C&S) may be required for ruling out bacterial encephalitis.
- Histopathologic examination is required for definitive diagnosis in many diseases causing structural lesions (e.g., masses). Tissue samples can be obtained via surgical excision or stereo-tactic brain biopsy (see p. 1214).

TREATMENT

TREATMENT OVERVIEW

Definitive treatment for vestibular disease is based on diagnosis of the underlying cause.

ACUTE GENERAL TREATMENT

- Meclizine (25 mg PO q 24 h in dogs; 12.5 mg PO q 24 h in cats) or diazepam (0.1-0.5 mg/kg PO q 8 h in dogs) may help alleviate clinical signs of nausea and vomiting. Meclizine causes less sedation than diazepam and can be purchased as an over-the-counter drug. Oral diazepam should be used with caution in cats because of the reported incidence of idiosyncratic hepatic necrosis.
- Idiopathic vestibular disease: clinical signs improve spontaneously over 1-2 weeks; no treatment has been shown to accelerate natural resolution of the disorder.
- Otitis media/interna: systemic antibiotics ± antifungals for 4-6 weeks, ideally based on bacterial C&S. Surgical treatment (bulla osteotomy and total ear canal ablation) may be required to remove infected tissues.
- Nasopharyngeal polyps: bulla osteotomy
- Hypothyroidism: thyroid supplementation (see p. 588)
- Neoplasia: surgical excision may be possible for meningioma and choroid plexus tumors depending on lesion location. Surgical excision of tumors in the middle and inner ear may be possible but is difficult. Radiation therapy may provide some relief of clinical signs, and consultation with an oncologist is recommended in these cases.
- CDV and FIP encephalomyelitis: no specific therapy is available. Nonspecific supportive therapy with antibiotics and corticosteroids may alleviate signs temporarily (see pp. 317 and 383).
- Rickettsial encephalitis: doxycycline (5 mg/kg PO q 12 h) or chloramphenicol (50 mg/kg PO q 8 h) for 3-4 weeks.
- Fungal encephalitis: fluconazole (5 mg/kg PO q 12 h) penetrates the CNS to a greater degree than other antifungal medications. Itraconazole and amphotericin B can be used with blastomycosis. Oral treatment should be continued for at least 6 months, barring adverse reactions, and may be required long term to control clinical signs.
- GME: immunosuppressive dose of prednisone, initially at 2 mg/kg PO q 12 h for 1-2 days, then 1 mg/kg PO q 12 h for at least 2 weeks. Then slowly taper the drug over 4-8 months to reach the minimal effective dose (see p. 457).
- Protozoal encephalitis: clindamycin (10 mg/kg PO q 12 h to q 8 h) for 4 weeks; or combination of trimethoprim/sulfadiazine (TMS; 15 mg/kg PO q 12 h) and pyrimethamine (1 mg/kg PO q 24 h)
- Metronidazole toxicosis: discontinue metronidazole. In dogs, diazepam administration (0.5 mg/kg IV once, followed by 0.5 mg/kg PO q 8 h until resolution of signs) appears to shorten the duration of clinical signs. Oral diazepam should be used with extreme caution in cats, owing to the reported incidence of idiosyncratic hepatic necrosis.

POSSIBLE COMPLICATIONS

A permanent mild head tilt may persist after resolution of other clinical signs.

RECOMMENDED MONITORING

- Serial neurologic exam every 4 weeks
- Serial infectious disease titers if indicated

PROGNOSIS AND OUTCOME

- Prognosis for most PVDs is good with specific treatment, with the exception of neoplasia, which carries a guarded to poor prognosis.
- CDV and FIP encephalomyelitis: poor even with treatment
- Rickettsial and protozoal encephalitis: good with early and specific treatment
- Fungal encephalitis: fair to guarded. Long-term treatment may be required to control clinical signs.
- GME: fair to guarded. Many dogs respond initially to treatment; however, relapse is common. In some dogs, corticosteroids eventually can be discontinued.
- Neoplasia: generally poor long-term prognosis

- Metronidazole toxicosis: excellent

PEARLS & CONSIDERATIONS

COMMENTS

- Compensation for vestibular diseases will occur in many animals regardless of lesion location, and clinical signs may improve slightly if the lesion is slow growing.
- In general, animals with PVD carry a good prognosis for recovery following specific therapy.
- The long-term prognosis for animals with CVD is variable depending upon the specific cause; however, treatment should be attempted to alleviate clinical signs.

PREVENTION

- Thyroid supplementation in dogs with hypothyroidism
- Avoidance of high doses and/or prolonged courses of metronidazole treatment. A common error is to prescribe a high dose of the drug (e.g., 30-65 mg/kg PO q 12 h). The recommendation is to limit the maximum daily dose to 30 mg/kg/day, divided into two daily doses.

CLIENT EDUCATION

Head tilt may be persistent.

SUGGESTED READING

Sanders SG, Bagley RS: Disorders of hearing and balance: the vestibulocochlear nerve (CN VIII) and associated structures. In Dewey CW, editor: A practical guide to canine and feline neurology, ed 2, Ames, IA, 2008, Wiley-Blackwell, pp 261–285.

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Ventricular Septal Defect

BASIC INFORMATION

DEFINITION

Well-recognized, anomalous communication between the right ventricle (RV) and left ventricle (LV), resulting in interventricular shunting of blood

SYNONYMS

Interventricular septal defect, VSD

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Dogs and cats
- First or second most common congenital heart defect in cats
- Typically diagnosed at a young age
- No sex predilection

GENETICS & BREED PREDISPOSITION

- Hereditary in a family of English springer spaniels and keeshonden
- Predisposed breeds: Akita, basset hound, bloodhound, English bulldog, English springer spaniel, keeshonden, Lakeland temer, Old English sheepdog, West Highland white terrier

ASSOCIATED CONDITIONS & DISORDERS

- Aortic valvular insufficiency (AI) due to decreased support of aortic valve
- Pulmonic stenosis, overriding aorta, atrial septal defects

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- In small animals, ventricular septal defect (VSD) most commonly involves the high membranous septum below the aortic valve on left side and below the tricuspid valve on the right side (perimembranous VSD).
- Left to right (L→R) shunting across the VSD is most common.
- A very large VSD or VSD accompanied by other defects that increase RV pressure (e.g., severe pulmonic stenosis or pulmonary hypertension) may result in shunting of blood from right to left (R→L, “reverse shunting”).

HISTORY, CHIEF COMPLAINT

- Usually there are no overt clinical signs reported by the owner (incidental finding of heart murmur during routine exam).
- In the case of a large L→R VSD or in R→L VSD, the following may be observed:
  - Exercise intolerance
  - Dyspnea, tachypnea
  - Cough (L→R)
  - Cyanosis (R—>L)
  - Syncope

PHYSICAL EXAM FINDINGS

- Systolic murmur, loudest around the fourth intercostal space (ICS) on the ventral thorax to the right of the sternum (most common) or left base
- If substantial AI is present, a diastolic murmur may be heard on the left cranial thorax (heart base, third ICS).
- Tachycardia, dyspnea, tachypnea, crackles may be apparent if left-sided congestive heart failure (CHF) is present

- R→L shunt: cyanosis, generally no murmur unless another malformation is present (e.g., pulmonic stenosis)

ETIOLOGY AND PATHOPHYSIOLOGY

- Magnitude and direction of shunting and thus clinical consequences depend on size of defect, relative pulmonary and systemic vascular resistances, and presence of other cardiopulmonary defects.
- L→R shunting VSD causes volume overload of pulmonary circulation and left side of the heart; ultimately the result may be left-sided CHF and/or pulmonary hypertension.
- R→L shunting VSD (much less common) causes systemic arterial hypoxemia, which can lead to polycythemia and hyperviscosity syndrome.

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

While very strong clinical suspicion of VSD may be based on physical examination alone (typically, systolic murmur with a point of maximal intensity on the right hemithorax), definitive diagnosis requires echocardiography.

DIFFERENTIAL DIAGNOSIS

- Other congenital causes of systolic murmurs: aortic/subaortic or pulmonic stenosis, atrio ventricular (AV) valve dysplasia, tetralogy of Fallot (of which VSD is one component)
- Acquired heart diseases: acquired AV valve regurgitation (dogs), dilated cardiomyopathy (dogs or cats), hypertrophic cardiomyopathy (cats)

INITIAL DATABASE

- CBC/serum biochemistry panel:
  - Typically normal
  - Polycythemia if R→L shunting
- Thoracic radiographs:
  - Normal with small VSD
  - Larger L→R VSD: left-sided cardiomegaly, pulmonary overcirculation, ± pulmonary edema, ± right ventricular enlargement
  - R→L VSD: right-sided cardiomegaly, variable pulmonary artery pattern (e.g., normal to enlarged if pulmonary arterial hypertension; normal or small if pulmonic stenosis)
- Electrocardiogram (ECG):
  - Often normal
  - Left atrial (LA) and/or LV enlargement if large L→R shunt or RV enlargement if R→L shunt
  - ± Wide and/or notched Q wave, representing abnormal septal activation
- Echocardiography:
  - A visible defect in the interventricular septum may be noted. Beware of artifactual defects (“septal drop-out”).
  - L→R VSD: turbulent jet from LV to RV with color Doppler, ± LA enlargement, ± LV enlargement
  - Peak velocity (V in m/s) of VSD jet with continuous wave Doppler reflects the pressure gradient (ΔP [mm Hg]) between LV and RV according to modified Bernoulli equation ($\Delta P = 4V^2$), which generally speaks to size of defect (small VSD: V > 4.5 m/s; moderate-size VSD: 3 < V < 4.5 m/s; large VSD: V < 3 m/s). Beware of underestimation of velocity due to erroneous/oblique alignment of Doppler sample.
  - R→L VSD: right ventricular hypertrophy, flattening of the interventricular septum, main pulmonary artery dilation
  - ± AI with color and spectral Doppler

ADVANCED OR CONFIRMATORY TESTING

- Contrast echocardiography (bubble study) to confirm R→L shunt
- Cardiac catheterization for angiography, shunt quantification, and measurement of cardiac pressures (virtually never used; mainly preoperative if open-heart surgery)

TREATMENT 

TREATMENT OVERVIEW

- Often no treatment is required, since the majority of VSDs are small and do not result in volume overload of the left ventricle or other significant clinical consequences.
- Treatment of large L→R VSDs is directed at decreasing the shunt volume and preventing or eliminating the signs of CHF.
- Treatment of R→L VSDs tends to be palliative only.

ACUTE GENERAL TREATMENT

- L→R VSD with significant left-sided volume overload (moderate to marked left ventricular enlargement):
  - Surgical repair via thoracotomy uncommon (requires cardiopulmonary bypass, which is available at very few referral institutions)
  - Percutaneous transcatheter repair using a variety of devices has been described and may be available at some referral institutions.
  - Pulmonary artery banding is a palliative surgical technique to decrease L→R shunt.
  - Arterial vasodilators used with caution to decrease L→R shunt; contraindicated if complex malformations or R→L shunt
  - If CHF present, may use angiotensin-converting enzyme (ACE) inhibitors, diuretics, ± pimobendan, ± digoxin (see p. 468)
- R→L VSD:
  - Surgical repair contraindicated
  - Phlebotomy to palliate signs and maintain PCV at 55%-65%

CHRONIC TREATMENT

- Treatment of CHF as already described (see p. 470)
- Periodic phlebotomy ± hydroxyurea as needed if R→L shunt

POSSIBLE COMPLICATIONS

- Left-sided CHF
- Pulmonary hypertension
- Shunt reversal (R→L) over time (Eisenmenger's complex); rare in dogs and cats

RECOMMENDED MONITORING

- Following diagnosis in puppies/kittens with no clinical signs, examination at 6 months, 1 year, then yearly thereafter
- Frequent monitoring for animals with overt decompensation and requiring treatment

PROGNOSIS AND OUTCOME

- Excellent prognosis for small, uncomplicated VSD
- Guarded prognosis for larger VSD (risk CHF and/or pulmonary hypertension)
- Concurrent substantial AI carries poor prognosis.
- Guarded to poor prognosis for R→L shunts; severe exercise limitations

PEARLS & CONSIDERATIONS

COMMENTS

- In L→R shunting VSDs, the RV and pulmonary arterial circulation essentially act as conduits for VSD flow. The LA and LV, however, receive increased venous return, resulting in increased diastolic pressures. In addition, effective forward flow into the systemic circulation is reduced as a result of the shunt flow. The latter two points account for the increased LV workload and predominant occurrence of left heart failure, not right heart failure, in L→R VSDs.
- VSD and tricuspid dysplasia are the two main differential diagnoses for a systolic murmur heard best on the right side of the chest in dogs or cats (murmurs due to subaortic stenosis may radiate prominently to the right side in some cases; hypertrophic cardiomyopathy is another common differential in cats).
- Most VSDs are relatively small, well tolerated, and do not require therapy.

PREVENTION

Genetic basis possible but unproven in the breeds listed previously. Consider discouraging breeding of affected animals.

SUGGESTED READING

Oyama MA, Sisson DD, Thomas WP, et al: Congenital heart disease. In Ettinger SJ, Feldman EC, editors: Textbook of veterinary internal medicine, ed 7, St Louis, 2010, Elsevier Saunders, pp 1250–1298.

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Ventricular Arrhythmias

Additional Images Available on Website

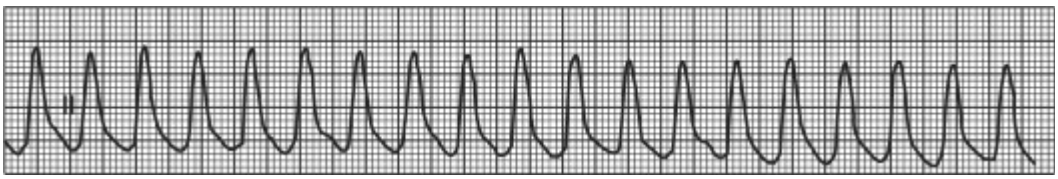
BASIC INFORMATION

DEFINITION

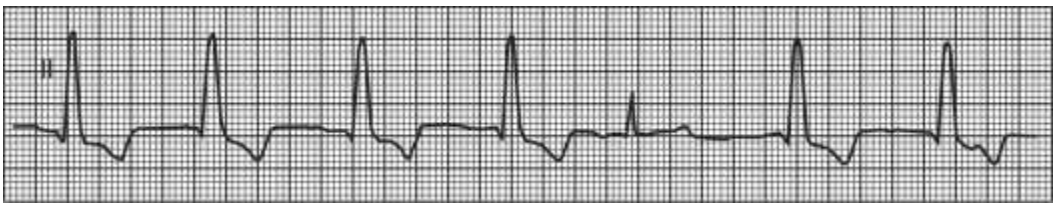
- Ventricular arrhythmias are excessive electrical discharges occurring spontaneously and prematurely in the ventricles.
- By definition, the term *premature ventricular complex(es)* (PVCs) applies to one, two, or three consecutive premature ventricular impulses, whereas four or more in a row are defined as ventricular tachycardia (VT).
- By definition, ventricular tachycardia involves a ventricular rate of 180 beats per minute (bpm) or more in dogs and 240 bpm or more in cats.
- Strictly speaking, these are ventricular tachyarrhythmias (to distinguish them from ventricular escape rhythms); for simplicity, the term *ventricular arrhythmia* will be used here for designating PVCs and VT.

SYNONYMS

- Ventricular ectopy, extrasystoles, or tachyarrhythmias
- *PVCs* are synonymous with ventricular premature complexes or contractions (VPCs), premature ventricular depolarizations (PVDs), and similar variations.



VENTRICULAR ARRHYTHMIAS Lead II ECG in a dog with ventricular tachycardia, 50 mm/sec, 10 mm/mV. The ventricular tachycardia is monomorphic (PVCs all of the same shape) and extremely rapid (375 bpm) in this critically septic dog.



VENTRICULAR ARRHYTHMIAS Single-lead ECG in a dog with immune-mediated hemolytic anemia and an ausculted arrhythmia, 50 mm/sec, 5 mm/mV. The 5th beat is a normal sinus beat; the remaining beats are of ventricular origin. Despite the ventricular arrhythmia, the rate is not rapid (115 bpm) and likely only slightly faster than the underlying sinus rate. This is accelerated idioventricular rhythm, a benign rhythm that does not require therapy beyond proactive treatment of its inciting cause (here, anemia).

EPIDEMIOLOGY

SPECIES, AGE, SEX: Any can be affected.

GENETICS & BREED PREDISPOSITION

- Boxers: arrhythmogenic cardiomyopathy (see p. 90)
- Doberman pinschers and other breeds: dilated cardiomyopathy
- German shepherds: inherited ventricular tachycardia of young adults
- Large-breed dogs: splenic masses
- Large-breed dogs (Great Danes, setters, retrievers, and many others): gastric dilatation/volvulus (GDV)
- Cats (male > female): hypertrophic cardiomyopathy

RISK FACTORS: Outdoor, roaming dogs: traumatic myocarditis (hit by car). Primary heart disease or any systemic disturbance, if sufficiently severe, can cause ventricular arrhythmias.

GEOGRAPHY AND SEASONALITY: Chagas' disease: myocarditis (southern parts of the United States and Latin America)

ASSOCIATED CONDITIONS & DISORDERS: Syncope (rapid VT)

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Incidental finding
- Clinically overt (e.g., causing syncope)
- Accelerated idioventricular rhythm

HISTORY, CHIEF COMPLAINT

Incidental finding (more common):

- Animal is presented for evaluation of a disorder other than syncope.
- Arrhythmia is noted during physical examination or subsequent monitoring.

Clinically overt:

- Syncope/episodic collapse
- Episodic stumbling, disorientation, confusion
- Animal may be well (and even playful and active) before and after episodes or may be lethargic, weak, or anorexic.

PHYSICAL EXAM FINDINGS

Incidental finding:

- Physical exam findings reflect the underlying disorder; however, an arrhythmia is noted on physical exam.

Common Causes of Ventricular Arrhythmias

Hypokalemia*,†
Hypoxemia (e.g., due to cardiogenic pulmonary edema, pleural effusion, primary lung disease)*
Cardiomyopathy
Gastric dilatation/volvulus*
Traumatic myocarditis/hit by car
Abdominal mass, especially splenic or hepatic*
Advanced valvular heart disease
Hypomagnesemia*,†
Acidosis*
Intoxication (digitalis; oleander, foxglove, lily of the valley, azalea, and yew plants; many over-the-counter, prescription, or illicit drugs)

* Potentially correctable/curable.

† Presence makes ventricular antiarrhythmic drugs such as lidocaine, procainamide, and mexiletine ineffective.

- With ventricular tachycardia, the arrhythmia is rapid and may be irregular (usually polymorphic on electrocardiogram [ECG]) or regular (usually monomorphic on ECG).
- Pulse deficit:
  - Premature heartbeat ausculted, without a corresponding palpable pulse for that beat
  - Common with ventricular arrhythmias
  - Depends on the degree of prematurity of PVCs (“How underfilled are the ventricles when the PVC causes them to contract again?”)

- Clinically overt:
- Wide range of presentations, from clinically normal and alert if arrhythmia is intermittent, to profoundly weak and hemodynamically collapsed with very rapid, sustained ventricular tachycardia
- Regularity or irregularity and pulse deficit, as for incidental finding (above)

ETIOLOGY AND PATHOPHYSIOLOGY

- Enhanced or abnormal automaticity, microreentry, and triggered activity (early or delayed after depolarizations) are mechanisms that underlie ventricular arrhythmias.
- These mechanisms can be activated or potentiated by systemic disturbances such as those previously listed (see Associated Conditions & Disorders, above).
- The result is one or more spontaneous electrical depolarizations originating prematurely in the ventricles. The prematurity is manifested on the electrocardiogram (ECG) as a shorter R-R interval. The ventricular origin results in a QRS complex that is of a different shape than a sinus QRS complex.
- A greater degree of prematurity of PVCs (or a higher rate of ventricular tachycardia) reduces the time the ventricles have for filling prior to contracting. Therefore, faster ventricular arrhythmias compromise diastolic filling time more severely and are more likely to produce clinical signs or hemodynamic deterioration (e.g., poor pulse, cerebral hypoperfusion) than slower or infrequent ventricular arrhythmias.
- Accelerated idioventricular rhythms are seen commonly in hospitalized patients in association with noncardiac diseases (e.g., GDV surgery, splenic disease, immune-mediated hemolytic anemia, post trauma, and neurologic disease). These are often benign, the rate is not rapid, and they often do not require therapy.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Ventricular arrhythmias can be suspected on history (syncope), physical exam (premature beats), and ECG (classically, wide and bizarre QRS complexes occurring prematurely). Careful inspection of the ECG allows differentiation from other similar-appearing but clinically very different ECG deflections.

DIFFERENTIAL DIAGNOSIS

- PVCs can occur in many situations and do not automatically equate to an underlying serious cardiac disorder. Additionally, they can be seen in normal animals in low numbers (<50 per 24 hour period). They are very commonly associated with noncardiac disease, possibly secondary to myocardial ischemia, electrolyte abnormalities, or other factors surrounding the underlying disease.
- Physical examination:
  - Supraventricular premature beats, marked respiratory sinus arrhythmia
- ECG (wide, bizarre, and/or predominantly negative QRS complexes in lead II):
  - Right or left bundle branch block
  - Ventricular escape rhythm
  - Right ventricular enlargement
  - Motion artifact
  - Accelerated idioventricular rhythm (ventricular rhythm at a rate of ≈120-170 bpm). This is a fancy term for slow ventricular tachycardia, but it is an appropriate name because a ventricular myocyte is now firing as a pacemaker cell at an accelerated rate.

INITIAL DATABASE

ECG (see p. 1253) remains the gold standard for diagnosis of cardiac arrhythmias. Criteria for ventricular arrhythmias:

- PVC is substantially different from normal sinus QRS complexes:
  - Wide and bizarre QRS (<90% like the normal beat). This is because the impulse originates below the bundle of His and therefore cannot take advantage of the specialized conduction system. It therefore must travel through the ventricular myocardium muscle cell to muscle cell. This is slow and produces a wide, bizarre complex. QRS complexes can be positive in lead II or negative, depending on the site of origin within the ventricle.
- PVC occurs prematurely. The R-R interval from the preceding normal sinus beat to the PVC is shorter than the interval between two normal sinus beats.
- Large, bizarre T wave; because depolarization is abnormal, repolarization is also abnormal.
- P waves continue to occur regularly during ventricular arrhythmias, but they are not related to PVCs and often are lost within the PVCs.

ADVANCED OR CONFIRMATORY TESTING

- 10- or 12-lead ECG: improved visualization of certain features of ventricular arrhythmias (e.g., better ability to see P waves not associated with the wide, bizarre QRS complexes of PVCs)
- CBC, serum biochemistry profile, urinalysis: especially to assess systemic proarrhythmic abnormalities like hypokalemia
- Thoracic radiographs: particularly if suspicion of primary cardiac disease, hypoxemia, or thoracic trauma
- Echocardiogram: if a primary cardiac problem is suspected or if no other cause is identified
- Abdominal imaging: if there is suspicion of an abdominal problem or if a primary cause for the arrhythmia is not found
- Arterial blood gas (ABG) analysis: if acid-base or oxygenation abnormalities are suspected

TREATMENT 

TREATMENT OVERVIEW

- To control the arrhythmia to such a degree that adequate organ perfusion is present and there is a resolution or control of any arrhythmia-related clinical signs (e.g., syncope)
- Decisions regarding treatment for a ventricular arrhythmia should be made based on whether the patient is experiencing or will experience hemodynamic compromise due to the arrhythmia. The goal is to treat the patient, not the ECG!
- The goal is not to abolish every PVC or otherwise try to “normalize” the ECG, because overzealous treatment of arrhythmias may be detrimental.
- see algorithm, .

ACUTE GENERAL TREATMENT

- First, determine if the arrhythmia is a ventricular arrhythmia (PVC, VT) by ruling out common impostors (see Differential Diagnosis, above).
- Second, identify and address any relevant underlying causes (see table).
- Third, determine if there are overt clinical signs associated with the ventricular arrhythmia (e.g., syncope). If so, antiarrhythmic treatment is warranted.
- Fourth, if the ventricular arrhythmia is sustained at a rapid rate (>180/min in large-breed dogs, >220/min in smallbreed dogs, >260/min in cats) despite the three steps described so far, then antiarrhythmic treatment should be considered. The following are recognized treatments for ventricular arrhythmias:
    - Lidocaine, 1-2 mg/kg (dog) or 0.25-1 mg/kg (cat) IV bolus (can repeat up to three times in 10-15 minutes); can be followed with IV constant rate infusion (CRI) at 40-80 mcg/kg/min (dog) or 10-20 mcg/kg/min (cat)
        - To make lidocaine CRI: withdraw 25 mL from a 500-mL bag of crystalloid fluid (e.g., lactated Ringer's solution) and replace with 25 mL of 2% lidocaine. Concentration in bag is 1000 mg/mL. Administer IV at usual fluid maintenance rate *(66* mL/kg per day) assuming congestive heart failure (CHF) is not present. Infusion at this rate will be 50 mcg/kg/min.
    - Procainamide, 6-15 mg/kg (dog) or 1-2 mg/kg (cat) slow IV bolus; may follow with IV CRI at 25-50 (dog) or 10-20 (cat) mcg/kg/min. Usually administered instead of lidocaine if lidocaine was ineffective, but both may be given together.
    - see treatment algorithm, .

CHRONIC TREATMENT

- Ongoing management of the underlying cause
- Oral antiarrhythmic drugs may be used for treating rapid and/or clinically overt (syncopal) ventricular arrhythmia. Options include one of the following:
    - Sotalol, 0.5-2 mg/kg PO q 12 h (dogs); 10-20 mg per cat PO q 12 h
    - Mexiletine, 4-8 mg/kg PO q 12 h to q 8 h; and atenolol, 0.2-0.75 mg/kg PO q 12 h (dogs)
    - Amiodarone, 10 mg/kg PO q 12 h for 1 week (loading), then 5-8 mg/kg PO q 24 h (dogs)
    - Atenolol (cats), 6.25-12.5 mg per cat PO q 24 h to q 12 h
    - Procainamide sustained release (dogs) has been given at 10-20 mg/kg PO q 8 h to q 6 h, but variable dissolution of tablets makes pharmacokinetics unpredictable.

DRUG INTERACTIONS

Digoxin can cause ventricular arrhythmias (see p. 309).

POSSIBLE COMPLICATIONS

Uncontrolled ventricular arrhythmias may progress to ventricular flutter and ventricular fibrillation (cardiac arrest); however, normalization of the ECG to sinus rhythm using antiarrhythmic drugs alone has never been shown to improve the prognosis for

survival. Therefore, complications can be minimized by treating/correcting inciting factors (see table), reserving ventricular antiarrhythmic drugs for cases in which overt signs such as syncope are present or in which a very high rate (e.g., >220 bpm in dogs, >260 bpm in cats) is present despite management or correction of the underlying cause.

RECOMMENDED MONITORING

- ECG as dictated by clinical evolution; ranges from continuous ECG with ventricular tachycardia in an unstable animal to periodic ECG or Holter monitoring during visits in stable animals
- Follow-up tests as listed for initial diagnosis to monitor underlying condition

PROGNOSIS AND OUTCOME

- Ventricular arrhythmias that occur at a faster rate are more likely to produce clinical signs and carry a more guarded prognosis than slower ventricular arrhythmias.
- Ventricular arrhythmias that fail to respond to correction of the underlying problem (or for which the underlying problem cannot be corrected) usually indicate cardiac manifestations of a serious problem that carries a guarded short-term prognosis. Long-term prognosis depends on the exact nature of the underlying problem.

PEARLS & CONSIDERATIONS

COMMENTS

- Virtually any disease or disorder, if sufficiently severe to have systemic effects, can cause ventricular arrhythmias.
- Ventricular escape beats and PVCs often look identical. Ventricular escape beats occur at a rate of 40-100 bpm against a background of second- or third-degree AV block or asystole—they are saving the heart from arrest and should never be treated with ventricular antiarrhythmics. By contrast, PVCs are excessive, unwanted ventricular complexes that occur in addition to the heart's usual rhythm.
- The most common correctable underlying causes of ventricular arrhythmias are hypokalemia, hypoxia, GDV, abdominal masses, anemia, metabolic acidosis, and pain.
- The most common treatable but non-correctable causes of ventricular arrhythmias are cardiomyopathy, degenerative valvular heart disease, and traumatic myocarditis (hit by car).
- Ventricular arrhythmias most commonly are manifestations of an underlying disorder. Attempting to eliminate ventricular arrhythmias with antiarrhythmic drugs in a stable animal is analogous to “shooting the messenger.” Rather, the underlying cause needs to be found and addressed. Perhaps no antiarrhythmic drug is as beneficial to a patient with ventricular arrhythmias as correction of the underlying cause.

TECHNICIAN TIP

Impostors for ventricular arrhythmias are common on in-hospital telemetry monitors, but ventricular arrhythmias are an important signal requiring attention. Unusual-appearing heartbeats on an ECG monitor should be printed and reviewed with the attending veterinarian.

PREVENTION

Ventricular arrhythmias are clues to a primary cardiac or systemic disturbance; therefore, preventing them relies on identifying and managing the underlying disease whenever possible.

CLIENT EDUCATION

Ventricular arrhythmias are serious disturbances of the cardiac rhythm. Their impact can range from minimal to life threatening, and sudden cardiac death is always possible when an animal has a disorder that causes ventricular arrhythmias.

SUGGESTED READING

Côté E, Ettinger SJ: Electrocardiography and cardiac arrhythmias. In Ettinger SJ, Feldman EC, editors: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Elsevier, pp 1040–1076.

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Vasculitis

BASIC INFORMATION

DEFINITION

Vasculitis is an uncommon pathologic syndrome of inflammation and necrosis of the vessel wall, characterized by purpura, edema, necrosis and ulceration, often involving the extremities. Vasculitis may be limited to the skin (see online chapter: Vasculitis, Cutaneous) or may be an early sign of systemic disease.

SYNONYMS

Inflammatory vasculopathy, angiitis

EPIDEMIOLOGY

SPECIES, AGE, SEX: Vasculitis is rare in cats and when it occurs, is often associated with neoplasia such as lymphangiosarcoma.

GENETICS & BREED PREDISPOSITION: Dogs: Jack Russell terriers, Scottish terriers, German shepherds, greyhounds (cutaneous and renal vasculopathy), dachshunds, rottweilers, beagles (rare: juvenile polyarteritis syndrome, [JPS], primary polyarteritis). Poodles, Maltese, bichon frise are reported to experience vaccine reactions more commonly.

RISK FACTORS

- Dogs: infectious diseases (Rocky Mountain spotted fever [RMSF], ehrlichiosis, babesiosis, bacteremia, canine corona virus, canine parvovirus, leishmaniasis, dirofilariasis, sarcocystosis, staphylococcal hypersensitivity); drug exposure, vaccination (rabies vaccine), blood component transfusions (human albumin), flea bite or food hypersensitivity
- Cats: infectious diseases (feline infectious peritonitis [FIP], feline leukemia virus [FeLV], feline immunodeficiency virus [FIV]), drug exposure, vaccination (rabies, herpesvirus/calicivirus panleukopenia)

CONTAGION & ZOONOSIS

- Dogs: canine corona virus (dog-to-dog only), canine parvovirus (dog-to-dog only) leishmaniasis (potential zoonosis)
- Cats: FIP, FeLV, FIV (cat-to-cat only)

GEOGRAPHY AND SEASONALITY: Regional variation in etiology (i.e., RMSF)

ASSOCIATED CONDITIONS & DISORDERS: Multisystemic clinical signs are uncommonly reported, including anemia, thrombocytopenia, polyarthropathy, myopathy, neuropathy, hepatopathy.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Cutaneous vasculitis is more common than systemic vasculitis.
- Vasculitis is more commonly secondary; a careful history including all medications/vaccinations received in the most recent 3 months is critical to identifying the etiology.
- Primary vasculitis is diagnosed by exclusion.

HISTORY, CHIEF COMPLAINT

- Nonspecific signs: lethargy, inappetence, or anorexia
- +/− Medications/vaccination in past 3 months
- Erythema, plaques, papules/pustules, necrosis/ulcers
- Bruising
- Ventral or dependent edema (limbs, ventrum, prepuce)

PHYSICAL EXAM FINDINGS

- Lesions in dependent/ventral regions, over pressure points, extremities (pinna, tail):

- Nonblanching erythema typically sharply demarcated from adjacent “normal” tissue; may be focal or generalized.
- Plaques, papules/pustules, necrosis/ulcers
- Petechia or ecchymotic hemorrhages
- Dependent edema
- +/− Fever
- +/− Peripheral lymphadenopathy

ETIOLOGY AND PATHOPHYSIOLOGY

- Toxic, immune-mediated, infectious, inflammatory and neoplastic disorders can all result in vasculitis.
- >50% of cases are idiopathic.
- Secondary vasculitis more common than primary vasculitis; search for underlying cause.
- Type III hypersensitivity is the predominant mechanism of cutaneous vasculitis.
- Vasculitis is characterized histologically by inflammatory cells in and around the vessel wall. Histologic classifications include neutrophilic, eosinophilic, lymphocytic, granulomatous, mixed and cell-poor forms. Neutrophilic vasculitis can be further classified into leukoclastic or nonleukoclastic (more common).
- Damage to vascular endothelium results in increased permeability, inflammation, and microvascular thrombosis.

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on the presence of nonblanching dermal erythema with or without edema; diagnosis is confirmed by skin biopsy. Vasculitis is a clinical problem with many etiologic possibilities, rather than a diagnosis, and efforts should be directed at identifying the underlying etiology.

DIFFERENTIAL DIAGNOSIS

Coagulopathy, disseminated intravascular coagulation (DIC), systemic lupus erythematosus, cold agglutinin disease, discoid lupus, bullous pemphigoid, lymphoreticular neoplasia, hypersensitivity (primarily urticaria)

INITIAL DATABASE

- CBC: changes related to underlying disease +/− mild leukocytosis
- Serum biochemistry panel: changes related to underlying disease +/− hyperglobulinemia, mild hypoalbuminemia
- Urinalysis: +/− proteinuria if renal involvement
- Skin biopsy: confirmatory test of choice

ADVANCED OR CONFIRMATORY TESTING

- Rickettsial testing (dogs), viral serology (FeLV/FIV, cats)
- Coagulation testing (platelet count, prothrombin time (PT), activated partial thromboplastin time (APTT), fibrin degradation products (FDPs)
- Direct immunofluorescence, immunohistochemical testing: often not needed in diagnosis, short window for sampling (within 4-24 hours of lesion formation)

TREATMENT 

TREATMENT OVERVIEW

Vasculitis may be acute and nonprogressive or chronic and recurrent. The therapeutic goal is to identify the underlying cause and minimize end organ damage if there is systemic involvement. Treatment of idiopathic cases is immunosuppressive or immunomodulatory. For treatment to be successful, the underlying cause must be treated or removed if possible.

ACUTE GENERAL TREATMENT

- Discontinue all unnecessary drugs until the inciting cause is identified.
- Glucocorticoids: prednisone or prednisolone (cats), 2-4 mg/kg PO q 24 h:
  - Use caution with immunosuppressive doses if underlying infectious etiology
- Supportive care including IV fluids and analgesics, based on clinical judgment

- Sulfasalazine: 20-40 mg/kg q 8 h in dogs for cases refractory to glucocorticoids or if dermal involvement only:
  - Monitor for side effects: anemia, thrombocytopenia, KCS, elevated ALT, and more serious side effects such as neuropathy, nephropathy
- May require addition of second immunosuppressive if not responding or prednisone intolerant:
  - Azathioprine, chlorambucil, and cyclophosphamide have been reported.

CHRONIC TREATMENT

- Glucocorticoids: slowly taper to lowest effective dose.
- Pentoxifylline: 10 mg/kg q 8-12 h, tapered over 1-3 months to q 12-24 h:
  - May take 1-3 months for response, synergistic action with glucocorticoids
- Therapy may be able to be tapered and discontinued over 4-6 months.

NUTRITION/DIET

Vitamin E therapy has been reported, as has a combination of tetracycline and niacinamide.

DRUG INTERACTIONS

Immunosuppressive doses of glucocorticoids may complicate treatment of underlying infectious etiology and should be used with extreme caution in these cases.

POSSIBLE COMPLICATIONS

- Necrosis: predisposes to infection or necessitates surgical débridement or amputation
- Consumptive coagulopathy (DIC) in severe cases
- Glomerulonephritis (GN) if immune complex deposition in the kidneys
- Hypoalbuminemia with severe or diffuse vasculitis or GN
- Glucocorticoids: immunosuppression, iatrogenic hyperadrenocorticism
- Sulfasalazine: side effects (above)

RECOMMENDED MONITORING

- Recheck in 3-5 days to assess response to initial therapy (extent and severity of lesions); reassess blood work if abnormalities present.
- CBC and serum biochemistry profile in 7 days if using sulfasalazine; every 4-6 weeks during initial treatment
- Reassess potentially infarcted dermal regions daily for evidence of necrosis; surgically address when patient stable.

PROGNOSIS AND OUTCOME

- Open depending on the underlying cause
- Drug-induced vasculitis tends to have a favorable prognosis once the inciting cause is eliminated, but chronic therapy may be required to limit the recurrence of clinical signs.

PEARLS & CONSIDERATIONS

COMMENTS

- Most cases of vasculitis are secondary, so aggressive efforts to identify the etiology should be made; however, 50% of cases remain idiopathic.
- A skin biopsy including the junction between affected and normal skin is critical to diagnose vasculitis and may be helpful in identifying the possible underlying etiology.

PREVENTION

Mark patient charts with medications/vaccinations associated with vasculitis to prevent potential administration in the future.

TECHNICIAN TIPS

Obtain a detailed history from owners.

CLIENT EDUCATION

Medical therapy may involve combinations of medications and multiple dose adjustments until therapeutic goal is reached. Frequent reassessment is critical to treatment success.

SUGGESTED READING

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Vasculitis, Cutaneous

BASIC INFORMATION

DEFINITION

A well-recognized condition characterized by blood vessel damage that results in ischemia of the skin and resultant tissue necrosis

SYNONYM

Cutaneous vasculopathy

EPIDEMIOLOGY

GENETICS & BREED PREDISPOSITION: Any breed, but certain syndromes show breed predisposition:

- Familial cutaneous vasculopathy (autosomal recessive): Jack Russell terrier, Scottish terrier, German shepherd
- Alabama rot (see p. 491): greyhounds
- Thrombovascular pinnal vasculitis: dachshund, weimaraner
- Rabies vaccine injection-site vasculitis (see p. 610): rottweiler, miniature poodle, bichon frise, silky terrier, Yorkshire terrier, Pekingese, Maltese, and miniature pinscher
- Familial canine dermatomyositis (see p. 291): collie, Shetland sheepdog, and Beauceron shepherd

RISK FACTORS

- Drug therapy (oral or injectable)
- Malignancy
- Infection (viral, bacterial, fungal, rickettsial)
- Immune-mediated diseases
- Insect bites
- Food allergy/hypersensitivity

ASSOCIATED CONDITIONS & DISORDERS

- Systemic lupus erythematosus (SLE)
- Familial canine dermatomyositis

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Clinically the lesions can be localized, regional, or multifocal to generalized.
- They are classified as small-vessel necrotizing vasculitis, hypersensitivity vasculitis, and large-vessel vasculitis.
- They are categorized histologically as neutrophilic (leukocytoclastic, nonleukocytoclastic), eosinophilic, lymphocytic, granulomatous, or cell-poor.

HISTORY, CHIEF COMPLAINT: Patients may present with crusted or ulcerative macules or patches that may be a source of self-trauma. Patients with urticarial vasculitis may present with erythematous and often pruritic wheals. These patients are often anorexic and lethargic.

PHYSICAL EXAM FINDINGS

- Description of the lesions varies according to the disease. Fever is often present.
- Thrombovascular pinnal vasculitis: notching of pinnal margins at tip and/or well-demarcated ulcers on the concave aspect of the pinna.
- Idiopathic vasculitis: well-demarcated necrosis and ulceration, particularly at the extremities and pressure points; may include edema, alopecia, or crateriform ulcers on the central aspect of the footpads. Some of these cases could be a rare manifestation of rabies vaccine-induced generalized ischemic dermatopathy.
- Urticarial vasculitis: generalized pruritus associated with papules, purpura, and wheals

- Familial canine dermatomyositis: erythema, ulceration, and mild crusting in the young dog. Affected areas include face, pressure points, digits, and tail tip.

ETIOLOGY AND PATHOPHYSIOLOGY

- Suspected type III hypersensitivity, although multiple pathomechanisms likely play a role. Antigen-antibody complexes become trapped along the basement membrane of vessel walls and activate the complement cascade.
- Other mechanisms proposed include direct antibody binding to the vessel wall and the release of toxic mediators, leading to a bystander reaction.
- In many cases, the exact mechanism is not known.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Cutaneous vasculitis is first suspected based on the appearance of skin lesions. The definitive diagnosis is based on a detailed drug history and skin biopsy. Unremarkable hematologic and biochemical profiles help confirm that the problem is "skin deep." It is often wise to consider the option of submitting tissue samples for fungal and bacterial culture at the time of biopsy.

DIFFERENTIAL DIAGNOSIS

- Cold-agglutinin disease
- Disseminated intravascular coagulation
- Frostbite
- Demodicosis (focal lesions)
- Dermatophytosis (focal lesions)

INITIAL DATABASE

- Thorough history to assess risk of drug-induced vasculitis
- Routine CBC, serum biochemical profile, urinalysis: results are typically within normal limits.
- Skin scrapings for focal (not ulcerated) lesions
- Diascopy (hemorrhagic lesions [e.g., vasculitis] do not blanch when a glass slide is pressed over the top, in contrast to vascular dilation/congestion).
- Biopsy: histopathologic evaluation reveals varying degrees of neutrophilic, eosinophilic, lymphocytic, granulomatous, or cell-poor vasculitis.

ADVANCED OR CONFIRMATORY TESTING

Selected according to signalment and clinical features of case:

- Bacterial serologic titers (dogs: *Rickettsia rickettsii, Ehrlichia canis, Borrelia burgdorferi)*
- Viral serologic titers (cats: feline leukemia virus [FeLV], feline immunodeficiency virus [FIV])
- Coagulation profile, Coombs' test, antinuclear antibody (ANA) test, and rheumatoid factor test may be indicated based on history, physical exam, and initial database supporting immune-mediated disease.
- Blood culture if sepsis is suspected
- Tissue culture of nodular or granulomatous lesions
- Hypoallergenic dietary trial (urticarial form of food hypersensitivity)

TREATMENT

TREATMENT OVERVIEW

The goal of treatment is to improve circulation to the affected area (e.g., using pentoxifylline, which increases RBC plasticity), control self-trauma, and suppress the immune reaction (e.g., using corticosteroids or other immunosuppressors) while evaluating for the inciting cause.

ACUTE GENERAL TREATMENT

- Discontinue current drug therapies.

- Bandage pressure points and keep wounds clean.
- Prevent self-trauma (Elizabethan collar).

CHRONIC TREATMENT

One or more may be indicated:

- Pentoxifylline: 25-35 mg/kg PO q 12 h following a meal
- Tetracycline and macinarmele: >10 kg. 500 mg of each drug PO q 8 h (<10 kg, 250 mg of each drug) for a minimum of 3 months; tapering is based on a favorable response.
- Prednisone or prednisolone: 2-4 mg/kg PO q 24 h starting dose, tapering based on a favorable response
- Azathioprine (dogs): 2.2 mg/kg PO q 24-48 h (with prednisone or prednisolone)
- Chlorambucil (cats): 0.1-0.2 mg/kg PO q 24-48 h (with prednisone or prednisolone)
- Dapsone: 1 mg/kg PO q 8 h in dogs
- Sulfasalazine: 22-44 mg/kg PO q 8 h in dogs
- Cyclosporine: 5 mg/kg PO q 12-24 h
- Tacrolimus 0.1% topically q 12 h can be considered in cases with focal disease, especially as a substitute for topical corticosteroids. Wear gloves to apply.

POSSIBLE COMPLICATIONS

Tissue necrosis and secondary infection: septicemia

RECOMMENDED MONITORING

- Response to therapy
- Monitor as appropriate for adverse reactions to therapy.

PROGNOSIS AND OUTCOME

- Some cases resolve, whereas others are chronic or recurrent. Damage to other organs (renal, neurologic) will also affect prognosis.
- Thrombovascular pinnal vasculitis: variable response (may wax and wane)
- Idiopathic: may require long-term/indefinite treatment
- Urticarial: dependent on identification of underlying etiology; rule out food allergy (see p. 400).

PEARLS & CONSIDERATIONS

COMMENTS

- Multiple skin biopsies for histopathologic evaluation are the key to diagnosis.
- Do not use drugs of similar classes to those used prior to development of the disease (owing to possibility of drug reaction).
- Monitor closely for adverse reactions to therapy.

PREVENTION

Vaccinate dogs IM if there is a history of rabies vaccine-induced vasculitis; increased risk of an anaphylactic reaction has been suggested.

CLIENT EDUCATION

Long-term treatment (4-6 months, sometimes indefinitely) is often needed.

SUGGESTED READING

Nichols PR, Morris DO, Beale KM: A retrospective study of canine and feline cutaneous vasculitis. Vet Dermatol 12:255–264, 2001.

AUTHOR: STEPHEN WAISGLASS

EDITOR: MANON PARADIS

Vascular Ring Anomaly

BASIC INFORMATION

DEFINITION

Congenital malformation of one or more parts of the aortic arch during embryogenesis such that vessels encircle the esophagus and trachea, causing chronic compression

SYNONYMS

Vascular ring malformation, persistent right aortic arch (PRAA; most common vascular ring anomaly)

EPIDEMIOLOGY

SPECIES, AGE, SEX

- More common in dogs than in cats
- Clinical signs usually develop shortly after weaning.
- No sex predilection

GENETICS & BREED PREDISPOSITION

- The majority of dogs with PRAA are of large breeds (>15 kg expected adult weight).
- Heritability is suspected in German shepherds and greyhounds.

ASSOCIATED CONDITIONS & DISORDERS

- Persistent left cranial vena cava and patent ductus arteriosus (PDA) can be associated vascular anomalies.
- Megaesophagus and aspiration pneumonia are secondary problems associated with chronic partial esophageal obstruction.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT: Most dogs and cats develop clinical signs once they start to ingest solid food, because the vascular ring obstructs passage of food down the esophagus. Postprandial regurgitation is the usual presenting complaint, and the majority of cases are diagnosed before 6 months of age. Occasionally, animals may have coughing or respiratory distress due to aspiration pneumonia or tracheal compression.

PHYSICAL EXAM FINDINGS: Animals have a good appetite but may be thin as a result of chronic regurgitation. An enlarged esophagus may occasionally be palpated in the thoracic inlet, especially after eating. In dogs with a concurrent PDA (minority of cases), a continuous left basilar murmur is ausculted; however, in the absence of PDA, cardiac auscultation is normal. Animals with aspiration pneumonia may be febrile with harsh ventral lung sounds.

ETIOLOGY AND PATHOPHYSIOLOGY

- Normal embryogenesis:
  - In the embryo, the great vessels are formed from six aortic arches that connect paired ventral and dorsal aortas. During development, these vessels undergo regression and reconnection that normally result in a left-sided aorta, left-sided ligamentum arteriosum, and normal branching of the brachiocephalic trunk and left subclavian arteries off the ascending aorta.
- Pathophysiology:
  - Developmental anomalies of the great vessels appear to be relatively common; however, these anomalies are only clinically important when the vessels entrap the esophagus and trachea within a vascular ring.
  - Passage of food down the esophagus is impeded by the vascular ring, causing esophageal dilation, food stasis, and regurgitation. Regurgitation with aspiration can cause pneumonia.
- PRAA (most common in dogs):
  - The normal left aortic arch regresses, while the right aortic arch is retained. The left ligamentum arteriosum passes over the esophagus, connecting the right aortic arch to the left-sided pulmonary artery and compressing the esophagus at the base of the heart.
  - PRAA can also occur with an aberrant left subclavian artery. This causes an incomplete ring that dorsally compresses

the esophagus (the left subclavian arises from the right aorta and courses dorsally over the esophagus).

- Double aortic arch:
  - Both left and right aortic arches persist, encircling the esophagus and trachea as the two vessels merge to form the descending aorta.
- Persistent right ligamentum arteriosum with normal left aorta is an uncommon cause of a vascular ring anomaly. It is important to note that correction by a left lateral thoracotomy is more difficult for this malformation than for the other vascular ring anomalies.
- An aberrant right subclavian artery with a normal left aorta can cause an incomplete ring because the aberrant vessel courses over and dorsally compresses the esophagus.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

A history of regurgitation beginning immediately after weaning is highly suggestive; plain thoracic radiographs provide the basis for a diagnosis of vascular ring anomaly (e.g., ventral and leftward tracheal deviation, dilated cranial esophagus) and also screen for associated aspiration pneumonia.

DIFFERENTIAL DIAGNOSIS

- Differential diagnoses for regurgitation include congenital megaesophagus, stricture, foreign body, neoplasia, granuloma, hiatal disorder, and esophageal diverticulum.
- Esophageal stricture is the major differential diagnosis to consider for radiographic esophageal dilation that terminates at the base of the heart.

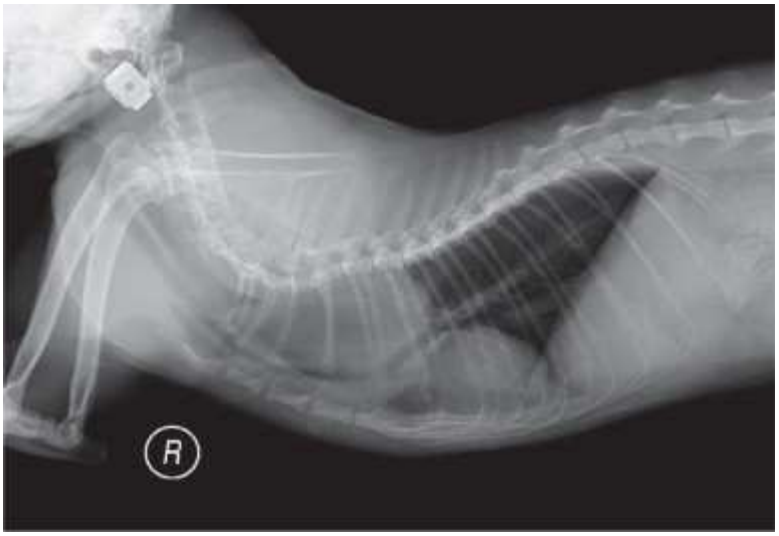
INITIAL DATABASE

- Thoracic radiographs:
  - The esophagus may appear dilated up to the base of the heart on plain films. Its visualization may be enhanced by residual food. Lateral radiographs often show ventral deviation of the trachea cranial to the heart, and the tracheal lumen may be narrowed in this deviated segment.
  - Leftward curvature of the trachea near the cranial border of the heart on the dorsoventral (DV) or ventrodorsal (VD) view reliably differentiates dogs with vascular ring anomalies from dogs with generalized megaesophagus. These radiographic findings may obviate the need for a barium esophagram.
- CBC is indicated if there is evidence of aspiration pneumonia.

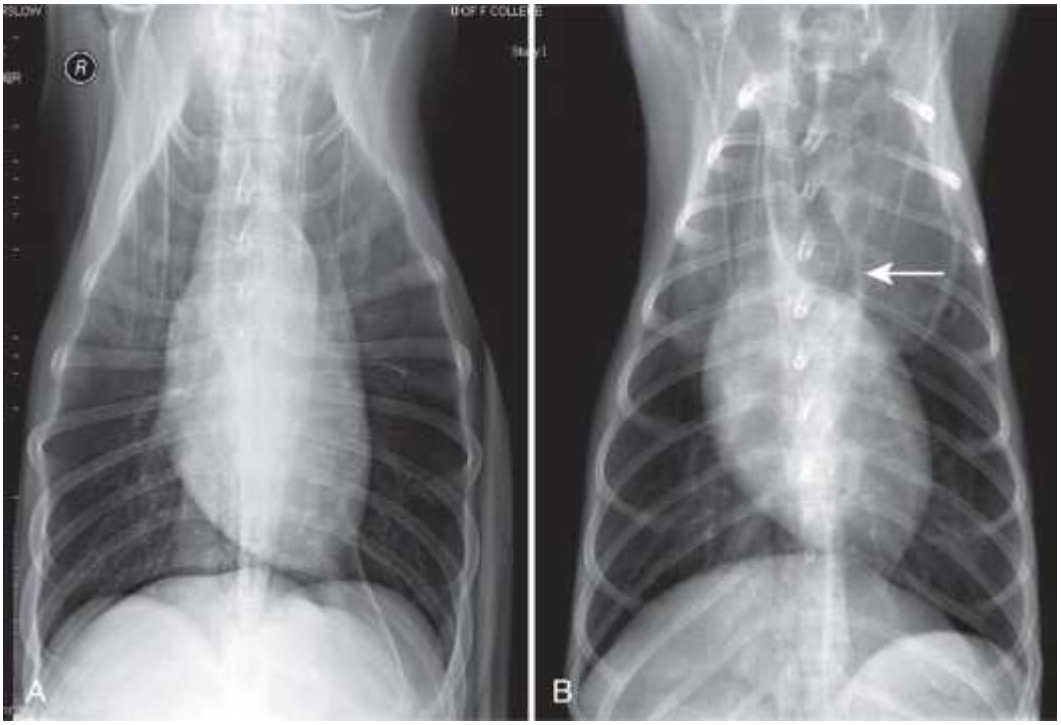
ADVANCED OR CONFIRMATORY TESTING

Often unnecessary when a working diagnosis is made from thoracic radiographs.

- Barium esophagram: barium given in food can be used to radiographically outline the focal dilation of the esophagus that narrows at the base of the heart. Although this finding is diagnostic for a vascular ring anomaly, it does not reveal the type of anomaly present.
- Nonselective CT angiography has been used for producing a 3-dimensional anatomic reconstruction of the anomalous vasculature for diagnosis and to assist in surgical approach.



VASCULAR RING ANOMALY Lateral thoracic radiograph demonstrating marked ventral deviation of the trachea and severe esophageal filling with fluid/soft-tissue opacity material cranial to the carina. The cause was a vascular ring anomaly.



VASCULAR RING ANOMALY A, Ventrodorsal thoracic radiograph of a normal dog. **B**, Ventrodorsal thoracic radiograph of a dog with vascular ring anomaly. Leftward deviation of the trachea *(arrow)* is characteristic of vascular ring anomaly.

TREATMENT

TREATMENT OVERVIEW

Esophageal constriction caused by vascular ring anomalies is treated surgically by ligation and division of the aberrant vessel, with the ultimate goal being a reduction or elimination of regurgitation. Intensive pre- and postoperative care may be required for debilitated patients.

ACUTE GENERAL TREATMENT

- Young malnourished animals may benefit from fluid therapy with dextrose.
- Animals with aspiration pneumonia require antibiotic therapy prior to surgical intervention.
- Surgical division of the vascular ring:

- For the vast majority of vascular ring anomalies, the preferred surgical approach is a left fourth intercostal thoracotomy.
- Ventilation is required after entering the thorax (thoracostomy tube after surgery for 24 hours to evacuate air).
- When the vascular ring is caused by PRAA, the left ligamentum arteriosum is ligated and divided, releasing the constriction on the esophagus.
- When the vascular ring is caused by an aberrant subclavian artery coursing over the esophagus, this artery is ligated and divided. No adverse effects are noted from this ligation, as the vertebral artery supplies adequate collateral flow.
- When a double aortic arch is present, the smaller arch is ligated and divided.
- Thoracoscopic ligation of a left ligamentum arteriosum (with PRAA) has been reported as a less invasive surgical option.

NUTRITION/DIET

- Severely malnourished animals may require nutritional support prior to surgery, including elevated feedings of slurried food or, in some cases, placement of a gastrostomy tube (see p. 1270).
- Give slurried food to the patient from an elevated position for several weeks after surgery. After feeding, the patient should be kept in a vertical position for 10 minutes. Then introduce solid food from an elevated position. If no regurgitation occurs, most dogs can be returned to a normal feeding regimen 1-2 months after surgery.

POSSIBLE COMPLICATIONS

- Most common complication: aspiration pneumonia. Regurgitation may continue after surgical disruption of the vascular ring because of loss of neuromuscular esophageal function. Some animals may never be able to ingest solid food and may need to be fed a slurry diet indefinitely.
- Other possible complications are related to thoracic surgery and include lung lobe laceration, intraoperative hemorrhage, or thoracic duct injury leading to postoperative chylothorax.

RECOMMENDED MONITORING

Thoracic radiographs should be used to monitor for postoperative aspiration pneumonia and document resolution of megaesophagus.

PROGNOSIS AND OUTCOME

- Prognosis is dependent on age at the time of surgical therapy, severity of malnourishment, presence of aspiration pneumonia, and degree of esophageal constriction.
- A study found that 6 months after surgery, the majority (92%) of dogs did not regurgitate, and the remainder regurgitated only occasionally.

PEARLS & CONSIDERATIONS

COMMENTS

- Oral passage of a stomach tube into the esophagus by an assistant during surgery can help locate the stricture and facilitates dissection around the esophagus.
- Intraoperative balloon dilation of the esophagus is particularly helpful to remove constricting fibrous bands after the ring has been resected.

CLIENT EDUCATION

Although the prognosis is good for most dogs following surgical therapy, counsel owners about the potential for continued esophageal dysfunction.

SUGGESTED READING

Buchanan JW: Tracheal signs and associated vascular anomalies in dogs with persistent right aortic arch. J Vet Intern Med 18:510–514, 2004.

Kyles AE: Esophagus. In Slatter DH, editor: Textbook of small animal surgery. Philadelphia, 2003, WB Saunders, p 577.

AUTHORS: DARCY B. ADIN, CHRISTOPHER A. ADIN

EDITOR: ETIENNE CÔTÉ

Vaginitis

Additional Images Available on Website

BASIC INFORMATION

DEFINITION

Inflammation/irritation of the vagina

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Spayed or intact bitches
- Prevalence <1%
- Juvenile onset: bitches 8 weeks to 1 year of age. Adult onset: bitches >1 year of age

RISK FACTORS: Anatomic abnormalities (strictures or septa), perivulvar dermatitis with atrophic juvenile vulva and excessive skin folds, perivascular dermatitis in overweight dogs with urinary incontinence, systemic illness (e.g., diabetes mellitus, hyperadrenocorticism)

CONTAGION & ZOONOSIS: *Bruceila cants,* canine herpesvirus

GEOGRAPHY AND SEASONALITY: Hot and humid climates may trigger or exacerbate vaginitis.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Juvenile onset versus adult onset
- Acute versus chronic

HISTORY, CHIEF COMPLAINT

- Vulvar discharge (chronic, if present for >1 month)
- In juvenile-onset vaginitis, bitches usually are not systemically ill.
- Pollakiuria, discomfort (e.g., excessive vulvar licking, pain when urinating)
- Clinical signs of concurrent disease (e.g., polyuria/polydipsia, urinary incontinence, pruritus, infertility) may be contributing causes of vaginitis.

PHYSICAL EXAM FINDINGS

- Vulvar mucoid, purulent, occasionally blood-tinged discharge
- Vulvar hyperemia
- Digital vaginal examination (see p. 1360) may reveal vaginal stenoses or septa
- Atrophic or juvenile vulva with excessive skin folds, with concurrent perivulvar dermatitis
- Overweight dogs with urinary incontinence, with excessive perivulvar skin folds and persistent moisture and urine scalding

ETIOLOGY AND PATHOPHYSIOLOGY

- Physical abnormalities impede normal evacuation of secretions, compromise natural barrier. Systemic diseases may compromise immunity (e.g., diabetes mellitus, hyperadrenocorticism) or infect reproductive tract directly (e.g., brucellosis).
- Many dogs have idiopathic vaginitis.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is generally suspected as a result of vulvar discharge. Vaginoscopy +/− bacterial culture are used for confirming the

diagnosis.

DIFFERENTIAL DIAGNOSIS

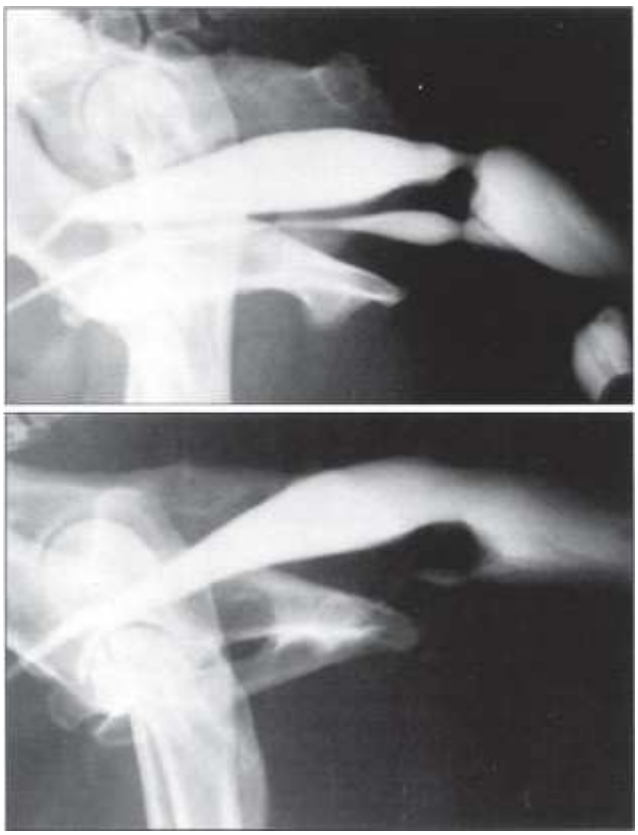
- Urinary tract infection
- Metritis
- Cystic endometrial hyperplasia/pyometra
- Uterine stump pyometra
- Vulvar, vaginal, or uterine tumor
- Brucellosis
- Canine herpesvirus infection

INITIAL DATABASE

- CBC, serum biochemistry profile: generally unremarkable
- Serologic titer for *Brucella canis* (see p. 162)
- Vaginoscopy assesses discharge present in the vagina; vesicular lesions (e.g., canine herpesvirus associated or lymphoid follicles) seen as nonspecific indicators of inflammation; urine pooling, masses, foreign bodies possible.
- Vaginal Cytologic examination shows WBCs with or without bacteria.

ADVANCED OR CONFIRMATORY TESTING

- Vaginal bacterial culture: moderate to heavy growth of 1 to 2 bacterial types (more might suggest normal flora).
- Urinalysis and bacterial culture: concurrent urinary tract infection (UTI) is common.
- Contrast radiography, biopsy: rarely if ever needed



VAGINITIS Contrast vaginogram showing vestibulovaginal stenosis with marked narrowing of vagina cranial to urethral papilla. *Top,* Preoperatively. *Bottom,* Five months after surgical resection of the stenosis and vestibulovaginal anastomosis.

(From Kyles AE, Vaden S, Hardie EM, et al: Vestibulovaginal stenosis in dogs: 18 cases (1987-1995). J Am Vet Med Assoc 209:1889-1893, 1996.)

TREATMENT

TREATMENT OVERVIEW

- Correction of the underlying cause is the cornerstone of effective long-term resolution. In adult-onset vaginitis, treatment of the underlying cause is usually curative.
- Most therapy for vaginitis is supportive and nonspecific because most cases are idiopathic. Many cases resolve spontaneously in both juvenile- and adult-onset vaginitis, particularly when there is no identifiable underlying cause.

ACUTE AND CHRONIC TREATMENT

- If the primary problem is UTI (up to 60% of cases with identifiable underlying cause):
  - Antibiotics based on culture and sensitivity testing (empirical antibiotics acceptable for first 48-72 h pending culture results)
  - Antibiotics, if used, should be administered for 4 weeks and based on a guarded sample collected from the cranial vagina and culture and sensitivity.
- Diethylstilbestrol (DES), 0.1-0.2 mg/kg PO, maximum dose = 1 mg, q 24 h for 5 days, tapering to 2× a week; or phenylpropanolamine, 1-1.5 mg/kg PO q 8-12 h. Note: Do not use DES in dogs that have not reached adult stature (may induce premature long-bone physeal closure).
- In overweight urinary-incontinent dogs with excessive perivulvar skin folds, vulvoplasty (episioplasty) is recommended.
- If the primary problem is vaginal anatomic anomalies (up to 36% of cases with identifiable underlying cause), surgical repair may be indicated.
- If the primary problem is systemic disease (up to 15% of cases with identifiable underlying cause): treat the underlying systemic disease.
- If the primary problem is idiopathic:
  - DES to treat subclinical urinary incontinence
  - Glucocorticoids may be beneficial in some bitches (do not use in cases of concurrent urinary incontinence).
- Treatment for atopic dermatitis if present concurrently (see p. 106)
- Vaginal douches with antiseptics or antibiotics have not been reported to be an effective treatment.
- Owners should be instructed to keep the perivulvar skin folds clean.

POSSIBLE COMPLICATIONS

- Ascending UTIs can result from chronic vaginitis.
- Self-mutilation can result from excessive licking of the perivulvar skin secondary to vaginitis.

RECOMMENDED MONITORING

Recheck animals showing any signs of systemic illness, and look for complications such as metritis.

PROGNOSIS AND OUTCOME

With spontaneous remission, future reproductive success is not compromised.

PEARLS & CONSIDERATIONS

COMMENTS

- Urethral sphincter mechanism incompetence (see p. 1134) may be misdiagnosed as vaginitis, especially when there is positive response to treatment for suspected vaginitis with DES or phenylpropanolamine.
- Daily record of the frequency and severity of clinical signs (e.g., vulvar discharge, vulvar licking) will help the veterinarian to assess response to therapy.
- Limited understanding of the causes of vaginitis makes it difficult to predict when and if clinical signs will resolve.

CLIENT EDUCATION

Owners should consider not breeding bitches with poor vulvar conformation or congenital vaginal defects to avoid perpetuating these problems in the female offspring.

SUGGESTED READING

Root Kustritz MV: Vaginitis in dogs: a simple approach to a complex condition. Vet Med 103:562–567, 2008.

AUTHOR: CARLOS GRADIL

EDITOR: MICHELLE A. KUTZLER

Vaginal Hyperplasia and Vaginal Prolapse

BASIC INFORMATION

DEFINITION

Edematous swelling of the vaginal mucosa cranial to the urethral orifice; an uncommon disorder that occurs during estrogen stimulation in the intact bitch. It may progress to vaginal protrusion through the vulvar lips.

SYNONYMS

Vaginal edema, hypertrophy, hyperplasia, eversion, or protrusion

EPIDEMIOLOGY

SPECIES, AGE, SEX: Intact bitch, any age (7 months to 16 years old)

GENETICS & BREED PREDISPOSITION

- More common in large-breed dogs
- Breeds predisposed: bulldog, mastiff, boxer, dalmatian, German shepherd, Saint Bernard, Labrador and Chesapeake Bay retrievers, weimaraner, Walker hound, springer spaniel, Airedale terrier, and American pit bull terrier

RISK FACTORS

- Young bitch under the influence of estrogen during proestrus or estrus; may occur or recur during diestras, pregnancy, or parturition
- Can be observed as side effect of estrus induction with estrogen

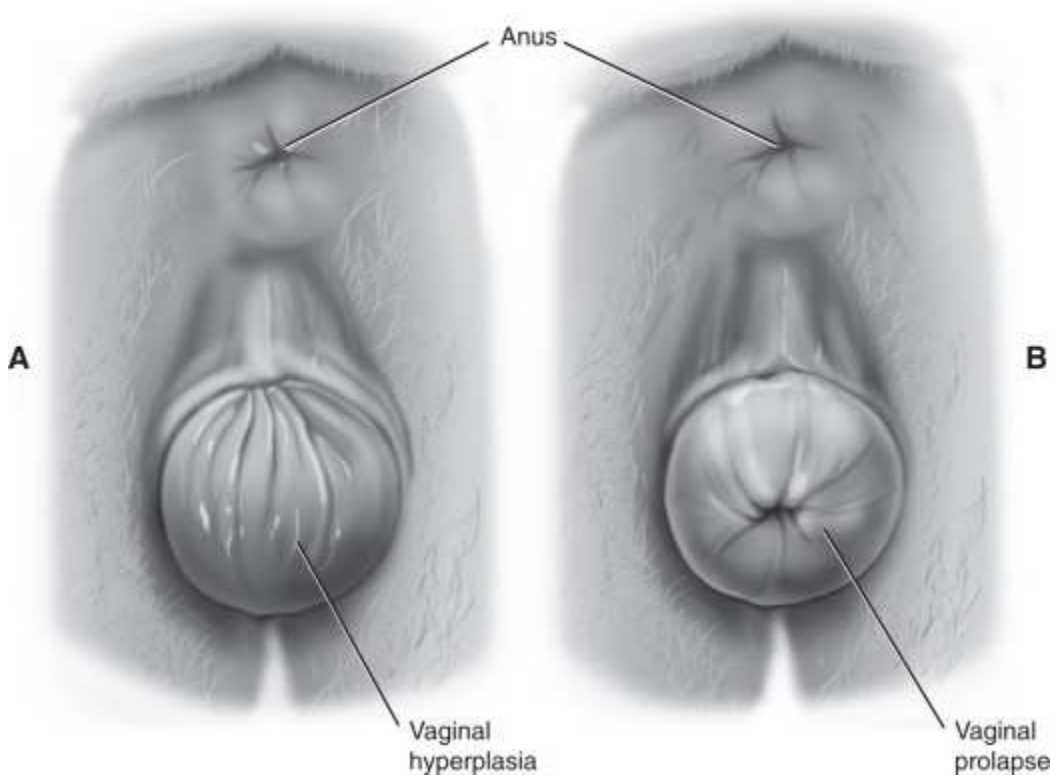
ASSOCIATED CONDITIONS & DISORDERS: Markedly prolapsed vaginal tissue is subject to self-mutilation and may be dry, ulcerated, necrotic, and devascularized; possible dysuria or pollakiuria.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

Vaginal hyperplasia:

- Type I: slight to moderate eversion of the vaginal floor cranial to the urethral orifice; confined to the vestibulum, appearing as a bulge at the perineum.
- Type II: well-developed swelling of the vaginal floor, which may include the lateral vaginal walls, protruding through the vulvar lips. The swelling appears dome shaped.



VAGINAL HYPERPLASIA AND VAGINAL PROLAPSE A, Well-developed swelling of vaginal floor, which may include lateral vaginal walls, protruding through vulvar lips. Swelling appears dome-shaped (type II vaginal hyperplasia). **B**, Well-developed protrusion of entire circumference of vaginal wall through vulvar lips. Swelling appears doughnut shaped (vaginal prolapse).

- Type III: well-developed protrusion of the entire circumference of the vaginal wall through the vulvar lips. The swelling appears doughnut shaped and is a vaginal prolapse.

HISTORY, CHIEF COMPLAINT

- Previous occurrence of vaginal hyperplasia
- Onset of proestrus or estrus
- Licking or irritation of the vulva
- Mass protruding from vulva or bulge at the perineum
- Dysuria or pollakiuria
- Failure to allow intromission during breeding
- Tenesmus

PHYSICAL EXAM FINDINGS: Bulge at the perineum or protrusion of a pink dome-shaped or doughnut-shaped mass from vulva; surface of protrusion may be dry, necrotic, or ulcerated. Vaginal examination reveals:

- A urethral orifice located ventrally in all three types of vaginal hyperplasia
    - A vaginal lumen located dorsally in types I and II but centrally located in type III
- By contrast, uterine prolapse is distinguished by the presence of tubular masses within the vagina or protruding from the vulva.

ETIOLOGY AND PATHOPHYSIOLOGY

- Vaginal hyperplasia: an exaggerated response of the vaginal mucosa to estrogen (hyperemia, edema, keratinization). The swelling begins as an eversion in the vaginal floor, cranial to the urethral orifice.
- With vaginal prolapse: histopathologic examination of affected vaginal tissue is consistent with submucosal edema rather than with hyperplasia or hypertrophy.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is suspected based on the presence of a vulvar swelling or protrusion in a young intact bitch.

DIFFERENTIAL DIAGNOSIS

- Benign or malignant vaginal neoplasia
- Vaginal polyp
- True vaginal prolapse with concurrent entrapment of visceral organs (rare)
- Uterine prolapse
- Urethral neoplasia

INITIAL DATABASE

- Stage of hormonal cycle based on vaginal cytologic examination
- Vaginal examination to locate the urethral orifice, vaginal lumen, origin of the protruding mass, and the size of its base (see p. 1360)
- Ensure that the animal is able to urinate.

ADVANCED OR CONFIRMATORY TESTING

- Biopsy of vaginal mass confirms diagnosis in atypical bitches.
- In severe cases, survey radiographs can be used to evaluate for visceral organ involvement; contrast radiography can confirm the location of the urethral orifice and vaginal lumen.

TREATMENT

TREATMENT OVERVIEW

Treatment goals are to prevent drying, necrosis, and devitalization of exposed vaginal tissue, prevent future recurrence, and prevent urethral obstruction.

ACUTE GENERAL TREATMENT

- Insertion of a urethral catheter to relieve obstruction when present
- Ensuring that vaginal tissue is kept clean
- Topical application of sterile water-soluble lubrication or antibiotic ointment
- Application of an Elizabethan collar or protective pants
- Provision of a clean environment to minimize tissue trauma
- Scheduling an ovariohysterectomy, which prevents recurrence and may hasten resolution; regression of tissue is reported to occur within 21 days.
- Recognition that spontaneous regression at end of estrus is common

CHRONIC TREATMENT

- Ovariohysterectomy prevents recurrence in nonbreeding bitches.
- Surgical excision of prolapsed vaginal tissue in bitches intended for breeding or in those with severely inflamed or devitalized vaginal tissue:
    - May prevent recurrence during subsequent estrous cycles or at parturition
    - Various surgical techniques are described involving circumferential incision at the base of the prolapse.
    - Episiotomy may be needed.
- Manual reduction of prolapsed tissue and placement of stay sutures in the vagina do not prevent recurrence and may cause the bitch discomfort.
- Artificial insemination can be performed in breeding bitches.
- Induction of ovulation during a nonbreeding cycle may hasten regression of vaginal tissue by decreasing estrogenic stimulation: gonadotropin-releasing hormone (2.2 mcg/kg IM) or human chorionic gonadotropin (1000 IU IM, irrespective of body weight as a single injection, or 500 IU IM, irrespective of body weight and repeated in 48 hours); a 1-week regression follows ovulation. Treatment is ineffective if given after ovulation.

DRUG INTERACTIONS

Avoidance of progestational drugs that contribute to pyometra

POSSIBLE COMPLICATIONS

- Necrosis, infection, and devascularization of vaginal tissue
- Evisceration of abdominal organs
- Urination and defecation difficulties

RECOMMENDED MONITORING

- Monitor viability of prolapsed vaginal tissue.
- Evaluate ability to urinate.

PROGNOSIS AND OUTCOME

- Good prognosis with ovariohysterectomy
- Recurrence rate is 66% in untreated bitches

PEARLS & CONSIDERATIONS

COMMENTS

- Vaginal hyperplasia may progress to vaginal prolapse (type lll), but other disorders less commonly may also cause vaginal prolapse.
- If excision of vaginal tissue is performed in late estrus or early diestrus, bleeding is minimized.
- If ovariohysterectomy is performed in anestrus (serum progesterone concentrations <2 ng/mL), development of pseudopregnancy is minimized.
- Catheterize urethra during excision of vaginal tissue to help prevent inadvertent urethral trauma.

PREVENTION

- Ovariohysterectomy
- Surgical excision of redundant vaginal tissue may prevent recurrence during the following estrous cycle.

CLIENT EDUCATION

Discuss heritability and intended plans for the bitch; ovariohysterectomy is the recommendation for nonbreeding bitches.

SUGGESTED READING

Alan M, Cetin Y, Sendag S, et al: True vaginal prolapse in a bitch. Anim Reprod Sci 100: 411–414, 2007.

Schaefers-Okkens AC: Vaginal edema and vaginal fold prolapse in the bitch, including surgical management. International veterinary information service. April 10, 2001: http://www.ivis.org.

AUTHOR: KRISTINE L. GONZALES

EDITOR: MICHELLE A. KUTZLER

Vaginal Congenital Abnormalities in the Bitch

BASIC INFORMATION

DEFINITION

Malformations that reduce the diameter of the vestibulovaginal junction (bands) and may cause secondary infertility, vaginitis, or cystitis include incomplete dissolution or fusion of the paramesonephric ducts (Müllerian), hymenal remnants, and hypoplasia of the vestibulovaginal junction.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Congenital vaginal abnormalities are present at birth but are usually undetected until the appearance of clinical signs. Young-adult female dogs are most commonly affected.

GENETICS & BREED PREDISPOSITION: Large-breed dogs may be over-represented.

ASSOCIATED CONDITIONS & DISORDERS: Female dogs with ectopic ureters often have coincident congenital vaginal abnormalities.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Double vagina
- Hypoplasia of the vaginal vault
- Imperforate hymen
- Vaginal stenosis
- Vaginal stricture

HISTORY, CHIEF COMPLAINT

- Unsuccessful breeding attempts, obvious pain during breeding, avoidance of male during breeding attempts
- Purulent, often recurrent vaginal discharge
- Persistent urinary tract infection (UTI), urine dribbling

PHYSICAL EXAM FINDINGS

- Vaginal discharge may be present.
- Narrowing of vestibulovaginal junction may be apparent during manual vaginal exam (see p. 1360).

ETIOLOGY AND PATHOPHYSIOLOGY

- Incomplete fusion of the paramesonephric ducts can result in persistent dorsoventral bands.
- Vestibulovaginal hypoplasia causes concentric narrowing of the vestibulovaginal junction.
- Incomplete dissolution of the hymen can compromise the vestibulovaginal junction.
- Any type of vestibulovaginal stricture can interfere with breeding, owing to pain produced during penetration by a male dog.
- Anatomic abnormalities of the vestibulovaginal junction can inhibit drainage of vaginal secretions, which can lead to vaginitis or ascending UTI.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Clinicians should suspect vestibulovaginal abnormalities in bitches or queens with a history of difficult or unsuccessful breeding. The diagnosis is usually made during vaginal examination.

DIFFERENTIAL DIAGNOSIS

- Behavioral abnormalities in breeding bitches in estrus who are reluctant to stand for a male
- Urolithiasis is a much more common cause of chronic UTI.
- Vaginal discharge may be associated with juvenile-onset vaginitis or pyometra.

INITIAL DATABASE

- Vaginoscopy using a flexible or rigid endoscope (see p. 1361)
- Heavy sedation or general anesthesia is necessary.

ADVANCED OR CONFIRMATORY TESTING

Contrast radiography: retrograde vaginography (see p. 1158)

TREATMENT

TREATMENT OVERVIEW

Remove obstruction/narrowing at vestibulovaginal junction.

ACUTE GENERAL TREATMENT

- Digital dilation of vestibulovaginal junction (effective for treatment of hymenal remnants or mild [membranous] vestibulovaginal stenosis)
- Resection of dorsoventral paramesonephric duct remnants or bands if present
- For severe (fibrous) vestibulovaginal stenosis: resection and anastomosis of vestibulovaginal junction via an extended episiotomy

CHRONIC TREATMENT

After manual or surgical dilation, antibiotic therapy (based on culture and sensitivity [C&S]) may have to be extended up to 6 weeks for treatment of ascending UTI if present.

BEHAVIOR/EXERCISE

Bitches with previous painful breeding episodes may be reluctant to accept a male after treatment of vestibulovaginal abnormalities. Use of an experienced breeding male may be helpful.

POSSIBLE COMPLICATIONS

- Stricture secondary to resection and anastomosis
- Inadequate resection does not resolve clinical signs.

RECOMMENDED MONITORING

Observe the animal for recurrence of signs; initial treatment may have to be repeated if stricture occurs secondary to resection or traumatic dilation.

PROGNOSIS AND OUTCOME

- Prognosis is good if clinical signs are caused by hymenal remnants or mild vaginal stricture.
- Prognosis for resolution of clinical signs is fair to good for severe vaginal stricture treated by vestibulovaginal resection and anastomosis.

PEARLS & CONSIDERATIONS

COMMENTS

- Do not confuse normal narrowing at the vestibulovaginal junction with a pathologic condition:

    - The diameter of the vestibulovaginal junction must be less than 30% of the diameter of the maximal diameter of the vagina to be considered pathologic.
- Most congenital vaginal abnormalities do not cause clinical signs.

PREVENTION

Since most vestibulovaginal abnormalities are congenital but not hereditary, there are no recommendations against breeding affected bitches or queens once the abnormality is treated.

TECHNICIAN TIPS

Although digital vaginal examination is helpful in making a diagnosis of vestibulovaginal abnormality, direct visual inspection using vaginoscopy permits a much more accurate diagnosis.

CLIENT EDUCATION

- Breeding bitches that are reluctant to stand for a male may have vestibulovaginal abnormalities that cause painful breeding.
- Congenital vaginal anomalies may be present without causing clinical signs.

SUGGESTED READING

Crawford JT, Adams WM: Influence of vestibulovaginal stenosis, pelvic bladder, and recessed vulva on response to treatment for clinical signs of lower urinary tract disease in dogs: 38 cases (1990-1999). J Am Vet Med Assoc 221:995, 2002.

Kyles AE, et al: Vestibulovaginal stenosis in dogs: 18 cases (1987-1995). J Am Vet Med Assoc 209:1889, 1996.

AUTHOR: JAMES A. FLANDERS

EDITOR: MICHELLE A. KUTZLER

Vacuolar Hepatopathy

BASIC INFORMATION

DEFINITION

Benign, reversible hepatic lesion of glycogen accumulation that occurs commonly in dogs in response to excess glucocorticoids and/or as a reactive change secondary to systemic disorders

SYNONYMS

Glucocorticoid hepatopathy, hepatic glycogen accumulation, steroid hepatopathy

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs only; age and sex dependent on underlying cause. Older dogs may have spontaneous hyperadrenocorticism or idiopathic vacuolar hepatopathy.

GENETICS & BREED PREDISPOSITION

- Poodles, dachshunds, beagles, boxers, terrier breeds: pituitary-dependent hyperadrenocorticism
- German shepherd, Labrador retriever, poodle, dachshund, terrier breeds: functional adrenal tumor
- Scottish terriers: idiopathic vacuolar hepatopathy

RISK FACTORS: Glucocorticoid administration

ASSOCIATED CONDITIONS & DISORDERS: Hyperadrenocorticism including atypical forms (increased adrenal steroids other than cortisol, or aberrant adrenocortical disease [see p. 6]); secondary reactive change associated with stress from other systemic inflammatory, infectious, or neoplastic disorders.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Incidental finding of increased serum alkaline phosphatase (ALP) activity; subsequent fine-needle aspirate (FNA) and Cytologic examination or liver biopsy show vacuolar change
- Clinical signs of glucocorticoid excess
- Clinical signs of primary systemic disorder

HISTORY, CHIEF COMPLAINT

- For glucocorticoid excess, clinical signs reflect systemic effects of hyper-cortisolism rather than hepatic disease: polyuria and polydipsia (PU/PD), polyphagia, panting.
- If iatrogenic, a history of glucocorticoid administration (oral, injectable, topical: eyes, ears, skin) within last 3-6 months (depends on route, preparation, duration of therapy, and individual sensitivity) is expected.
- Other signs depend on primary systemic disorder.
- The patient may show no clinical signs (incidental finding) or mild polydipsia: idiopathic vacuolar hepatopathy, Scottish terriers.

PHYSICAL EXAM FINDINGS

- For iatrogenic or spontaneous hyperadrenocorticism: hepatomegaly (may be massive); abdominal enlargement, thin haircoat or truncal alopecia, thin skin
- Other findings dependent on primary systemic disorder
- May be unremarkable

ETIOLOGY AND PATHOPHYSIOLOGY

- Excess glucocorticoids (exogenous, or spontaneous hyperadrenocorticism):

    - Dogs are uniquely susceptible to hepatic effects of glucocorticoids.
    - Gradual hepatic glycogen accumulation and hepatomegaly occur within the first 2 weeks of daily prednisolone administration.
    - Preceded by increased serum ALP activity
    - Marked individual variation
    - Lesions identical with exogenous or endogenous corticosteroids
    - Hepatic function is typically normal.
    - Reversible
- Aberrant adrenocortical disease ("atypical hyperadrenocorticism;" see p. 6)
    - Increased adrenal steroid hormones other than cortisol (especially progesterone and 17-α hydroxyprogesterone)
    - Progesterone has glucocorticoid-like effects on the liver.
- Scottish terriers:
    - Increased serum ALP activity (predominantly steroid-induced isoenzyme)
    - No overt clinical signs; cause unknown
    - No association between progesterone or 17-α hydroxyprogesterone levels and serum ALP elevations
    - Reactive hepatopathy:
    - Common lesion in dogs with other systemic illnesses (including neoplastic, neurologic, immune-mediated, and gastrointestinal tract disorders) and severe dental disease.
    - Acute or chronic illness can be associated with stress-induced hypercortisolemia resulting in vacuolar hepatopathy.
- Hepatic nodular hyperplasia or regeneration:
    - Etiology unknown; may be associated with nutritional factors or the result of focal areas of ischemia
- Congenital or acquired hepatobiliary disease:
    - Acute and chronic inflammation, hepatotoxicity, and congenital portosystemic shunt may have vacuolar changes. With acquired hepatobiliary disease, necrotic or inflammatory lesions predominate.
- Idiopathic vacuolar hepatopathy:
    - Excess corticosteroids or other adrenal steroid hormones cannot be documented; absence of systemic disease; usually associated with no clinical signs; clinical significance unknown.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

- Initially suspected based on findings of increased serum ALP activity (steroid-induced isoenzyme predominates), normal liver function, and hepatomegaly.
- Abdominal ultrasound to evaluate for other causes of liver disease and to evaluate adrenal glands; FNA cytologic examination of liver shows characteristic vacuoles (though common false-positive finding with FNA).
- Screen for excess exogenous or endogenous glucocorticoids (endocrine testing for hyperadrenocorticism if compatible with history and physical exam), then evaluate for systemic disorders causing reactive change; if no diagnosis, consider liver biopsy to evaluate for primary hepatobiliary disorders.

DIFFERENTIAL DIAGNOSIS

- Other hepatopathies (inflammatory, neoplastic)
- Nodular hyperplasia or regeneration
- Hyperlipidemia:
    - Diabetes mellitus
    - Hypothyroidism
    - Familial in miniature schnauzers, Shetland sheepdogs, others
- Superficial necrolytic dermatitis (hepatocutaneous syndrome)
- Exocrine pancreatic insufficiency
- Chronic pancreatitis
- Tetracycline administration
- Glycogen or lysosomal storage disease

INITIAL DATABASE

- CBC: lymphopenia, eosinopenia (excess glucocorticoids), other abnormalities depending on primary systemic disorder
- Serum biochemistry panel: serum ALP activity increased, may be marked, predominantly due to steroid-induced isoenzyme of ALP. Serum alanine aminotransferase (ALT) activity shows mild to moderate increases (or levels may be normal). Increased serum cholesterol concentration (excess glucocorticoids). Other biochemistry values typically normal (bilirubin, albumin).
- Serum bile acids concentration normal to mildly increased
- Abdominal radiographs: hepatomegaly (may be marked)

- Abdominal ultrasound: diffusely hyperechoic liver; may also be mottled and/or nodular; adrenomegaly (hyperadrenocorticism)

ADVANCED OR CONFIRMATORY TESTING

- FNA and cytologic evaluation of liver:
  - Ballooned hepatocytes with decreased cytoplasmic density, commonly described as *vacuolar hepatopathy*
  - Vacuolar hepatopathy is a common false-positive finding with FNA
- Liver biopsy and histopathologic evaluation:
  - Patchy distribution of ballooned hepatocytes with decreased cytoplasmic density. Glycogen accumulation is characteristic. Glycogen accumulation can be differentiated from hydropic degeneration with periodic acid-Schiff (PAS) stains for glycogen; oil red O (ORO) stain to differentiate lipid vacuoles
  - No evidence of inflammation, necrosis, or cholestasis
- Rule out spontaneous hyperadrenocorticism:
  - Review clinical history and physical exam
  - Low-dose dexamethasone suppression test or adrenocorticotropic hormone (ACTH) stimulation test to screen for hyperadrenocorticism
  - Endogenous ACTH level, high-dose dexamethasone suppression test, and adrenal gland ultrasonography to differentiate pituitary from adrenal causes
  - Adrenal steroid profile before and after ACTH to diagnose aberrant adrenocortical disease
- Evaluate for other systemic disorders that could cause secondary reactive vacuolar hepatopathy.

TREATMENT

TREATMENT OVERVIEW

Focus therapeutic efforts on treating underlying disorder.

CHRONIC TREATMENT

- If the patient is receiving high doses of glucocorticoids and is showing clinical signs of hepatic disease (e.g., lethargy or depression, difficult to distinguish from underlying condition), other immunosuppressive drugs such as azathioprine or cyclosporine may be warranted to allow dose reduction of glucocorticoids.
- Idiopathic vacuolar hepatopathy:
  - If no clinical signs are present, treatment may not be warranted.
  - Necessity or clinical effectiveness of hepatoprotective drug therapy (*S*-adenosylmethionine, vitamin E) unknown.

POSSIBLE COMPLICATIONS

- Hyperadrenocorticism (see p. 548) and complications involving glucocorticoid excess
- Severe vacuolar hepatopathy has been associated with development of gallbladder mucocele.

RECOMMENDED MONITORING

Idiopathic vacuolar hepatopathy: because some dogs may eventually develop spontaneous hyperadrenocorticism, monitor for clinical signs and follow up with screening tests (low-dose dexamethasone suppression test or ACTH stimulation) as needed.

PROGNOSIS AND OUTCOME

- Idiopathic vacuolar hepatopathy; vacuolar hepatopathy of Scottish terriers:
  - Benign clinical course
  - Good long-term prognosis
  - Some dogs may eventually develop clinical hyperadrenocorticism
- Exogenous glucocorticoid therapy:
  - Vacuolar hepatopathy is reversible once glucocorticoids are discontinued; may require weeks to months.

PEARLS & CONSIDERATIONS

COMMENTS

- Diagnostic and therapeutic efforts should be directed at identifying and correcting causes of glucocorticoid excess or primary systemic disorders.
- Hepatic function is typically preserved. If serum ALT > ALP or if hypoalbuminemia, hyperbilirubinemia, or markedly increased serum bile acids concentration are present, a more serious primary hepatobiliary disorder may be present and should be identified and treated. In rare instances, severe vacuolar hepatopathy has been associated with overt hepatic dysfunction, which may be fatal.
- Presence of increased serum ALP activity and vacuolar hepatopathy does not preclude continued use of corticosteroids if their administration is necessary. Liver function is generally preserved; benign lesion. Whenever possible, make an attempt to minimize systemic effects of glucocorticoids with alternate-day therapy using lowest effective dose possible (prednisolone or prednisone), and/or use other immunosuppressive drugs (azathioprine, cyclosporine).
- Cats that are receiving glucocorticoids (or with hyperadrenocorticism) rarely develop vacuolar hepatopathy.

PREVENTION

If long-term glucocorticoid therapy is necessary, give oral prednisolone or prednisone (rather than oral dexamethasone or injectable long-acting forms) at the lowest dose possible on alternate days to minimize the systemic (including hepatic) effects of glucocorticoids. Also consider administering other immunosuppressive drugs (e.g., azathioprine, cyclosporine) to allow dose reduction of glucocorticoids.

CLIENT EDUCATION

Idiopathic vacuolar hepatopathy appears to be clinically benign.

SUGGESTED READING

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Sepesy LM, Center SA, Randolph JF, et al: Vacuolar hepatopathy in dogs: 336 cases (1993-2005). J Am Vet Med Assoc 229:246, 2006.

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Wolff-Parkinson-White Syndrome

BASIC INFORMATION

DEFINITION

A cardiac disorder characterized by extremely rapid, inappropriate tachycardias. The underlying defect is an accessory pathway or additional conductive fiber connection between atria and ventricles, separate and parallel to the normal atrioventricular (AV) node-bundle of His connection. The accessory pathway can participate as one limb of a rapid re-entrant tachycardia.

SYNONYMS

Premature activation of the ventricles by the atria:

- Accessory AV pathway (or bypass tract)
- Ventricular pre-excitation

Macro re-entrant tachycardia:

- AV reciprocating tachycardia

EPIDEMIOLOGY

SPECIES, AGE, SEX: Any; most commonly identified in dogs <6 years old

GENETICS & BREED PREDISPOSITION: Labrador retrievers and brachycephalic breeds appear to be predisposed.

ASSOCIATED CONDITIONS & DISORDERS: In dogs, there is a possible association between tricuspid valve dysplasia and accessory AV pathways.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Manifest accessory AV pathway: capable of antegrade (atrioventricular) conduction, bypassing the AV node. The result is ventricular pre-excitation during normal sinus rhythm. Manifest accessory pathways can also participate as the antegrade or retrograde limb of a tachyarrhythmia.
- Concealed accessory AV pathway: capable of retrograde conduction (ventricle to atrium) only. Therefore, there is no ventricular pre-excitation. Concealed AV pathways can participate as the retrograde limb of a tachyarrhythmia.

HISTORY, CHIEF COMPLAINT: Related to resultant tachyarrhythmias:

- Decreased exercise tolerance/weakness
- Vomiting, inappetence
- Racing heart/pulsing ears or head
- Dyspnea/coughing
- Abdominal distension
- Acute collapse
- Sudden death

PHYSICAL EXAM FINDINGS: Patient may be normal at the time of exam or may show any of the following signs:

- Tachyarrhythmia
- Decreased femoral pulse quality
- Tachypnea/dyspnea
- Abdominal fluid wave
- Mucous membrane pallor

ETIOLOGY AND PATHOPHYSIOLOGY

- The accessory AV pathway is composed of working myocardial fibers that exist outside the confines of the normal conduction system and connect atrial and ventricular myocardium.
- The antegrade (atria to ventricles) conduction of an atrial impulse over the accessory AV pathway activates a portion of the ventricular myocardium early and then spreads in a myocyte-to-myocyte fashion. The result is a short PR interval and a wide, abnormal QRS complex (i.e., ventricular pre-excitation).
- Retrograde (ventricles to atria) conduction of a ventricular impulse over the accessory AV pathway activates a portion of the atrium and then spreads in a cell-to-cell fashion, eventually reaching the AV node. If the AV node conducts the impulse to the ventricles, this cycle can be repeated in a self-perpetuating loop and result in a narrow complex tachyarrhythmia.
- If a tachyarrhythmia is frequent or sustained, it can lead to tachycardia-induced cardiomyopathy, a dilated poorly contractile heart that is indistinguishable from idiopathic dilated cardiomyopathy, except that it can be reversible with control of the tachyarrhythmia. Pathways capable of rapid antegrade conduction can conduct atrial tachyarrhythmias rapidly to the ventricles, bypassing the normal delay imposed by the AV node.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Electrocardiographic identification of ventricular pre-excitation during sinus rhythm or an atrial tachycardia definitively identifies an accessory pathway. This will not be found with concealed accessory pathways. A narrow complex, regular tachyarrhythmia with specific ECG features is suggestive, but electrophysiologic study is required for confirmation.

DIFFERENTIAL DIAGNOSIS

- Electrocardiographic (ECG): narrow complex, regular tachyarrhythmias: automatic or re-entrant atrial tachycardias, AV re-entrant tachycardia, junctional tachycardias. Pre-excited tachyarrhythmias: ventricular tachycardias.
- Radiographic/echocardiographic (in cases progressing to tachycardia-induced cardiomyopathy): idiopathic dilated cardiomyopathy

INITIAL DATABASE

- ECG (see 1253):
  - Ventricular pre-excitation may be present during sinus rhythm: short PR interval (usually <0.06 seconds); initial portion of the QRS slurred (i.e., slowly rises or descends; “delta wave”); QRS duration prolonged (> 0.06 seconds); QRS axis may be abnormal
  - Tachyarrhythmias: tend to be narrow complex (QRS < 0.06 seconds), 250-400+ bpm; when patients are not on antiarrhythmic drugs, the ECG may have a visible deflection in ST segment (retrograde P wave); tachyarrhythmias are often intermittent, so they are not necessarily captured on a baseline ECG. Holter monitoring is more helpful than a single baseline ECG but may still be normal on a given day.
- Echocardiogram (see 1253):
  - May be normal
  - May mimic dilated cardiomyopathy
  - Assess for congenital heart defects, examine tricuspid valve
- Thoracic radiographs:
  - Assess cardiac silhouette (normal to severely enlarged)
  - Assess pulmonary vasculature and lung fields (for congestion and edema)
- Physical tests:
  - Vagal maneuver: may terminate a tachyarrhythmia by inducing AV nodal blockade but generally unsuccessful (see 1359)

ADVANCED OR CONFIRMATORY TESTS

- Holter monitoring: can be helpful in capturing intermittent pre-excitation or tachyarrhythmias.
- Drug administration: IV diltiazem can terminate AV reciprocating tachycardia by inducing AV block; however, it can terminate certain other tachyarrhythmias as well. Blood pressure (BP) monitoring and resuscitation equipment should be available.
- Electrophysiologic testing: definitively establishes the presence or absence of an accessory pathway and its location along the AV groove.

TREATMENT

TREATMENT OVERVIEW

Goals of treatment are to terminate any tachyarrhythmia present, control its reoccurrence, and control signs of congestive heart failure and hypotension.

ACUTE GENERAL TREATMENT

- Incessant narrow complex tachyarrhythmias: aimed at slowing AV nodal conduction or blocking the accessory pathway: diltiazem (0.125-0.35 mg/kg, slow IV over 3-4 minutes) or procainamide (6-20 mg/kg slow IV over 30 minutes) most commonly used.
- Synchronized direct current (DC) cardioversion can be used once the patient is anesthetized or unconscious if drugs are unsuccessful.

CHRONIC TREATMENT

- Antiarrhythmic drug therapy to control tachyarrhythmias
- Radiofrequency catheter ablation of the accessory pathway is a curative procedure.

BEHAVIOR/EXERCISE

Restricted exercise is recommended until antiarrhythmic control and control of congestive heart failure signs is achieved.

DRUG INTERACTIONS/CONTRAINDICATIONS

Potential interactions between digoxin and several antiarrhythmic and commonly used drugs. Beta agonists or other stimulants are contraindicated.

POSSIBLE COMPLICATIONS

- Tachycardia-induced cardiomyopathy
- Congestive heart failure (CHF)
- Sudden death
- Side effects of antiarrhythmic drugs

RECOMMENDED MONITORING

- Follow-up exam, ECG, and Holter monitoring: frequency dependent on the severity of the tachyarrhythmias documented
- Radiographic and echocardiographic monitoring for dogs with tachycar-dia-induced cardiomyopathy: with adequate control of tachyarrhythmias, myocardial function and chamber dilation should improve within 3 months.

PROGNOSIS AND OUTCOME

- Excellent with radiofrequency catheter ablation
- Fair long term with antiarrhythmic drug administration
- Poor if tachyarrhythmias are not controlled: progressive cardiomyopathic changes (eventually not completely reversible) and recurrent CHF result. Sudden death becomes more common.

PEARLS & CONSIDERATIONS

COMMENTS

- Should be a differential diagnosis in a young (<6 years old) dog presenting with dilated cardiomyopathy (DCM)-like signs
- May require repeated Holter monitoring for documentation
- Even dogs with tachycardiomyopathy and CHF can be cured with successful ablation of the accessory pathway.

CLIENT EDUCATION

- Monitor heart rate carefully at home.
- Sustained tachyarrhythmias are life threatening.
- Curative procedures are available.

SUGGESTED READING

Wright KN: Assessment and treatment of supraventricular tachyarrhythmias. In Bonagura JD, editor: Kirk's current veterinary therapy XIII. Philadelphia, 2000, WB Saunders, pp 726–730.

AUTHOR: KATHY WRIGHT
EDITOR: ETIENNE CÔTÉ

Whipworm Infection

Client Education Sheet Available on Website

BASIC INFORMATION

DEFINITION

Infection of the cecum (and possibly ileum and colon) with *Trichuris vulpis* (canine); rare in cats *(T. campanula* or *T. serrata)*

SYNONYM

Trichuriasis

EPIDEMIOLOGY

SPECIES, AGE, SEX: Primarily in dogs; rarely a problem in cats

RISK FACTORS

- Roaming
- Exposure to feces or a contaminated environment

CONTAGION & ZOONOSIS: Humans are rare aberrant hosts.

GEOGRAPHY AND SEASONALITY

- Common in the eastern and southern United States
- Ova are extremely resistant in the environment, surviving 4-5 years and demonstrating no seasonality.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Large-bowel diarrhea (mucoid stool, hematochezia, tenesmus) of variable degrees of severity
- Hypoadrenocorticism-like syndrome: hyponatremia, hyperkalemia, azotemia, metabolic acidosis
- Rarely, typhlitis or cecocolic intussusception may occur.

HISTORY, CHIEF COMPLAINT

- None (incidental finding on fecal flotation)
- Clinical signs of large-bowel diarrhea: frequent, urgent defecation of loose or watery feces, possibly containing mucus or fresh blood (hematochezia). Tenesmus, flatulence possible.
- Occasionally associated with weight loss and protein-losing enteropathy
- In dogs with hypoadrenal-like illness, lethargy, vomiting, or severe diarrhea may be present.

PHYSICAL EXAM FINDINGS

- Commonly, animals with mild whipworm infections have a normal physical examination.
- Vague signs of midabdominal pain/tenderness, often characterized by flank licking, have been associated with granulomatous typhlitis.
- Rarely, physical signs of systemic disease are present (weight loss/cachexia) with hypoadrenal-like illness related to whipworm infection.

ETIOLOGY AND PATHOPHYSIOLOGY

- Direct life cycle begins with ingestion of embryonated eggs.
- Ova hatch in small intestine, and larvae burrow into mucosa for a 1-week period, not causing clinical signs.
- Young adults emerge, relocate to the cecum/colon, and deeply embed the thread-like head (the “whip”) into the mucosa to feed on blood and tissue fluids.
- 3-month prepatent period (range: 70-107 days) precedes appearance of ova in feces

- Host response varies from mild localized inflammation to mucosal hyperplasia to granulomatous inflammation, resulting in variable degrees of gastrointestinal (GI) clinical signs.
- Affected animals can develop large-bowel diarrhea that ranges in severity from intermittent soft stool to severe, copious mucoid or hemorrhagic diarrhea with tenesmus.
- Whipworm-related enteritis may produce biochemical changes falsely suggesting hypoadrenocorticism.
  - Hyponatremia: due to concurrent diarrhea-associated sodium loss, water consumption, and anorexia
  - Hyperkalemia: due to metabolic acidosis, decreased kaliuresis from reduced flow in the distal renal tubules, and/or laboratory artifact (normal platelet K^+ release when clotting)
  - Primary enteritis-associated hyponatremia and hyperkalemia are not caused by aldosterone deficiency (hypoadrenocorticism), as confirmed by normal adrenocorticotropic hormone (ACTH) stimulation test results.
- Whipworm infection has been suggested as a cause for cecocolic intussusception.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Whipworm infection should be suspected on any dog with clinical signs of chronic colitis. Multiple fecal analyses should be pursued but may yield negative results despite parasite infection (intermittent shedding). Therefore monitoring the initial response to two courses of anthelminthic treatment (2 weeks apart), even with negative fecal analysis results, is an important step prior to pursuing costly diagnostics in any patient with solitary signs of intermittent bloody and/or mucoid diarrhea.

DIFFERENTIAL DIAGNOSIS

- *Capillaria* spp. infection (ova appear similar, but *Capillaria* spp. do not cause enteritis)
- Dietary-responsive large-bowel diarrhea
- *Clostridium perfringens* enterotoxicosis
- Inflammatory bowel disease (large intestine)
- Chronic colitis (e.g., histiocytic ulcerative colitis)
- Eosinophilic colitis
- Histoplasmosis (large bowel)
- Neoplasia (carcinoma, lymphoma)
- Hypoadrenocorticism
- Protein-losing enteropathy
- Intussusception

INITIAL DATABASE

- Serial fecal flotations to identify characteristic golden-brown bioperculated smooth ova: they are dense and intermittently shed—often in low numbers—making multiple examinations necessary with adequately dense flotation solution (specific gravity >1.200; e.g., sugar or zinc sulfate).
- CBC: occasional eosinophilia and mild to moderate anemia
- Serum biochemistry profile: hyponatremia, hyperkalemia, azotemia, hypoalbuminemia, metabolic acidosis are occasionally seen.
- Rectal cytologic examination (see p. 1334): insensitive for ova but may demonstrate clostridial spores, inflammatory cells, neoplastic cells
- ACTH response testing is recommended to rule out hypoadrenocorticism in dogs with hyponatremia and hyperkalemia.

ADVANCED OR CONFIRMATORY TESTING

Colonoscopy is an expensive and complex way to detect the presence of adult worms in the cecum and proximal colon.

TREATMENT

TREATMENT OVERVIEW

Therapeutic goals are to eliminate parasites from the GI tract. Three treatments are needed to completely eliminate parasites, owing to prepatency period.

ACUTE GENERAL TREATMENT

- Anthelmintic therapy:
  - Fenbendazole, 50 mg/kg PO q 24 h × 3 days is the preferred treatment.
  - Febantel, 10 mg/kg PO q 24 h × 3 days is an acceptable alternative.
  - Drontal Plus (contains febantel) is also an appropriate therapy.
- Retreat in 3 weeks and again in 3 months because of the long prepatent period.
- Supportive care (e.g., intravenous fluids) for electrolyte abnormalities and azotemia in severe cases
- Typhlectomy for granulomatous typhlitis or cecocolic intussusception (rare)

CHRONIC TREATMENT

Milbemycin oxime is an effective preventive for chronic, recurrent trichuriasis.

DRUG INTERACTIONS

Dogs should be evaluated for presence of heartworm infection before instituting milbemycin oxime.

POSSIBLE COMPLICATIONS

Possible adverse reaction with milbemycin oxime in heartworm-positive dogs

RECOMMENDED MONITORING

Frequent fecal examinations for chronic infections

PROGNOSIS AND OUTCOME

- Excellent with appropriate therapy
- Reinfection likely as a result of environmental contamination with resistant ova.

PEARLS & CONSIDERATIONS

COMMENTS

- *T. vulpis* is a common cause of large-bowel diarrhea in dogs in the eastern and southern United States.
- Empirical treatment is recommended in uncomplicated cases before pursuing a lengthy, expensive diagnostic workup.
- The potential for hypoadrenocorticism-like findings with trichuriasis must be recognized when hypoadrenocorticism is suspected in any dog based on history, clinical signs, and serum biochemistry/electrolyte results.
- Seizures have been reported in dogs with trichuriasis, most likely associated with profound hyponatremia.

PREVENTION

Milbemycin oxime in endemic areas or with chronic infections is an excellent preventive against *T. vulpis* and *Dirofilaria immitis* infection. Because of the prepatent period, a three-treatment course regime with fenbendazole is recommended for acute infections.

CLIENT EDUCATION

Environmental contamination is the source for reinfection and is difficult to eliminate; monthly prophylaxis is recommended after treatment.

SUGGESTED READING

Allenspach K: Diseases of the large intestine. In Ettinger SJ, Feldman ED, editors: Textbook of veterinary internal medicine, ed 7, St Louis, MO, 2010, Saunders Elsevier, pp 1573–1594.

Graves TK, et al: Basal and ACTH-stimulated plasma aldosterone concentrations are normal or increased in dogs with trichuriasis-associated pseudohypoadrenocorticism. J Vet Intern Med 8:287–289, 1994.

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West Nile Virus Infection

BASIC INFORMATION

DEFINITION

Mosquito-borne virus that affects humans and animals but rarely causes clinically significant illness in dogs and cats

EPIDEMIOLOGY

SPECIES, AGE, SEX: Wild birds are the principal hosts of West Nile virus. More than 150 species of birds have been infected in North America. Horses and humans, particularly if older, may also develop clinical signs of infection. Dogs and cats appear to be more resistant to clinical illness, with lower morbidity and mortality.

RISK FACTORS: Infection in dogs and cats has been associated with being stray, residing exclusively outdoors, and not receiving heartworm medication. In humans, advanced age, alcohol abuse, diabetes mellitus, immunosuppression, requirement of mechanical ventilation, history of stroke, and being homozygous for a defective allele have been associated with increased risk of encephalitis, death, or a poor prognosis. In some studies, horses were at greater risk of death or euthanasia if they were older, had not received West Nile vaccination, or had collapsed or become recumbent.

CONTAGION & ZOONOSIS: Exposure to domestic animals is not considered a risk factor for acquisition or amplification of West Nile virus.

GEOGRAPHY AND SEASONALITY: Infections are more common during warm seasons in manmade and natural environmental conditions supportive of the transmitting mosquito species.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Most infections with West Nile virus are subclinical.

HISTORY, CHIEF COMPLAINT: Dogs or cats with clinical West Nile virus infection could present with signs related to joint, cardiac, or neurologic infection, as well as sudden death.

PHYSICAL EXAM FINDINGS: Lethargy, anorexia, weight loss, lameness, depression, neurologic involvement (central neurologic deficits), and myocarditis (e.g., cardiac arrhythmia on auscultation, pulse deficits) may be expected in advanced cases. The physical exam is likely often normal, and the infection is not suspected (nor necessarily of clinical concern).

ETIOLOGY AND PATHOPHYSIOLOGY

- West Nile virus is a mosquito-borne disease. The natural hosts are wild passerine birds (e.g., robins, sparrows, finches, blackbirds, warblers), which predominantly experience latent infection. However, high mortality has been reported in crows and blue jays. Mosquitoes (primarily *Culex* spp. in the United States) feed on infected birds and are vectors, transmitting disease to other animals and to people.
- Pathologic findings usually mirror clinical signs and can include gross brain hemorrhage; lymphoplasmacytic encephalitis; enlargement, necrosis, and hemorrhage of the spleen and liver; myocardial degeneration; and pancreatitis.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Clinical cases in dogs and cats are rare and will require submission of specimens to a veterinary diagnostic laboratory with capability of West Nile virus testing.

DIFFERENTIAL DIAGNOSIS

Causes of encephalitis, myocarditis, lameness

INITIAL DATABASE

Because dogs and cats are rarely clinically ill with West Nile infection, no routine diagnostic testing regimens are likely to be of value but should be considered to rule out other causes of clinical signs.

ADVANCED OR CONFIRMATORY TESTING

- For ill animals, serologic testing methods are most commonly used for diagnosis, particularly paired acute-phase and convalescent-phase serum samples.
- Tissues including brain, spinal cord, heart, liver and kidneys from animals that have died or been euthanized can be submitted for viral detection through cell culture, RT-PCR, and immunohistochemistry.

TREATMENT

TREATMENT OVERVIEW

Supportive care, which in horses has included administration of antiinflammatory drugs, vitamins, fluids, and antimicrobials to minimize co-infections

ACUTE GENERAL TREATMENT

- As determined by clinical manifestations of disease
- Neurologic manifestations (see pp. 314 and 1009)
- Myocarditis: treatment of arrhythmias if negatively affecting perfusion (see pp. 111 and 1165)

PROGNOSIS AND OUTCOME

For clinical cases, prognosis depends on severity of illness.

PEARLS & CONSIDERATIONS

COMMENTS

- West Nile virus is now the leading cause of human arboviral encephalitis in the United States.
- Domestic animal species, except for horses, are rarely ill with West Nile infection and do not develop sufficient viremia to serve as a source of infection for mosquitoes.
- Dead birds, particularly crows, may indicate that the risk of West Nile infection has increased in an area.

PREVENTION

- Control of West Nile virus is best accomplished by control of mosquito populations, particularly by removal of standing, stagnant water in artificial basins (pools, tires, pots).
- Keeping animals and people indoors at times of high mosquito activity (e.g., dusk and dawn) may help prevent infection.
- Topical application of insect repellents can be effective at repelling mosquitoes, but only products approved for specific species should be used.
- Vaccination appears to be effective in horses and has also been used in animals from zoological collections.

CLIENT EDUCATION

- Prevention of mosquito breeding grounds and mosquito exposure is the most effective method of preventing infection with West Nile virus.
- Domestic animal species are not a risk for transmitting West Nile virus to people.

SUGGESTED READING

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Weight Loss

BASIC INFORMATION

DEFINITION

Decrease in body mass; may be intended (as in the treatment of obesity) or an unintended consequence of disease

SYNONYMS

Cachexia, emaciation

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dog or cat, any age, either sex

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

With or without localizing gastrointestinal (GI) signs

HISTORY, CHIEF COMPLAINT

- Thin appearance, lethargy, decreased appetite
- It is important to determine:
  - Quantity, quality, and appropriateness of the diet
  - Appetite (increased or decreased)
  - Daily activity/caloric expenditure
  - Presence of physiologic conditions that may increase energy requirements (e.g., growth, pregnancy, lactation)
  - Presence of localizing GI signs (dysphagia, regurgitation, vomiting, diarrhea)

PHYSICAL EXAM FINDINGS

Poor body condition (or decrease in weight in comparison to historic body weight) +/− poor haircoat, muscle atrophy

ETIOLOGY AND PATHOPHYSIOLOGY

- Body weight is affected by caloric intake, absorptive capacity, metabolic demand, and nutrient losses.
- Weight loss may result from (1) inadequate quantity or quality of diet, (2) inability to prehend or swallow food, (3) regurgitation or vomiting of ingesta, (4) anorexia (loss of desire to eat), (5) inability to digest or absorb ingested nutrients, (6) inability to utilize absorbed nutrients (e.g., diabetes mellitus), (7) increased metabolic rate, (8) increased catabolism, (9) loss of nutrients.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Weight loss is a nonspecific clinical sign. When it is confirmed to not be deliberate (i.e., no weight-loss diet), a broad systemic evaluation beginning with fecal flotation and routine blood and urine tests is indicated. The diagnostic approach is then adapted to results of these tests, the history, and the physical exam.

DIFFERENTIAL DIAGNOSIS

- Weight loss with localizing GI signs:
  - Inability to prehend or masticate food:
    - Dental disease
    - Head trauma
    - Temporomandibular joint disease

        - Masticatory myositis
    - Dysphagia:
        - Neuromuscular disorders
        - Oropharyngeal neoplasia
        - Nasopharyngeal polyp
    - Regurgitation:
        - Esophageal disorders
    - Vomiting (see p. 1175)
    - Small-bowel diarrhea (see p. 305; e.g., protein-losing enteropathies)
    - Large-bowel diarrhea:
        - Does not cause weight loss
- Weight loss due to anorexia/decreased appetite:
    - All GI causes of vomiting
    - Systemic diseases leading to anorexia
    - All systemic causes of vomiting
    - Neoplasia (anywhere)
    - Chronic infections:
        - Viral: feline leukemia virus (FeLV), feline immunodeficiency virus (FIV), feline infectious peritonitis (FIP)
        - Mycotic: blastomycosis, histoplasmosis, cryptococcosis, coccidioidomycosis
        - Bacterial: endocarditis, chronic pneumonia, rickettsial infections (e.g., chronic ehrlichiosis), mycobacterial infections
        - Protozoal: leishmaniasis, hepatozoonosis
    - Chronic pancreatitis
- Weight loss despite normal to increased appetite:
    - Unrecognized vomiting or regurgitation
    - Dietary:
        - Inadequate quantity
        - Poor-quality diet
    - Increased energy demand:
        - Pregnancy
        - Lactation
        - Increased exercise
        - Growth
    - Increased metabolic rate or increased catabolism:
        - Hyperthyroidism (cats)
        - Congestive heart failure
        - Chronic inflammation
    - Inability to utilize nutrients:
        - Diabetes mellitus
    - Nutrient loss:
        - Protein-losing nephropathies (see p. 926):
            - Rarely, protein-losing enteropathies cause weight loss without diarrhea

INITIAL DATABASE

- CBC, biochemistry panel, urinalysis
- FeLV/FIV testing (cats)
- T4 (cats >5 years old)
- Fecal flotation

ADVANCED OR CONFIRMATORY TESTING

- Trypsinlike immunoreactivity (TLI), if there is small-bowel diarrhea, to rule out exocrine pancreatic insufficiency (EPI)
- Fecal α1-protease inhibitor activity if PLE is suspected but no diarrhea
- Abdominal ultrasound to identify GI tract thickening or layer loss, neoplasms, granulomas, pancreatitis
- Upper GI endoscopy to rule out esophageal or gastric foreign body, ulcerations, or luminal neoplasms
- GI biopsies via endoscopy or exploratory laparotomy
- Bile acids to rule out liver failure (portosystemic shunt)
- Urine protein/creatinine (UPC) ratio to rule out protein-losing nephropathy
- Adrenocorticotropic hormone (ACTH) stimulation test to rule out hypoadrenocorticism
- Infectious disease testing when indicated

TREATMENT

TREATMENT OVERVIEW

Treat underlying disease and provide nutritional support.

ACUTE GENERAL TREATMENT

- Improve appetite/symptomatic therapy:
  - Diet change
- Antacids (H2 blockers [famotidine, ranitidine] or proton pump inhibitors [omeprazole])
- Antinausea medications (metoclopramide, ondansetron, maropitant) unless contraindicated
- Appetite stimulants (mirtazapine [dogs], cyproheptadine [cats])
- Increase caloric intake.

CHRONIC TREATMENT

Treat underlying disease and maintain adequate caloric intake.

NUTRITION/DIET

- Enteral nutrition is preferred in animals that have a functioning GI tract.
- Assisted feeding through a nasoesophageal, esophagostomy, gastrostomy, or jejunostomy tube may be required (see p. 1267).
- Parenteral nutrition may be necessary in animals that cannot tolerate enteral feeding or if enteral feeding alone cannot meet caloric requirements.
- Caloric requirements are estimated by calculating resting energy requirements (RER) and illness energy requirements (IER):
  - RER (in kilocalories) can be calculated as:
    - 70 × (body weight [BW] in kilograms)$^{0.75}$
  - IER is calculated by multiplying RER by an illness factor (1.2 to 1.4 for dogs; 1.1 to 1.2 for cats).

BEHAVIOR/EXERCISE

Exercise should not be encouraged until weight is controlled.

POSSIBLE COMPLICATIONS

- Refeeding syndrome if anorexia is chronic and/or severe
- Aspiration pneumonia in patients that are regurgitating, vomiting, or being force-fed

RECOMMENDED MONITORING

- Body weight
- Other testing based on underlying cause

PROGNOSIS AND OUTCOME

Weight stabilization occurs in the majority of surviving patients through treatment of the underlying disease and appropriate nutrition.

PEARLS & CONSIDERATIONS

COMMENTS

- If the patient has other clinical signs (e.g., vomiting, diarrhea, fever, etc.), the diagnostic approach should not focus on the weight loss alone.
- In the initial stages of therapy, changes in body weight often reflect changes in fluid dynamics.

PREVENTION

Dependent upon the underlying cause

CLIENT EDUCATION

Weight loss is caused by a wide array of diseases; many are treatable. Obtaining a diagnosis often requires extensive testing.

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Zinc-Responsive Dermatosis

Additional Images Available on Website

BASIC INFORMATION

DEFINITION

Uncommon but well-recognized zinc-responsive scaling disorder of the skin; can be hereditary or secondary to a dietary imbalance

EPIDEMIOLOGY

SPECIES, AGE, SEX

- Syndrome I: age of onset is typically 1-3 years; range: 2 months to 11 years
- Syndrome II: most common in young, rapidly growing dogs

GENETICS & BREED PREDISPOSITION

- Syndrome I: northern canine breeds, such as Alaskan malamute, Siberian husky, and Samoyed; also reported in Doberman pinschers and Great Danes
- Syndrome II: any breed; Great Dane, Doberman pinscher, beagle, German shepherd, German short-haired pointer, Labrador retriever, Rhodesian ridgeback, and standard poodle may be predisposed.

RISK FACTORS: Rapidly growing puppies fed diets deficient in zinc or high in phytates (high plant/grain content) or calcium

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES

- Syndrome I: hereditary
- Syndrome II: dietary

HISTORY, CHIEF COMPLAINT

- Owner may note scaling and crusting dermatosis.
- Pruritus may precede development of other clinical signs and is present in nearly half of cases.

PHYSICAL EXAM FINDINGS

- Focal cutaneous erythema and alopecia progress to scaly and crusted lesions.
- Secondary microbial (bacterial and yeast) dermatitis
- Predilection sites: periocular, ears, bridge of the nose, perioral, footpads, pressure points on limbs. Scrotum, prepuce, perianal region, and vulva may also be affected.
- Dull, dry coat
- Some puppies with syndrome II present with depression, anorexia, delayed growth, fever, and lymphadenopathy.

ETIOLOGY AND PATHOPHYSIOLOGY

- Genetic defect involving zinc absorption reported in Alaskan malamutes.
- Diets high in calcium or phytates (plant/grain products) bind zinc, decreasing absorption.
- Zinc absorption is also negatively affected by essential fatty acid deficiency, high levels of iron in water, or prolonged diarrhea.
- It is suspected that low zinc levels cause poor lytic enzyme function (thus affecting epidermal maturation) or increased epidermal turnover rate (leading to hyperkeratosis).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

The diagnosis is based on identification of lesions both clinically and histopathologically in an animal of a breed that is at risk, an animal that has a current history of nutritional inadequacy (high in phytates, high iron-content drinking water), or an animal with chronic diarrhea.

DIFFERENTIAL DIAGNOSIS

- Superficial necrolytic dermatitis (hepatocutaneous syndrome)
- Dermatophytosis
- Nutritionally deficient diets
- Demodicosis
- Pemphigus foliaceus

INITIAL DATABASE

- Skin scrapings: generally negative
- Fungal (dermatophyte) culture: expect negative result
- If diarrhea is noted, perform fecal flotation and any additional appropriate testing.

ADVANCED OR CONFIRMATORY TESTING

- Skin biopsy: epidermal parakeratotic hyperkeratosis is the most common finding, and follicular parakeratosis is highly suggestive.
- Zinc concentration in serum or hair: not used in small animal clinical dermatology. Overall, lower levels are present in zinc-responsive dermatosis patients, but substantial overlap exists with the normal range.

ZINC-RESPONSIVE DERMATOSIS Alopecia and crusting of the face in a Siberian husky with zinc-responsive dermatosis.

(Courtesy Dr. Stephen Waisglass.)

TREATMENT

TREATMENT OVERVIEW

The goals of treatment are to resolve the scaling +/− alopecia and inflammation, control the secondary microbial dermatitis, and ensure the patient is eating a nutritionally balanced diet.

ACUTE GENERAL TREATMENT

- Assess and correct dietary deficiencies.
- Treat secondary bacterial or yeast dermatitis (see pp. 682 and 951).
- Keratomodulating shampoos (e.g., salicylic acid/sulfur shampoos) to remove scales and crusts
- Syndrome I: Supplementation is recommended at 1-3 mg/kg of elemental zinc daily. Start at the lower dose, but in some cases doses in the order of 2-3 mg/kg may be needed. Zinc gluconate (generic) 5 mg/kg PO q 24 h, or zinc sulfate 10 mg/kg PO q 24 h. Response to treatment is usually noted within 6 weeks. Lifelong treatment is required.
- Syndrome II: Correct diet. Lesions improve within 2-6 weeks in most cases. Some animals require zinc supplementation, as

above.
- Essential fatty acid supplementation (omega-3 and omega-6) may aid zinc absorption.

CHRONIC TREATMENT

- Treatment for patients with syndrome I is usually lifelong.
- It has been suggested that low (0.15 mg/kg PO q 24 h) doses of prednisone or prednisolone can be added to the regimen to aid gastrointestinal (GI) absorption if response is inadequate. Improved response may also be due to an antiinflammatory effect on the skin.
- Different forms of zinc may be tried if there is poor response to therapy. It has been suggested that IV sterile zinc sulfate administration (10-15 mg/kg diluted 1:1 with saline and infused slowly) may help animals that do not respond to oral supplementation because of poor intestinal absorption. Treat weekly for at least 4 weeks (monitor with electrocardiogram [ECG] when administering), then every 1-6 months as maintenance.

DRUG INTERACTIONS

- Zinc salts may reduce the absorption of some fluoroquinolones and chelate oral tetracycline, reducing the absorption of zinc.
- Penicillamine and ursodiol may inhibit zinc absorption.

POSSIBLE COMPLICATIONS

- Emesis: zinc in the form of methionine or acetate may be less likely to cause stomach irritation. If vomiting occurs, lower the dose or give with food.
- Large doses of zinc can inhibit copper absorption in the intestine. Carefully consider the use of zinc in copper-deficient animals.
- IV zinc sulfate treatment may result in cardiac arrhythmias. Always monitor ECG during administration.

PROGNOSIS AND OUTCOME

- Syndrome I: fair to good prognosis in most animals
- Syndrome II: excellent prognosis if cause is of dietary origin

PEARLS & CONSIDERATIONS

COMMENTS

- Zinc chelated as an amino acid such as methionine offers greater bioavailability than sulfate or gluconate, but response has been noted using all forms. If one form is not working, try another.
- Zinc plus linoleic acid (e.g., safflower oil) has been shown to improve skin and coat condition in normal dogs eating a properly balanced diet.
- Avoid confusion regarding zinc formulations: note whether dosed as mg/kg of the compound or mg/kg elemental zinc. Zinc sulfate contains 1 mg element zinc/4.4 mg zinc sulfate; zinc acetate contains 1 mg elemental zinc/3.33 mg zinc acetate; zinc gluconate contains 1 mg elemental zinc/7.14 mg zinc gluconate.

CLIENT EDUCATION

- Syndrome I: animals should not be used for breeding purposes.
- Syndrome II: nutritional counseling on benefits of feeding good-quality diets

SUGGESTED READING

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Zinc Toxicosis

BASIC INFORMATION

DEFINITION

Syndrome that occurs after ingestion of zinc-containing objects such as pennies, scrap metal pieces, wires, and hardware. Clinical signs arise due to acute gastrointestinal (GI) irritation or hemolysis (zinc-mediated red blood cell [RBC] injury) and possible renal and hepatic damage.

SYNONYMS

Elemental zinc; Zn

EPIDEMIOLOGY

SPECIES, AGE, SEX: Toxicosis is reported mostly in dogs (all breeds and ages, both sexes) from ingesting zinc-containing objects; cats are less likely cases.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Inappetence, lethargy, protracted vomiting, diarrhea
- Red-colored urine
- Animal occasionally may vomit pennies or other metallic objects or pass pennies in the feces
- Animal owners often are unaware of ingestion of any foreign metallic object by their pets
    - In these cases, zinc toxicosis becomes suspected based on hemolytic anemia and/or presence of metallic object in the GI tract on radiographs or in vomitus/feces.

PHYSICAL EXAM FINDINGS

- As already described
- Signs of abdominal discomfort or pain on palpation
- Pale mucous membranes
- Icterus
- Discolored urine (hemoglobinuria)

ETIOLOGY AND PATHOPHYSIOLOGY

Source:

- Metallic zinc is used in galvanizing, welding, and soldering. Zinc salts are used as astringents, antiseptics, deodorants; in galvanized nuts and cage wires; and in smoke generators, wood preservatives, pigments, and insecticides. Zinc gluconate is about 14% elemental zinc and is frequently found in cough drops. Zinc oxide (10%-40%) is found in ointments and sunblocks (see p. 1180).
- U.S. pennies minted after 1982 weigh 2.5 g and are 97.6% zinc and 2.4% copper. Canadian pennies prior to 1997 were approximately 98% copper and 1.75% zinc. From 1997 to 2001, Canadian pennies were made with 96% zinc and 4% copper. Since 2001, Canadian pennies have been made of copper-plated steel (94% steel, 1.5% nickel, 4.5% copper).

Mechanism of Toxicosis:

- Zinc has an antagonistic effect on copper and iron. It can interfere with iron absorption, making RBCs susceptible to hemolysis. Zinc also causes direct, severe GI mucosal irritation.
- Zinc leaches from metallic objects owing to an acidic gastric pH, providing continuous GI absorption. Toxicosis occurs when zinc-containing objects are retained or embedded in the GI tract.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Suspicion of zinc toxicosis arises in one of three contexts: observed ingestion or vomiting/defecation of metallic objects; incidental finding of metallic object on abdominal palpation or radiography; or investigation of hemolytic anemia. A patient in any of these categories should undergo a minimum database of a CBC (hemolytic anemia), serum biochemistry profile, urinalysis, and abdominal radiography. Protracted vomiting, lethargy, diarrhea, inappetence and hemoglobinuria lend further support to the diagnosis. Toxicosis should be confirmed (or ruled out) by measuring concentration of zinc in serum, whole blood or urine.

DIFFERENTIAL DIAGNOSIS

- Other toxicoses: onions/garlic, acetaminophen, mothballs (naphthalene), local anesthetics
- Immune-mediated hemolytic anemia
- Tickborne diseases

INITIAL DATABASE

- CBC: regenerative anemia, hemoglobinemia, reticulocytosis, spherocytosis; neutrophilic leukocytosis
- Serum biochemistry profile: azotemia; elevation in serum bilirubin, liver enzymes, amylase, lipase
- Urinalysis: hemoglobinuria, proteinuria

ADVANCED OR CONFIRMATORY TESTING

Definitive diagnosis: blood or tissue zinc levels

- For blood collection, use special tubes (royal-blue top) and syringes that contain no rubber grommets. Do not use traditional syringes, rubber grommets, and Vacutainer tubes, because the rubberized surfaces contain some amount of zinc and may give erroneous results.
- Toxic levels in dogs:
  - Serum: 10-54 ppm (adequate levels 0.7-2 ppm)
  - Whole blood: 45 ppm has been fatal
  - Liver: 130-436 ppm (adequate levels 30-70 ppm)
  - Kidney: 175-295 ppm (adequate levels 16-30 ppm)
  - Urine: 10-25 ppm (adequate levels 2-5 ppm)

TREATMENT

TREATMENT OVERVIEW

Life-threatening abnormalities, if present, must be identified and managed first: severe anemia may require transfusion, pigment nephropathy should be addressed with intravenous fluids, and GI tract perforation may require medical treatment with or without surgical correction. Then the source of zinc should be removed from the GI tract. Finally, general supportive care is indicated during recovery. Chelation with calcium EDTA or dimercaprol or D-penicillamine is rarely needed after the source of zinc has been removed.

ACUTE GENERAL TREATMENT

- Management of life-threatening abnormalities if present:
  - Anemia: if severe (e.g., hematocrit <20%), consider blood transfusion (see p. 1347).
  - Azotemia, if concurrent with severe hemolysis: brisk intravenous fluid therapy (e.g., 90-130 mL/kg/h, barring preexisting heart disease)
  - Peritonitis from GI tract perforation (see p. 865)
- Removal of zinc source from GI tract:
  - Emesis (see p. 1364): do not induce if animal is already vomiting; always feed the animal first (to avoid unproductive vomiting).
  - Removal through an endoscope: may be possible if the metallic object is small and present in the stomach, but difficult/impossible if there is food in the stomach or with smooth, slippery objects
  - Surgical removal (gastrotomy/enterotomy): last resort, weighing all the risks and benefits before performing surgery; stabilize the animal first (fluids, blood transfusion as needed).
  - Activated charcoal is not indicated because it does not adsorb zinc well.
  - Early and sustained use of antacids until source is removed (calcium carbonate, 70-185 mg/kg/d PO) and/or H2 blockers (famotidine, 0.5-1 mg/kg PO q 12-24 h) to decrease leaching and absorption of zinc.
- Chelation therapy: Note that most cases of zinc poisoning do not require chelation therapy. Animals with zinc toxicosis usually respond well to fluid therapy and other supportive measures once the source of zinc has been removed. In the rare case that

requires chelation, options for chelation therapy include one of the following treatments:
    - Calcium EDTA *(6.6%* solution, equals *66* mg/mL) in dogs: dilute to 10 mg CaEDTA/mL in 5% dextrose and give 25 mg/kg SQ at different sites q 6 h for 2-5 days. Do not exceed 2 g per day, and do not treat for more than 5 consecutive days. In cats: 27.5 mg/kg in 15 mL of 5% dextrose SQ q 6 h for 5 days. Use with caution and monitoring because of risk of nephrotoxicity.
    - Dimercaprol: 2-4 mg/kg SQ or IM q 8-12 h for 2 days
    - D-penicillamine: 27.5 mg/kg/d PO q 6-8 h for 7-14 days
    - Efficacies of dimercaprol and D-penicillamine have not been validated for zinc toxicosis.
- Supportive care:
    - As above. Control severe vomiting with maropitant, 1 mg/kg SQ q 24 h or 2 mg/kg PO q 24 h for 5 days; or metoclopramide, 0.2-0.5 mg/kg SQ q 8 h if needed, provided GI obstruction is ruled out.

POSSIBLE COMPLICATIONS

Liver and renal compromise

RECOMMENDED MONITORING

- CBC
- Serum biochemistry profile (serum bilirubin, renal, and liver values for 1-3 days or until resolution of signs)
- Hematocrit
- Urinalysis

PROGNOSIS AND OUTCOME

- Good with intensive supportive care after removing the source
- Poor if there is overt clinical evidence of multiple organ system damage or failure (liver, kidney, and/or pancreas)

PEARLS & CONSIDERATIONS

COMMENTS

- Toxicosis not likely to occur if zinc-containing objects move out of the GI tract quickly.
- The hematologic and clinical findings in animals with zinc toxicosis are similar to those found for immune-mediated hemolytic anemia (IMHA).
- Zinc toxicosis can cause a positive direct antiglobulin test (Coombs' test) result. Therefore, Coombs' test is not a reliable method of differentiating between IMHA and zinc toxicosis.
- The LD50 of zinc chloride is approximately 100 mg/kg PO.
- The greatest amounts of zinc are present in blood, liver, kidney, skin, lung, brain, heart, and pancreas. Excretion of zinc occurs through the bile and kidneys.

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Zinc Phosphide Intoxication

BASIC INFORMATION

DEFINITION

Zinc phosphide is a metallophosphide rodenticide available as 0.5%-10% bait. Acute toxicosis occurs from ingestion of bait and is characterized by progressive bloody vomiting, agitation, discomfort, constant movement or running, vocalization, bruxism (teeth grinding), respiratory distress, muscle tremors, seizures, and death.

SYNONYMS

Gopher or mole killer; Zn3P2, trizinc diphosphide

EPIDEMIOLOGY

SPECIES, AGE, SEX: All species are susceptible; dogs are more frequently involved.

GENETICS & BREED PREDISPOSITION: Animals that do not vomit are at greater risk of toxic effects.

GEOGRAPHY AND SEASONALITY: Increased incidence during greater rodent activity and mobility following harvest.

CONTAGION & ZOONOSIS: Public health significance to veterinary personnel: human inhalation of phosphine off-gas during decontamination procedures can occur (risk of pulmonary and other effects in humans). Typical garlic or dead fish odor of phosphine may not be detectable at low yet hazardous concentrations to humans. If handling a phosphine-intoxicated animal, ensure good ventilation and contact regional hazardous materials authority for safest procedure guidelines; see Acute Treatment, below.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- History of exposure
- Vomiting, often with blood
- Agitation, discomfort, constant movement or running
- Vocalization, teeth grinding
- Muscle tremors, seizure

PHYSICAL EXAM FINDINGS

- As above
- Dyspnea, harsh lung sounds (due to pulmonary edema)
- Signs of cranial abdominal pain
- Cardiac arrhythmias
- Shock
- Slight garlic or rotten fish odor

ETIOLOGY AND PATHOPHYSIOLOGY

Source

- Baits are available as commercial grain-based pellet, tracking powder, or paste.
- Fumigants aluminum phosphide and magnesium phosphide are similar to zinc phosphide in toxicity.
- Some commercial names are Sweeneys Poison Peanuts Mole and Gopher Bait, Dragon Gopher and Mole Killer Pellets, and Dexol Gopher Killing Pellets 2.

Mechanism of Toxicosis

- Onset of clinical signs in most cases is 15 minutes to 4 hours after ingestion; occasionally delayed up to 18 hours.
- Corrosive effects of zinc phosphide can cause signs of cranial abdominal (gastric) pain and bloody vomiting.
- Gastric acid hydrolysis of zinc phosphide liberates highly toxic phosphine gas, which is rapidly absorbed by passive diffusion.

- Phosphine disrupts cellular respiration by interfering with electron transport (cytochrome C) in the mitochondrion, leading to cellular hypoxia, generation of reactive oxygen species, and lipid peroxidation, especially in tissues of high oxygen demand.
- Death is from cardiac arrest most commonly resulting from hypotensive shock, seizures, and pulmonary compromise.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Tentative diagnosis must be based on history of exposure and clinical signs (vomiting, agitation, vocalization, tremors, seizures), as timely testing is not available. Characteristic rotten fish or garlic smell supports diagnosis but poses risk of pulmonary toxicosis to humans. Diagnosis can be confirmed by presence of zinc phosphide in the stomach contents, liver, or kidney (collect samples in airtight jar) through a diagnostic laboratory.

DIFFERENTIAL DIAGNOSIS

- Strychnine intoxication
- Metaldehyde intoxication
- Organophosphate or carbamate insecticides intoxication
- Arsenic intoxication
- Primary central nervous system (CNS) disease (neoplasia, encephalitis, other)
- Hepatic encephalopathy

INITIAL DATABASE

- Chest radiographs: pulmonary edema
- Acid-base status: respiratory and metabolic acidosis
- Electrocardiogram (ECG): arrhythmias, nonspecific evidence of myocardial ischemia (e.g., ST segment elevation or depression)
- Baseline CBC and serum chemistries generally unremarkable:
  - Baseline electrolytes: possibly decreased Mg^{++}, Ca^{++}
- Coagulation profile: increased

ADVANCED OR CONFIRMATORY TESTING

- Freeze gastric contents, vomitus, liver, and kidney in airtight containers for zinc phosphide analysis.
- Silver nitrate paper qualitative screen of gastric fluid may help detect presence of phosphine gas. Phosphine reacts with silver nitrate, changing the test paper color to black and indicating a positive reaction (follow label directions).

TREATMENT

TREATMENT OVERVIEW

Because of human health risk of phosphine gas, owners or veterinary staff should feed the patient margarine/oil and magnesium hydroxide to help with toxin neutralization. Then treatment goals are early decontamination (induction of vomiting in a well-ventilated area and administration of activate charcoal) for patients not showing any clinical signs. Additional treatment is implemented based on the occurrence of signs: seizure control, treatment of noncardiogenic pulmonary edema, and supportive care to minimize or prevent renal/hepatic failure, while protecting the veterinarians and staff.

ACUTE GENERAL TREATMENT

- Reduce liberation of phosphine gas:
  - 1-3 tbsp (15-45 mL) margarine or olive/corn/vegetable oil (high in unsaturated lipids) fed on a piece of bread to an affected, conscious animal PO may help quench reactive oxygen species from phosphine in the stomach. Useful prior to presentation and vomiting induction.
  - Magnesium hydroxide 10-60 mL PO/animal prior to presentation and vomiting induction to increase gastric pH. A commonly available preparation of magnesium hydroxide is Milk of Magnesia.
- Decontamination of patient:
  - Emesis (see p. 1364). Indicated in patients not showing clinical signs. Apomorphine is preferred: 0.04 mg/kg IM or IV, or part of a crushed tablet dissolved in water instilled into conjunctival sac. Note: Use of 3% hydrogen peroxide, 1-2 mL/kg PO, maximum 45 mL in dog is not contraindicated. However, it is possible that its use may enhance liberation of

phosphine gas (weigh pros and cons before using in well-ventilated area).
    - Activated charcoal, 1-3 g/kg PO (Caution: aspiration risk in vomiting animal; see p. 1281).
- Control seizures. One of the following may be used:
    - Diazepam, 0.5-2 mg/kg IV; repeat as needed.
    - Pentobarbital, 10-30 mg/kg IV to effect, repeat as needed.
    - Propofol, up to 5-6 mg/kg slow IV to effect, then constant rate IV infusion 0.1-0.6 mg/kg/min titrated to effect
- Stabilize respiratory, cardiovascular, and neuromuscular systems:
    - Place endotracheal tube if needed, with proper gas evacuation.
    - Supplemental oxygen
    - Treat hypovolemic shock with crystalloid or colloid fluids; crystalloid dose 80-90 mL/kg/h for dogs, 40-60 mL/kg/h for cats. Synthetic colloid dose approximately 20 mL/kg/d for dogs, 10-20 mL/kg/d for cats (adjust based on case parameters).
    - Corticosteroids (dexamethasone, 0.1-0.2 mg/kg IV) if needed
    - Monitor acid-base status, and correct metabolic or respiratory acidosis with sodium bicarbonate as needed.
    - Monitor electrolytes; correct any deficiency (Ca^{++}, Mg^{++}, and K^{+}).
    - Control pain with narcotic analgesics (e.g., fentanyl transdermal patches 25-100 mcg/h; injectable opiates first if acute pain).
    - Monitor serum biochemistry profiles for 72 hours for delayed hepatic and renal injury.
- Exogenous scavengers:
    - *N*-acetylcysteine reduced myocardial injury in laboratory animals exposed to aluminum phosphide: loading dose 140-280 mg/kg PO or slow IV, then 70 mg/kg PO q 6 h for six treatments.

POSSIBLE COMPLICATIONS

Renal, cardiac, and/or hepatic compromise

RECOMMENDED MONITORING

Respiratory, cardiac, hepatic, and renal functions for 72 hours after exposure

PROGNOSIS AND OUTCOME

- Good for animals not showing clinical signs 8-16 hours after exposure
- Guarded to poor if cardiac arrhythmias, shock, or pulmonary edema develop; death usually within 6 hours
- Fair to good for cases surviving 24 hours

PEARLS & CONSIDERATIONS

COMMENTS

- Early vomiting may reduce risk of serious toxicity in dogs.
- Human inhalation of phosphine off-gas during decontamination procedures can occur and is hazardous. Typical garlic/dead fish odor of phosphine may not be detectable at low yet hazardous concentrations to humans.
- Baits may retain potency for 3 years in a dry environment.
- Toxic dose in dogs and cats is 20-40 mg/kg.
- Only 1 tbsp of 2% pellet bait contains approximately 180 mg zinc phosphide, a significant risk for a 10-kg dog.
- Delayed hepatic or renal injury is possible 48-72 hours following exposure.

TECHNICIAN TIPS

- As with any toxicosis, having the owner bring the container can confirm active ingredients (label and/or brand name search); technicians who speak to owners on the telephone should encourage this if the dog is likely to have ingested zinc phosphide, and technicians should also recommend the owner take immediate measures to reduce phosphine gas (see Acute General Treatment, above).
- Do not wash vomitus down drain, as water will liberate phosphine gas. Double-bag and dispose of in the trash.

CLIENT EDUCATION

- Keep all baits away from dogs.
- Dogs can dig mole/gopher holes and retrieve the bait in the yard/garden.

SUGGESTED READING

Knight MW: Zinc phosphide. In Peterson ME, Talcott PA, editors: Small animal toxicology, ed 2, St Louis, 2006, Saunders Elsevier, pp 1101–1118.

Centers for Disease Control: http://www.atsdr.cdc.gov/tfactsx7.html.

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Zinc Oxide Toxicosis

BASIC INFORMATION

DEFINITION

Generally acute self-limiting vomiting, lethargy, and anorexia occurring after ingestion of concentrated (10%-40%) zinc oxide–containing products such as diaper rash ointments, creams, hemorrhoid preparations, calamine lotion, and some sun blocks

SYNONYMS

Zinc oxide: Chinese white, zinc white, ZnO

EPIDEMIOLOGY

SPECIES, AGE, SEX: All animals susceptible; cases commonly involve dogs.

RISK FACTORS: Younger, unsupervised pets are most likely to ingest products containing zinc oxide.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- Acute onset of vomiting
- White-colored material present in the vomitus (looks like product ingested) within hours of the ingestion
- Presence of teeth marks on the container
- Animals usually remain bright, alert, and responsive.

PHYSICAL EXAM FINDINGS: Unremarkable, aside from nausea, vomiting, and mild lethargy

ETIOLOGY AND PATHOPHYSIOLOGY

- Zinc oxide–containing ointments or creams are used as topical skin protectants, astringents, and bactericidal agents.
- Most zinc oxide ointments or creams contain 10%-40% zinc oxide.
- Some commercial zinc ointment preparations may also contain varying concentrations of vitamin A or D or local anesthetics (benzocaine), cod liver oil, beeswax, petrolatum, or mineral oil.
- Zinc salts are usually irritating to gastrointestinal (GI) mucosa.
- Mild to moderate vomiting occurs secondary to acute gastric irritation.
- Vomiting is self-limiting but may be exacerbated if unlimited water ingestion is allowed before resolution.
- Some dogs will occasionally show an allergic-type reaction (urticaria, angioedema).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Evidence of exposure to zinc oxide–containing product and presence of self-limiting gastritis should be considered diagnostic.

DIFFERENTIAL DIAGNOSIS

- Dietary indiscretion/indigestion/garbage ingestion
- Pancreatitis
- Parvoviral enteritis
- Differentiation: zinc oxide characteristically gives vomit a white color.

INITIAL DATABASE

Not generally required; no systemic signs are expected, and diagnostic testing is rarely indicated (self-resolving problem)

TREATMENT

TREATMENT OVERVIEW

Withhold food and water for 2 hours. Control vomiting and maintain hydration as needed (rarely necessary).

ACUTE GENERAL TREATMENT

- Nothing by mouth (NPO) until 2 hours after last episode of vomiting
- Consider using antiemetics (rarely needed) such as maropitant, 1 mg/kg SQ q 24 h in dogs; or metoclopramide, 0.2-0.5 mg/kg SQ q 6-12 h in dogs, if vomiting is severe and no longer productive (zinc oxide-containing product has been expelled), and gastrointestinal tract obstruction (e.g., with the container as a foreign body) has been ruled out.
- Most cases do not require IV fluids, because clinical signs resolve within 12 hours. Allergic reactions may persist longer (24 hours).
- For allergic reaction: diphenhydramine (dogs: 2-4 mg/kg PO q 8-12 h or 1 mg/kg IM or SQ q 8-12 h; cats: 0.5-mg/kg PO q 12 h or 2 mg/kg IM q 12 h)

POSSIBLE COMPLICATIONS

GI foreign body if the container was ingested

PROGNOSIS AND OUTCOME

- Expect rapid and complete recovery within 24 hours.
- Ingestion is not expected to result in zinc toxicosis (hemolytic anemia, renal damage), because most dogs vomit. Unlike a solid zinc-containing object, which tends to remain in the GI tract long enough to allow absorption of zinc, ointment/cream is readily removed from stomach.

PEARLS & CONSIDERATIONS

COMMENTS

- Single acute ingestion of zinc oxide–containing ointments or creams is not likely to result in zinc toxicosis.
- Repeated use of concentrated zinc oxide–containing products can result in zinc toxicosis, however. Zinc toxicosis has been reported in a dog when 40% zinc oxide ointment was applied dermally for 4 days and dog licked most of the ointment after application.
- Cod liver oil in products containing zinc oxide makes them attractive to dogs.

TECHNICIAN TIP

Prevention of licking (via application of an Elizabethan collar, for example) helps reduce the likelihood of toxicosis when zinc oxide creams are applied to dogs' skin, such as in the treatment of superficial dermatitis or with sunscreen in dogs sensitive to ultraviolet light (immune-mediated skin disease, hairless skin).

PREVENTION

Keep diaper rash products out of pet's reach.

SUGGESTED READING

National Library of Medicine, Medline Plus (human toxicology summary): http://www.nlm.nih.gov/medlineplus/ency/article/002571.htm.

Welch SL: Oral toxicity of topical preparations. Vet Clin North Am Small Anim Pract 32(2):443–453, 2002.

AUTHOR & EDITOR: SAFDAR A. KHAN

1ST EDITION AUTHOR: MARY M. SCHELL

Yew Toxicosis

BASIC INFORMATION

DEFINITION

Toxicosis resulting from accidental ingestion, typically by dogs, of dried or fresh yew plant material followed by development of vomiting, muscle weakness, seizures, cardiac arrhythmias, coma, and death

EPIDEMIOLOGY

SPECIES, AGE, SEX: Dogs are more likely to be involved than cats; all breeds, ages, and both sexes are susceptible.

RISK FACTORS

- Yews are toxic both as green and dried plant material.
- All parts of the yew are toxic except for the red, fleshy fruit surrounding the hard seed. The hard seed coat is resistant to digestive enzymes. Clinical signs are unlikely if the seed is swallowed whole, but absorption from a cracked or partly chewed seed is possible.
- *Taxus brevifolia* contains only minimal concentrations of toxic alkaloids and therefore has lower toxic potential than other yews.

GEOGRAPHY AND SEASONALITY

- The most common ornamental yews are *T. baccata* (English yew) and *T. cuspidata* (Japanese yew).
- In the eastern United States, *T. canadensis* (American yew) is the most common native yew; in Florida, *T. floridana* is the most common native species; and in the western United States, *T. brevifolia* (Western or Pacific yew) is most frequently seen.
- Taxine content is often higher in the winter than in the summer.

CLINICAL PRESENTATION

HISTORY, CHIEF COMPLAINT

- History of exposure to dried or fresh plant material.
- Recent history of vomiting, with the presence of plant material noted in the vomitus.
- The onset of systemic clinical signs is extremely rapid (within 30 minutes to 3 hours post ingestion), and progression to death may happen within a few hours.
- In increasing degree of severity over time, the spectrum of clinical complaints includes vomiting, muscle weakness, seizures, coma, and death.

PHYSICAL EXAM FINDINGS

- Signs of abdominal pain
- Mydriasis
- Tachycardia or bradycardia (both occur fairly commonly with yew toxicosis)
- Hypotension
- Respiratory distress or arrest

ETIOLOGY AND PATHOPHYSIOLOGY

- *Taxus* spp. (yew) are commonly used as ornamental evergreen shrubs (Japanese yew *[Taxus cuspidata],* English yew *[Taxus baccata],* American yew *[Taxus canadensis],* Chinese yew *[Taxus chinensis],* Pacific or Western yew *[Taxus brevifolia],* Florida yew *[Taxus floridana]*).
- Yew alkaloids (taxines) are calcium and sodium ion channel blockers that gradually induce bradycardia and ultimately cardiac arrest.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Generally based on known or possible ingestion of yew; confirmation is via identification of plant parts in vomitus. Extremely rapid course of toxicosis means that diagnosis is often retrospective (made at postmortem exam).

DIFFERENTIAL DIAGNOSIS

- Cardiac glycoside-containing plants (e.g., oleander, foxglove)
- Calcium channel blockers (diltiazem, verapamil) toxicosis
- Caffeine toxicosis (methylxanthines)

INITIAL DATABASE

- CBC, serum biochemistry profile, urinalysis: hypokalemia possible
- Electrocardiogram (ECG; see 1253): a wide variety of arrhythmias is possible and fairly common, most commonly atrioventricular (AV) block, ventricular tachycardia, and (ultimately with severe intoxications) ventricular fibrillation/cardiac arrest.
- Blood pressure (see 1209) (hypotension possible)

ADVANCED OR CONFIRMATORY TESTING

- Taxines (or metabolites) can be identified in vomitus and stomach contents by gas chromatography, mass spectrometry, and silica gel thin-layer chromatography, although the lengthy turnaround time of such advanced testing usually precludes its use clinically.
- Necropsy: the diagnosis of yew poisoning is generally based on the presence of yew plant in the gut. Taxine affects electrical activity of the heart, so no significant lesions are typically found on necropsy. Fatty degeneration of the kidney, congestion of lungs, and inflammation of the gastrointestinal (GI) tract are possible.

TREATMENT

TREATMENT OVERVIEW

Given the rapid course of progression and possibility of fatal intoxication, yew toxicosis is considered a medical emergency. Induction of vomiting, followed by administration of activated charcoal can be lifesaving, particularly if implemented within 2 hours of ingestion prior to the onset of clinical signs of toxicosis. If clinical signs are present, general treatment consists of managing cardiac arrhythmias, controlling seizures, and providing supportive care as needed.

ACUTE GENERAL TREATMENT

- Evacuation of ingested plant material: in animals not showing clinical signs:
  - Apomorphine, 0.03-0.04 mg/kg IV or IM, or crush tablet portion with water and instill into conjunctival sac and rinse following emesis; or hydrogen peroxide 3%, 2 mL/kg PO (max 45 mL [in large dogs]), repeat in 10 to 15 minutes if no vomiting. Emesis may not remove all plant material from the GI tract. If the ingestion was small and/or the patient has not eaten anything else, some clinicians feed a tasty meal immediately prior to inducing vomiting, to allow mixing and agglutination of plant material with food that is then vomited.
  - Gastric lavage (plant material not easily removed through tube)
  - Endoscopic removal of plant parts
  - Activated charcoal (1-2 g/kg PO) with a cathartic such as sorbitol (70%) 1-3 mL/kg; mix with charcoal; use labeled dose for commercial products.
- Treat cardiac arrhythmias as needed:
  - Ventricular tachyarrhythmias (see 1165): correct hypokalemia if present and consider lidocaine (dogs: 2 mg/kg IV; cats: use with caution), procainamide (dogs: 6-8 mg/kg IV; cats: 1-2 mg/kg IV), propranolol 0.1 mg/kg slow IV, or esmolol 0.2-0.5 mg/kg slow IV to effect.
  - Sinus bradycardia: atropine, 0.04 mg/kg IV
- Control seizures (see pp. 353 and 1009): diazepam (dogs/cats: 0.25-0.5 mg/kg IV) or phenobarbital (dogs/cats: 2-5 mg/kg IV, higher doses often used in dogs)
- IV fluids and oxygen as needed
- Correct electrolyte abnormalities as needed.

DRUG INTERACTIONS

Sodium channel blockers (proarrhythmia), calcium channel blockers may potentiate arrhythmias.

RECOMMENDED MONITORING

- ECG (arrhythmias)
- Blood pressure (hypotension)
- Serum electrolytes
- Central nervous system (CNS) signs
- Respiratory rate and effort

PROGNOSIS AND OUTCOME

- Good if treated early and aggressively (prior to onset of clinical signs)
- Poor if systemic effects are present, especially cardiac arrhythmias

PEARLS & CONSIDERATIONS

COMMENTS

- All species of yews should be considered toxic, but there is great variability in taxine content.
- Tetanic epileptiform seizures are reported clinically in dogs but not reproduced experimentally.
- Toxic dose for dogs is 30 g (approximately 2 tbsp) of plant material.

TECHNICIAN TIP

Ensure that vomitus and ingesta are disposed of safely, to avoid consumption and reintoxication by other dogs (or the same dog).

PREVENTION

Keep pets away from yew bushes and clippings.

CLIENT EDUCATION

Dried shrubbery and trimmings are still toxic.

SUGGESTED READING

Burrows GE, Tyrl RJ: Taxaceae. In Burrows GE, Tyrl RJ, editors: Toxic plants of North America. Ames, IA, 2001, Iowa State Press, pp 1149–1157.

Cope RB: The dangers of yew ingestion. Vet Med, 2005, pp 646–650.

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Xylitol Toxicosis

BASIC INFORMATION

DEFINITION

Xylitol is a 5-carbon sugar alcohol used as a sweetener in gums, candies, confectionery/baked goods, and in some medications. Toxicosis is characterized by hypoglycemia leading to weakness, lethargy, disorientation, seizures, and ataxia usually within 12 hours after ingestion. Hepatotoxicity can occur in 12-48 hours in some dogs and may be idiosyncratic (individual susceptibility). Toxicosis has been fatal in some dogs.

SYNONYMS

- Xylite, Eutrit, Newtol, Xyliton
- Chemical names are 1,2,3,4,5-pentapentanol or 1,2,3,4,5-pentahydroxypentane.
- Many “sugar-free” products contain xylitol as a sweetener.

EPIDEMIOLOGY

SPECIES, AGE, SEX: Toxicosis has been documented in dogs only. No known age, sex, or breed predisposition.

RISK FACTORS

- Animals with preexisting liver disease may be at increased risk for hepatotoxicosis.
- Young animals may be more prone to developing hypoglycemia.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES: Xylitol toxicosis is an acute syndrome.

HISTORY, CHIEF COMPLAINT

- Evidence of chewed up package; gum or wrappers in the vomitus/stool
- Lethargy, vomiting, weakness, disorientation, ataxia, seizures, typically 30 minutes to 12 hours after ingestion.
- Some dogs develop both hypoglycemia and acute liver failure. Some dogs do not show evidence of hypoglycemia but may have signs of acute hepatic injury (see p. 503) in 12-48 hours.

PHYSICAL EXAM FINDINGS

- Nonspecific lethargy, vomiting, weakness
- With marked hypoglycemia: ataxia, disorientation, seizures
- Evidence of bleeding disorder is common: petechiae, ecchymoses, gastrointestinal hemorrhage, oozing from venipuncture sites.
- Vital signs usually within normal range (body temperature, respiratory rate and character, heart rate)

ETIOLOGY AND PATHOPHYSIOLOGY

- Toxicosis occurs acutely when dogs eat large amounts of xylitol-containing products.
- In humans, xylitol does not cause significant increase in insulin or blood glucose levels, but in dogs, xylitol causes a rapid and dose-dependent increase in blood insulin and concomitant decrease in blood glucose concentration.
- Mechanism of hepatotoxicosis in dogs may be necrosis of hepatocytes due to adenosine triphosphate (ATP) depletion, resulting in cell necrosis; or production of reactive oxygen species, resulting in damage to cell membranes and macromolecules.

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Diagnosis rests on any combination of history (observed or suspected ingestion), physical exam (signs consistent with hypoglycemia and/or liver failure), and results of routine laboratory testing (hypoglycemia +/− signs of acute liver injury +/− coagulopathy). No specific confirmatory test exists.

DIFFERENTIAL DIAGNOSIS

- Rule out other causes of hypoglycemia:
  - Toxicologic: Insulin overdose, anti-diabetic medications overdose (sulfonylureas)
  - Nontoxicologic: Insulinoma, juvenile hypoglycemia, starvation, sepsis
- Rule out other causes of hepatotoxicosis:
  - Toxicologic: acetaminophen, blue-green algae, sago palm, mushrooms (*Amanita* type), zinc phosphide, mycotoxin (aflatoxins), nonsteroidal antiinflammatory drug (NSAID) toxicosis
  - Nontoxicologic rule outs: bacterial hepatitis, idiopathic chronic hepatopathy, viral hepatitis, leptospirosis

INITIAL DATABASE

- CBC: thrombocytopenia common; mean = 137 × 10^9 platelets/L
- Serum biochemistry profile, specifically including glucose, electrolyte, and liver enzyme levels (baseline on presentation):
  - Hypoglycemia (mild to severe; lowest reported = 26 mg/dL [1.5 mmol/L])
  - Marked liver enzyme elevations common (e.g., ALT: 1000 to >10,000 IU/L; normal <120 IU/L).
  - Hyperbilirubinemia common (mean 4.1 mg/dL; normal <0.6 mg/dL)
  - Mild to marked hyperphosphatemia
- Coagulation panel:
  - Prothrombin time (PT) often elevated (36 to >100 seconds)
  - Activated partial thromboplastin time (APTT) markedly elevated (>100 seconds) in many/most dogs

ADVANCED OR CONFIRMATORY TESTING

Necropsy findings include icterus, hepatic necrosis, peritoneal and gastrointestinal (GI) petechiae and ecchymoses, hemorrhage into the GI tract, and mediastinal hemorrhage.

TREATMENT

TREATMENT OVERVIEW

Mainstays of therapy are to treat seizures (likely due to hypoglycemia) if present; induce vomiting if ingestion occurred within 6 hours and patient is not yet showing clinical signs, to manage delayed hepatotoxicosis if present; and to address bleeding tendencies prophylactically. The clinical presentation and evolution of the case dictates which aspects of treatment are necessary.

ACUTE GENERAL TREATMENT

- Management of hypoglycemia and associated signs, including seizures:
  - 5% dextrose, 20 mL/kg IV bolus followed by 2 mL/kg/h IV; adjust according to blood glucose level measured q 2-4 h.
  - Oral source of dextrose (e.g., Karo syrup) to lick if dog is able to swallow; give small frequent meals.
- Decontamination in asymptomatic patient:
  - Induce vomiting with oral administration of 3% hydrogen peroxide or apomorphine (see p. 1364)
  - Activated charcoal: do not give; not expected to be effective.
- Gastric lavage (see p. 1281): only if large dose has been ingested and vomiting cannot be induced.
- Treat liver damage (see p. 503).
- Treat bleeding disorders:
  - Significant (>double, with or without overt bleeding) elevations in PT and/or APTT warrant fresh frozen plasma transfusion (see p. 1347).
  - Severe thrombocytopenia, especially if solely associated with bleeding (i.e., coagulation times are normal), may warrant replacement via whole-blood transfusion.

CHRONIC TREATMENT

S-adenosyl-L-methionine (SAMe), 18 mg/kg PO q 24 h for 1-3 months if evidence of hepatotoxicosis

NUTRITION/DIET

- Karo syrup, honey, or corn syrup, together with frequent feeding of small meals, may be helpful initially for hypoglycemia.

- Optimal protein diet for liver damage (see p. 513)

DRUG INTERACTIONS

Metabolism and pharmacokinetic parameters of many medications can change due to liver damage. Dose adjustments should be made accordingly.

POSSIBLE COMPLICATIONS

- Coagulopathy secondary to acute liver failure and/or disseminated intravascular coagulation
- Hyperthermia secondary to seizures

RECOMMENDED MONITORING

- Monitor blood glucose every 2-4 hours for 12-24 hours in all patients (whether showing overt signs of hypoglycemia or not).
- Recheck serum biochemistry profile (liver enzyme levels) at 24, 48 hours. If high, monitor until return to normal.
- Recheck coagulation profile at 24, 48 hours.
- Neurologic signs of hypoglycemia

PROGNOSIS AND OUTCOME

Prognosis is good with control of hypoglycemia. Guarded if hepatic necrosis and coagulopathy develops.

PEARLS & CONSIDERATIONS

COMMENTS

- Hypoglycemia can occur at doses of >75-100 mg/kg.
- Hepatotoxicity typically occurs at higher doses >500-1000 mg/kg, but since it is possibly an idiosyncratic reaction, monitoring liver enzymes is suggested in most cases, especially if hypoglycemia develops.
- Amount of xylitol in gums and candies varies widely; sugar-free gums can contain as little as 9 mg of xylitol per piece, and some brands may contain up to 2 g per piece.
- Some medications, rinses, toothpastes may also contain xylitol (variable amount).
- Sorbitol, maltitol, or maltitol syrup present in some sugar-free products are not believed to induce hypoglycemia or liver damage in dogs.
- Splenda (sucralose), Sweet'n Low (saccharin, dextrose, and cream of tartar), and Equal (aspartame, dextrose, and maltodextrin) do not contain xylitol.

PREVENTION

Keep xylitol-containing products out of reach of dogs.

TECHNICIAN TIPS

Label may provide information on the amount of xylitol or other sugar-free alcohols present in the product.

CLIENT EDUCATION

Keep xylitol containing gum, cookies, oral hygiene products, and other sources away from dogs.

SUGGESTED READING

Dunayer EK, Gwaltney-Brant SM: Acute hepatic failure and coagulopathy associated with xylitol ingestion in eight dogs. J Am Vet Med Assoc 229:1113–1117, 2006.

Web source: http://xylitol.org/ Accessed: December 2009.

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Introduction to Diseases and Disorders

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Overview

This section, Diseases and Disorders, aims to summarize the most important clinical entities in small-animal practice. These entities include specifi c disease syndromes and general clinical signs. The following pages summarize several hundred of the most frequently encountered diseases and disorders. Over 100 more, which are encountered less frequently but are well recognized in veterinary practice and are equally complete and up to date, are accessible online in this same format at www. clinicalvetadvisor2.com.

BASIC INFORMATION

DEFINITION

a brief explanation of the meaning of this disease or disorder

SYNONYMS

where appropriate, other terms used interchangeably to name this disease or disorder

EPIDEMIOLOGY

SPECIES, AGE, SEX

the typical signalment of affected individuals

GENETICS & BREED PREDISPOSITION:

information regarding possible hereditary factors

RISK FACTORS

elements that might predispose a patient to this disease or disorder

CONTAGION & ZOONOSIS:

important information regarding infectious spread of certain diseases

GEOGRAPHY AND SEASONALITY:

features that would help to raise or lower the clinician's index of suspicion for a disease or disorder, based on environment and timing of occurrence

ASSOCIATED CONDITIONS & DISORDERS:

entities that occur simultaneously or as a result of this disease/ disorder

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES:

if applicable, the different variants of a disease a clinician should consider

HISTORY, CHIEF COMPLAINT

the information provided by the owner or caretaker (history), together with the primary reason for seeking veterinary attention (chief complaint)

PHYSICAL EXAM FINDINGS

the relevant abnormalities—or, if important, relevant normal findings—associated with the disease/disorder

ETIOLOGY AND PATHOPHYSIOLOGY

The mechanisms and pathways according to which the disease or disorder begins and then evolves

DIAGNOSIS 

DIAGNOSTIC OVERVIEW

New to this edition, this segment is a brief summary that states what is appropriate to achieve a functional clinical diagnosis in most cases of the disorder. The goal of the Diagnostic Overview is to give direction to the reader/practitioner for applying the information provided subsequently. The result is diagnostic guidance, rather than just a list of possible diagnostic tests.

DIFFERENTIAL DIAGNOSIS

Other diseases or disorders that may mimic the one under discussion, and about which the reader should be aware

INITIAL DATABASE

A summary of basic clinical tests that are appropriate when this disease/disorder may be present. These are largely tests that should be accessible in most outpatient clinics or facilities.

ADVANCED OR CONFIRMATORY TESTING

Diagnostic tests that are performed if the initial database is insuffi cient for establishing the diagnosis. Some of these tests may be performed easily in any clinic or hospital, whereas others may require referral to a specialty center.

TREATMENT 

TREATMENT OVERVIEW

Like the Diagnostic Overview, a new section that summarizes the goals and priorities of treatment. The purpose is to offer guidance in the application of treatment information.

ACUTE GENERAL TREATMENT

Those forms of treatment that are instituted promptly, either because treatment is simple or because of immediate need

CHRONIC TREATMENT

When necessary, ongoing treatment typically provided at home

NUTRITION/DIET

Previously grouped within the preceding two segments, this area covers alterations of food intake or food type that may assist in treatment.

BEHAVIOR/EXERCISE

Information pertaining to deliberate changes in physical activity (increase, decrease, or new) and any forms of treatment related to behavioral modifications.

DRUG INTERACTIONS

Relevant information regarding incompatibility of two or more medications commonly used in the treatment of the disease/disorder. This section by necessity is perhaps one of the least comprehensive; the reader is advised to seek information from clinical pharmacology sources to assist in identifying potential or real problems..

POSSIBLE COMPLICATIONS

Selected, recognized problems that may occur as a result of the disease process alone or as a complication of treatment to be sought and addressed if it occurs

RECOMMENDED MONITORING

Methods the reader/practitioner should use for ensuring that treatment and/or resolution of the disease or disorder is proceeding as expected

PROGNOSIS AND OUTCOME 

The expected evolution of the disease or disorder, with or without treatment. Important elements include survival time, survival rate, and expected variations in clinical progression.

PEARLS & CONSIDERATIONS 

PEARLS

Single items of counterintuitive observations, pitfalls to avoid, and other important points

PREVENTION

Methods to avoid recurrence or reduce occurrence of new cases

TECHNICIAN TIPS

New to this edition, this segment provides information relevant to nursing care and the role of the veterinary technician in managing cases of this disease disorder.

SUGGESTED READING

Every disease and disorder has at least one outside source for additional consultation. In most cases, there are others as well. In addition to the Suggested Reading in the printed version of this text, be sure to check the online version for expanded lists at: www.clinicalvetadvisor2.com.

Artificial Insemination

OVERVIEW AND GOAL

To effectively deliver fresh, chilled, or frozen-thawed semen into the cranial vagina

INDICATIONS

Convenience (geographic separation of dam and sire), maximizing use of valuable semen, ineffective natural mating (e.g., inexperienced/uncooperative male)

CONTRAINDICATIONS

Poor timing/incorrect detection of estrus; systemic illness or other medical disorder likely to compromise successful fertilization; poor technique and/or materials and equipment; semen quality is not optimal, or the total number of viable sperm is not adequate (arbitrarily, <50 million motile sperm for small or toy breeds or <100 million motile sperm for medium, large breeds), which is a relative contraindication because acceptable results may be obtained, especially if switching to transcervical insemination (see p. 1346) or surgical intrauterine insemination.

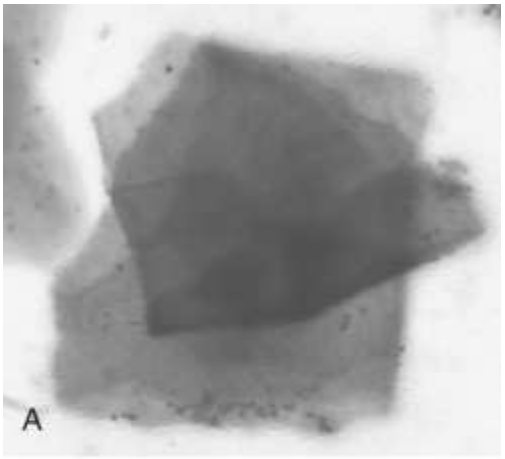
EQUIPMENT, ANESTHESIA

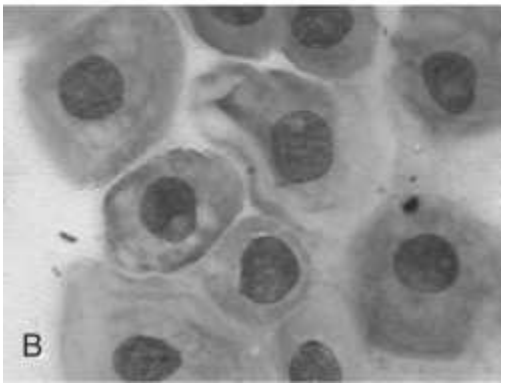
The procedure is generally performed awake. Required materials and equipment include:

- Latex examination gloves
- Sterile water-soluble lubricant
- Semen in sterile pipette or straw
- Sterile syringe for expelling the semen in the pipette

ANTICIPATED TIME

10 minutes

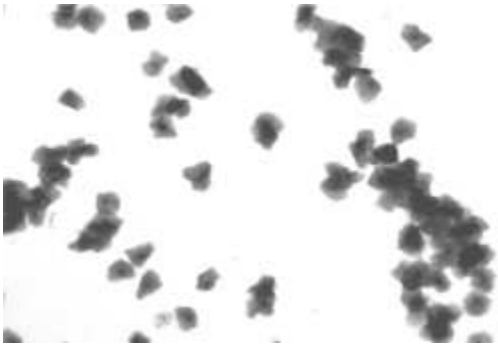




ARTIFICIAL INSEMINATION Vaginal smears stained with Romanowski stain and observed with bright-field microscopy. **A**, Estrus; superficial epithelial cells observed at 1000× magnification. **B**, Diestrus; parabasal epithelial cells observed at 400× magnification.

PREPARATION: IMPORTANT CHECKPOINTS

- Above all, the insemination process should be timed as optimally as possible. This means inseminating 1-4 days after ovulation.
- For optimal results, 2 inseminations should be planned 24-72 hours apart in this window of time.
- Methods for estrus detection and estimation of anticipated time of ovulation require hormonal assays, vaginoscopy, vaginal cytologic examinations (see figure), or a combination thereof (see pp. 155 and 1361).
- Semen which has been properly handled and is of good quality must be available.
- The help of one or two assistant(s) is very useful for basic restraint and handling of the bitch.



ARTIFICIAL INSEMINATION Vaginal smear depicting 100% cornification (superficial and large intermediate squames), consistent with estrus. Smear stained with Romanowski stain and observed with bright-field microscopy at 100× magnification.

POSSIBLE COMPLICATIONS AND ERRORS TO AVOID

- Urethral catheterization with the pipette; avoided by advancing the pipette along the lateral (left or right) aspect of the vagina
- Vaginal injury; avoided by concurrent gentle palpation of the vagina and cervix abdominally, and avoidance of pressure if resistance is met while advancing the pipette
- The semen should be deposited specifically in the cranial-most part of the vagina as close to the cervix as possible to increase the likelihood of success.

PROCEDURE

- The bitch is placed standing in a location that is comfortable for the inseminator, typically an examination table for small dogs and the ground for medium- to large-breed dogs.
- An assistant restrains the bitch and draws her tail to one side (or this can be done by a second assistant).
- The inseminator dons gloves and holds the semen-filled pipette in the right hand if the inseminator is right-handed.
- The inseminator parts the labia and elevates the vulva dorsally using the hand not holding the pipette.
- The pipette tip is placed in the vestibule and elevated dorsal to the brim of the pelvis, and lateral (left or right) to avoid the urethral papilla.
- The pipette is advanced gently. The inseminator releases the labia and uses the non-pipette hand now to palpate the abdomen and locate the cervix.
- The pipette continues to be advanced until its tip is felt with the fingertips, transabdominally, to be immediately caudal to the cervix.
- At this time, the bitches hindquarters are elevated at a 30- to 45-degree angle; the inseminator then delivers the semen by depressing the plunger on the syringe connected to the pipette.

POSTPROCEDURE

- With insemination into the cranial vagina, it is considered advantageous to maintain the bitch's hindquarters elevated for 5-10 minutes to improve delivery of semen to the uterus. In the dog, spermatozoa first reach the uterus 30-120 seconds after insemination into the cranial vagina when the bitch is positioned with elevated hindquarters, but this process is hindered when the bitch is left in a horizontal (normal) posture after vaginal artificial insemination.
- “Feathering” of the vulva and perineum may be performed while the bitch's hindquarters are elevated, to induce uterine contractions and further favor movement of spermatozoa into the uterus.

ALTERNATIVES AND THEIR RELATIVE MERITS

Fertile dogs experience normal pregnancy rates and litter sizes following intravaginal inseminations; however, intracervical or surgical uterine inseminations may be advised for breeding bitches with frozen-thawed semen or low sperm doses.

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Johnston SD, Root Kustritz MV, Olson PN: Vaginal cytology. In Johnston SD, Root Kustritz MV, Olson PN, editors: Canine and feline theriogenology. Philadelphia, 2001, WB Saunders Co, pp 32–40.

AUTHOR: CARLOS PINTO

Arthroscopy

OVERVIEW AND GOALS

Arthroscopy is the use of a rigid endoscope—fitted with a lens, a fiberoptic light source, a video camera, and a fluid ingress—to magnify, view, and assess the intraarticular anatomy of a joint. Assisted manipulation and structural alteration of intraarticular ligaments, tendons, joint capsule, and cartilage are routinely performed under arthroscopic visualization.

INDICATIONS

Diagnostic: confirmation of suspected joint trauma and degeneration initially assessed by palpation and imaging

- Forelimb:
  - Shoulder: osteochondritis dissecans (OCD) flap, biceps tendon avulsion/sprain, supraspinatus and subscapularis tendon trauma, medial and lateral glenohumeral ligament damage
  - Elbow: fragmentation of medial coronoid process, humeral trochlear OCD, ununited anconeal process, humero-ulnar conflict, radio-ulnar joint incongruity, condylar fracture, incomplete ossification of humeral condyle, cartilage damage secondary to elbow joint dysplasia
  - Carpus: intercarpal ligament damage
- Hindlimb:
  - Hip: acetabular labral avulsion, femoral head ligament rupture, cartilage damage secondary to hip dysplasia
  - Stifle: cranial and caudal cruciate ligament damage, medial and lateral meniscal avulsion and tearing, long digital extensor tendon avulsion, lateral femoral condylar OCD, femoropatellar and femorotibial cartilage degeneration
  - Hock: talar OCD, intraarticular tibiotarsal fracture

Therapeutic: débridement and removal of damaged and noncompetent ligament, tendon and osteochondral lesions under arthroscopic visualization

CONTRAINDICATIONS

Lack of comprehensive training, supervised initial exposure, and well-maintained modern arthroscopy equipment

EQUIPMENT, ANESTHESIA

Equipment:

- Rigid arthroscope; there is a wide range of scope diameters and length; the commonly used diameters in small animal arthroscopy are 1.9 mm, 2.3 mm, and 2.7 mm. Arthroscope length varies from short (6-10 cm) to long (12-18 cm). The most commonly used arthroscopes are the 2.3 mm and 2.7 mm short arthroscopes.
- Arthroscopic cannula and blunt trocar matched to arthroscope size and used for joint introduction
- Endoscopic video camera mounted to the arthroscope and connected by cable to a camera control box and video screen monitor
- Compatible tungsten-halogen or xenon lamp and intensity regulator
- Digital image collection system; video loop capability is optional and advantageous
- Fluid ingress system for joint distension and lavage. Gravity-assisted, pressure-bag, or mechanical pump systems are all used with success. Initial joint aspiration and distension achieved with 22- to 18-gauge needles and 6- to 12-mL syringes.
- Joint fluid outflow egress cannula-trocar or large-gauge needles (18-20 gauge)
- Hand instruments; a variety of probes, grasping forceps, cutting forceps, biting forceps, push and hook knives is needed to manipulate, débride and remove intraarticular structures.
- Motorized sheathed shavers and burrs with concurrent suction and adjustable rotatory speed allow for mechanical débridement of intraarticular fat pads, damaged ligaments, and cartilage defects.
- Intraarticular electrocautery and radio-frequency units enable accurate control of intraarticular bleeding and soft-tissue débridement.
- Instrument cannulas may be utilized to minimize periarticular trauma by repeated introduction of hand instruments through tissue ports.

Anesthesia:

- Routine induction and anesthesia maintenance of patient on airway-intubated gas anesthesia
- Regional local anesthesia often employed with axillary nerve block for thoracic limb procedures and epidural analgesia for pelvic limb procedures

- Intraarticular local anesthesia with lidocaine or bupivacaine is used by some surgeons to further analgesic coverage.

ANTICIPATED TIME

About 20-60 minutes depending on surgeon experience and skill level. Diagnostic joint exploration followed by significant intraarticular débridement and treatment may exceed 60 minutes in select cases.

PREPARATION: IMPORTANT CHECKPOINTS

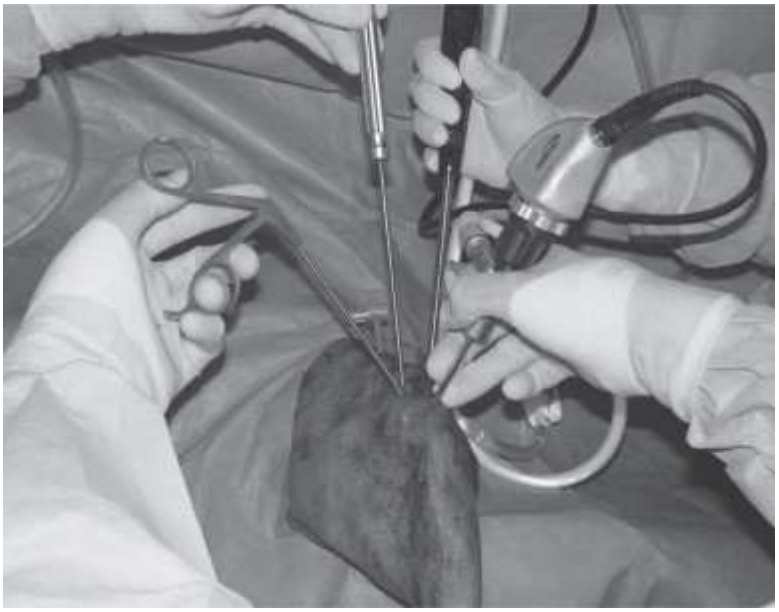
- To minimize the occurrence of technical difficulties, the video camera, video screen monitor, light source, image collection system, fluid supply, and their relevant control units should be connected and tested prior to patient induction. The components of the arthroscopic equipment are best stored and operated from a mobile equipment tower that can be easily moved to an optimal position.
- The arthroscopic control tower with the video monitor should be located in the surgical theater to allow easy access to the control units by nonsterile technical staff during the procedure and an uninterrupted view of the monitor by the sterile surgical team.
- Correct patient positioning on the surgical table is very important to minimize iatrogenic joint trauma during arthroscopic instrumentation and allow for maximal visualization of intraarticular structures.
- The use of arthroscopic positioning braces allows the examined joint to be placed in an optimal position and secured in that position for the duration of the procedure.
- All arthroscopic supplies and equipment should be available, sterilized as appropriate, and organized on the surgical table in a consistent and logical fashion.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

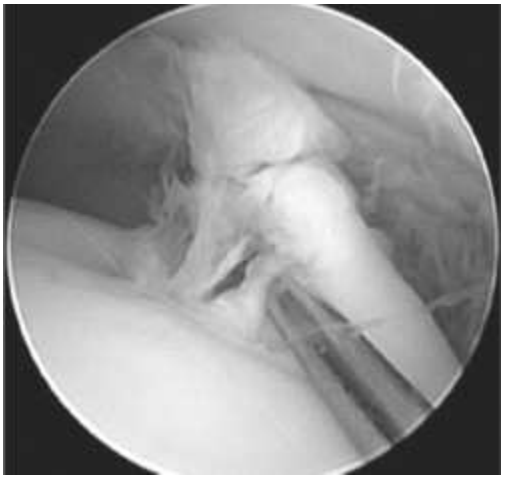
- Technical issues with endoscopic equipment are not uncommon, and it is imperative that technical staff be completely familiar with the various components of the arthroscopic tower and be able to troubleshoot technical issues as they arise during the procedure.
- Difficulty with initial distension, lavage, or instrumentation of the joint during the procedure, or loss of intraarticular visualization due to joint capsule collapse during prolonged procedures with multiple arthroscopic ports, may necessitate open arthrotomy to complete diagnostic and therapeutic goals.
- Pooling of arthroscopic ingress fluids in the periarticular tissues due to difficulties with egress ports and cannulas may make secondary procedures planned for the joint difficult due to alteration of standard tissue dissection planes.

PROCEDURE

- Patient positioning will depend upon the surgical joint and which aspect of the joint is being instrumented:
    - Shoulder: lateral or dorsal recumbency with lateral or hanging distal traction of the surgical limb
    - Elbow: dorsal recumbency with limb abduction and lateral bracing for medial instrumentation, medial bracing for lateral instrumentation
    - Carpus: dorsal or ventral recumbency with carpus hyperflexed
    - Hip: lateral recumbency with pelvic limb distally distracted
    - Stifle: dorsal recumbency with stifle flexed at table end and femur stabilized
    - Tarsus: ventral recumbency with tarsus flexed off table end
- The locations of the camera portal and instrument portals in each joint vary with the location of the intraarticular lesion of greatest interest, the overall aim of the individual procedure, and the arthroscopic surgeon's personal preference.
- Distension of the surgical joint with isotonic fluid and/or local anesthetic via an 18- to 12-gauge needle and 6-mL syringe allows for placement of the arthroscope cannula and trocar through a small stab incision directly adjacent to the distension needle.
- Care should be taken to not damage critical neurovascular tracts, transarticular ligaments, and tendons and to minimize periarticular and intraarticular trauma during the instrumentation procedure.
- Replacement of the arthroscopic trocar with the arthroscope and initiation of egress fluid flow should allow visualization of the cartilage surface and joint capsule.
- Establishing the location of the instrument portal into the joint will depend upon the ability to triangulate with the visual field of the arthroscope, the presence of vital structures that must be avoided, the instruments needed, and the specific intraarticular treatment planned.
- Crucial to effective ongoing visualization and manipulation of joint structures are stable limb position, reliable and adjustable ingress fluid flow, maintenance of an unobstructed and consistent visual field within the joint, a reliable and easily used instrument portal, lack of fluid leakage into the periarticular tissue, and minimal intraarticular hemorrhage.
- Following systematic examination of the joint, interventions may include removal of osteochondral flaps, debridement of damaged articular ligaments, partial meniscectomy and meniscal release, etc. Initial technical challenges are generally overcome with increased surgeon experience.



ARTHROSCOPY Left stifle arthroscopy with arthroscope in distal lateral portal, double instrumentation of medial portal, and joint distractor in second proximal lateral portal.



ARTHROSCOPY Left shoulder arthroscopic image with partially elevated osteochondritis dissecans (OCD) flap.

POSTPROCEDURE

- Articular ports are closed with skin sutures that should be removed in 10-12 days.
- Cold packing of the surgical joint area for 15-20 minute periods over the first 24-48 hours post surgery will assist in patient comfort and recovery.
- Placement of a light support dressing for the first 24-72 hours post surgery may assist in patient comfort, absorb postsurgical fluid leakage from the arthroscopy ports, and minimize early contamination of port sites.
- Use of postsurgical medications including opioids, nonsteroidal antiinflammatories, and sedatives may allow for better patient recovery and compliance with postsurgical exercise restriction.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Open arthrotomy and direct visualization of intraarticular structures is more invasive, causes more periarticular trauma, has a higher incidence of joint contamination and development of septic arthritis, provides less accurate visualization of joint lesions, allows less accurate treatment of articular lesions, and has a higher complication rate and slower patient recovery with potentially a less successful endpoint in treatment recovery.
- Open arthrotomy should only be employed in patients that do not have access to arthroscopic surgeons or in joint conditions that require an arthrotomy to achieve the surgical goal.

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AUTHOR: IAN GORDON HOLSWORTH

Arthrocentesis

SYNONYMS

Joint tap, joint aspirate, synovial tap

OVERVIEW AND GOAL

To use a needle and syringe to obtain a sample of fluid from a synovial (joint) space for analysis

INDICATIONS

- Joint pain (arthralgia)
- Joint swelling, joint effusion
- Radiographic evidence of joint disease
- As part of evaluation of nonspecific systemic signs

CONTRAINDICATIONS

Severe bleeding disorder (risk of hemarthrosis)

EQUIPMENT, ANESTHESIA

- Generally performed with mild sedation but not local or general anesthesia
- Skilled clinicians sometimes use no sedation or anesthesia unless the animal shows signs of resentment or discomfort.
- The procedure may be performed during general anesthesia if the animal is anesthetized for another reason.
- Hair clippers
- Surgical scrub solution, rubbing alcohol, and gauze/sponge for prepping skin
- 6-10 4 × 4 gauze pads
- Microscope slides (at least 10), cleaned and spread out on a table or tray
- 5-10 sterile needles (20-, 22-, or 23-gauge, depending on the animal's size)
- 3-4 sterile syringes (1, 3, or 6 mL)
- Red-top test tube
- Lavender-top test tube
- Sterile culture swab
- Sterile gloves

ANTICIPATED TIME

About 10-30 minutes

PREPARATION: IMPORTANT CHECKPOINTS

- The joints to be aspirated should be clearly identified in the medical record.
- As a general rule, the carpi, tarsi, and stifles are the most easily accessed joints.

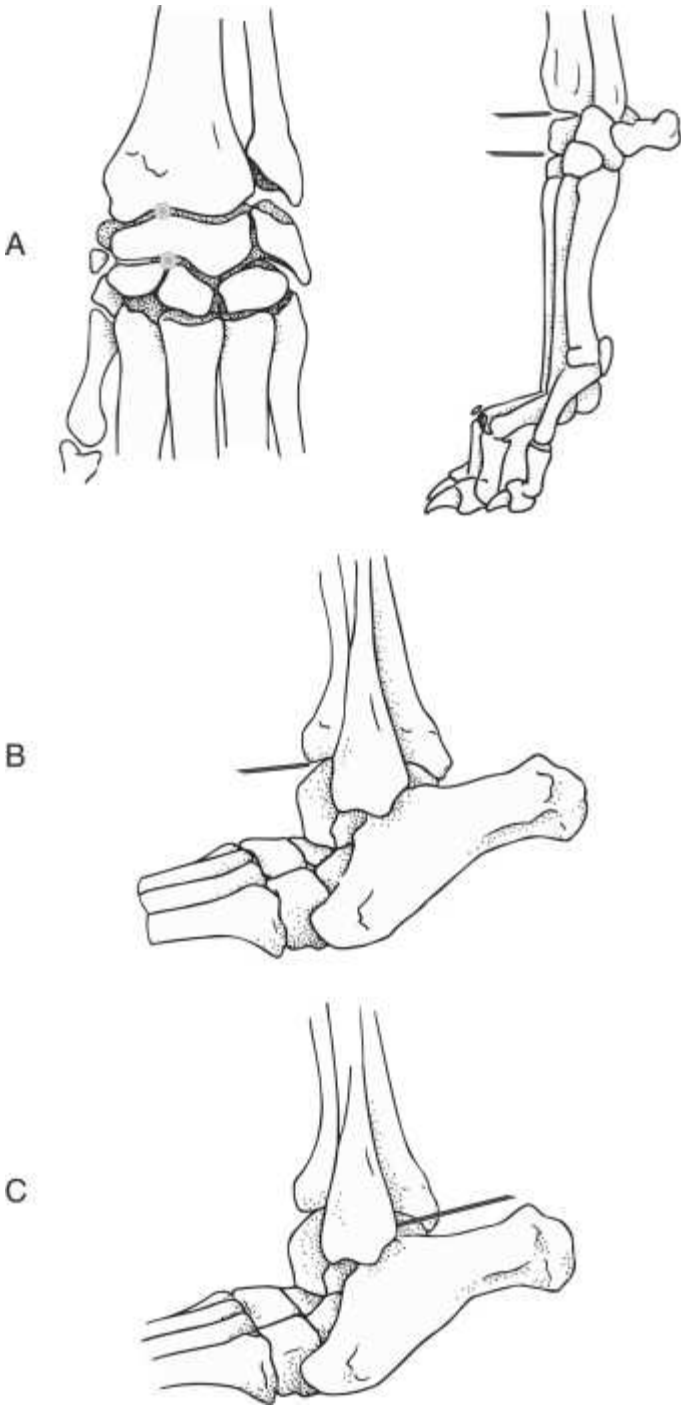
POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Blood contamination of sample: very common and detrimental to obtaining an accurate diagnosis. Be sure to release negative pressure on syringe before withdrawing needle from joint.
- Iatrogenic hemarthrosis: very uncommon unless underlying bleeding disorder
- Lameness induced by procedure: very rare

PROCEDURE

- The skin is clipped and aseptically prepped over the relevant joint(s).
- Bony landmarks are palpated to have the most direct access to the joint space.

- Note: An important rule of thumb is to first palpate a joint in a gentle and superficial manner to find areas of gross joint swelling. When they occur, joint swellings can often be felt as soft, fluctuant, "puffy" subcutaneous pockets of synovial fluid and are the easiest source of access to a joint. This is especially true for the carpi, tarsi, and stifles.



ARTHROCENTESIS Schematic representation of recommended sites for arthrocentesis in the dog and cat. **A**, Carpus: partially flex joint. Palpate and enter craniomedial aspect of carpometacarpal or radiocarpal space. **B**, Hock: cranial approach. Palpate space between tibia and tibiotarsal bone on craniolateral surface of hock; insert needle in shallow, palpable space. **C**, Hock: lateral approach. Partially flex joint, and insert needle under (distal to) lateral malleolus of fibula.

(Reprinted with permission from Nelson RW, Couto CG: Small animal internal medicine, ed 4, St Louis, 2009, Mosby, pp 1122–1124.)

CARPUS:

- On the cranial-most surface of the flexed carpus, a space is delineated by the distal radius proximally, the carpal bones distally, and the tendons of the extensor carpi radialis and common digital extensor on either side.
- The space is 2-3 mm in diameter in a medium-size dog.

- It is a natural depression that is best felt when the carpus is flexed.
- An assistant maintains the carpus in a gently but fully flexed position to open the radiocarpal angle and increase access to the joint space during the procedure.

TARSUS:

- The tarsal joint is not excessively flexed or extended.
- The caudal aspect of the tarsus presents both medial and lateral access to the tarsal joint.
- The lateral and medial malleoli of the distal tibia are palpated; immediately medial and caudal to each one is a depression in which the joint space can be accessed.

STIFLE:

- The stifle joint is not excessively flexed or extended.
- From a cranial approach, the needle is passed laterally or medially to the patellar tendon and is directed caudally and toward the center of the tibial plateau.

Once the landmarks have been established for the chosen joint(s):

- Aseptically scrub the site once more.
- Open sterile syringes onto sterile field (e.g., onto opened paper wrapper for sterile gloves).
- Put on both sterile gloves.
- With the help of an assistant, attach sterile needle to sterile syringe.
- Have assistant hold joint in the desired position to maximize access with needle.
- Palpate landmarks once more.
- Advance needle and syringe, applying gentle negative pressure with syringe once the needle tip is below the skin until synovial fluid is seen in the needle hub and syringe.
- Often, the needle tip will strike bone. If so, the pressure should be released from the syringe, and the needle tip “walked” off the bone and further into the joint space. “Walking” refers to gentle probing using the needle tip, seeking out a path of lesser resistance within a few millimeters of the site where bone was encountered. The needle is partially withdrawn—but remains below the skin surface—and is redirected and readvanced during “walking.”
- When the needle tip advances without striking bone, negative pressure may be reapplied with the syringe until synovial fluid enters the hub of the needle and the syringe.
- If blood is encountered, the procedure should be stopped and then restarted with a new needle and syringe.
- At least 1 mL should be sought if possible, but many successful arthrocentesis procedures will produce < 0.5 mL of joint fluid.
- It is essential to release negative pressure from the syringe prior to withdrawing the needle to avoid blood contamination from vessels in the joint capsule and skin.

POSTPROCEDURE

- Immediate assessment of the synovial fluid includes:
  - Turbidity; the fluid should be clear and pale tan or pale yellow.
  - Viscosity test; a drop of fluid placed between two slides, which are then separated, should appear somewhat viscous or gummy. Synovial fluid that has little viscosity (like water) is abnormal.
  - Odor; none is expected in normal synovial fluid. Note: If an airborne zoonotic organism is part of the differential diagnosis, assessing the odor may be hazardous and should be avoided.
- Laboratory samples to be submitted include (in general order of priority because volume of fluid retrieved maybe small):
  - Fresh smears on microscope slides
  - Whole fluid in red-top tube
  - Whole fluid in lavender-top tube
  - Culture swab
- Routine sedation/anesthetic recovery as needed

ALTERNATIVES AND THEIR RELATIVE MERITS

- Radiographs:
  - Useful for detecting subchondral bone lesions
  - Do not replace synovial fluid analysis
- Bone scan:
  - Identifies multiple joint involvement
  - Identifies relative degree of severity between joints
  - Does not give etiologic diagnosis

- Synovial biopsy:
    - Appropriate if joint capsule is thickened or deformed (grossly, radiographically) and synovial fluid analysis is unrewarding

AUTHOR: ETIENNE CÔTÉ

Arterial Blood Sampling and Arterial Catheterization

SYNONYMS

Arterial phlebotomy, arterial puncture

OVERVIEW AND GOALS

To access the peripheral artery with a needle or catheter, typically for arterial blood gas (ABG) analysis or for arterial blood pressure (BP) monitoring, respectively

INDICATIONS

- Assessment of ABG and acid-base status, usually in animals with systemic illness or a respiratory problem
- Placement of an arterial catheter for BP measurement, usually in critically ill or anesthetized animals

CONTRAINDICATIONS

Bleeding disorder: assess for overt signs of bleeding or history of bleeding

EQUIPMENT, ANESTHESIA

Sedation or general anesthesia not usually required; manual restraint only; one or two assistants may be needed and:

- Hair clippers
- Sterile scrub material
- 6-10 3 × 3 gauze squares
- Arterial catheter (standard over-the-needle IV-type catheter):
  - Cats, dogs < 10 kg: 24- or 25-gauge
  - Dogs 10-25 kg: 22-gauge
  - Dogs > 25 kg: 20-gauge
- White tape, 2 cm (1 inch) width
- Heparinized sterile saline flush
- Pressure transducer and monitor (if continuously monitoring direct arterial pressure)

For arterial blood sample (one time):

- 1-mL heparinized syringe
- Needles (guidelines for size same as for arterial catheters, above)

ANTICIPATED TIME

- About 5 minutes (arterial blood sample)
- About 10-15 minutes (arterial catheter)

PREPARATION: IMPORTANT CHECKPOINTS

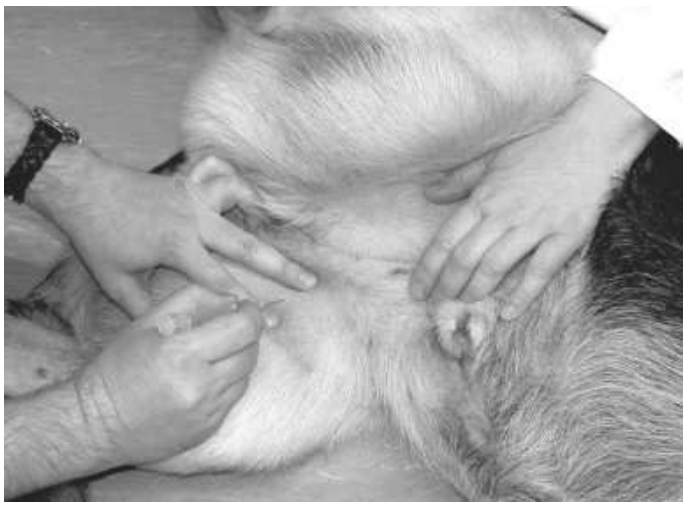
- Thoracic radiographs are indicated prior to or concurrently with ABG sampling when the purpose of arterial sampling is to assess arterial oxygen or CO2 levels.
- Samples for venous blood gas measurement generally are easier to obtain and may be useful for measuring certain parameters in arterial blood (e.g., pH, Pco2, $Hco^{-}3$).
- Confirmation of normal platelet count
- Confirmation of absence of overt signs of bleeding disorders or history of bleeding

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Pressing excessively firmly on the artery when palpating for the pulse to locate the proper site for puncture; excessive pressure abolishes the pulse and makes accurate puncture virtually impossible
- Inserting the needle or catheter without having convincingly identified the course of the artery (by repeated palpation of the arterial pulse)
- Crossing both artery and vein with the needle, resulting in venous contamination of arterial sample (artifactual low Po2 result)
- Mistakenly advancing the needle or catheter with the bevel up rather than down
- Inadequate manual pressure on the site after the procedure:
  - Hematoma possible if inadequate direct pressure is applied after the procedure or if animal has a bleeding disorder or vasculitis.
- Artery may not be patent after arterial catheterization, but the effect of this loss of patency on the animal typically is minimal (limits the source of access for arterial blood samples in the immediate future but rarely causes ischemia distal to the site of puncture).

PROCEDURE

- Clip hair over the area of interest (dorsal metatarsus: dorsal surface of distal hind limb, from hock to beginning of phalanges; inguinal area: femoral triangle, from inguinal crease [medial side of proximal hind limb where thigh meets caudal abdomen] toward stifle).
- Restrain animal in lateral recumbency (example here: left lateral):
  - Dorsal metatarsal arterial approach:
    - Right-handed clinician: fully extend animal's hock by drawing paw of upper hind limb (right paw if animal is in left lateral recumbency) toward self using the left hand.
    - While keeping leg extended using traction on the right hind paw with the left hand, palpate the dorsal metatarsal pulse with the tips of the index and middle fingers of the right hand on the dorsal surface of the right metatarsus. The artery lies between the third and fourth metatarsal bones.
    - Palpating the dorsal metatarsal pulse simultaneously with two fingers reveals the course of the dorsal metatarsal artery.
    - Caution: The course of the metatarsal artery must be identified convincingly by repeated palpation of the dorsal metatarsal pulse before beginning to insert the needle or catheter.
    - Then proceed as described further below (after “Femoral arterial”): “Both dorsal metatarsal and femoral approaches.”
  - Femoral arterial approach:
    - Right-handed clinician: Fully extend the animal's dependent hind limb (e.g., left hind leg, if in left lateral recumbency) to expose the medial inguinal area of that leg. In cooperative (or anesthetized) cats and dogs, the leg may be restrained minimally or not at all. In recalcitrant animals, a second restrainer is needed to hold the leg in an extended stable position.
    - Palpate the femoral pulse at its dorsal-most location, near the inguinal crease. It should be palpated with the tips of the index and middle fingers of the right hand (for a right-handed clinician). The femoral artery lies midway between the cranial-most and caudal-most aspects of the thigh, at the usual location for palpation during physical examination.
    - Palpating the pulse of a femoral artery simultaneously with two fingers 1-2 cm apart reveals the course of the femoral artery, namely a straight line between the two points on the artery where the pulse is palpated (i.e., between the two fingers).
    - Caution: This line (the artery) must be identified convincingly by repeated palpation of the femoral pulse before beginning to insert the needle or catheter.
  - Both dorsal metatarsal and femoral approach:
    - Repeat brief aseptic scrubbing procedure once pulse has been palpated satisfactorily.
    - There is no need for the assistant to “hold off” or “raise” the vessel, as is done for venous samples, because of the normal arterial pressure.
    - Break the seal in the syringe by withdrawing and depressing the plunger once. The syringe (with needle) is held in the right hand like a pen. It enters the skin obliquely at 45°. If placing an arterial catheter, the 45° angle between skin and catheter is also necessary, but the catheter is held the same way an IV catheter is normally held.
    - The bevel of the needle/catheter points down, not up (contrary to venous blood samples and IV catheters).
    - The needle is introduced under the skin and into the artery, again advancing while maintaining a 45° angle between the syringe and the vessel.
    - A flashback of blood indicates successful entry into the artery. Pulsatile flow is visible when an uncapped catheter is used. With a needle and syringe, arterial pressure will slowly but steadily “self-fill” the syringe, and negative pressure (as with a venous blood sample) is not necessary.
    - Typically, a sample for ABG analysis requires approximately 0.5 mL of blood, which should be placed in an ice bath if analysis in the following 10 minutes is not possible.
    - An arterial catheter should be fixed in place, capped, and flushed, or it should be connected to a pressure transducer for pressure measurement. It should be identified clearly with a label as being arterial.



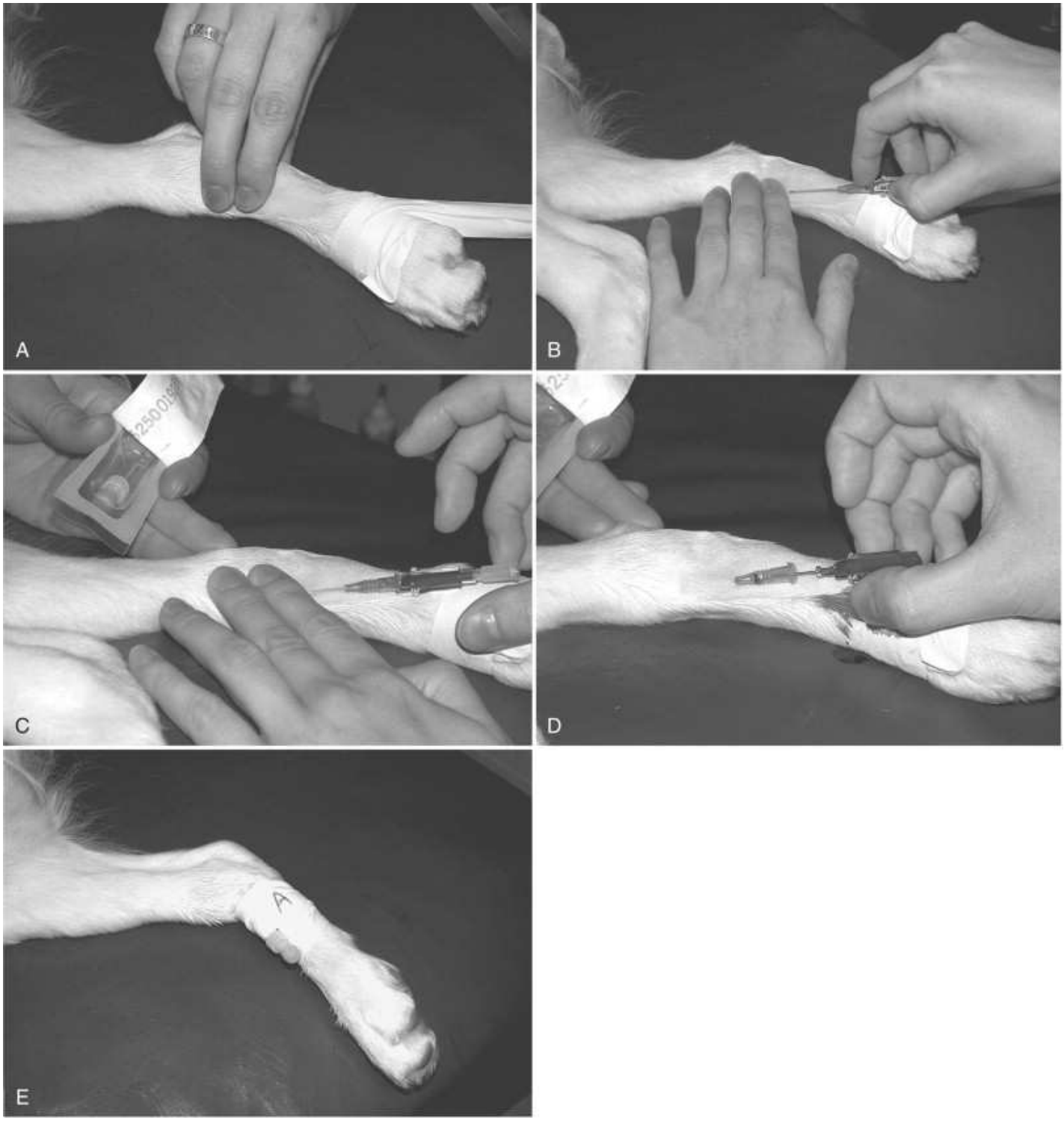
ARTERIAL BLOOD SAMPLING AND ARTERIAL CATHETERIZATION Blood sampling from femoral artery, dog in left lateral recumbency. Cranial is to lower right. Assistant holds right hind limb elevated and prepuce retracted. Phlebotomist identifies course of left femoral artery between middle and index fingers by palpation of femoral pulse with both fingers and prepares to enter artery, needle bevel down.

POSTPROCEDURE

Successful outcome:

- Successful arterial puncture for blood gas measurement improves animal care via treatment adjustments.

- Successful arterial catheter placement improves animal care via minute-by-minute adjustments of factors that influence arterial BP (e.g., IV fluids, pressor drugs, anesthetic agents) in anesthetized or critically ill animals.



ARTERIAL BLOOD SAMPLING AND ARTERIAL CATHETERIZATION Placement of arterial catheter in a dog's right metatarsal artery. **A**, Palpation of arterial pulse. **B**, Introduction of catheter, using right hand while simultaneously palpating arterial pulse for orientation using left hand (right-handed clinician). **C**, Flashback of blood confirms proper placement. **D**, Removal of stylet in preparation for placement of catheter cap. **E**, Capped catheter is flushed with heparinized saline, wrapped, and clearly marked as arterial.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Repeat thoracic radiographs:
  - Noninvasive; provides information on lesions of respiratory system only. Minimal usefulness for assessing subtle, moment-by-moment changes.
- Venous blood gas analysis:
  - Sampling is easier.

    - Few other advantages over arterial blood, unhelpful regarding Po2
- Arterial cutdown for arterial blood sampling:
    - Easier access to vessel
    - More invasive

AUTHOR: ETIENNE CÔTÉ

Angiogram, Nonselective

SYNONYMS

Nonselective radiographic contrast study of the heart

OVERVIEW AND GOAL

To perform an IV contrast study that highlights the venous return to the heart and the right-sided cardiac structures

INDICATIONS

- Suspected venous obstruction (see p. 263)
- Ill-defined abnormalities of the right side of the heart when echocardiography is equivocal or unavailable
- Pulmonary thromboembolism: rarely diagnostic as a nonselective procedure (often requires power-injected contrast through large-bore catheter in pulmonary artery)

CONTRAINDICATIONS

- Lesions that are equally or better defined without the administration of contrast (i.e., via echocardiography)
- Hypersensitivity to contrast material
- Acute renal failure (decreased ability to excrete contrast material and/or risk of contrast-induced renal failure)
- Arteriovenous (AV) fistulae are not an indication for this procedure. AV fistulae shunt from artery to vein and require selective arteriography.

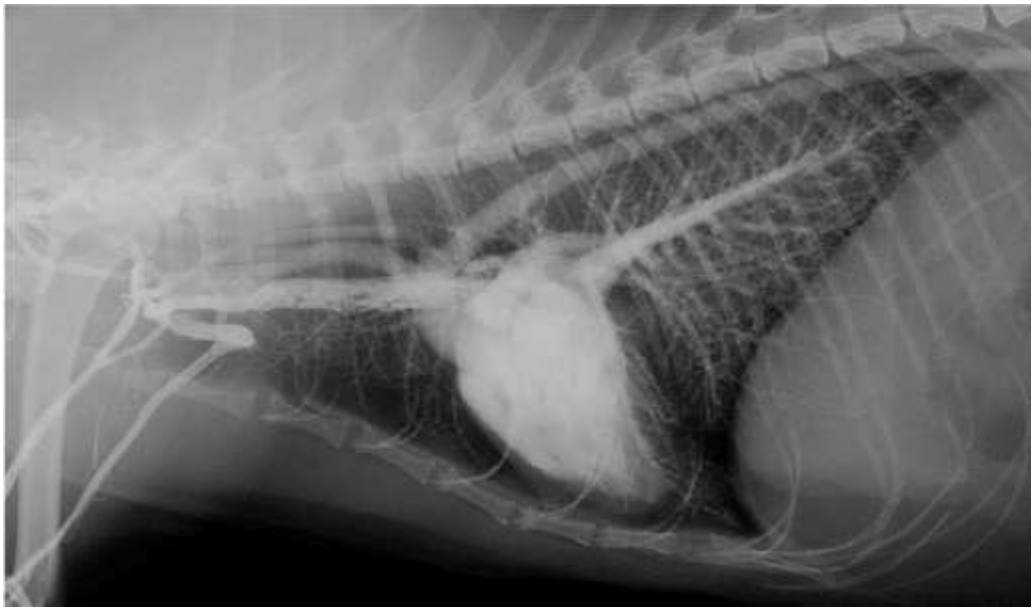
EQUIPMENT, ANESTHESIA

- Can be done with or without anesthesia; sedation in most patients (see end pages inside text cover).
- Hair clippers
- Surgical scrub solution, rubbing alcohol, and gauze/sponge for prepping skin
- IV catheter (jugular or peripheral)
  - A 19- or 20-gauge catheter for cats or small dogs; a 16- or 18-gauge catheter for medium or large dogs
- The catheter cap or T-port should be a screw tip to avoid detachment under high pressure of contrast injection.
- ± Sterile surgical gloves if using a nonsheathed jugular catheter
- ± Lidocaine for local anesthesia if large-bore jugular catheter (e.g., 18 gauge or larger)
- Routine tape and bandage material for catheter fixation to skin
- ± Suture material (e.g., 3-0 nylon), needle holders, and suture scissors if anchoring jugular catheter to skin of neck
- Syringe for IV contrast material. A syringe with a screw tip is recommended to avoid pressure-induced separation of the syringe from the T-port or catheter cap during high-pressure injection of contrast.
- Transparent, aqueous IV contrast material (iodinated, ionic; e.g., Renografin-76, Renovist 69%, Hypaque-M75, Conray 60%); maximal total cumulative dose given during procedure, assuming maintenance IV fluid administration to promote diuresis: 3 mL/kg
- Radiographic facility, including radiographic machine, films and cassette, and developer and/or fluoroscopic unit

Adapted from Wise M: Nonselective angiocardiography in the normal dog and cat, Vet Radiol 23:144–151, 1982.

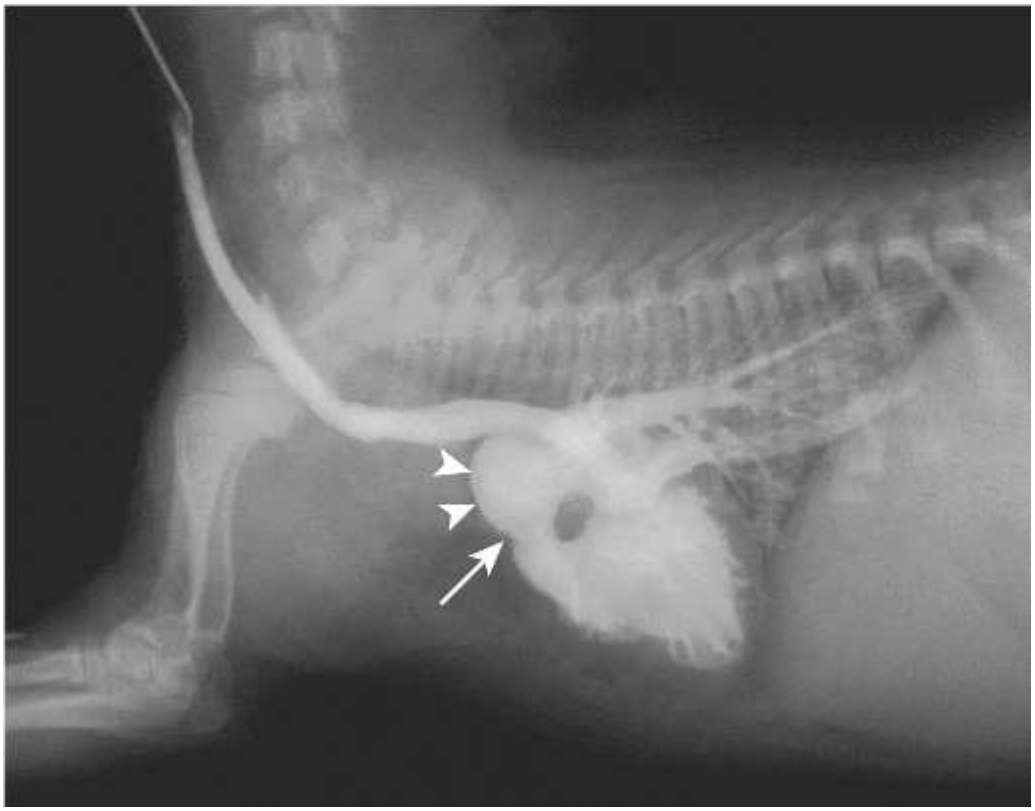
	DOG	CAT
Site Enhanced by Contrast	**Time (sec) from Start of Injection**	**Time (sec) from Start of Injection**
Cranial vena cava	1–2.5	0.5–1.5
Right ventricle	2–3	1.5–2.5
Pulmonary arteries	2–3	1.5–2.5
Left atrium	4–5.5	4.5–7
Left ventricle	4.5–6	5–7

	DOG	CAT
Site Enhanced by Contrast	**Time (sec) from Start of Injection**	**Time (sec) from Start of Injection**
Aorta	4.5–6.5	5–7



ANGIOGRAM, NONSELECTIVE Lateral nonselective angiogram in a normal cat. Contrast was injected in a cephalic vein; right side of the heart and pulmonary circulation are opacified, and early opacification of left side of the heart and aorta is also seen.

(Courtesy Dr. Brett Kantrowitz.)



ANGIOGRAM, NONSELECTIVE Lateral nonselective angiogram in a dog with valvular pulmonic stenosis. Contrast was injected in a jugular vein. Narrowing (stenosis) is seen at the level of the pulmonic valve *(arrow)*. Marked poststenotic dilatation of the pulmonary trunk is apparent *(arrowheads)*.

(Courtesy Dr. Brett Kantrowitz.)

ANTICIPATED TIME

About 15-30 minutes after catheter placement

PREPARATION: IMPORTANT CHECKPOINTS

- Thoracic radiographs: must precede contrast study, because a diagnosis may be apparent from these alone.
- Congestive heart failure must be controlled prior to procedure.
- Clipping of hair over vein to be catheterized (typically jugular or cephalic); jugular may be preferable in small animals (<10 kg) because the cephalic can be too small to allow easy flow of viscous contrast solution through catheter.
- A 12-hour fast if sedating animal
- Placement of IV catheter
- Discuss possible complications with owner as indicated in the following paragraphs (see p. 1293).

POSSIBLE COMPICATIONS AND COMMON ERRORS TO AVOID

Nondiagnostic study; improve likelihood of diagnostic result by:

- Using large-diameter catheter
- Using fluoroscopy instead of serial radiographs
- Injecting contrast rapidly
- Injecting adequate volume of contrast

PROCEDURE

- Catheter patency is checked.
- Animal is placed on radiographic table, usually in lateral recumbency.
- Position of radiographic beam is set over area of interest (usually thorax, neck, or limb).
- Contrast is injected IV by hand as quickly as possible (maximal manual pressure). Recommended single dose is 1-2 mL/kg (440 mg iodine/kg).
- Radiographic views are obtained at the appropriate times, or the flow of contrast is observed in real time with fluoroscopy.

POSTPROCEDURE

IV fluid diuresis is provided if appropriate. The goal is to increase excretion of contrast medium, but excessive volume load must be avoided if heart disease exists.

ALTERNATIVES AND THEIR RELATIVE MERITS

- An echocardiogram and thoracic radiographs should be performed prior to angiography:
  - Noninvasive, excellent diagnostic yield
- Vascular ultrasound:
  - Noninvasive but limited by lungs: poor visualization of intrathoracic vessels
- Arterial blood gas (ABG) analysis:
  - If pulmonary vascular disease
- Selective angiography/cardiac catheterization:
  - If cardiac or pulmonary vascular lesion still unclear

AUTHORS: ETIENNE CÔTÉ, BRETT KANTROWITZ

Acupuncture

Additional Images Available on Website

OVERVIEW AND GOAL

- Acupuncture may be used in concert with other methods of integrative pain management for the control of acute or chronic pain.
- Most clinicians report that acupuncture either resolves the clinical problem or serves well as a maintenance therapy for a lifelong condition in 80% of cases.
- There are several indications for the use of acupuncture as an adjunct treatment for specific visceral organ diseases.
- The many different techniques used for stimulating an acupuncture point may be a source of confusion (e.g. heat, ultrasound, laser, or implant). Each method has its purpose and particular virtues in a given clinical setting.
- There are several neurophysiologic mechanisms which describe acupuncture effects. Spinal gates, central nervous system (CNS) endorphin release, and viscerocutaneous reflex arcs are a few of these.
- The teaching and clinical applications of acupuncture may be based on any of several different methodologies. The principle systems are known as *traditional Chinese medicine (TCM); the eight principles;*and *medical, empirical,*and *French energetic acupuncture.*The essential differences between them are matters of history and clinical philosophies. Each system uses the same needles and inserts them into the same acupuncture points. Differences of clinical outcome between these methodologies are difficult to measure and appear to be slight.

INDICATIONS

- Chronic orthopedic pain, especially:
  - Hip dysplasia
  - Cranial cruciate ligament injury
  - Elbow dysplasia
  - Other degenerative joint disease
- Postoperative (acute) pain
- Back pain (including nonsurgical intervertebral disk disease [IVDD])
- Asthma syndromes
- Demodectic mange
- Acral (lick) granuloma
- Malaise of chemotherapy
- Inflammatory bowel disease

Note: In the abstract, acupuncture is capable of influencing virtually any disease process or organ system in the body. Although we may accept the theoretical basis for this point of view, there are numerous medical and practical reasons to avoid considering acupuncture as an isolated treatment modality. Acupuncture may be helpful as the sole treatment for hypothyroidism, for example, but thyroid supplementation is known to be successful, cost-effective, and safe.

The use of particular acupmuncture points and related techniques (tongue and pulse diagnosis) to suggest or confirm a diagnosis is established in TCM of human beings. While the development of this aspect of acupuncture clinical science in animals is progressing, there is less validated information to advocate its use for this purpose on a routine basis.

CONTRAINDICATIONS

- Pregnancy and tumors are often cited as relative contraindications. Use of acupuncture therapy in patients with these conditions should be reserved for clinicians with advanced knowledge of safe protocols.
- There are specific cautions for the use of electroacupuncture, which should be understood by practitioners who use this modality.

EQUIPMENT, ANESTHESIA

- Needles, 28-38 gauge, sterile, disposable, solid, acupuncture needles
- Microamperage electrostimulator
- Moxa (an herbal product)
- Milliwatt diode laser equipment is useful for younger animals, birds, ferrets, and pocket pets.
- Anesthesia is not indicated; sedation is rarely needed.

ANTICIPATED TIME

- Varies from 15-60 minutes for each treatment session
- Particular problems may be resolved following a single treatment, but most will need from 3-8 treatments.
- Maintenance treatments for chronic conditions (e.g., hip dysplasia, epilepsy) may be performed at intervals from 1-6 months.

PREPARATION: IMPORTANT CHECKPOINTS

- Acupuncture may be performed on the sedated or anesthetized patient, but this is seldom indicated and may cause more problems than it prevents.
- Acupuncture will almost always be less difficult and more acceptable when performed without physical restraint.
- Medium- and large-breed dogs typically will be more relaxed when treated on a low bench or on a blanket on the floor instead of the typical exam table.
- Quiet surroundings and the presence of the owner can provide reassurance, especially for cats.
- There is no requirement for preparation of the skin at the site of needle insertion, even in immunosuppressed patients.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO BE AVOIDED

- Clinically relevant complications of acupuncture in animals are rare, and patients do not require hospitalization.
- It is common for patients to experience somnolence for 12-24 hours following treatment.
- A stuck or “frozen” needle (resists removal) will often occur: this is easily resolved by further manipulation of the needle for a few more minutes.
- Immediately following the first treatment, patients may show a transient increase in disease signs of the condition being treated.
- Concurrent use of pharmaceuticals is not a contraindication for acupuncture.
- Local infection or seizures occur in <0.1% of patients.

PROCEDURE

- Acupuncture is normally performed on an outpatient basis.
- While some practitioners find simple (minimal) methods of restraint to be needed for some cases, most patients will be treated without forceful or unpleasant restraint.
- Most patients do not feel most needles; when they do, the clinician may elect its removal.
- Needles remain in place for an average of 10-20 minutes before removal.
- Treatments are repeated at intervals from 24 hours to several weeks.
- Following the appearance of a useful response to treatment by the patient, supportive or maintenance treatments may be needed in some cases, especially for chronic pain conditions in older animals.
- For a number of visceral organ, immune system, dermatologic, and cases of back pain, there may not be a requirement for maintenance treatments.

POSTPROCEDURE

- Other than occasional somnolence, there are few postprocedure considerations following routine acupuncture.
- It is common to find that the requirement for systemic analgesic or antiinflammatory drugs is reduced following acupuncture.

ALTERNATIVES AND THEIR RELATIVE MERITS

- The relative merit of pharmaceutical alternatives varies widely with the disease being treated.
- For treatment of pain, nonsteroidal antiinflammatory drugs (NSAIDs) can be equally effective but carry the risk of a number of adverse drug reactions in a significant percentage of patients.
- Treatment of chronic orthopedic pain is best accomplished with multimodal therapies, and the combination of a low-dose NSAID and acupuncture is often very effective and reduces the likelihood of renal or gastrointestinal injury from the use of NSAIDs alone.
- For conditions likely to persist for the rest of the patient's life (e.g., osteoarthritis), it may be appropriate to place a permanent implant in the acupuncture points which have been successful in treatment of the problem. Small rods or spheres of sterile metallic 0.999 gold are often used in this way for long-term treatment of degenerative joint disease, for example.
- When acupuncture fails to provide adequate clinical results or cannot be continued for other reasons, it may be necessary to consider pharmaceutical or surgical options.

AUTHOR: ARTHUR I. ORTENBURGER

Abdominocentesis

SYNONYMS

Abdominal paracentesis, abdominal tap, belly tap

OVERVIEW AND GOAL

To use a needle and syringe to obtain a sample of abdominal fluid

INDICATIONS

- Visible abdominal distention with palpable fluid wave
- Ultrasound-detected ascites
- Generally diagnostic, not therapeutic (versus abdominal drainage as already described, p. 1192)

CONTRAINDICATIONS

- Abdominal enlargement due to mass or organomegaly, without ascites, because of risk of organ damage without benefit of fluid retrieval for analysis
- Bleeding disorders

EQUIPMENT, ANESTHESIA

- Procedure is done with manual restraint only and without anesthesia (local or general), except in fractious or excited animals.
- Note: Pressure of large-volume ascites on the diaphragm may distress animals during restraint. In such cases, sedation should not be administered, but rather the procedure may be performed with the animal in lateral recumbency or in standing position.
- Hair clippers
- Surgical scrub solution, rubbing alcohol, and gauze/sponge for prepping skin
- 6-10 4s × 4 gauze pads
- Needles (1-5; 2 inches long; 20-, 22-, or 25-gauge based on animal size and body wall thickness); a 22-gauge needle is generally preferred.
- Syringes (1-3, 6 mL or greater)
- Sterile tubes for cytologic examination and fluid analysis (red and lavender tops)
- Ultrasound guidance optional

ANTICIPATED TIME

About 1-10 minutes

PREPARATION: IMPORTANT CHECKPOINTS

- Assess for risk of bleeding disorder if indicated overtly (e.g., epistaxis, hematuria, melena, petechiae/ecchymoses) or suspected via primary diagnosis (e.g., hepatopathy).
- Use ultrasound guidance if necessary for small volumes of ascites.
- Advise owner of possible complications, as listed in the following paragraphs.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- “Dry tap,” no fluid withdrawn: insufficient abdominal fluid (check with ultrasound); fluid is too viscous or particulate (change needle and syringe because clot may be in needle; check fluid appearance with ultrasound); wrong area was sampled (change animal's posture—e.g., try with animal standing—or site of centesis).
- Centesis not representative of underlying process: assess for extraabdominal causes of ascites such as cardiovascular, hypoalbuminemia, and vasculitis as indicated, and pursue primary intraabdominal causes further, beginning with abdominal ultrasound. If negative, consider nonexfoliating intraabdominal disease.
- Laceration of organ with needle tip. Decrease risk with:

    - Good animal restraint (sedation if animal is fractious or excited)
    - Ultrasound guidance if volume of ascites is small
    - Single-dimensional, in-out motion of needle, with minimal or no redirecting
- Pooling of ascitic fluid subcutaneously postprocedure; usually resolves on its own

PROCEDURE

- Place animal in dorsal recumbency or lateral recumbency. If dyspnea is present, lateral recumbency is preferable. Very small, dyspneic animals (cats, toy-breed dogs) that are cooperative may be restrained in an upright sitting position ("begging" posture) in a technician's arms; muzzling is recommended owing to proximity to technician.
- Aseptically scrub and prepare the clipped area, which typically will be on the midline just cranial or just caudal to the umbilicus. Position adjusted according to any known risk (e.g., cavitated abdominal mass in that location).
- Connect needle to syringe and advance needle through skin and body wall, directing the needle cranially and dorsally into the abdomen. The needle is meant to pass through the linea alba/body wall slightly obliquely, such that the tract left when the needle is removed can close on itself. The obliquity comes from the dorsocranial orientation of the needle on the midline instead of direct dorsal orientation.
- Once tip of needle is just under the skin, pull back on syringe plunger intermittently or continuously and observe for fluid "flashback" into syringe.
- Depth of penetration (2-3 mm to 3 cm) is relative to the animal's size and amount of body fat.
- Once fluid flow is established, the desired amount of fluid can be aspirated, and then the needle is withdrawn from the abdomen smoothly and quickly.
- Immediate tests that can be performed include:
    - Visual inspection for turbidity and color. Note: Hemorrhagic samples with hematocrit > 5% appear as red as blood.
    - Odor; foul smell commonly associated with anaerobic infections. Note: Be aware of the possibility of airborne zoonoses if applicable (e.g., systemic fungal, other), and avoid assessing odor in such cases.
    - Hematocrit: compare to peripheral blood to rule out hemorrhage.
    - Total protein: compare to peripheral blood to rule out hemorrhage, exudative process.
    - Creatinine, potassium: compare to peripheral blood to rule out uroabdomen.
    - Cytologic evaluation
- The fluid should be fractionated into two tubes (EDTA [lavender-top tube], and sterile glass [red-top tube]), and a sample should also be saved on a sterile swab for bacterial culture. The two tubes are submitted for standard fluid analysis including cytologic evaluation. The bacterial swab can be submitted for culture immediately if bacterial infection is suspected clinically, or it can be saved for later submission in case cytologic results indicate the possibility of bacterial infection.

POSTPROCEDURE

Subcutaneous pooling of ascitic fluid is common with partial drainage of large-volume ascites; may resolve spontaneously or require abdominal wrap (barring dyspnea).

ALTERNATIVES AND THEIR RELATIVE MERITS

- Repeat centesis under ultrasound guidance:
    - Better ability to reach small pockets of ascites
- Diagnostic peritoneal lavage (see online chapter: Diagnostic Peritoneal Lavage):
    - Increases ability to sample small volumes of ascites
    - Often poorly diagnostic, somewhat cumbersome
    - Generally replaced by ultrasound-guided centesis
- Laparoscopy (see p. 1298) or exploratory laparotomy for nonexfoliating, primary intraabdominal disorders causing ascites:
    - Definitive diagnosis for abdominal masses, mesothelioma/carcinomatosis, and other similar conditions

AUTHOR: ETIENNE CÔTÉ

Abdominal Drainage

SYNONYMS

Large-volume abdominal paracentesis, peritoneal drainage

OVERVIEW AND GOAL

To evacuate large-volume ascites via percutaneous placement of a sterile tube into the abdomen

INDICATIONS

- Tense ascites caused by chronic passive congestion (right heart failure, chronic hepatopathies)
- Abdominal compartment syndrome

CONTRAINDICATIONS

- Hemoabdomen: voids autotransfusion; delays control of cause of hemoabdomen
- Coagulopathy: risk of hemorrhage if laceration of abdominal organ occurs with needle tip

EQUIPMENT, ANESTHESIA

- Local anesthesia
- Manual restraint; sedation needed only rarely. Note: Animals often are restless during restraint owing to pressure of ascites on diaphragm; in such cases, the procedure may be preceded by large-volume needle centesis or may need to be performed with the animal in standing position.
- Hair clippers
- Surgical scrub solution, rubbing alcohol, and gauze/sponge for prepping skin
- Use 0.5-15 mL 2% lidocaine for local anesthesia. The volume is based on body weight, 1-70 kg. Discomfort from lidocaine infusion can be reduced by adding 0.05-0.2 mL sodium bicarbonate for injection (8.4% = 84 mg/mL = 1 mEq/L) and by warming solution to body temperature (armpit method).
- Alligator forceps (preferable) or mosquito hemostats, 1 pair
- Red rubber feeding tube: sterile 5-16 Fr tube, based on body size
- Sterile surgical gloves
- Suture material (e.g., nylon 2-0) and needle
- A#11 sterile scalpel blade
- Sterile needle holders
- Sterile suture scissors
- Elizabethan collar
- Sterile gauze squares (postprocedure)
- Tissue glue (postprocedure)

ANTICIPATED TIME

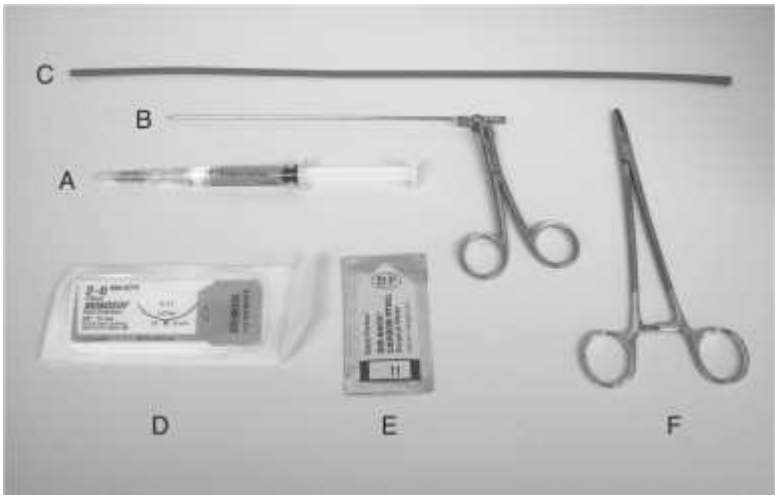
15-40 minutes, plus drainage time

PREPARATION: IMPORTANT CHECKPOINTS

- Weigh animal immediately before procedure (to quantify volume of fluid lost).
- Advise owner of possible drawbacks:
    - Hair clipping required
    - Procedure generally palliative; underlying problem not corrected
    - Low risk of infection or other complications
- Have Elizabethan collar ready to place on the animal as soon as tube placement is complete.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Overall, complications very uncommon; approximately 5%-10% incidence of irritation or dehiscence of incision, responding to topical treatment. Major complications are <1%.
- Concerns for hypovolemia, hypotension, hypoalbuminemia, and ascending bacterial peritonitis appear unjustified, given lack of occurrence in large case series (unpublished data).
- Elizabethan collar must be on the animal at all times during drainage to avoid self-induced damage to the tube.
- Once in place in the standing animal, the tube ± stopcock may be caught in the grate flooring of the cage when the animal lies down. Covering the grate on the floor of the cage with towels helps prevent this complication.

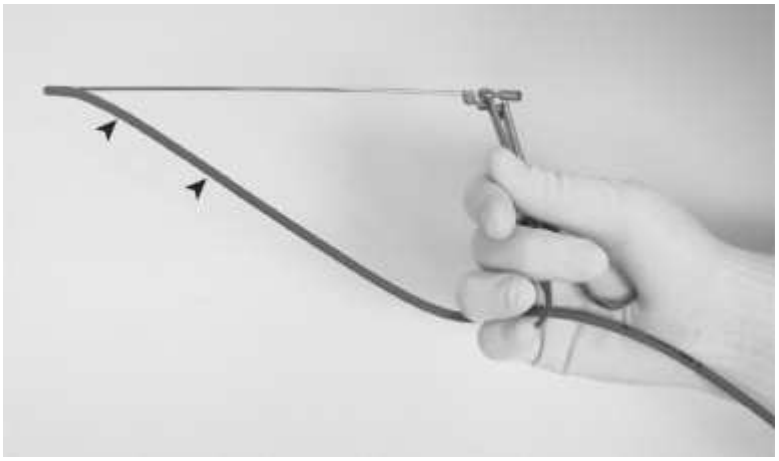


ABDOMINAL DRAINAGE Equipment and materials used for abdominal drainage. **A**, 0.5-15 mL 2% lidocaine for local anesthesia. **B**, Alligator forceps. **C**, Sterile red rubber feeding tube, 5-16 Fr gauge. **D**, Suture material (e.g., nylon 2-0) and needle. **E**, #11 sterile scalpel blade. **F**, Sterile needle holders.

PROCEDURE

- Clip hair widely (ventral abdomen), with umbilicus approximately at center of clipped area. Since the procedure does not require surgical draping, long hair must be trimmed back extensively.
- Restrain in lateral recumbency.
- Wide surgical scrub and prep, centered on ventral abdominal midline and just cranial to the umbilicus.
- Lidocaine infusion at planned point of entry; on abdominal midline, generally just cranial to the umbilicus. Use multiple (e.g., 6-8) small subcutaneous boluses.
- Note: More cranial is better in most males (greater distance from prepuce, so less risk of contamination), but it is important to avoid too cranial in animals with hepatomegaly (right-sided heart failure, some liver diseases).
- Note: Lidocaine infusion must be wide (cranial-caudal, left-right) and deep (reaching all layers, including peritoneum) and involves injecting many small pockets of lidocaine throughout the region of the planned incision.
- Caution: When redirecting, avoid subcutaneous tissue laceration with the needle tip. After each infiltration of a small pocket of lidocaine, partially withdraw the needle, redirect it, and then readvance it for the next infiltration. The multiple infiltrations can all be accomplished via a single point of needle entry (i.e., radial redirection of the needle).
- After opening the sterile gloves, keep the paper wrapper flat and use as a sterile surface. Wear the sterile gloves from this point onward. Use the suture scissors for making three to five additional drainage holes in the red rubber feeding tube to avoid omental plugging during drainage.
- Note: To make extra holes prior to inserting the tube into the abdomen, kink the red rubber feeding tube with thumb and forefinger and snip off the corner of the folded edge; unfolded edge reveals a small oval hole (needs to be <50% of tube's circumference to prevent weakening it). Repeat to make several holes along the distal half of the tube. The suture scissors are kept sterile for later in the procedure.
- Using the #11 scalpel blade, make a stab incision cranial to the umbilicus on the ventral abdominal midline at the center of the lidocaine-infiltrated area.
- Note: To avoid an excessively large incision, hold the #11 scalpel blade between the thumb and forefinger. The point at which the blade is held between the thumb and forefinger leaves a maximal width of the exposed blade that is the same as, or just slightly greater than, the diameter of the red rubber feeding tube to be inserted; that is, the fingertips act as a guard to prevent excessive insertion of the blade. For example, if a 10 Fr red rubber feeding tube will be used (approximate outer diameter of tube is 6 mm), then the scalpel blade should be held such that the maximum exposed width of the blade (at the fingertips) is 6 or 7 mm.
- The blade is set aside but kept sterile in case enlargement of the incision is necessary.
- The tube is inserted into the abdomen. Tube insertion is facilitated by grasping the tip in the lower jaw of an alligator forceps, closing the forceps, and advancing tube and forceps through the hole. Mosquito forceps are an acceptable alternative. Often the hole in the skin and the hole in the body wall are not exactly aligned because of imperceptible shifting of the tissue planes. Blunt probing with the tube and forceps may be necessary to find the hole in the abdominal wall. If excessive

pressure is required, the incision may need to be enlarged using the #11 scalpel blade.
- Any sign of discomfort on the animal's part is an indication for additional lidocaine infiltration at and around the insertion site.
- Once the tube is inserted appropriately (a release of pressure may be apparent as the tube pierces the peritoneum and initiates voluminous flow of ascites), it is advanced until it protrudes from the abdominal wall by only 1-2 inches (several cm).
- The tube is sutured in place, using 2-0 or 3-0 nylon, with both a circumferential purse string and a transfixation (suture through the tube) ligature.
- If a rapid flow of fluid occurs, a clamp or partially closed three-way stopcock (usually requiring a “Christmas tree” type of adapter to fit most red rubber feeding tubes) can be used for moderating the rate of flow.
- Complete drainage is possible in minutes (often 15-20 minutes) or 2-6 hours (animal is placed in a cage with a grated floor to allow drainage; towels are placed on top of the grate to prevent a clamp/stopcock from becoming caught in the grate).
- Caution: An Elizabethan collar is essential for preventing the animal from chewing at and transecting the tube.
- The system may be closed (drainage bag) or open; if open, as is done most commonly, the animal must be monitored for ongoing drainage, and the tube should be removed immediately when flow ceases to reduce the risk of ascending infection.
- When drainage has ended, the animal is again restrained in lateral recumbency, and the nylon ligatures are cut. The tube is removed, taking care not to withdraw omentum. The skin incision may be dried with a sterile gauze, and tissue glue may be applied to close it. If the incision is >5 mm, a skin suture or staple may be placed.



ABDOMINAL DRAINAGE Sterile red rubber feeding tube with additional holes in its distal part *(arrowheads)*. Tube is grasped in jaws of alligator forceps and passed into abdominal cavity through a small incision on ventral abdominal midline.

POSTPROCEDURE

- Weigh the animal; record weight of lost fluid (for future reference and also to know accurate lean body weight for medication dosages).
- Dripping of ascitic fluid from incision is common despite tissue glue and generally resolves in minutes to hours. If it is persistent, a skin suture or staple may be necessary.
- Dripping and any subcutaneous pooling of ascitic fluid are minimized by allowing complete rather than partial drainage during procedure.

ALTERNATIVES AND THEIR RELATIVE MERITS

Abdominocentesis with needle and syringe:

- Less invasive
- Very time-consuming for large volumes (e.g., 1 l or more)
- Generally ineffective at removing most or all of ascites

Abdominocentesis with suction/vacuum:

- Faster
- May aspirate omentum or other abdominal structure
- Drainage less complete

AUTHOR: ETIENNE CÔTÉ

Buccal Mucosal Bleeding Time

SYNONYMS

Bleeding time, BMBT

OVERVIEW AND GOALS

To quickly and easily assess primary hemostasis and evaluate formation of a platelet plug

INDICATIONS

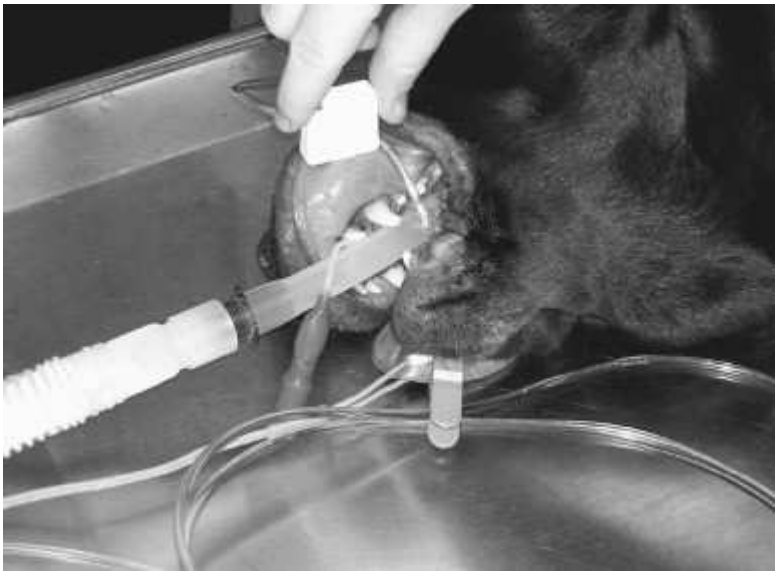
Presence of mucosal hemorrhage (petechiae/ecchymoses, gingival bleeding, epistaxis, melena, hematuria) in animals with a normal platelet count. May also be used for assessing primary hemostasis in preoperative animals.

CONTRAINDICATIONS

Thrombocytopenia

EQUIPMENT, ANESTHESIA

- Anesthesia is generally not required in dogs.
- Sedation or general anesthesia necessary in cats
- Template bleeding device (device with a spring-loaded blade that creates a standard incision in the buccal mucosa)
- Filter paper or gauze for blotting blood
- Muzzle gauze (or equivalent)
- Stopwatch



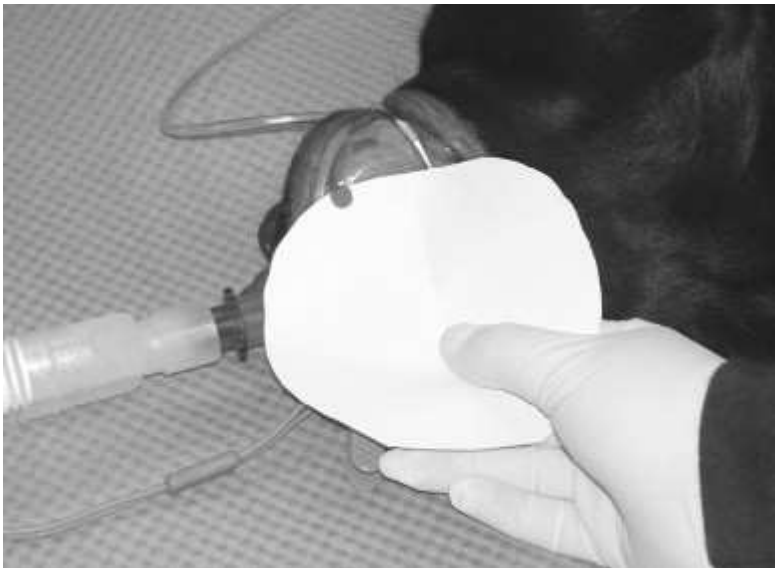
BUCCAL MUCOSAL BLEEDING TIME Template bleeding device placed against buccal mucosa.

ANTICIPATED TIME

A total of 5-10 minutes

PREPARATION: IMPORTANT CHECKPOINTS

Evaluate platelet count prior to evaluating buccal mucosal bleeding time (BMBT).



BUCCAL MUCOSAL BLEEDING TIME Blotting blood below the incision.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Animal may become agitated; use sedation as needed to keep animal still for entire test.
- Do not manually disrupt clot while assessing clotting time.

PROCEDURE

- Place animal in lateral recumbency.
- Evert upper lip and secure in everted position with muzzle gauze. This allows exposure of the buccal mucosa and causes the vessels to become slightly engorged.
- Place template firmly on mucosa, and activate the blade.
- Begin timing when the incision is made.
- Hold filter paper beneath the incision to absorb blood.
- Continue timing until a clot has formed and bleeding has ceased.
- Normal BMBT is about 3 minutes in cats and about 4 minutes in dogs.

POSTPROCEDURE

After the clot has formed and the test is completed, it may be necessary to apply pressure as needed if the clot becomes disrupted and bleeding resumes.

ALTERNATIVES AND THEIR RELATIVE MERITS

Cuticle (“toenail”) bleeding time; less reliable as a measure of primary hemostasis and more painful to the animal.

AUTHOR: ERIKA DE PAPP

Bronchoscopy

OVERVIEW AND GOALS

To view and assess both the anatomy (mucosal, structural) and function (dynamic collapse) of the airways from larynx to distal bronchi and to obtain samples from the distal airways for analysis

INDICATIONS

- Diagnostic: evaluation of lower airway and parenchymal disease (culture/cytologic examination, biopsy) and documentation of airway caliber disorders (malacia, collapse, compression, bronchiectasis, bronchial stenosis)
- Therapeutic: foreign body/secretion removal

CONTRAINDICATIONS

- Major: severe hypoxemia, unstable cardiac arrhythmias, heart failure
- Minor: significant resting expiratory effort, bronchomalacia, inexperience

EQUIPMENT, ANESTHESIA

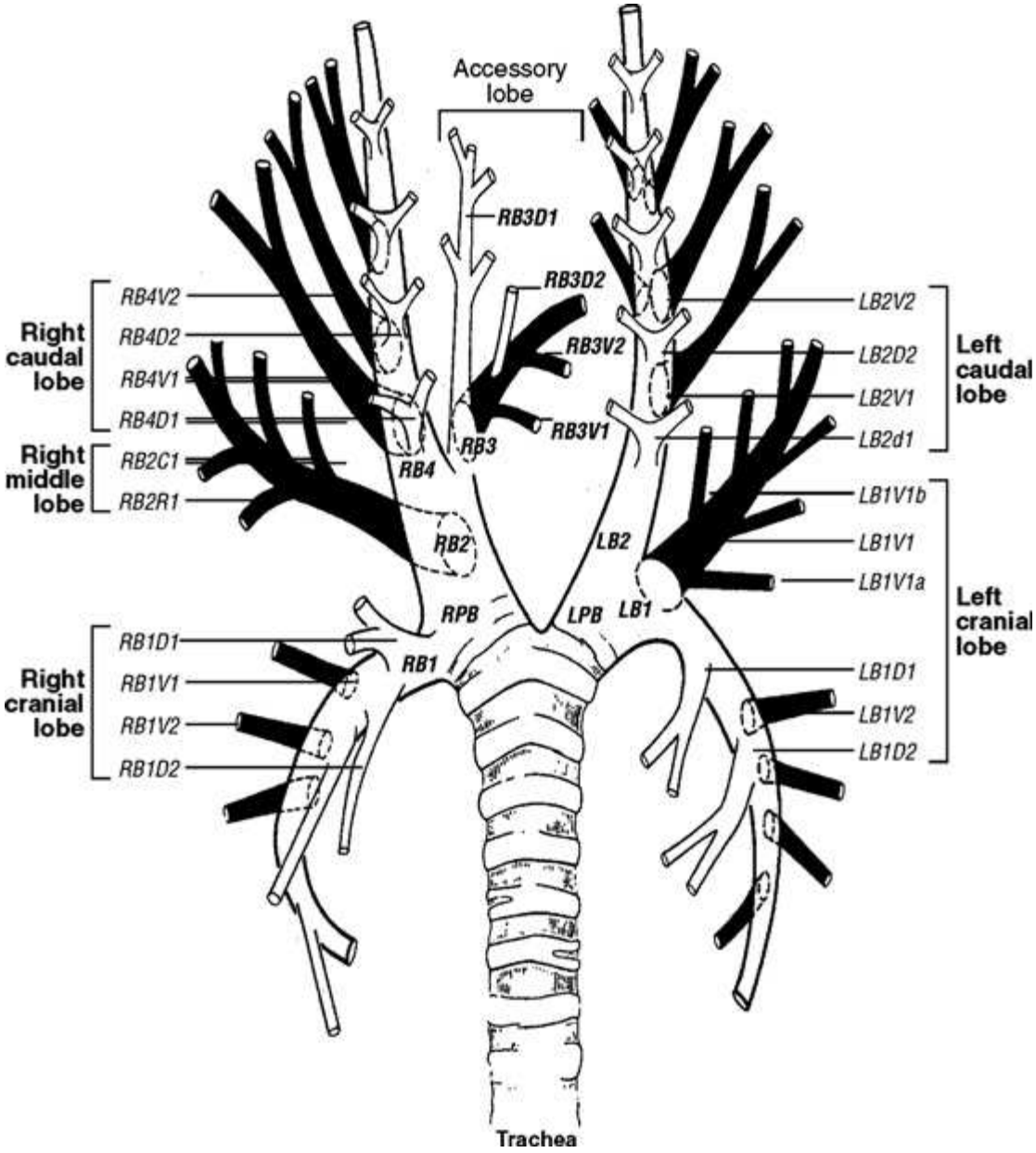
- Equipment:
  - Flexible endoscope: 3-5 mm in diameter, 55-85 cm in length
  - Mouth gag, sterile gauze, suction capabilities
  - Sterile saline:
    - Preloaded in 3 or 4 10- to 20-mL syringes for bronchoalveolar lavage (BAL)
    - For rinsing and cleaning
  - Sterile, water-soluble lubricant
  - Forceps: if foreign body removal or mucosal biopsy is required
- Anesthesia:
  - Pretreatment with a bronchodilator is recommended, especially in small dogs and all cats; use injectable terbutaline, 0.01 mg/kg SQ at least 15 minutes prior to the procedure.
  - IV catheter for administration of a short-acting injectable anesthetic protocol: either atropine, 0.02-0.04 mg/kg IM; or glycopyrrolate, 0.01-0.02 mg/kg IM; in addition, butorphanol, 0.05-0.1 mg/kg IM and diazepam, 0.1 mg/kg IV followed by propofol, 3-6 mg/kg, slow IV titrated to effect, with repeated miniboluses of propofol (1 mg/kg) as needed over the duration of the procedure to maintain anesthetized state.
  - Intubation is rarely used for the procedure; an anesthesia “T” piece is required if the scope will be passed through the tube; jet ventilation can be used if available.
  - Provide oxygen before, during, and after the procedure; insufflate oxygen through the endoscope channel or via a 3-8 Fr urinary catheter passed alongside the scope during the procedure; use an endotracheal tube or a face mask for oxygen administration before and after.
  - Topical 2% lidocaine if needed to decrease pharyngeal/laryngeal sensation, excessive coughing, and movement
  - Doxapram HCl, 2.2 mg/kg IV once to assist with the evaluation of intrinsic laryngeal function
  - Electrocardiogram (ECG), oximetry, blood pressure (BP) cuff, and other monitoring equipment

ANTICIPATED TIME

A complete bronchoscopy and bronchoalveolar lavage can be completed within 10-20 minutes by an experienced endoscopist; animal recovery time is additional and varies with the type of anesthetic used.

PREPARATION: IMPORTANT CHECKPOINTS

- The bronchoscopist must have a good understanding of normal bronchial mucosa and lung anatomy to diagnose subtle airway abnormalities.
- The bronchoscope should be cleaned and ready for use.
- All supplies and equipment should be available before starting the procedure; anesthetic monitoring and image capture equipment should be turned on and ready to use.
- Antibiotics should be discontinued at least 72 hours prior to the procedure for accurate culture results.
- Chest radiographs are useful to help select specific lung regions for examination and for BAL.



BRONCHOSCOPY Diagrammatic representation of the normal canine tracheobronchial tree.

(Reprinted with permission from Amis T, McKiernan BC: Systematic identification of endobronchial anatomy during bronchoscopy in the dog, Am J Vet Res 47:2649–2657, 1986.)

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Contamination of the BAL sample is possible if care is not taken to avoid touching the upper airways during insertion of the scope. Guarded catheters may be used for decreasing the potential for BAL contamination, although catheter cost limits their use.
- Pulmonary barotrauma (tracheobronchial or lung rupture) is possible if the oxygen insufflation rate exceeds the ability of the gas to exit the lungs; this is of concern in smaller animals when the bronchoscope diameter is close to the tracheal size and pressure builds up in the lungs as active insufflation continues.
- Airway collapse during recovery can result in severe hypoxemia; anticipate when active expiratory effort is noted prior to anesthesia; slow recovery from anesthesia helps minimize this concern.

PROCEDURE

- Sternal recumbency is the recommended position in cats and dogs.
- Topical anesthesia (1%-2% lidocaine) may be applied to the pharyngeal/laryngeal mucosa to minimize laryngospasm or excessive coughing.

- Provide oxygen as already outlined.
- Evaluate the oropharyngeal/laryngeal region; use IV doxapram HCl (2.2 mg/kg once) to stimulate intrinsic laryngeal motion.
- Insert the bronchoscope into the airways, noting changes in shape (stenosis, stricture), dynamic caliber (malacia, collapse), and mucosa (secretions, erythema, edema, masses).
- In the normal animal, the dorsal tracheal membrane is taut so that there is little if any redundancy (no visible protrusion or collapse into the airway).
- The healthy tracheobronchial mucosa is a smooth, light-pink surface with a rich supply of submucosal capillaries; if these capillaries are not visible, mucosal edema or cellular infiltration is likely present.
- Healthy mucosa has a slightly glistening appearance; mucosal edema is readily apparent because it imparts a gelatinous appearance to the epithelial surface.
- The clinician should examine the carina for abnormalities (widening, compression, mucosal infiltration) before evaluating each lobar and as many segmental and/or subsegmental bronchi as possible (as both the animal and endoscope size will allow).
- Airway bifurcations beyond the carina are referred to simply as a *spur.* Like the carina, these should also form a sharp V, but they become widened and appear U shaped with chronic airway inflammation and/or mucosal edema.
- Small polypoid mucosal nodules are commonly encountered in the bronchi of dogs with chronic bronchitis.
- Small amounts of white or slightly opaque mucus may be noted in a healthy animal, but larger accumulations or secretions of unusual color are abnormal.
- The normal monopodial branching system results in a gentle, smooth tapering of the airways. Changes may be focal or generalized and include those of shape and size of the airway lumen, such as an intraluminal stricture/tumor, external compression (tumor or lymphadenopathy), bronchiectasis, or dynamic collapse (malacia).
- Whether or not abnormalities are noted, samples should be obtained for culture and cytologic examination. Following the initial airway evaluation, the endoscope is removed from the animal and cleaned by alternatively suctioning the channel with sterile saline and air immediately prior to reinsertion.
- The BAL site (lobe and bronchus) is chosen based on both radiographic and gross bronchoscopic findings. If no site is clearly abnormal, BALs from both “middle” lung lobes should be collected.
- To perform a BAL, the bronchoscope is first gently wedged into a segmental or smaller bronchus. Aliquots of 10-20 mL sterile saline (depending on the size of the animal) are instilled into the airway (via the suction channel or a washing pipette) and then immediately aspirated using slow, gentle hand suction.
- Ideally, at least two different sites (lung lobes) should be lavaged, with two aliquots per site.
- A 40%-90% return of the volume instilled is expected. Difficulty in fluid recovery results when a proportionately large endoscope is used (prevents wedging into a small bronchus) or if malacic airways collapse when suction is applied.
- If there is enough time and anesthetic depth is appropriate, the nasopharynx should also be examined.

POSTPROCEDURE

- Provide supplemental oxygen until fully recovered.
- Crackles are commonly noted on auscultation for a short time following a BAL procedure.
- Process samples immediately.
    - Quantitated aerobic cultures should be made if possible.
    - *Mycoplasma* and anaerobic cultures are processed using Amies transport media, or submit fluid in a sterile tube.
    - Cytologic analysis:
        - Total white blood cell (WBC) and differential cell counts should be done.
        - The predominant cell in all species should be the alveolar macrophage (70+%), with usually less than 3%-8% of all other cell types (except the cat, which may have up to 20+% eosinophils and still be normal).
- Handling the scope:
    - Immediately rinse/wipe the scope down when finished to prevent secretions from drying.
    - Clean and sterilize the scope as outlined in the manufacturer's manual.
    - Store the scope hanging up (to fully dry it) in a protected space/closet.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Tracheal wash procedures are less expensive and easier to perform, but they lack the ability to direct sampling into specific sites, provide no information regarding anatomic, structural, or functional airway abnormalities, and have no therapeutic capability.
- Fine-needle lung aspiration biopsy has been used successfully to sample consolidated lung lobes and larger masses.

AUTHOR: BRENDAN C. MCKIERNAN

Breeding Soundness Exam: Male Dog

OVERVIEW AND GOAL

Evaluate the physical and physiologic parameters of the breeding male

INDICATIONS

- Prior to breeding, especially with a virgin male, a male with a history of systemic disease or when the male has not been used for breeding for several months
- Less than 50% whelping rate
- Prepurchase evaluation of a male intended for breeding

EQUIPMENT, ANESTHESIA

- Scrotal calipers
- A semen collection vessel such as:
  - 15-mL centrifuge tube and plastic cone
  - Sterile urine cup
  - Whirl-Pak bag
- Microscope
- Morphology stain (eosin-nigrosin) and Diff-Quik stain for cytologic analysis
- Hemocytometer and WBC Unopette
- Ultrasound

ANTICIPATED TIME

30-90 minutes

PREPARATION: IMPORTANT CHECKPOINTS

- 1 week sexual rest recommended prior to a breeding soundness exam (BSE)
- It is recommended to fill out an evaluation form when performing a BSE, as this will help ensure all important points are covered and provide a valuable record. An evaluation form is available from the Society for Theriogenology.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO BE AVOIDED

- It is important to prevent thermal, mechanical, or chemical injury to the semen once collected.
- A poor-quality semen sample, especially one with low sperm numbers, should be interpreted with caution, as it may be an incomplete ejaculate. Seminal alkaline phosphatase (ALP; of epididymal origin) can be used to distinguish between an incomplete ejaculate and true azoospermia. Normal ALP of a complete ejaculate would be between 5000 and 40000 IU/L. An incomplete ejaculate usually would usually measure <1000 IU/L.

PROCEDURE

- History:
  - Obtain a general health history including nutrition, vaccination history, systemic diseases and previous illnesses with attention to anything that may have resulted in thermal injury (fever) or trauma to the penis or scrotum. Include all previous medications, especially corticosteroids, anabolic steroids, chemotherapeutics, anthelminthics, and antifungal agents.
  - Obtain a thorough reproductive history including libido, presence of a tie at each breeding, and the details for all bitches bred. This would include their age and parity, type of breeding management used, dates bred, method of pregnancy diagnosis, their whelping dates, and litter sizes. The results from any previous semen evaluations, cytologic evaluation, and cultures should also be included.
- Perform a general physical exam, noting any musculoskeletal pain that may affect mating ability and potential hereditary or congenital defects. Chronic conditions such as obesity, skin disease, and endocrine disorders can also negatively impact fertility.
- Scrotal width should be measured by calipers. This correlates with testicular volume and sperm production.

- The testes and epididymides should be palpated for symmetry and consistency. The testes lie horizontally in the scrotum, with the tail of the epididymis at the caudal pole; the body and head of the epididymis lie along the cranial-dorsal aspect. It is abnormal for the testes to be either soft or hard, which may indicate degeneration, hypoplasia, neoplasia, fibrosis, or abnormal development.
- Prostate evaluation involves rectal and abdominal palpation. For rectal palpation, it may be necessary to simultaneously exert dorsal pressure on the abdomen to lift the bladder and prostate higher into the pelvic inlet. On rectal exam, the prostate should be smooth and bilobed and lie 2-3 cm caudal to the brim of the pelvis. Size, texture, and pain should be evaluated:
    - An ultrasound exam is warranted if any abnormalities are noted. If the prostate cannot be reached by rectal exam, it may be evaluated by transabdominal ultrasound or radiography.
- The prepuce is examined for discharge and the presence of paraphimosis. Preputial discharge may be the result of posthitis or balanoposthitis. The penis is best examined during semen collection. If semen collection is not to be performed, the prepuce should be reflected and the penis evaluated.
- Semen collection:
    - Before starting, the collection vessels should be prepared and within reach of the collector.
    - If possible, the male and teaser bitch should be allowed to interact. When the male becomes sexually excited, the collector should step in and begin to stimulate the penis through the prepuce.
    - The bulbus glandis is stimulated inside the prepuce until an erection is established, then the prepuce is retracted caudal to the bulbis glandis to expose the penis.
    - The collector encircles both hands around the base of the bulbus glandis. To simulate the tie, the dog may want to step over the collector's arm. The dorsal aspect of the penis remains dorsal as the collector turns the penis 180° until it is directed caudally.
    - The ejaculate should be fractionated such that each fraction is collected in a separate vessel. The first fraction is the pre-sperm fraction consisting of 1-2 mL of clear prostatic fluid. The second fraction is the sperm-rich fraction and consists of 1-3 mL of an opaque to creamy white fluid. The third fraction is clear prostatic fluid and will continue to be produced as long as the erection is maintained.
    - After the collection is complete, placing a small amount of water-soluble lubricant around the bulbus glandis will aid retraction into the prepuce.
- Semen evaluation:
    - Color:
        - The first and third fractions should be colorless, and the second should be slightly white to cream colored. In cases of prostatic disease, such as benign prostatic hyperplasia, the third fraction maybe pink, red, or brown colored. A yellow color indicates urine contamination; an Azostix can be used to confirm the presence of urea.
    - Semen analysis:
        - Motility is evaluated by placing a drop of semen on a warm slide and adding a cover slip. Gross motility is evaluated at low power (10-20), and individual motility is evaluated at 40. Normal motility is >70% with good forward progression.
        - A morphology slide is prepared by placing a drop of semen on a warm slide along with a drop of an eosin-nigrosin morphology stain. The two drops are mixed together, spread evenly across the slide and allowed to air dry. Alternatively, the slide can be prepared by smearing the semen drop across the slide and stained using Diff-Quik. If this method is used, the slide should remain in the purple and red stain for 10 minutes each to ensure stain penetration of the sperm cells. The slide must be evaluated under oil immersion (100×). Normal morphology should be >70%. Primary defects should not be greater than 10%, and secondary defects should not be greater than 20%.
        - A concentration is obtained by creating a 1 : 100 dilution, either using a WBC Unopette or by manually pipetting 20 L of semen into 2 mL of distilled water, and counting the central square on a hemocytometer. This is the concentration in million per milliliter.
        - Volume should be between 1 and 30 mL total, with the sperm rich fraction comprising 1-12 mL.
        - Total sperm/ejaculate should be between 200 million and 2 billion. This is dependent on the body weight of the dog but should be greater than 22 million per kilogram of body weight.
    - Cytologic analysis:
        - Normal cytologic examination should contain <2000 WBC/mcL. There should not be more than 6 leukocytes per high-power field in any portion of the ejaculate.
        - Abnormalities include red blood cells, tumor cells, and spermatocytes.
    - Culture:
        - >105 gram-negative organisms/mL and an inflammatory cytologic profile indicates bacterial infection (typically prostatitis).
    - pH: between 6.3 and 6.7
- Blood should be collected for a baseline database including *Brucella canis*titer, CBC, serum biochemistry, and thyroid function tests.

POSTPROCEDURE

- If there is a high number of morphologically abnormal sperm, the semen analysis should be repeated in ~60 days.
- Additional tests not part of a routine BSE but which can be performed to further investigate an infertility problem include:

- Staining for intact acrosomes
- Endocrine assays
- Karyotype
- Testicular ultrasound
- Testicular biopsy

AUTHOR: BRONWYN CRANE

Breeding Soundness Exam: Female Dog

OVERVIEW AND GOAL

Evaluate the physical and physiologic parameters of the breeding female to determine her likelihood for normal fertility.

INDICATIONS

- Prior to breeding, to ensure general health and likelihood of a healthy litter
- Prepurchase evaluation of a female intended for breeding
- A breeding female with a history of abnormal estrous cycles or failure to conceive when bred to a fertile male with appropriate breeding management

EQUIPMENT, ANESTHESIA

- Canine vaginal speculum
- Pediatric protoscope and a penlight
- Cotton-tip swab, slides, and Diff-Quik stain for vaginal cytology
- Culturette for vaginal culture, if needed. Double-guarded swabs for mares will work well.
- Blood collection supplies
- Ultrasound
- If vaginoscopy is required:
    - Rigid endoscope
    - Sedation/anesthesia

ANTICIPATED TIME

30-90 minutes

PROCEDURE

- The reproductive history will often outline a cause for infertility or reveal an area for improvement in the breeding management. A complete reproductive history should be obtained and include the following:
    - Fertility of dam, sire, and littermates
    - Date and age at first estrus
    - Duration of estrus
    - Duration of interestrus intervals
    - Progesterone/vaginal cytologic analysis results and dates from previous estrous cycles
    - Insemination dates and semen evaluation (if performed)
    - Date(s) and method(s) of pregnancy diagnosis
    - Whelping dates and litter sizes
    - Dates and results of *Brucella canis* tests
    - Vaccination and general health history: general health history should take into account factors and diseases that could potentially alter fertility. This would include thyroid disorders, prolonged treatment with corticosteroids (e.g., for skin problems), and potential exposure to reproductive pathogens such as canine herpesvirus.
- The following diagnostic samples should be collected:
    - Serum progesterone: result should coincide with the expected stage of the estrous cycle
    - Vaginal cytologic sample: result should also coincide with the stage of the estrous cycle and could potentially reveal inflammation.
    - *Brucella canis* serologic test (see p. 162): initial screening test is usually a highly sensitive test. This will result in a higher number of false positives but fewer false negatives. The rapid slide agglutination test (RSAT), the modified RSAT (MERSAT) and the tube agglutination test (TAT) are the most common screening tests performed. Antibodies for *Bordetella* spp. may cross-react with the *Brucella canis* tests. A positive test should be followed up with a more specific test such as agar gel immunodiffusion, blood culture, or histopathologic examination of tissue.
    - CBC and serum biochemistry profile
    - Thyroid function tests
- A complete physical exam should be performed. This includes careful palpation of the mammary glands and a digital vaginal exam. Physical factors which may reduce fertility include abnormal vulvar conformation, vaginal strictures, and a persistent median septum. Potential hereditary disorders such as orthopedic disorders (hip dysplasia, elbow dysplasia, cranial cruciate

ligament rupture), ophthalmic disorders, and heart conditions should be evaluated and brought to the attention of the breeder if present.

- Vaginal speculum exam is performed using a canine vaginal speculum and/or the pediatric proctoscope (if available). This will allow visualization of the caudal vagina only. The degree of vaginal crenulation as well as the presence or absence of vaginitis can be observed.
- Vaginoscopy requires a rigid or flexible endoscope at least 30 cm long (depending on the size of the bitch). This will allow visualization of the entire vagina and external cervical os. Strictures, persistent median septa, and other abnormalities may be observed.
- Vaginal culture should be obtained after a sterile prep of the vulva and careful retraction of the vulvar lips or insertion of a sterile vaginal speculum:
    - Contamination can be prevented by using a double guarded swab.
    - Careful interpretation of the vaginal culture is required, as most cultures will be positive for one or more bacteria considered part of the normal flora. If high numbers of potentially pathogenic bacteria are cultured, this result may be considered significant.
    - Vaginal culture should be interpreted together with the history and vaginal cytology:
        - If there is no evidence of infertility or inflammation, a positive culture—even with a potential pathogen—is most likely insignificant.
    - If *Mycoplasma canis* is a concern, the diagnostic lab receiving the sample should be contacted regarding the culture procedures and shipping requirements prior to obtaining a sample.
- Ultrasonography of the uterus and ovaries should be part of a complete breeding soundness exam. In larger bitches, it can be difficult to image the ovaries consistently. The uterus is located dorsal to the bladder and should be followed to the horn tips:
    - The features of the uterus will vary with the stage of the estrous cycle. During proestrus and estrus, the uterus will be edematous and appear have a heterogenous echotexture. There may be a small amount of fluid present in the lumen at this time. During diestrus, the uterus will have a more homogenous echotexture and may have a convoluted course. Cystic structures within the endometrium are abnormal at any stage of the estrous cycle and may indicate cystic endometrial hyperplasia. The presence of luminal fluid in diestrus is also abnormal and indicates mucometra or pyometra. Ovarian structures should coincide with the stage of the estrous cycle. Follicles larger than 8 mm are most likely anovulatory follicles. These could be significant if signs of prolonged proestrus exist (estrogen exposure) and may be estrogen-producing cysts. During diestrus, the ovaries will contain corpora lutea and some small follicles. During anestrus, the ovaries will have only small follicles and may be difficult to locate.

POSTPROCEDURE

Additional tests:

- An abnormal or unexpected progesterone or vaginal cytologic analysis should be followed by serial tests every 2 days.
- A positive *Brucella* RSAT or TAT should be followed by a more specific test such as agar gel immunodiffusion or culture.
- Suspected vaginal abnormalities can be further evaluated by a vaginography or vaginoscopy.
- Karyotyping should be performed on females with abnormal external or internal genitalia, with irregular estrous cycles or failure to cycle.

AUTHOR: BRONWYN CRANE

Brainstem Auditory Evoked Response (BAER) Test

SYNONYMS

Hearing test, auditory brainstem response (ABR)

OVERVIEW AND GOALS

- A noninvasive way of evaluating hearing and brainstem function by recording the electrical response in the brainstem to an external auditory stimulus.
- An average of 256 and 1000 time-locked recordings result in a characteristic waveform with five to seven discernable waves (I-VII).
- Wave I is generated by the ipsilateral cochlear nerve. Waves II-V are generated by nuclei within the medulla, pons and midbrain.
- The brainstem auditory evoked response (BAER) test does not actually assess conscious perception of hearing; however, because there are very few diseases that would interrupt the hearing pathways after they have left the brainstem, it is accepted as a valid test of hearing.
- Conductive (obstruction to sound in the ear canal or middle ear) and sensorineural (abnormality with the nerves or receptors in the inner ear) deafness both can result in an abnormal BAER test.
- Congenital sensorineural deafness typically results in a flat BAER recording.
- With conductive disorders, the latency from stimulus to the appearance of wave I is delayed, and there is often decreased amplitude which increases when the intensity is raised from 80 to 100 dB.
- With brainstem lesions, the interpeak latencies (I-III, I-V) may be prolonged relative to normal reference range or the opposite side, and the wave V/I amplitude ratio may be reduced.
- Brainstem death results in a BAER that is either flat or has only a wave I.
- Although BAER testing is commonly used for identifying congenital deafness (an absolute yes/no assessment), it can also be used for assessing the level of hearing function by performing threshold analyses. Most dogs can hear sounds at a level of sound intensity of 0-5 dB. By gradual reduction of the sound intensity during testing (from an initial level of 80 dB), the examiner can establish whether the threshold is abnormally increased.

INDICATIONS

- Suspected deafness or hearing loss (unilateral or bilateral). Screening for congenital deafness is the most common reason for BAER testing. It is frequently performed in puppies of those breeds commonly affected with congenital deafness (e.g., dalmatian, bull terrier, English setter).
- Suspected brainstem disease (neoplasia, encephalitis, infarction)
- Confirmation of brainstem death (complete loss of brainstem function)

EQUIPMENT, ANESTHESIA

- A computer with a signal averager and software capable of labeling and analysis of waveforms
- Subdermal electrodes
- Foam insert microphones, headphones or a bone conductor
- Otoscope
- Sedation may or may not be required, depending on how quiet the animal is and if it will lie still for 10-15 minutes. If sedation is required, light sedation is usually sufficient, and it will not significantly alter the characteristics of the recorded waveforms.

ANTICIPATED TIME

Usually 15-30 minutes depending on the animal's temperament and behavior

PREPARATION: IMPORTANT CHECKPOINTS

- Computer check to see that established protocols have been loaded appropriately and settings are correct.
- Impedance check (via computer software program) to ensure that all the electrodes are operating effectively.
- Otoscopic examination (see p. 1316): to ensure that ear canal is open and free from significant amounts of debris or exudate. A stenotic or occluded ear canal will not transmit sound to the tympanum and will result in subnormal waveform amplitudes and prolonged wave I latency. Ear canals may need to be cleaned thoroughly prior to the BAER test. Clinicians should

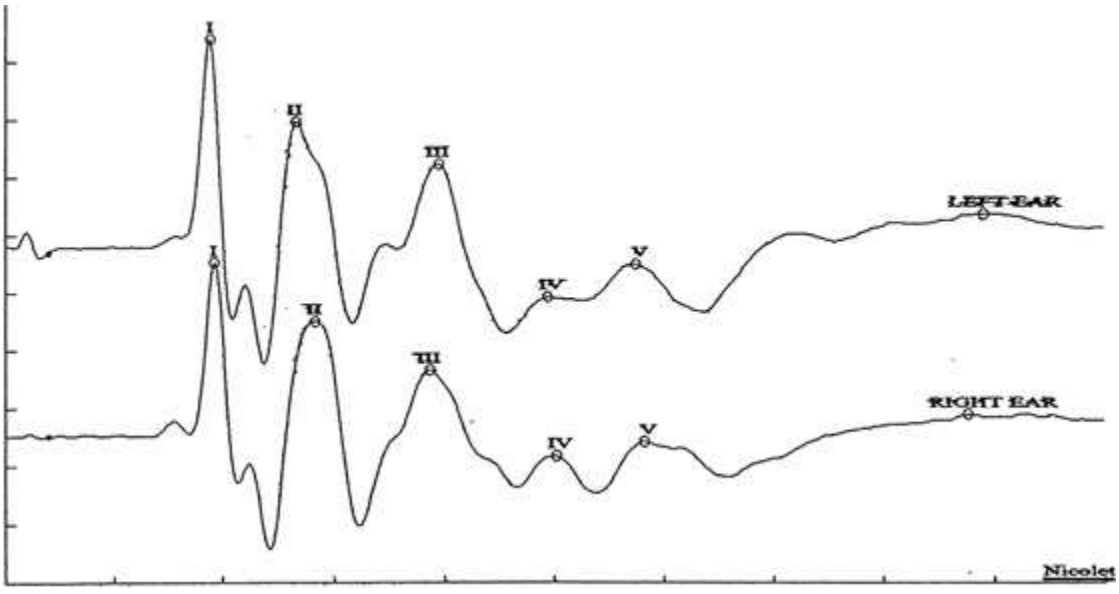
visually assess the integrity of the tympanic membrane.
- Ensure that right and left ear electrodes are appropriately placed and noted correctly on the computer.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Ear canals filled with exudate, cerumen, or debris
- Testing puppies that are too young. Puppies should be at least 6 weeks of age when tested.
- Although general anesthesia has little effect on the BAER, hypothermia will prolong latencies.
- Inserted microphones: not placed sufficiently deeply in the ear canal, or positioned such that the sound is directed into the wall of the ear canal instead of down the lumen
- Subdermal electrodes become dislodged.
- If flatline or grossly abnormal recording is obtained, always do a thorough technical check (e.g., computer working, sound is actually generated in the microphones, subdermal electrodes in place and not dislodged, inserted microphones placed appropriately in the ear canal) to ensure that the result is real. In some cases, a known normal dog should be checked to ensure there is not a technical problem and prevent incorrectly diagnosing deafness.

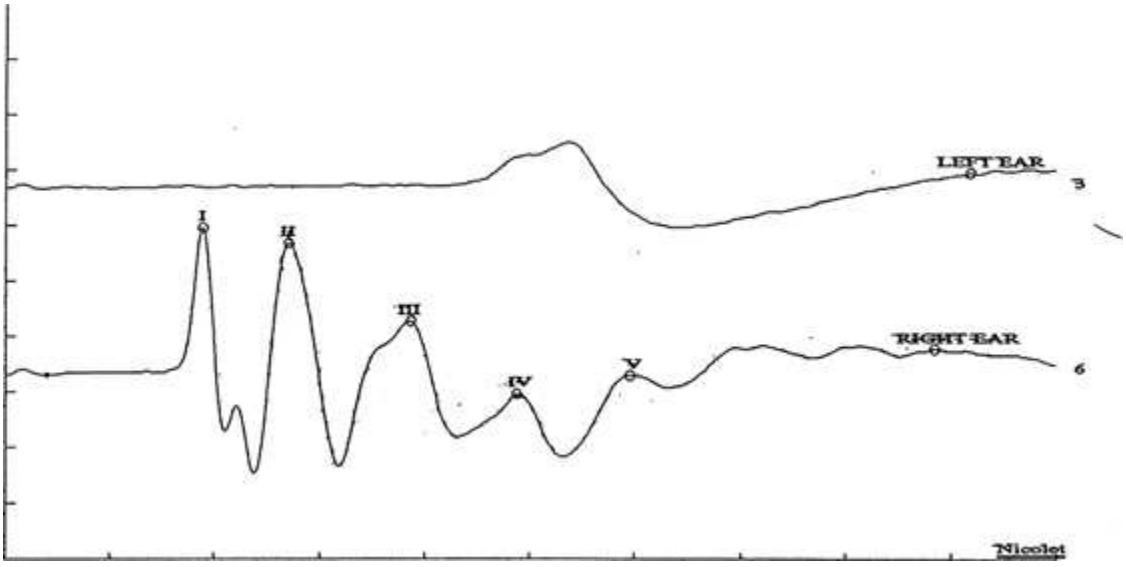
PROCEDURE

- Place animal in sternal recumbency or in a sitting position.
- Turn on computer, load appropriate software and protocols, and set up animal record.
- Perform an otoscopic examination and clean ears if necessary.
- Insert subdermal electrodes:
    - Reference: mastoid. Place electrode subcutaneously adjacent to where the horizontal ear canal begins just rostral to the base of the ear (usually at the caudal end of the zygomatic arch). The T1 reference may also be used just dorsal to the spinous process of T1.
    - Recording electrode: vertex. Place the electrode midline, halfway between the occipital crest and orbits.
    - Ground electrode: place the electrode midline over the second to fourth cervical vertebra.
- Check electrode impedance (usually in the computer software) to ensure that electrodes are working appropriately.
- Place foam insert microphones in right and left ear canals; place them so they are well seated in the upper (distal) third of the vertical ear canal. If using headphones, ensure that the pinnae are not obstructing the headphones and a snug seal is established over the ear canal.
- Set sound intensity at 80 dB. There is no established appropriate sound intensity to do initial screening, but this level has been determined to be comfortable for the animal and effective at identifying potential hearing deficits.
- Set signal averager to average 1000 signals (256 may be adequate for cats or uncooperative dogs if the waveform is clearly normal), and select right or left ear to begin recording.
- Each ear should be recorded twice, and the recorded waveforms should be compared. They should be very similar. If not, do a technical check and repeat the test.
- Once good-quality recordings have been recorded for both ears, the waveforms should be labeled and amplitudes and latencies calculated.
- Subdermal electrodes and inserted microphones are then removed, and the animal can be discharged.



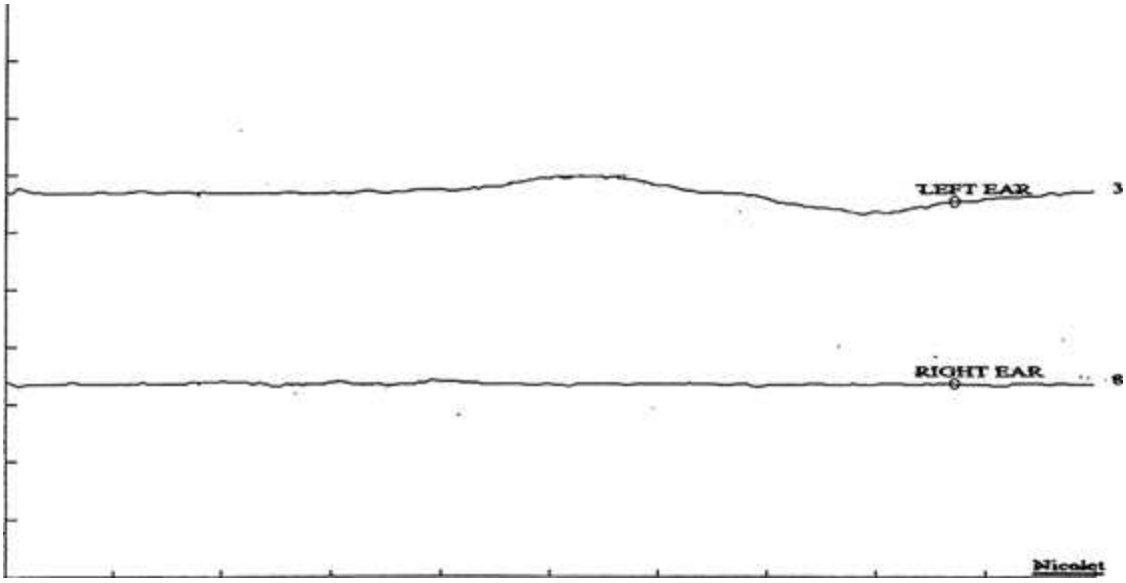
BRAINSTEM AUDITORY EVOKED RESPONSE (BAER) TEST Normal study.

(Courtesy Dr. Peter Foley.)



BRAINSTEM AUDITORY EVOKED RESPONSE (BAER) TEST Unilateral deafness in the left ear.

(Courtesy Dr. Peter Foley.)



BRAINSTEM AUDITORY EVOKED RESPONSE (BAER) TEST Bilateral deafness.

(Courtesy Dr. Peter Foley.)

POSTPROCEDURE

If the animal has been sedated, allow it to recover sufficiently before discharge.

ALTERNATIVES AND THEIR RELATIVE MERITS

There are no practical and accurate alternatives to establishing unilateral or bilateral deafness in dogs and cats. Bilateral deafness can usually be suspected but not confirmed by subjective assessment of the animal's response to loud noises.

AUTHOR: GREG KILBURN

1ST EDITION AUTHOR: DARCY SHAW

Brain Biopsy, CT-Guided Stereotactic

OVERVIEW AND GOAL

Neoplastic, vascular, infectious, or inflammatory diseases of dogs and cats frequently result in focal brain involvement. Although CT and MRI are sensitive in determining location, extent, and relationships of brain lesions to adjacent structures, both have limited specificity. For example, non-neoplastic lesions (such as those seen in association with infection, inflammation, or vascular diseases) may mimic the CT or MRI appearance of a neoplasm. In most instances, results of CT or MRI provide only a broad list of differential diagnoses for a focal brain lesion. Accurate histologic diagnosis of an intracranial lesion is critical before recommending a specific management or treatment strategy.

INDICATIONS

This procedure is used for obtaining tissue samples of areas within the brain that have CT or MRI imaging characteristics consistent with a neoplasm or an infectious/inflammatory lesion. The main indications for stereotactic biopsy are deep-seated focal lesions, multiple lesions, or disseminated lesions of the brain.

CONTRAINDICATIONS

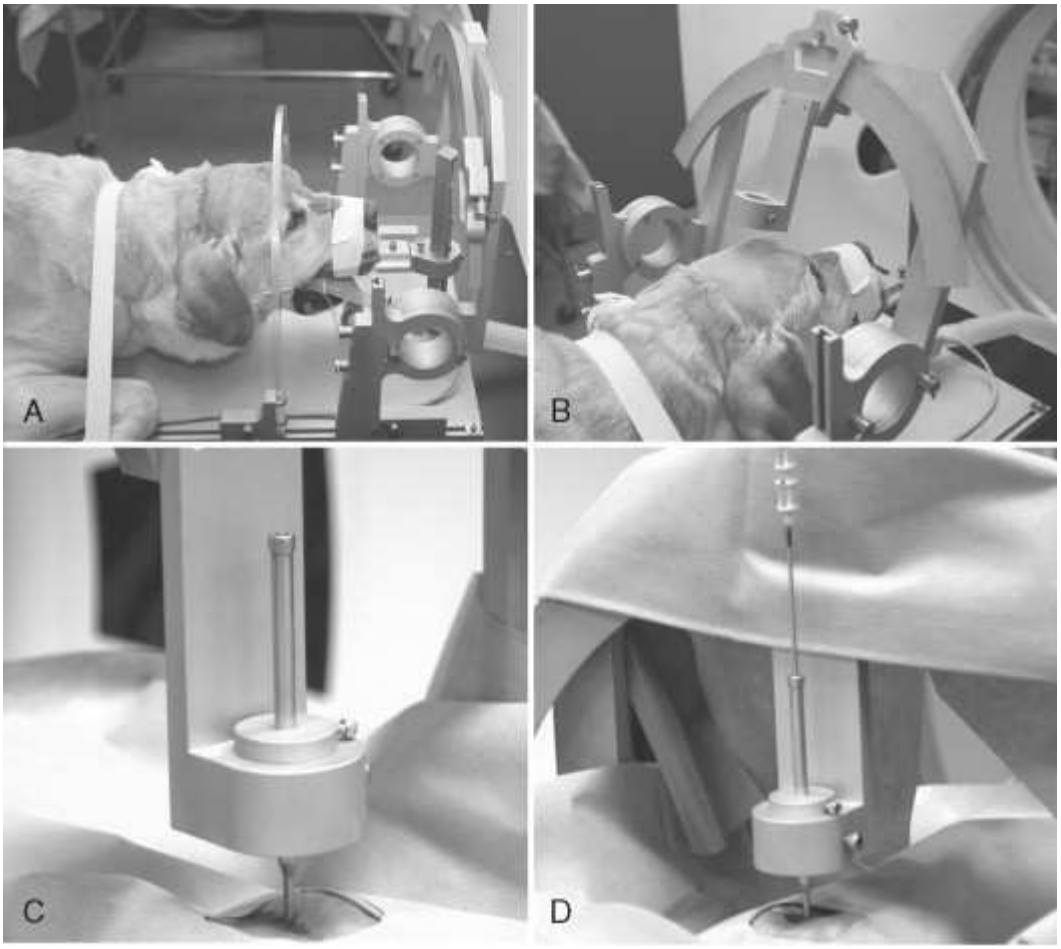
Brain biopsy should be approached with caution in animals with underlying bleeding disorders, clinical signs consistent with increased intracranial pressure (ICP), brainstem lesions, or systemic problems that result in increased anesthetic risk.

EQUIPMENT, ANESTHESIA

- Essentially all closed stereotactic brain biopsy methods rely on the three-dimensional CT-generated coordinates identifying the lesion location. These coordinates are used for plotting an optimal trajectory and depth needed for a biopsy needle to reach a target and obtain a diagnostic tissue sample.
- Technical impediments exist to the direct application of most human stereotactic systems to dogs and cats. Most commercially available systems use a cumbersome head frame and localizing system designed specifically for the human skull, and they require dedicated expensive computer software for the planning phase. Several different systems for image-guided stereotactic brain biopsy have been reported for use in dogs and cats.
- General anesthesia is required for stereotactic brain biopsy. Typically, pre-medication utilizes an opioid (a pure mu agonist because of using fentanyl in the maintenance phase). The dose and use of this drug will depend on the concern over changes in ICP and the mental status of the patient. General anesthesia usually is induced with propofol (± a benzodiazepine). Propofol (0.1-0.4 mg/kg/min to effect) and fentanyl (0.3-0.7 mcg/kg/minute to effect) are recommended for maintenance. Animals should be ventilated to maintain ETco2 at a value of 30-35 mm Hg. For recovery, the fentanyl should be stopped about 30 minutes before the end of the procedure.

ANTICIPATED TIME

2-3 hours, depending on the number of biopsy specimens collected and the number of trajectories planned



BRAIN BIOPSY Center-of-the-arc CT-guided stereotactic brain biopsy system. **A**, Dog positioned in biopsy frame. **B**, Biopsy frame positioned in appropriate trajectory for biopsy. **C**, Drill guide in place. **D**, Biopsy needle positioned in needle guide.

PREPARATION: IMPORTANT CHECKPOINTS

- Stereotactic biopsy begins with proper patient selection. The possibility of non-neoplastic disorders such as infection, cerebral infarction, or vasculitis must be considered and investigated, with other tests as appropriate prior to (or instead of) biopsy.
- When the differential diagnosis list is long and may include neoplasms and inflammatory lesions, the appropriate handling of tissue samples should be discussed with a neuropathologist in advance of the procedure.
- All patients should be tested for coagulation parameters (prothrombin time [PT], partial thromboplastin time [PTT]) prior to the procedure and should have a platelet count >100,000 mcL.
- Patients should not receive aspirin products for 1 week before surgery.
- Ideally, MRI or CT images should be completed within 10 days prior to completion of the biopsy procedure.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO BE AVOIDED

Although stereotactic brain biopsy is minimally invasive compared with open biopsy techniques, complications rarely may occur. Morbidity may include seizures, hemorrhage, development of biopsy-induced neurologic deficits, brain infection, tumor seeding, and lack of a definitive diagnosis.

PROCEDURE

- Biopsy generally is done on the CT-scanner table. For those lesions not well identified on CT images, MRI images that demonstrate a lesion may be used for localizing the lesion on CT images, using well-defined anatomic landmarks (e.g., lateral ventricles).
- Transverse CT images are used for defining the CT coordinates of reference markers and the biopsy target. Dorsal or sagittal images may be used for trajectory planning.
- An entry point should be selected that is associated with a low risk for neurologic deficit or hemorrhage (e.g., avoidance of dorsal sagittal sinus). Ependymal puncture should be avoided where possible.

- A small craniotomy (2-mm diameter) is made by means of a twist drill, the dura mater is punctured with an 18-gauge needle, and biopsies may be done with a side-cutting aspirator biopsy needle (Nashold Biopsy Needle [Integra Radionics, Burlington, Mass.]) with a 10-mm side opening. On average, one to three specimens are harvested.
- The intraoperative goal should be to confirm by means of smear or touch preparations whether tissue satisfactory for an eventual diagnosis has been obtained. A specific histologic diagnosis may require routine formalin fixation and paraffin embedding of the biopsy tissue.
- At the conclusion of the biopsy procedure, the needle is withdrawn in increments to assess any possibility of hemorrhage. In the case of hemorrhage, blood should be permitted to egress from the needle spontaneously until bleeding stops.

POSTPROCEDURE

- A series of CT images of the brain should be obtained immediately after completion of the biopsy procedure in order to assess the possibility of intracranial hemorrhage.
- Animals should be recovered in sternal recumbency with the head elevated slightly above the level of the heart.
- Animals should be observed for 12 hours postbiopsy before being discharged from the hospital.

ALTERNATIVES AND THEIR RELATIVE MERITS

Open (surgical) brain biopsy may be appropriate in certain clinical situations in which cortical architecture needs to be preserved, for leptomeningeal sampling, for superficially located lesions, and when a decompressive craniectomy with good cortical visualization may be helpful in addition to obtaining a biopsy sample.

AUTHOR: RICHARD A. LECOUTEUR

Bone Marrow Aspiration/Core Biopsy

OVERVIEW AND GOALS

To obtain a sample of bone marrow cells for cytologic (aspiration) and/or histologic (core biopsy) analysis

INDICATIONS

- Cytopenias without identifiable underlying cause
- Unusual blood cell morphologic abnormalities on blood smear
- Staging of neoplasia (notably lymphoma and mast cell tumor)

CONTRAINDICATIONS

- Contraindications to sedation or anesthesia
- Infection of overlying soft tissues
- Not a contraindication: thrombocytopenia

EQUIPMENT, ANESTHESIA

- Either sedation plus analgesia and local anesthesia may be used, or general anesthesia can be used.
- Typical protocol: butorphanol, 0.2 mg/kg IV, plus lidocaine 2% local infiltration (1-8 mL SQ for cats to large dogs, respectively); and propofol, 3-6 mg/kg IV to effect. Propofol and local anesthesia are inadequate without an analgesic such as butorphanol, because neither propofol nor lidocaine provides systemic analgesia, and aspiration is painful.
- Clippers for hair
- Antiseptic scrub solution, isopropyl alcohol, and gauze squares for preparing the skin
- Sterile surgical gloves
- A #11 scalpel blade.
- Bone marrow aspiration/biopsy needle, typically 18-gauge
- Microscope slides and/or laboratory container with anticoagulant and/or sterile test tube. The preferred method of submission varies from laboratory to laboratory.
- Tissue glue
- A 10% formalin and biopsy jar (if core biopsy)

ANTICIPATED TIME

About 20 minutes

PREPARATION: IMPORTANT CHECKPOINTS

- For larger patients (large-breed dogs, obese animals), the needle guard should be removed; otherwise, the exposed amount of needle shaft may not reach the marrow cavity.
- A whole-blood sample for CBC should be drawn before the procedure and submitted at the same time as the cytologic examination slides/biopsy specimen.
- The laboratory to which the sample is being submitted should be consulted beforehand. Some clinical pathologists require fresh smears, others require anticoagulated samples, and still others require clotted samples. Depending on the desired sample submission, anticoagulant may be placed in the aspirating syringe.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

Aspirate:

- Inadvertent clotting of sample; preventable by reducing the time between aspiration and smearing to a few seconds
- Sliding off the bone on initial approach, causing soft-tissue trauma; prevented with good anatomic landmarking, firm but not excessive pressure when advancing the needle, perpendicular positioning of the needle tip against the bone surface, and keeping one's hands close to one's own body for greater control when advancing the needle into bone.
- Submitting all slides for routine staining; it is worthwhile to keep one or two slides unstained because there may be additional indications (e.g., feline leukemia immunofluorescence, antimegakaryocyte antibody testing) that emerge later in the case and

for which additional slides would be useful.

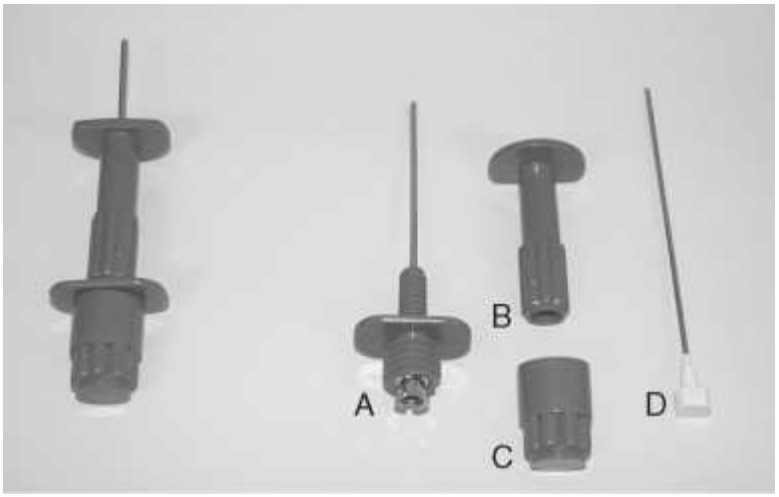
Core biopsy:

- Assumption that a core biopsy is superior to a marrow aspirate/cytologic examination. In most cases, a cytologic examination is as informative, if not more so.
- Sliding off the bone on initial approach, causing soft-tissue trauma: as already described.
- For core biopsies, failing to slightly rock the biopsy needle when it is fully embedded before withdrawing. This rocking motion breaks off deep attachments to the core and prevents the biopsy sample from remaining attached to bone and sliding out of the needle on withdrawal.

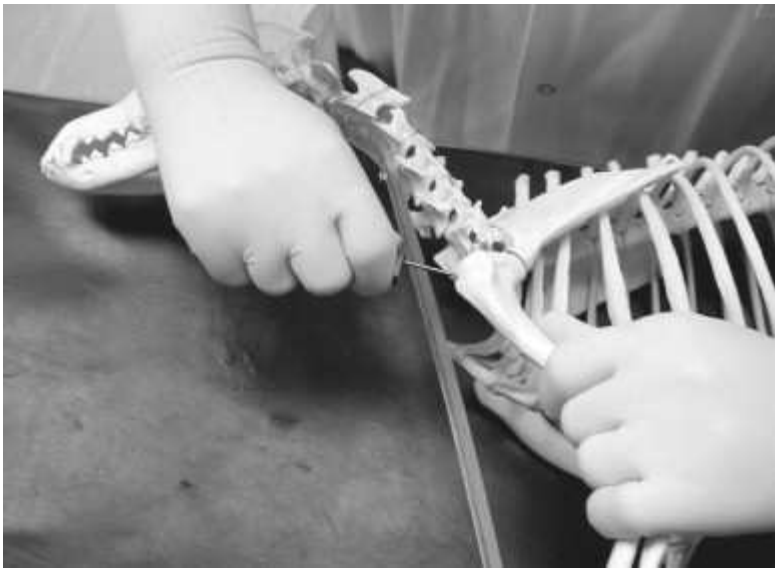
PROCEDURE

A humeral or ilial approach may be used. Aspirate: humerus:

- Sedation or general anesthesia is induced.
- For a right-handed clinician, the animal's left humerus is easiest. The animal is placed in right lateral recumbency on a table, and the clinician stands behind (dorsal to) the animal.
- The area over the animal's left shoulder is clipped of hair and aseptically scrubbed. Generally, a hairless, disinfected surface of skin that is a minimum of 3 × 3 inches (8 × 8 cm.) is necessary, centered on the point of the shoulder.
- Unless the animal is under general anesthesia, a local anesthetic is infiltrated (SQ and through the soft tissues to the level of the periosteum) according to the following landmarks:
    - The site of entry into the marrow cavity is the craniolateral proximal humerus, just distal to the joint space of the shoulder.
    - On palpation of the cranial aspect of the shoulder, a depression is felt (shoulder joint), and the site of entry with the needle is 3-10 mm (cat to large dog) distal and lateral to this point.
    - A broad surface of bone with little overlying muscle—the lateral, distal aspect of the greater tubercle—is the target. The needle should not enter the joint space.
- A brief aseptic scrub of the site is repeated after local anesthesia injection.
- The clinician puts on sterile gloves.
- Using his or her left hand, the clinician takes the animal's proximal left humerus firmly, holding the limb just distal to the aseptically scrubbed area. In this way, the left hand is no longer sterile but the right hand is still sterile.
- The landmarks just described are palpated again with the right hand; using the scalpel blade, the clinician makes a 2-3 mm skin incision over the lateral, distal greater tubercle.
- Using the right hand, the clinician places the bone marrow needle in the skin incision, exactly perpendicular to the bone surface, and advances it using a clockwise-counterclockwise rotatory motion and firm forward pressure. The bone marrow biopsy needle must be held firmly in the right hand, with the butt of the needle seated in the palm of the hand.
- If properly directed, the bone marrow needle should be difficult to advance and should feel firmly seated in bone.
- The needle is advanced 0.5-2 cm (cat to small dog/big dog) to reach the marrow cavity.
- The needle cap and stylet are then removed, a syringe is attached to the needle, and negative pressure is created by drawing back on the syringe plunger.
- Marrow (looks like blood) enters the syringe; 1-2 mL should be harvested if possible.
- As soon as marrow is in the syringe, the syringe and needle are withdrawn together, and the sample is instantly prepared for submission according to the laboratory's specifications.
    - Fresh smears: with the needle and syringe still connected to each other, a sample of marrow is expelled such that it partially (20%-50% of slide surface) floods the microscope slide. The sample is then reaspirated into the needle and syringe. This process leaves behind marrow spicules (1-2 mm specks) on the slide, and spicules contain the greatest concentration of marrow cells.
    - Anticoagulated samples: marrow is placed in a purpose-made dish with anticoagulant or in a lavender-top tube.
- The skin incision is closed with tissue glue, and mild direct pressure is applied for hemostasis.



BONE MARROW ASPIRATION/CORE BIOPSY Assembled *(left)* and disassembled *(right)* bone marrow needles. **A**, Needle. **B**, Needle guard. **C**, Cap. **D**, Stylet.



BONE MARROW ASPIRATION/CORE BIOPSY Position for bone marrow aspiration from the proximal humerus, using a skeleton for demonstration. This right-handed clinician is standing dorsal to the recumbent animal and is holding the humerus firmly. The needle tip is on the distal, lateral surface of the greater tubercle, ready to be advanced.

Aspirate: ilium:

- Sedation or general anesthesia is induced.
- The animal is placed in sternal recumbency.
- The skin over the dorsal-most aspect of the right or left ilial wing is clipped of hair and aseptically scrubbed. Generally, a hairless, disinfected surface of skin that is a minimum of 3 × 3 inches (8 × 8 cm) is necessary, centered on the palpable dorsal-most aspect of the wing of the ilium.
- Unless the animal is under general anesthesia, local anesthetic is infiltrated SQ and through the soft tissues to the level of the periosteum. The site of entry, and therefore the site requiring local anesthesia, is the dorsal-most/slightly medial aspect of the ilial wing.
- A brief aseptic scrub of the site is repeated after local anesthesia injection.
- The clinician puts on sterile gloves.
- Standing over the animal, the clinician palpates the dorsal wing of the ilium and makes a small (2-3 mm) skin incision using the scalpel blade.
- Using the right hand, the clinician places the bone marrow needle in the skin incision until it touches ilial bone and then advances it using a clockwise-counterclockwise rotatory motion and a moderate amount of forward (downward) pressure. The bone marrow biopsy needle must be held firmly in the right hand, with the butt of the needle seated in the palm of the hand.
- If properly directed, the bone marrow needle should be difficult to advance and should feel firmly seated in bone.
- The needle is advanced 0.5-2 cm (cat to small or big dog) to reach the marrow cavity.
- The needle cap and stylet are then removed, a syringe is attached to the needle, and negative pressure is created by

drawing back on the syringe plunger.
- Marrow (looks like blood) enters the syringe; 1-2 mL should be harvested if possible.
- As soon as marrow is in the syringe, the syringe and needle are withdrawn together, and the sample is instantly prepared for submission according to the laboratory's specifications.
    - Fresh smears: with the needle and syringe still connected to each other, a sample of marrow is expelled such that it partially floods the microscope slide. The sample is then reaspirated into the needle and syringe. This process leaves behind marrow spicules (1-2 mm specks) on the slide, and spicules contain the greatest concentration of marrow cells.
    - Anticoagulated samples: marrow is placed in a purpose-made dish with anticoagulant or in a lavender-top tube.
- The skin incision is closed with tissue glue, and mild direct pressure is applied for hemostasis.

Core biopsy: humerus or ilium:

- The same procedure as for bone marrow aspiration is followed, up to the point of advancing the needle into bone.
- When the needle is initially in bone (first few rotations, but before having advanced the full 0.5-2 cm), the procedure is stopped, the needle cap is unscrewed, and the stylet is removed.
- In this way, the cortex is not included in the sample (in contrast to bone biopsy, p. 1211).
- The cap is then replaced on the needle, and the procedure is continued, advancing the needle into the marrow cavity.
- No aspiration is involved. Rather, when the needle has been advanced a total of 0.5-2 cm (cat to small or big dog, respectively) without a stylet, a core of marrow should be in the shaft of the needle. The twisting and advancing motion is stopped, and the needle is gently tilted or rocked very slightly (perhaps 10° side to side) to break the core of marrow free from its attachments.
- The needle is then withdrawn and examined; a white plug of marrow should be obstructing the tip of the needle. This plug is expelled into 10% formalin using the stylet inserted in the normal (normograde) direction.

POSTPROCEDURE

Routine recovery from sedation/anesthesia and submission of samples for analysis

ALTERNATIVES AND THEIR RELATIVE MERITS

- Repeated CBC: assesses trends in cytopenias and morphologic blood cell abnormalities but does not show precursors and maturation sequence of blood cells
- Buffy coat examination: unreliable for malignant mast cell disease (poor sensitivity, poor specificity compared to bone marrow evaluation)

AUTHOR: ETIENNE CÔTÉ

Bone Grafting

SYNONYMS

Autogenous cancellous bone grafts (used most frequently in animals), allogenous corticocancellous bone grafts, allogenous cortical bone grafts, biosynthetic and synthetic bone graft substitutes

OVERVIEW AND GOALS

- Adjunct to surgical bone repair
- Autogenous cancellous bone grafts:
  - Enhance bone healing by osteogenesis, osteoconduction, and osteoinduction:
    - About 10% of donor cells survive and contain osteoblastic progenitor potential (osteogenesis).
    - Grafted cells serve as a trellis for ingrowing recipient vascular and cellular elements (osteoconduction).
    - Bone morphogenic proteins in graft stimulate recipient mesenchymal cells to form bone (osteoinduction).
- Allogenous corticocancellous and allogenous cortical bone grafts:
  - Enhance bone healing by osteoconduction and induction
  - Allogenous cortical bone provides structural support with cortical graft placed in bone defect.
  - Processed and banked
  - Derived from cadavers
- Biosynthetic and synthetic bone graft substitutes:
  - Consist of demineralized bone matrix, collagen, hydroxyapatite, tricalcium phosphate, calcium sulfate, or a combination of these minerals, special glass ceramics (bioactive glasses), and polymers
  - Serve as a structure on which new bone can grow
  - Many of these materials then dissolve over time, leaving only new bone behind
  - The degree to which the bone graft substitutes provide an osteoconductive structural framework or matrix for new bone ingrowth differs among implants

INDICATIONS

- Fractures
- Delayed unions or nonunions
- Osteomyelitis:
  - Infection of the recipient site is not a contraindication to autogenous cancellous bone grafting and selected synthetic and biosynthetic bone grafts.
  - The selected site from which the graft is harvested (donor site), however, must be aseptic.
- Arthrodesis
- Corrective osteotomies
- Ablation of bone cysts
- Limb-sparing surgery
- Minimize surgical time and donor site morbidity (allografts and bone graft substitute)

CONTRAINDICATIONS

- Prolonged anesthesia/operative time in compromised animal (autografts)
- Donor site comorbidity (autografts)

EQUIPMENT, ANESTHESIA

Standard orthopedic equipment and anesthesia are used during fracture repair, osteotomy, or arthrodesis.

ANTICIPATED TIME

An additional 15-30 minutes of operative time (autogenous cancellous bone grafting)

PREPARATION: IMPORTANT CHECKPOINTS

- Donor site for cancellous autograft
  - Common locations: proximal lateral humerus, proximal lateral femur, proximal medial tibia, or dorsolateral ilial wing
  - Needs to be aseptically prepared preoperatively

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

Cancellous autografts

- Hematoma formation
- Loss of graft by inadvertent discard of graft-laden sponge
- Contamination of donor site by infection or neoplasia from recipient site
- Inadequate graft harvest
- Iatrogenic fracture at donor site
- Iatrogenic physeal damage at donor siteAllografts and bone substitute
- Sufficient volume or size

PROCEDURE

For autogenous cancellous bone graft:

- Primary orthopedic procedure is performed, and then fresh graft is obtained from a separate (donor) site in the animal.
- Skin incision carried through subcutaneous tissues directly to bone at donor site
- Proximal cortex is penetrated by pin or drill bit
- Curette is used for collecting intramedullary contents: cancellous bone graft
- Material is collected in sterile container or gauze sponge and soaked with blood to prevent desiccation
- Graft is transferred to, and placed in, recipient site around implants and fracture(s)
- Routine closure of primary operative site and then donor site
- For autogenous corticocancellous graft from ilium:
    - Rongeurs or bone cutters are used for resecting ilium and collecting cortical and cancellous bone.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Commercial allograft preparations and bone substitutes eliminate donor site morbidity.
    - Unlimited supply, easy sterilization, and storage

SUGGESTED READING

Johnson AL, Hulse DA: Fundamentals of orthopaedic surgery and fracture management. In Fossum TW, editor: Small animal surgery, ed 2, St Louis, 2002, Mosby, pp 821–900.

Millis DL, Martinez SM: Bone grafts. In Slatter D, editor: Textbook of small animal surgery, ed 3, Philadelphia, 2002, WB Saunders, pp 1875–1891.

AUTHOR: JOSEPH C. GLENNON

Bone Biopsy

OVERVIEW AND GOAL

Percutaneous sampling procedure using a minimally invasive approach to obtain cortical and cancellous bone for histologic analysis

INDICATIONS

Investigation of primary bone lesions, most commonly suspected neoplasms or bony infections:

- Focal, palpable, hard bone swellings
- Radiographic evidence of lytic and/or productive focal bone lesions
- Pathologic fractures

CONTRAINDICATIONS

- Bleeding disorders
- If iatrogenic/pathologic fracture appears likely as a result of the procedure (radiographic appearance of severe osteolysis)

EQUIPMENT AND ANESTHESIA

- General anesthesia
- Clippers for hair
- Routine antiseptic surgical scrub material and isopropyl alcohol
- A 22-gauge needle
- A #11 scalpel blade
- Sterile surgical gloves
- Bone biopsy needle, either a purpose-made Jamshidi-type needle or a routine bone marrow aspiration needle and stylet

ANTICIPATED TIME

About 20-30 minutes plus anesthesia induction and recovery

PREPARATION: IMPORTANT CHECKPOINTS

- Radiographs of the region to be biopsied always are indicated first to confirm bony nature of enlargement.
- Thoracic radiographs (three views, metastasis check) if bony mass is cause for biopsy
- Platelet count; severe thrombocytopenia (<25,000 platelets/µl and/or overt systemic clinical signs of hemorrhage) is a contraindication for the procedure.
- Discuss risks with owner, including possible need for amputation if iatrogenic pathologic fracture occurs in the long bone of a limb.

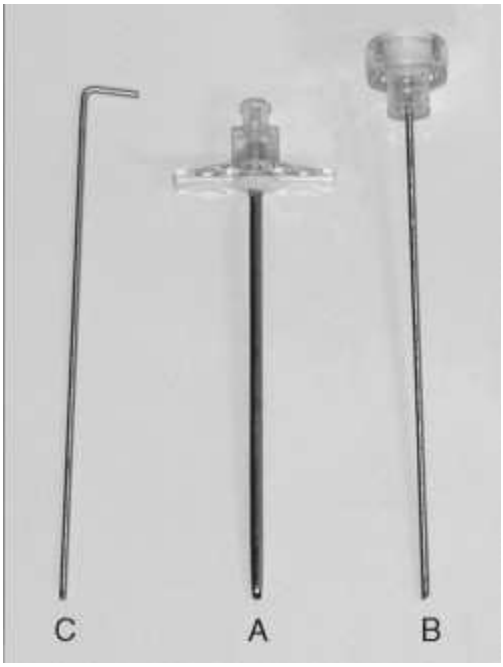
POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Bone biopsy tends to be unrewarding in cases of diffuse osteopenia. These animals benefit more from review of signalment and history and assessments of serum ionized calcium, phosphorus, parathyroid hormone (PTH), and vitamin D levels.
- Iatrogenic pathologic fracture: best avoided by ensuring that if serial samples are taken, they are taken at multiple different angles and positions on the bone to avoid circumferential or linear sets of biopsy punch holes.
- Iatrogenic nerve damage, vessel trauma: the course of regional nerves, veins, and arteries needs to be known and properly identified before proceeding. Doing so may require a “mini-cutdown” or keyhole (1-cm) skin incision and blunt dissection through the soft tissues to reach bone while avoiding these structures.

PROCEDURE

- The area of greatest bony abnormality is identified on the radiographs, and the hair over that area is clipped widely (usually at least 3 × 3 inches [8 × 8 cm]).
- An approximate measurement of the thickness of the lesion should be made from the radiographs (distance from skin to

marrow cavity) to anticipate the desired depth of needle penetration.
- General anesthesia is induced.
- The skin overlying the area of greatest radiographic abnormality is aseptically scrubbed. Surgical draping often can be avoided, provided a sufficiently wide area of hair has been clipped.
- The clinician puts on surgical gloves and pinch-elevates the skin to make a small (2-3 mm) stab incision using the scalpel blade. Caution: Be sure that nerves and vessels do not course in the chosen area.
- The biopsy needle is advanced into the lesion using gentle, consistent forward pressure and a rotatory, clockwise-counterclockwise twisting motion. Caution: The resistance of the abnormal tissue may be variable, and a sudden push could damage the bone or deeper structures on the other side of the lesion; the biopsy needle should therefore be “palmed” (butt of the needle in palm, needle shaft held firmly between index finger and thumb) so that the fingertips of the thumb and index act as a buttress.
    - The stylet is generally removed from the biopsy needle and set aside after the soft tissues have been passed and the needle first reaches bone.
- The biopsy needle has been sufficiently advanced when the cortex and marrow of one side of a bone (and its lesion) have been traversed (i.e., when the marrow cavity is reached, as estimated from the radiographs).
- Before withdrawing the needle, a gentle rocking of the needle (a few millimeters at most) side to side will break off any attachments of the biopsy core to deeper bone. Not doing this could cause the core biopsy to be retained in the bone rather than coming out with the needle.
- The needle is withdrawn, again with a rotatory clockwise-counterclockwise motion to decrease friction.
- The sample is expelled from the shaft of the needle. The stylet is inserted normograde (usual direction) if using a bone marrow aspirate–type needle; however, the stylet is inserted retrograde (up the tip of the needle) if using a Jamshidi-type needle, because these usually are tapered at the tip.
- Multiple (two or three) samples often are obtained during one procedure to increase diagnostic yield. The samples are obtained away from each other to reduce the risk of weakening/fracturing the bone.
- If a very small skin incision was made, then direct pressure alone (or possibly tissue glue) usually is sufficient for closure; larger incisions (rare) may require skin sutures or staples.



BONE BIOPSY Jamshidi-type needles for bone biopsies. **A**, Needle. **B**, Stylet that remains inside the needle while crossing the soft tissues but is removed before entering bone. **C**, Second stylet that is inserted retrograde into the needle after procedure is finished to expel biopsy specimen from the needle shaft.

POSTPROCEDURE

- Sedation/prolongation of recovery if animal flails its biopsied limb (to reduce risk of self-induced pathologic fracture)
- Radiograph biopsied limb if the animal experiences markedly worse lameness after the procedure (rule out pathologic fracture).
- Evaluate site several minutes later. If a hematoma is present, direct pressure is indicated.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Open biopsy; more invasive, but specimen is larger.
- Amputation (if area being biopsied is on a limb); indicated if pathologic fracture is present.

AUTHOR: ETIENNE CÔTÉ

Blood Pressure Measurement

OVERVIEW AND GOALS

- The goal of noninvasive blood pressure (BP) assessment in animals in a veterinary setting is to accurately measure arterial BP and detect abnormal BP, particularly systemic hypertension.
- Doppler sphygmomanometric methods or automated oscillometric methods may be used.
- Doppler methods deliver systolic BP values.
- Oscillometric methods deliver systolic, diastolic, and mean BP values.
- Systolic BP is the value of interest in most clinical cases of systemic hypertension (see p. 1068).

INDICATIONS

- Presence of clinical signs of systemic hypertension
- Presence of systemic disease known to be associated with systemic hypertension (e.g., renal disease, hyperthyroidism, hyperadrenocorticism, diabetes mellitus, pheochromocytoma)
- Random BP screening in young healthy animals is not recommended.

EQUIPMENT, ANESTHESIA

Doppler method (used in dogs and cats; the preferred method for cats):

- Commercial Doppler amplifier with attached piezoelectric crystal for detection of blood flow
- Sphygmomanometer previously calibrated for accuracy
- A variety of cuff sizes based on animal limb circumference
- Pliable measuring tape to measure animal limb circumference
- Ultrasound coupling gel
- Hair clippers and isopropyl alcohol, if desired, for preparation of site of piezoelectric crystal application

Oscillometric method (automated system; used in dogs, less reliable in cats):

- Commercial automated oscillometric BP monitor with either print or data storage capability
- A variety of cuff sizes based on animal limb circumference
- Pliable measuring tape to measure animal limb circumference

ANTICIPATED TIME

- Doppler method: approximately 10 minutes
- Oscillometric method: approximately 20 minutes

PREPARATION: IMPORTANT CHECKPOINTS

- Be sure the animal has acclimated to the clinic's environment and is calm and comfortable in lateral or sternal recumbency or sitting. BP values may be obtained in standing animals only if a tail cuff is used. Owner presence and assurance may help calm the animal.
- Be sure the cuff size used is appropriate and noted in the record for future reference. The width of the cuff should be (40% of the circumference of the limb or tail at the cuff site.
- During measurements with either method, the cuff should be at the level of the right atrium. This may involve elevating a forelimb during measurement if the animal is sitting.
- BP should be measured by well-trained individuals in the practice to maximize consistency. This is especially important when Doppler methods are used.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Erratic oscillometric readings may be obtained if an arrhythmia or very high heart rate is present.
- Turn volume knob to low or zero before turning Doppler amplifier on; then gradually increase volume to search for the pulse after contact is established between the crystal and the patient's skin. Failing to do this can produce extremely loud static noise that is startling to the patient (if using speakers) or deafening to the operator (if using headphones).

- For maximal accuracy in Doppler readings, be sure the audible signal is strong before beginning cuff occlusions.

PROCEDURE

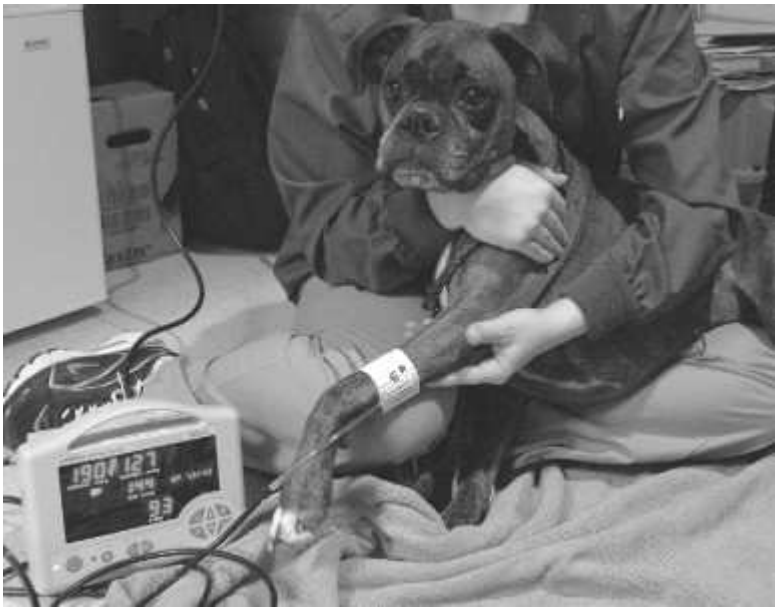
Doppler method:

- Restrain the animal in a comfortable position, and allow time and reassurance for acclimation. The position of the animal is dependent on the animal's temperament and mobility and on the planned position of the cuff.
    - Cuff on forelimb at level of radius: sternal or lateral recumbency or sitting position
    - Cuff on hind limb proximal to hock (tibial level): lateral recumbency preferred; sternal recumbency may be used if leg is in gentle extension during measurement.
- Measure the circumference of the limb or tail at the intended cuff site, and select an appropriately sized cuff (as already described when preparing the animal).
- Wrap the cuff snugly around the limb, and attach to sphygmomanometer.
- Clip or dampen hair as needed at site of Doppler crystal application distal to the cuff (palmar or plantar arterial arch, proximal to the metacarpal/metatarsal pad and slightly medial); apply coupling gel, and hold or tape crystal in position.
- The crystal is placed against the skin concave side down; the flat aspect of the crystal faces out.
- Turn volume knob to low setting, and turn amplifier on. Verify correct position of crystal by listening for clear pulsatile sounds of flow in the artery beneath the crystal. Adjust the crystal position or angle as necessary to improve signal strength if sounds are soft, distant, or muffled.
- Gently position limb so cuff is at the level of the right atrium during readings.
    - Sternum level if animal is in lateral position
    - Thoracic inlet level if animal is sternal or sitting
- While listening to sound of flow, inflate the cuff using the bulb manometer to approximately 20 mm Hg greater than the pressure needed to cut off flow sounds.
- Slowly deflate the cuff (1-3 mm Hg per second), and note the pressure at which pulsatile sounds of flow recur. This pressure is recorded as the systolic pressure.
- Completely deflate the cuff, and count the heart rate in the approximately 30 seconds between pressure readings. A contemporary heart rate can be recorded with each BP reading.
- Record at least 6 measurements in succession, allowing approximately 30 seconds to 1 minute between measurements to allow for limb reperfusion.
- Discard the first reading, and average the results of the remaining readings to obtain a representative number of systolic pressure and heart rate. High heart rate may indicate that increased levels of stress have affected readings.

Oscillometric method:

- Restrain the animal in a comfortable position, and allow time and reassurance for acclimatization. The position of the animal is dependent on animal's temperament and mobility and on the planned position of the cuff.
    - Cuff on forelimb at level of radius: sternal or lateral recumbency or sitting position
    - Cuff on distal hind limb at level of metatarsus (median artery): lateral recumbency preferred; sternal recumbency may be used if leg is in gentle extension during measurement.
    - Cuff on proximal tailhead: sternal or lateral recumbency or standing if animal is relatively immobile during readings (tailhead is preferred cuff site for oscillometric measurement technique in cats).
    - Limb cuffs should not be used in standing animals.
- Measure the circumference of the limb or tail at the intended cuff site, and choose an appropriately sized cuff (as already noted when preparing the animal).
- Wrap the cuff snugly around the limb, with the center of the inflatable bladder of the cuff positioned over the artery, and attach to the BP monitor.
- Gently position limb so cuff is at the level of the right atrium during readings (no repositioning required if tail cuff is used).
    - Sternum level if animal is in lateral position
    - Thoracic inlet level if animal is sternal or sitting
- Record at least 6 measurements in succession, allowing approximately 30 seconds to 1 minute between measurements to allow for limb reperfusion.
- Discard the first reading and any readings with clearly spurious results, and average the results of the remaining readings to obtain a representative number for systolic, diastolic, and mean pressures, respectively.
- Note the heart-rate readings associated with the BP readings. If heart rate is clearly incorrect, BP values may be spurious. In addition, high heart rate during recording may indicate high animal stress levels and possible elevated BP due to stress of procedure.

BLOOD PRESSURE MEASUREMENT Doppler method is used for estimating blood pressure (BP) in a cat. Note that animal is restrained in a calm, comfortable position. Cuff is applied to a distal forelimb, and limb is elevated such that cuff is at level of right atrium during readings. Coupling gel is applied to Dopple crystal (shown). After Doppler crystal is positioned over palmar arterial arch and a strong audible signal is obtained, bulb sphygmomanometer is used for inflating cuff and occluding arterial flow, then slowly deflated. Pressure at which arterial flow is again audible is recorded as the systolic BP.



BLOOD PRESSURE MEASUREMENT Automated oscillometric method used with a forelimb cuff to obtain systolic, diastolic, and mean blood pressure in a dog. Dog is restrained in a comfortable position, with intended cuff-site limb gently extended. Cuff is positioned at mid-radius level, and limb is positioned such that cuff is at level of right atrium during readings.

POSTPROCEDURE

- Record the average values in animal's record, with notation of method, cuff size, and cuff site used.
- Evaluate BP values in light of clinical findings and level of anxiety or excitement during BP measurement.

ALTERNATIVES AND THEIR RELATIVE MERITS

Invasive BP measurement involves acute arterial puncture (typically femoral artery) with a small-gauge needle attached to a pressure transducer, or catheter placement in a distal artery (typically dorsal pedal) and attachment to pressure tubing and a pressure transducer. A BP tracing is printed out, and systolic and diastolic pressure can be determined from the pressure tracing.

- Highly accurate information, since direct measure is used
- Local anesthesia is used for minimizing discomfort.
- Arterial puncture or arterial catheter placement requires more technical skill than noninvasive methods (see p. 1196).
- Bleeding may occur at site of femoral puncture if care is not taken to apply pressure for at least 5 minutes after the needle is withdrawn.
- Invasive methods are rarely used in conscious clinical patients, but indwelling arterial catheters are frequently used for continuous BP assessment in anesthetized or critically ill patients.

AUTHOR: REBECCA L. STEPIEN

Biopsy: Ultrasound-Guided Percutaneous

SYNONYMS

Tissue core biopsy, Tru-Cut biopsy

OVERVIEW AND GOAL

Procedure to obtain tissue core sample using ultrasound guidance and real-time monitoring of needle instrument placement

INDICATIONS

- Ultrasonographic detection of focal mass lesion
- Physical, ultrasonographic, or biochemical detection of diffuse or focal parenchymal organ abnormalities

CONTRAINDICATIONS

- Cavitated mass or bleeding disorder: risk of hemorrhage
- If abscess possible: risk of leakage, sepsis
- Intrathoracic masses not in contact with the chest wall: poor visualization
- Diffuse lung disease: risk of pneumothorax

EQUIPMENT, ANESTHESIA

- Biopsy instrument:
  - Automatic:
    - Manually advanced to a point 1.5-2 cm superficial to lesion
    - When triggered, cutting needle and external shaft automatically advance a specific distance
  - Semiautomatic:
    - Inner cutting needle manually advanced to desired depth
    - When triggered, external shaft automatically advances over cutting needle
  - Manual:
    - Operator controls depth of needle and length of tissue sampled.
    - Requires two hands to operate device
- Formalin container
- A #11 scalpel blade to incise skin
- A set of 25-gauge standard injection needles
- Hair clippers
- Surgical scrub, rubbing alcohol, gauze
- Sector or linear-array ultrasound transducer:
  - Sector transducers allow sampling of deep structures.
  - Linear-array transducers provide better resolution of superficial structures.
- ± Biopsy guide: easiest method, but angle of needle insertion fixed
- Anesthesia: IV or gas anesthesia required.

ANTICIPATED TIME

The procedure time is 10-15 minutes, plus anesthesia preparation/recovery time.

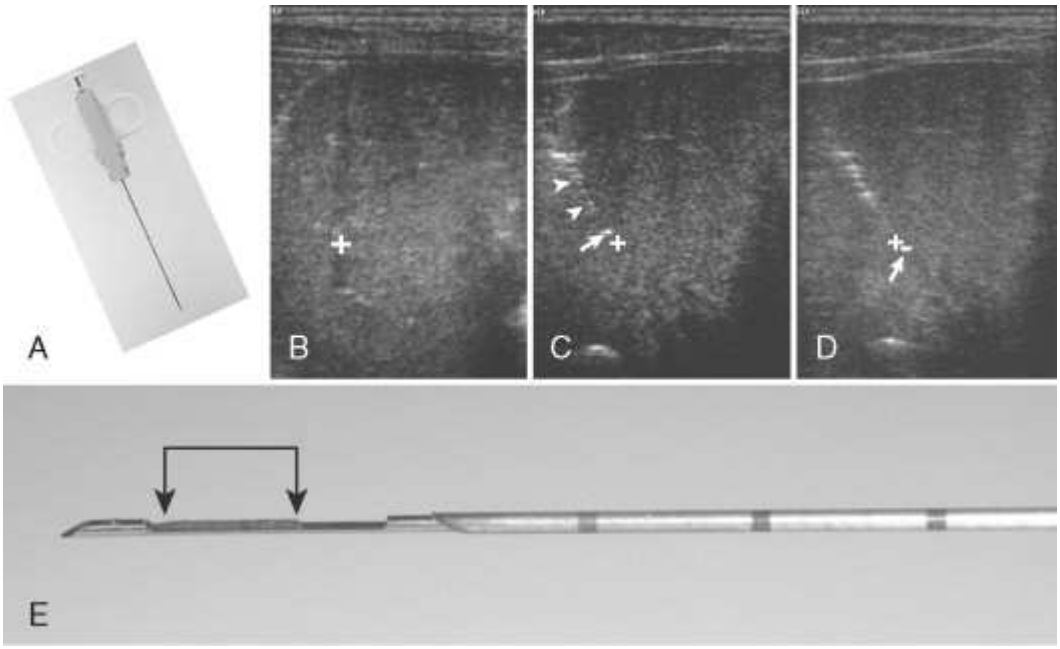
PREPARATION: IMPORTANT CHECKPOINTS

- Perform coagulation profile, platelet count, and blood pressure (BP) measurement.
- Place IV catheter.
- Ensure proper function of biopsy instrument.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Avoid overly rapid advancement and activation of the instrument:
  - A common, serious error of inexperienced veterinarians is to both advance and activate the instrument in one motion, which is contraindicated (poor placement/control of instrument tip).
  - The full extent of the instrument must be observed and monitored carefully and advanced with caution to the area to

be sampled.
- Identify and avoid large vessels in the organ being sampled or in those adjacent to the structure to minimize hemorrhage.
- Avoid penetrating bowel lumen, especially with larger-gauge instruments, owing to risk of peritonitis.
- Ensure that the ultrasound beam captures the full length and orientation of the instrument in the animal (see p. 1275).
- Sample the left aspect of the liver when possible to avoid the gallbladder and hilar vessels on the right. If the liver is small or cranially located, consider a caudal intercostal approach.
- In cases of bilateral renal abnormalities, the left kidney should be sampled because of its more caudal location.
- Sample the caudal cortex of a kidney to avoid the medulla and arcuate and hilar vessels.
- Do not pass through an organ other than the one being aspirated.
- Avoid using preanesthetic drugs that cause splenomegaly or panting whenever possible (e.g., acepromazine/phe-nothiazines, hydromorphone/opiates, respectively).



BIOPSY, ULTRASOUND-GUIDED A, Semiautomatic-type instrument used for ultrasound-guided core biopsy. **B**, Ultrasound of a dog's liver in preparation for core biopsy. Targeted area chosen for biopsy is marked (+). **C**, Ultrasound of same dog's liver, biopsy underway. Semiautomatic instrument shown in panel A has been advanced *(arrowheads)* until its tip *(arrow)* is immediately above the target. **D**, Internal stylet advancing. With instrument held immobile, internal stylet is slowly advanced, crossing through the targeted area or lesion. Once stylet is in the fully advanced/deployed position shown here, the instrument can be triggered, which obtains the sample. **E**, Core of liver tissue *(between arrows)* is shown within chamber of stylet.

PROCEDURE

- Restrain the animal in dorsal or lateral recumbency. A padded V-trough can be used.
- Clip hair from the ventral abdomen.
- Thoroughly evaluate area of interest sonographically, characterize lesion, identify adjacent or internal vessels to be avoided, and determine least traumatic location and direction of needle placement.
- Prepare skin with surgical scrub.
- Obtain ultrasound image of area to be sampled.
- Ensure that probe marker location on screen corresponds with desired needle course.
- Prepare biopsy instrument.
- Make a small skin incision with a scalpel blade at the site needle will be introduced.
- Introduce needle parallel to plane of ultrasound beam, visualizing it as it is advanced.
- Slowly fan transducer side to side to identify needle as necessary.
- Automatic:
    - Note the *throw length* of the biopsy device before triggering it. This is the additional distance the instrument advances when triggered.
    - Manually advance the needle, stopping at this distance superficial to desired biopsy site. Caution: When triggered, needle will advance the full predetermined throw length to obtain biopsy.
    - Trigger needle: cutting needle and external shaft will advance the predetermined throw length to obtain sample.
- Semiautomatic:
    - Manually advance the inner cutting needle to desired biopsy depth.
    - Trigger needle: external shaft will automatically advance over cutting needle to obtain sample.
- Manual:

    - Manually advance the inner cutting needle to desired biopsy depth.
    - Manually advance the external shaft over the cutting needle to obtain sample.
    - Requires two hands to operate, so two people are required for biopsy procedure.
- Withdraw needle from animal.
- Use a 25-gauge needle to gently lift sample from biopsy needle.
- Place sample in formalin container.
- Two to three samples of each organ or lesion are obtained.

POSTPROCEDURE

- Scan to evaluate for hemorrhage. A very small amount of hemorrhage is not uncommon.
- If small amount of hemorrhage is noted, reevaluate after several additional minutes, ensuring that the patient is monitored (mucous membrane color, blood pressure) and is kept recumbent with the biopsied side down (e.g., sternal recumbency if a liver biopsy was near or on the ventral midline).
- Hematuria is common following renal biopsy.

ALTERNATIVES AND THEIR RELATIVE MERITS

Laparoscopic (see p. 1298) and surgical biopsies are more invasive but have higher diagnostic quality in some cases.

SUGGESTED READING

Nyland TG, et al: Ultrasound guided biopsy. In Nyland TG, Mattoon JS, editors: Small animal diagnostic ultrasound, ed 2, Philadelphia, 2002, WB Saunders, pp 30–48.

Penninck DG, Finn-Bodner ST: Updates in interventional ultrasonography. Vet Clin North Am Small Anim Pract 28:1017–1040, 1998.

AUTHOR: WENDY D. FIFE

Behavioral Assessment

SYNONYMS

Behavioral problems: misbehavior, aggression, house soiling, destructiveness, barking

OVERVIEW AND GOALS

- To reestablish the owner/animal bond
- To protect the owner and the public from injury or loss of property

INDICATIONS

- Owner requests information on behavior.
- Better yet, practitioner asks the client how satisfied he or she is with the animal.
- It is often too late if the owners are already contemplating getting rid of the pet.

CONTRAINDICATIONS

If the dog or cat is very aggressive, the animal should probably be euthanized. Finding a new home for this animal is not an option. If the original owner cannot live with the animal, no one should have to.

EQUIPMENT, ANESTHESIA

- Assess-a-Hand
- Child-sized doll
- Closed-circuit television (camera and time-lapse video recorder)

ANTICIPATED TIME

About 1 hour for cats or 2 hours for dogs, including diagnosis and treatment

PREPARATION: IMPORTANT CHECKPOINTS

- Have a history form, preferably one for each species.
- Pictures of dogs and cat in various moods are very helpful.
- Have the most commonly used tools available, as appropriate:
    - Basket muzzle
    - Gentle Leader
    - Kong dog toy
    - Catalogs or websites of less commonly recommended products

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

Dealing with aggressive animals is a hazard, so liability is great. However, it is also essential to address an owner's problems correctly, or a life will be lost when the animal is euthanized.

PROCEDURE

The specific overall goal is to determine the exact nature of the problem, resulting in appropriate intervention and prognosis when possible. With the increased use of electronic communication, sending and receiving histories before the consultation is a convenient and time-saving strategy. A sample set of history forms can be found at www.vet.cornell.edu/abc. Note: Many owners are more willing to divulge behavioral information to technicians than to veterinarians. In addition, the technician can demonstrate training procedures and behavior modification techniques.

- Rule out medical disorders (e.g., urinary tract infection, feline lower urinary tract signs/disease, or ectopic ureters for soiling an area in the house; metabolic, central neurologic, endocrine, or pain-producing conditions for aggression), and treat appropriately if present.
- Clarify the nature of the environment surrounding the behavioral problem:
    - Number of people and animals in the household
    - Amount of space at the animal's disposal, both with owners at home and when absent

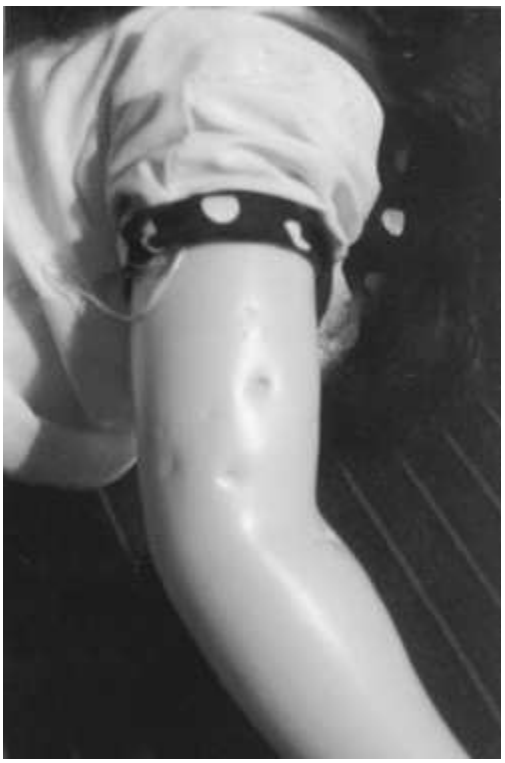
    - For cats, the location, type, and contents of litter boxes
    - Change in the people or pets in the household or their schedules
    - If the presenting problem is destructive behavior, soiling an area in the house, or barking, an important step is to determine whether these events occur when the owners are at home or only when they are gone.
- Clarify the reaction of the owners and others to the animal's misbehavior. Do they punish or soothe the animal?
- Help the owner to avoid misdirected intervention, such as punishing after the fact, physically punishing the dog for aggressive behavior, or rewarding jumping up.
- The owner should be given a reasonable treatment plan that does not involve risk to the owner or the public.
- A detailed history should be taken carefully. A destructive dog can be used as an example:
    - When is the animal destructive?
    - Where is the animal destructive?
    - With what methods have the owners tried to address the problem?

Note: It is always important to maintain a neutral attitude when taking a history, because any criticism of the owners' methods at this time will probably inhibit owners from volunteering any additional information as the interview continues. The dog's early history often gives clues regarding the cause of misbehavior:

- If the dog was obtained from a kennel at 6 months of age, it may neither have been house broken properly nor socialized to people during the socialization period of 7-14 weeks of age.
- If the dog was obtained as a 3-week-old puppy or was hand raised, it may be too dependent on people and not properly socialized with dogs.
- If the dog was obtained from a pound or an animal shelter, it may have been placed there because it was destructive or aggressive in the original home.

The owners should be able to supply this information and to indicate why they obtained the animal. Hand-raised kittens are frequently presented for aggression as adults, and feral or free-ranging cats may be reluctant to remain indoors and may vocalize, claw, or spray when confined.

- Note: Canine aggression is much more complicated. The victim, time, place, and circumstances of the aggressive episode must be known. The owner should be asked to describe the dog's posture: the position of its ears and tail as well as its vocalization and mouth position. Pupillary dilation and raised hackles indicate sympathetic stimulation. A temperament test should be performed. A toddler-sized doll can be walked toward the dog. Although some dogs are frightened, aggressive ones will bark at, and even bite, the doll. An artificial hand (Assess-a-Hand) can be used for determining how responsive the dog is to touching of its head, abdomen, paws, and tail. The artificial hand can also be used for pulling food from the dog in a safe manner.



BEHAVIORAL ASSESSMENT Bite marks on a doll's arm inflicted by an aggressive dog during a behavioral assessment.

Behavior history forms for cats can be shorter than those for dogs because cats rarely are trained and do not require the attention that dogs do. Because cats are much less likely to demonstrate their misbehavior during an interview, a video recording of the cat when it is aggressive is very helpful. If the problem is soiling an area in the house, time-lapse video recording can elucidate which cat in a multicat household is soiling and what its preelimination and postelimination behaviors are. Many cats visit the litter box but eliminate elsewhere, indicating an aversion to the litter or the box.

POSTPROCEDURE

Recheck the animal at 3 and 6 weeks to determine the success of the treatment and compliance of the owner.

ALTERNATIVES AND THEIR RELATIVE MERITS

Behavioral problems can be referred to trainers, but there is no quality assurance. Herbal remedies also lack quality control or controlled studies of their efficacy.

AUTHOR: KATHERINE ALBRO HOUPT

Barium Esophagram, Dynamic

SYNONYMS

Barium swallow, fluoroscopic esophagram

OVERVIEW AND GOAL

To administer a contrast agent per os (PO) and observe the oral and pharyngeal phases of swallowing and esophageal transit using fluoroscopy. The goal of the study is to define abnormalities of swallowing and/or esophageal transit.

INDICATIONS

Functional abnormalities of swallowing (dysphagia, abnormal esophageal motility). Can be used for evaluating mechanical abnormalities (mass, foreign body, extrinsic compression), but a static esophagram is usually sufficient for this purpose.

CONTRAINDICATIONS

- Evidence or risk of esophageal perforation
- Megaesophagus (not an absolute contraindication, but the study is not needed for diagnosis).

EQUIPMENT, ANESTHESIA

- Contrast agent:
  - Liquid barium (30% weight/volume and higher density)
  - Iodinated contrast agent:
    - Nonionic (iohexol, iopamidol, ioxaglate compounds)
    - Diluted 1:1 with water
- Highly palatable canned food
- Syringes for barium administration
- Bowl and utensil for mixing barium and food
- X-ray unit:
  - Fluoroscopic capability
  - Spot film capability
  - Video recording capability
- Protective clothing (lead aprons, gloves, thyroid shields) for personnel
- Paper towels or similar for cleanup of barium on animal and x-ray table

ANTICIPATED TIME

15-20 minutes

PREPARATION: IMPORTANT CHECKPOINTS

- Survey films of thorax and cervical region:
  - If contraindications are present (as previously mentioned), study should not be performed.
  - If plain films are diagnostic (i.e., megaesophagus), the study is unnecessary.
- Prepare contrast agents:
  - Barium:
    - Liquid barium in appropriately sized syringe
    - Liquid barium mixed with canned food. Only a small amount of barium ((5 mL) is needed, which also will keep the solid consistency of the food.
  - Nonionic iodinated contrast agent:
    - Iohexol, iopamidol, ioxaglate compounds
    - Liquid diluted 1:1
    - Diluted liquid is mixed with canned food.
- Personnel needed for procedure (restraint and administration of contrast). This may require two to three people, depending on animal's size and temperament.
- All personnel should have appropriate lead protective apparel (aprons, thyroid shield, gloves).
- Paper towels or other barrier drapes to limit excess contrast agent on table and animal

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Aspiration of contrast agent: study is always begun with a liquid contrast agent and no food. Animals with disorders requiring these evaluations may be prone to dysphagia and aspiration of contrast. If a small amount of liquid contrast agent is aspirated, it can be coughed up. If the animal aspirates a substantial amount of liquid contrast agent, the study should be aborted.
- Ionic iodinated contrast agents: these agents should not be used because clinically significant (potentially fatal) pulmonary edema can occur if they are aspirated. Ionic agents include diatrizoate, iothalamate, and iodamide compounds. All must be avoided.
- Nonionic iodinated contrast agents: these agents can be used if esophageal perforation is suspected.
- Leakage of contrast agent: evidence or risk of esophageal perforation is considered a contraindication for this study. If contrast agent leakage is suspected at any time, the study should be aborted.
- Assuming the procedure is not stopped because of aspiration of contrast agent or evidence of leakage of contrast agent, it is important to perform the study with both liquid contrast agent and liquid contrast agent mixed with food to give as full an assessment of esophageal function as possible.
- Fluoroscopic procedures involve a substantial radiation dose to the animal and to personnel. Radiation safety (e.g., proper protective clothing, collimation so that personnel are not included in the primary beam) is paramount.

PROCEDURE

Dynamic esophagram, barium:

- Survey films of thorax and cervical region (already described in preparation)
- Position animal in right lateral recumbency (if a C-arm fluoroscopy unit is used, it may be possible to place the animal in sternal recumbency and use a horizontal beam) with appropriate restraint.
- Activate fluoroscopy unit briefly to determine correct positioning and collimation.
- Activate the video recorder.
- Administer liquid barium PO (~5 mL for a cat and 5-10 mL depending on the size of the dog), and activate fluoroscopic unit. Image the oral and pharyngeal phases of swallowing (progression of barium from mouth to esophagus) and esophageal transit (progression from upper esophageal sphincter to stomach). Repeat two to three times even if no abnormality is defined.
- Spot film any areas of abnormality; lateral views are generally sufficient.
- Repeat above procedure with barium paste (optional).
- Administer barium and canned food mixture PO. Appropriately sized food balls (1-3 cm in diameter) may be fed to the animal or placed in the mouth. Activate fluoroscopic unit, and image the oral and pharyngeal phases of swallowing (progression of barium and food from mouth to esophagus) and esophageal transit (progression from upper esophageal sphincter to stomach). Repeat two to three times even if no abnormality is defined.
- Spot film any areas of abnormality; lateral views are generally sufficient.

Dynamic esophagram, iodinated contrast agent:

- This study may be performed if esophageal rupture is suspected or if endoscopy is to be performed immediately following the esophagram. If an esophageal perforation is suspected, a static esophagram is usually performed instead, using a nonionic iodinated compound.
- The dynamic esophagram using an iodinated contrast agent follows the same procedure as the barium esophagram.

POSTPROCEDURE

None

ALTERNATIVES AND THEIR RELATIVE MERITS

Static esophagram: a static esophagram (administration of barium and obtaining routine films) can be used in place of a dynamic study for certain indications. A static study does not require the use of a fluoroscopy unit and is generally sufficient for most suspected mechanical abnormalities of the esophagus (e.g., esophageal foreign body, esophageal mass, esophageal stricture). However, subtle abnormalities of swallowing and esophageal transit are rarely identified in this study, and it provides no information on the pharyngeal phase of swallowing.

SUGGESTED READING

O'Brien T: Esophagus. In O'Brien T, editor: Radiographic diagnosis of abdominal disorders in the dog and cat: radiographic interpretation, clinical signs, pathophysiology. Davis, CA, 1981, Covell Park Vet Company, p 141.

AUTHOR: PATRICIA L. ROSE

Barium Enema

SYNONYM

Large bowel/rectal contrast study

OVERVIEW AND GOAL

To perform a radiographic contrast procedure that provides information on the gross structure of the colon and rectum. This information generally is not available by other routine imaging means: abdominal ultrasound is limited by the presence of gas in the colon, and plain radiography cannot evaluate the mucosal surface of the colon and cannot evaluate colonic distensibility.

INDICATIONS

- Persistent tenesmus
- Pelvic canal/rectal mass effect on rectal palpation and/or on plain radiographs
- Severe constipation/obstipation not responsive to simple medical management

CONTRAINDICATIONS

Note: Organic iodine contrast material (e.g., sodium iothalamate, sodium diatrizoate, diluted 1 : 1 with water) should be used instead of barium if rectal or colonic perforation is suspected; contrast effect will be reduced, however (see p. 1284).

EQUIPMENT

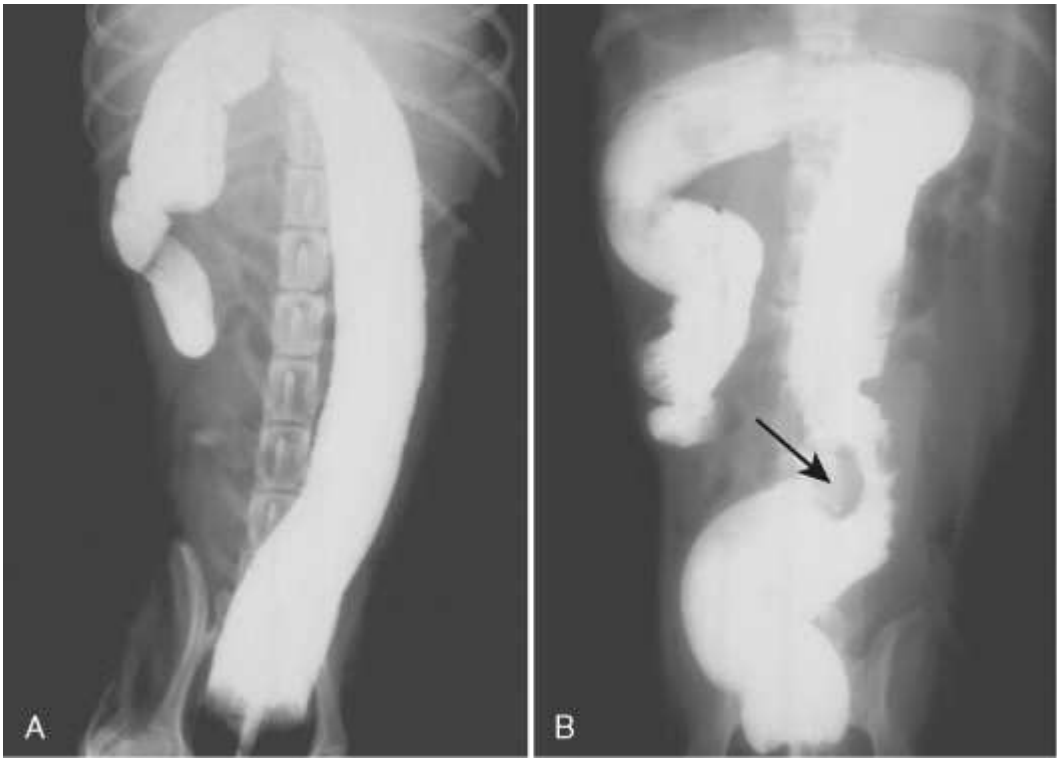
- General anesthesia is usually required; otherwise, barium is often expelled from the rectum by the animal's straining.
- Enema bag/set; for smaller animals, large syringes may be used instead.
- Barium sulfate suspension with concentration 15%-20% weight per volume
- Foley urinary catheter (e.g., 10-18 Fr tube for body range of cats to large dogs, respectively) or Bardex catheter
- Sterile, water-soluble lubricant

ANTICIPATED TIME

Approximately 40-60 minutes

PREPARATION: IMPORTANT CHECKPOINTS

- Fecal occult blood testing is highly specific using O-tolidine-based test kits and may be performed to further increase an index of suspicion for a colonic abnormality.
- Prepare an adequate volume of barium. Using too low a barium dose is a very common problem, causing pseudolesions or missing lesions altogether.
- Barring excessive anal pain, any dog weighing 6 kg or more needs to have a simple but complete rectal palpation prior to barium enema to better localize any focal lesions.
- Animal fasted 24 hours
- A maximum amount of feces is evacuated from the colon prior to the administration of the barium enema.
- Metastasis imaging (three-view thoracic radiographs; abdominal ultrasound to assess liver, lymph nodes, etc.) is indicated if malignancy is part of the differential diagnosis.



BARIUM ENEMA A, Ventrodorsal projection, normal study. **B**, Ventrodorsal projection, abnormal study. Large filling defect in distal colon *(arrow)* causes marked narrowing of lumen, suggesting a mass lesion.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

Perianal trauma and iatrogenic colonic perforation are very rare; use Foley catheter instead of rigid enema tube.

PROCEDURE

- Obtain preliminary abdominal radiographs to confirm adequate animal preparation (colon is as empty as possible) and to set radiographic technique. The barium contrast dose of 10 mL/kg is placed into enema reservoir.
- Lubricate catheter and insert sufficiently such that Foley balloon is well beyond the anus and within the rectum.
- Inflate Foley balloon to reduce or prevent outflow of contrast from the anus, and gently tug on catheter to bring Foley balloon to seal caudally and prevent contrast leakage from anus.
- Slowly administer barium, with the animal in right lateral recumbency, using gravity for colonic filling (raise the reservoir above the animal).
- Once the colon has been distended, clamp the infusion tubing to prevent backflow of the contrast material.
- Obtain both lateral and oblique views (45 degrees) and a ventrodorsal view.

POSTPROCEDURE

- Routine anesthetic recovery
- The clinician should tell the client that it is normal for the stools to be loose and grey or pale brown in color for several defecations after the procedure.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Endoscopy has largely replaced barium enemas.
- Abdominal ultrasound: the potential for visualizing the structure of the colonic wall is often severely restricted by the pelvis and by presence of air in the colon.
- Plain radiographs: diagnostic test of choice for bony obstruction of the pelvic canal (fracture, malformation, mass); poor sensitivity for soft-tissue lesions of the colon
- Colonic biopsy: diagnostic test of choice once a focal or diffuse mucosal lesion is suspected or identified

AUTHOR: LEEANN PACK

Cystoscopy

SYNONYMS

Transurethral cystoscopy, urethrocystoscopy, uroendoscopy

OVERVIEW AND GOALS

Transurethral cystoscopy (TUC) involves the use of rigid or flexible endoscopes for examination of the urinary bladder via passage through the urethra. Most anatomic structures of the lower urinary tract can be visualized: vulvar vestibule, vagina, urethral orifice, urethra, urinary bladder, and ureteral orifices. This procedure is done relatively commonly in specialty practice.

INDICATIONS

TUC is most often used in chronic conditions, but it may also be beneficial in cases with severe acute presentations. A differential diagnosis list for any of the following disorders or clinical signs could be an indication for transurethral cystoscopy:

- Anatomic abnormalities: vaginal strictures, persistent vaginal membranes, ectopic ureters
- Cystitis: chronic infectious, idiopathic, interstitial
- Posttraumatic or postsurgical assessment: pelvic fractures, abdominal trauma, prior surgery
- Hematuria: examination to identify origin of bleeding and observation of ureteral orifices (unilateral versus bilateral hematuria of renal origin)
- Urethritis: infectious, inflammatory, granulomatous (also known as proliferative)
- Stranguria
- Urinary incontinence: diagnostic identification of possible causes; therapeutic periurethral submucosal injections of glutaraldehyde cross-linked collagen for urethral sphincter mechanism incompetence
- Pollakiuria
- Calculi: urethral or cystic calculi retrieval and identification
- Tumor: urethral, urinary bladder, prostatic, vaginal
- Obstruction: tumor, stricture, calculi, hyperplasia (vaginal)
- Urethral stricture: diagnosis and dilations
- Removal of small polyps and tumors
- Ureteroscopy: for advanced endoscopists; requires concurrent fluoroscopy
- Holmium-doped yttrium, aluminum, garnet (Ho:YAG) laser: used for laser lithotripsy (see p. 1297); this is of growing interest and of proven benefit for the fragmentation of urinary calculi. These lasers have also been used for ablative treatment of intraluminal tumors and ectopic ureteral openings. As of 2009, the cost and advanced training involved have left the use of this laser as a procedure available at a few veterinary teaching hospitals and larger referral centers.

CONTRAINDICATIONS

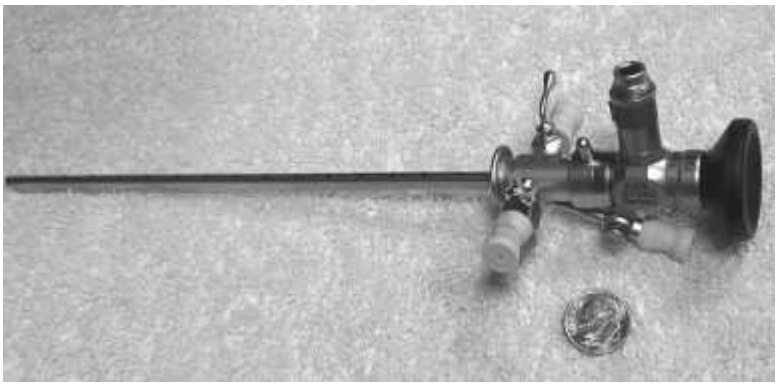
- Animal size and sex are the most common limiting factors; the exact limitations depend on endoscope size (external diameter) relative to the patient, as described in the following paragraphs.
- Known severe bacterial urinary tract infection is a relative risk factor.
- Known perforation or rupture of bladder or urethra

EQUIPMENT, ANESTHESIA

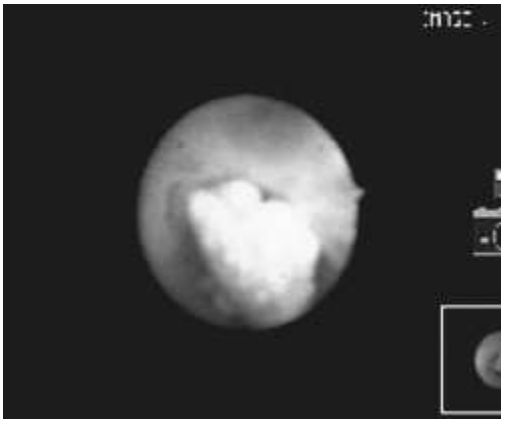
There is a wide array of possible equipment to use for transurethral cystoscopy. The marked differences between the male anatomy and female anatomy and between dogs and cats lead to the common veterinary statement “You can never have enough scopes.” To be prepared for any size and sex of animal may require a mix of six to seven flexible and rigid scopes.

- Review of the normal anatomy of the lower urinary tract
- Preparation of the preputial or perineal area by clipping interfering hair and gentle cleansing
- General anesthesia with tracheal intubation is required
- Between 1 and 2L of body-temperature sterile saline for flush and infusion during procedure via IV infusion set. A second IV infusion set is used for drainage and collection from the opposite port.
- Water-soluble sterile lubricant with or without lidocaine jelly
- Bacterial culture tubes
- Biopsy jars with 10% buffered formalin

- Flexible-tipped ureteral guide wires can be helpful for bypassing obstructions, strictures, and tears (serving a stylet-type function), then allowing catheters to be passed over them. Human ureteral dilation catheters can be used with the guide wires if urethral stricture is present.
- Accessory implements include sterile brushes, guide wires, biopsy forceps, balloon catheters, sterile catheters, stone retrieval baskets, and polypectomy snares (with or without electrocautery).
- Appropriate light source and light cable
- Documentation equipment (videocassette, digital video, prints)
- Flexible endoscopes:
    - Size of scopes varies by both anticipated length of the urinary tract segment to be assessed (cranial tip of filled bladder extending to perineum or preputial opening) and diameter of the urethra.
    - As examples: A larger female dog may be examined cystoscopically using a 5-mm, two-way deflecting fiberendoscope (e.g., bronchoscope), while a small male cat may only allow passage of a 1.2-mm pediatric ureterocystoscope.
    - Ancillary catheters, brushes, stone retrieval baskets, and biopsy forceps
    - Flexible endoscopes may require more positioning and manipulation of the animal because they tend to be deflected easily by external pressures.
- Rigid endoscopes:
    - A wide array of rigid endoscopes from human medicine can be used for transurethral cystoscopy, including purpose-designed cystoscopes, small laparoscopes, and adapted arthroscopes.
    - Rigid telescope sizes most commonly used range from 2.7-5 mm in diameter, with respective cannula (sheath) diameters ranging from 3.8-6 mm; length of the scopes ranges from 7-30 cm. The cannula usually includes the associated biopsy and infusion ports. Smaller scopes may have the outer cannula and ports combined into one single unit.
    - A 0° viewing angle may be better for viewing the urethra, and a 30° viewing angle may be preferred for viewing the bladder.
    - A "bridge" is used for connecting some scopes with their cannulas (cannula-bridge-scope) and to provide additional access ports (generally one or two) for flushing or infusion of saline and passage of other instruments.
    - The Albarrán lever is a "deflecting bridge" that forces flexible biopsy instruments to exit the bridge at an angle; this facilitates biopsy and grasping of structures that are almost parallel to the scope.
    - The Ellik evacuator allows for rapid saline lavage to provide for collection of small calculi when attached to a rigid cystoscope cannula.
    - Rigid scopes tend to provide superior images.

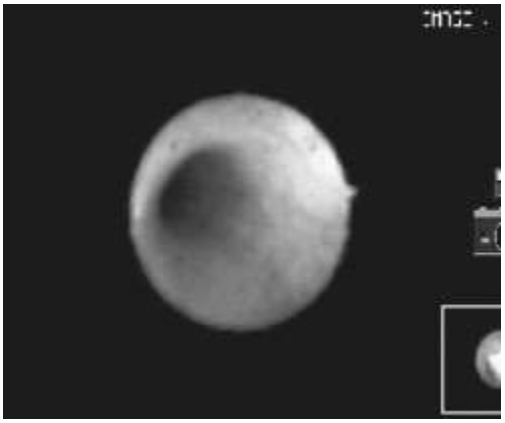


CYSTOSCOPY Assembled cystoscope and cannula/sheath.



CYSTOSCOPY Endoscopic view of urethra of a dog with severe stranguria and hematuria. A large urolith is occluding most of the lumen.

(Courtesy Dr. Etienne Côté.)



CYSTOSCOPY Endoscopic view of same site in same dog. Using an older set of dull biopsy forceps, urolith was fragmented into several pieces within the urethral lumen, and fragments passed easily through urethra during procedure. Moderate mucosal erythema remains (bottom half of image), but dog's recovery was uneventful and complete.

(Courtesy Dr. Etienne Côté.)

ANTICIPATED TIME

- About 30-75 minutes, depending onease of passage, extent of lesion(s), and whether the procedure is diagnostic or also therapeutic (e.g., stone retrieval)

PREPARATION: IMPORTANT CHECKPOINTS

- Have clear goals for the procedure based on case assessment.
- Know the appearance of normal structures in the lower urinary tract via textbooks and continuing education/training.
- Plan ahead for staff involvement with setup, procedural assistance, and cleaning the equipment.
- Discuss with owner that repeated procedures can be required (e.g., stone retrievals, stricture dilation, reassessments, etc.).
- Make alternative plans for surgery if goals are not achieved.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Mistaking the fossa clitoridis in female dogs for the urethral orifice
- Prior digital- or catheter-induced trauma to the urethral tubercle (papilla), thereby hindering entry of the endoscope into the urethra
- Iatrogenic urinary tract infections (UTIs)
- Rupture of the urinary bladder or urethra as a result of inappropriate technique (overfilling) or existing disease. Care should be taken while biopsying pathologic or thin areas of bladder wall (e.g., the site of remnant diverticula, intramural cancer).
- Urethral mucosal edema due to inherent trauma from endoscopy can be a limiting factor in uroendoscopy, particularly in the urethra of male dogs.
- Operator reliance on visual impressions rather than histopathologic or cytologic evaluation of samples

PROCEDURE

- If using small-diameter flexible endoscopes, if the urine is turbid and dark, or if there is gross hematuria, it may be best to empty the bladder prior to the procedure via urethral catheterization (see p. 1226).
- Transurethral cystoscopy can be done with the animal in either ventral or dorsal recumbency; the author prefers dorsal recumbency, but it can be necessary to reverse the selected position.
- Pre-procedure enemas can be done to reduce interference by colorectal feces (lessen mechanical depression of adjacent urinary structures, risk for fecal leakage contamination of perivulvar region during procedure).
- The perineum and prepuce or vulva are cleansed; it is preferable that an aseptic technique be the goal and any procedure-related materials be kept sterile (away from surrounding hospital-related contamination). However, it is expected that contamination from the animal will occur via the urethra, vulva, or prepuce.
- For female dogs and cats, the fiberendoscope or cannula with a rigid scope assembly is placed in the vulva, and the vulvar skin is gently pinched externally (by an assistant) to create a seal; then a saline infusion is started until the vault is distended. When the vulvovaginal area has been examined and the urethral orifice identified, the urethra is cannulated with the scope and distended with saline as the scope is passed to the bladder. The bladder is then emptied via the biopsy channel of the

fiberscope or cannula (remember that the rigid scope slides through the cannula) and then refilled with saline. It is important to visualize the appearance of mucosa both when the bladder is empty and when it is filled.

- For male dogs and cats, the technique is similar, except that the prepuce is held to form a seal around a flexible fiberendoscope. Male dogs may also have the pelvic and proximal urethral segments examined using a rigid urethrocystoscope via a temporary prepubic perineal urethrostomy.
- The bladder is examined in a methodical pattern inclusive of the apex of the bladder.
- The ureteral orifices are identified, and in many cases, pulsatile flow of urine can be observed. Then the trigonal area is examined. Biopsies are taken for histopathologic evaluation and culture. Calculi may be examined and samples taken for analysis. Calculi may be larger than the lumen of the cannula channel. If smaller than the urethral limitation, these larger stones may be drawn up to, and held against, the end of the scope. Then the scope and stone are withdrawn simultaneously. The size of the stone or stone fragments can limit the usefulness of this technique.
- The endoscope is withdrawn slowly while the clinician observes for abnormalities. Visualization of the urethral mucosa is often superior during withdrawal of the endoscope.
- Ectopic ureteral openings in the urethra can be identified in most cases with more accuracy than with the use of contrast radiography; multiple sites of ectopic openings might be identified.
- In the male dog, the colliculus seminalis is located dorsally and can be seen more prominently in intact dogs, as well as the associated prostatic and deferent duct openings into the proximal urethra.
- The vaginal area is then examined for irregularities to the level of the cervical os. Biopsies, brush cytologic analysis, and other procedures are done as warranted.
- The goals of the procedure should be reviewed prior to final withdrawal.

POSTPROCEDURE

- Consider antibiotic use when it is appropriate for the case.
- Postprocedural urethral obstruction can occur but is infrequent. It is usually correlated to the severity of the pathology present. Monitoring of micturition is advised until normal voiding is seen.
- Use appropriate pain management for the patient.

ALTERNATIVES AND THEIR RELATIVE MERITS

Laparoscopic-assisted suprapubic (pre-pubic) percutaneous cystoscopy can be done but is more involved with equipment and invasiveness. It may be used when larger tumors obstruct the trigonal region or urethra, for collection of greater numbers of small calculi, or for placing a retrograde guide wire to facilitate ante-grade catheterization of the urethra.

AUTHOR: MARK E. HITT

Cystogram

OVERVIEW AND GOALS

- On survey radiographs, the urinary bladder is often visualized. However, if further evaluation of the urinary bladder is needed or if the urinary bladder is not adequately seen on survey films, a cystogram may be needed.
- A cystogram is a radiographic study of the urinary bladder obtained following intraluminal administration of a positive contrast medium, negative contrast medium, or both. Evaluation of the urinary bladder with ultrasound has largely replaced many functions of the cystogram.

INDICATIONS

- Dysuria, pollakiuria, hematuria, stranguria
- Evaluation of caudal abdominal masses
- Increased or decreased opacity associated with the bladder
- Nonvisualization of the bladder after abdominal or pelvic trauma; suspected bladder rupture
- Abnormally-shaped or abnormally-located bladder
- Congenital abnormalities
- Recurrent or nonresponsive urinary tract infection (UTI)
- Suspected neoplasia
- Suspected polyp(s)
- Suspected radiolucent calculi
- Posturethral/cystic surgical evaluation

SPECIFIC STUDY FOR SUSPECTED DISEASE

- Negative-contrast cystogram: bladder position
- Positive-contrast cystogram: bladder rupture, bladder position
- Double-contrast cystogram: mucosal thickness (cystitis), mucosal margination, luminal contents (calculi), neoplasia

EQUIPMENT, ANESTHESIA

- General anesthesia or heavy sedation
- Agents:
    - Negative-contrast cystogram: room air, carbon dioxide, nitrous oxide
    - Positive-contrast cystogram: iodinated contrast medium (sodium iothalamate, sodium diatrizoate) or noniodinated contrast medium (iohexol, iopamidol) if clinically warranted
- Urinary catheter with inflatable bulb (Foley catheter) appropriately sized for the animal
- Tomcat catheter used for male cats
- Sterile lubricating jelly
- Surgical gloves
- Sterile syringe for contrast
- Sterile syringe for withdrawing urine from bladder
- Sterile syringe to inflate Foley balloon
- Mild surgical scrub solution and gauze/sponges for prepping the penis/vulva
- Sterile three-way stopcock
- Sterile catheter adapter (Christmas tree)
- Enema bag/set
- Sterile saline

ANTICIPATED TIME

Approximately 30 minutes

PREPARATION

- Animal fasted 24 hours
- Water ad libitum
- Enema given at least 2 hours prior to study to remove a maximum of fecal material from the colon to allow visualization of the

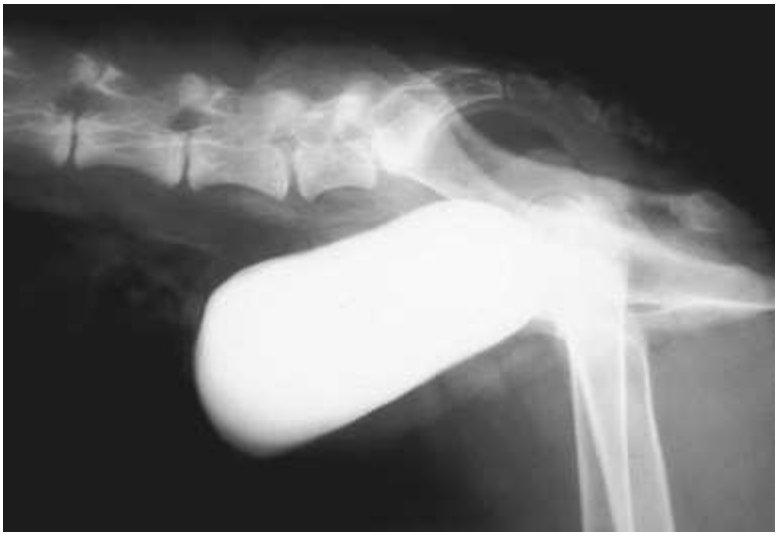
urinary bladder
- Sterile gloves should be worn from this point forward.
- Positive-contrast cystogram:
  - Dilute positive contrast agent to 15%-30% with sterile saline.
  - Dose of diluted contrast is 10 mL/kg.
  - Draw appropriate dose into a syringe.
- Negative-contrast cystogram:
  - Use 10 mL/kg of chosen negative agent (cats: 4-50 mL generally adequate).
  - Draw appropriate dose into a syringe.
- Double-contrast cystogram:
  - Use 10 mL of undiluted positive-contrast agent (cats: 2-4 mL).
  - Use 10 mL/kg of chosen negative-contrast agent (cats: 40-50 mL generally adequate).
  - Draw appropriate doses into syringes.
- Remove Foley catheter from packaging, using aseptic technique.
- Attach catheter adapter (Christmas tree) to Foley catheter.
- Attach three-way stopcock to catheter adapter.
- Draw appropriate amount of air into a syringe to inflate the Foley bulb.
- Attach syringe containing air to the three-way stopcock.
- Open three-way stopcock to allow air flow into the catheter bulb to ensure the bulb is intact. Fill the bulb to the recommended level, and close the three-way stopcock.
- Once it is clear the bulb will hold air, release the air from the bulb, leaving the air in the syringe.
- Attach the syringe filled with selected contrast onto the three-way stopcock (and fill the catheter with positive contrast if performing a positive contrast study).
- Close the stopcock to the contrast material, and open to the syringe filled with air for bulb inflation.
- In male cats, a sterile tomcat catheter is used. Contrast material is drawn into the syringe, and the syringe is attached directly to the catheter.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

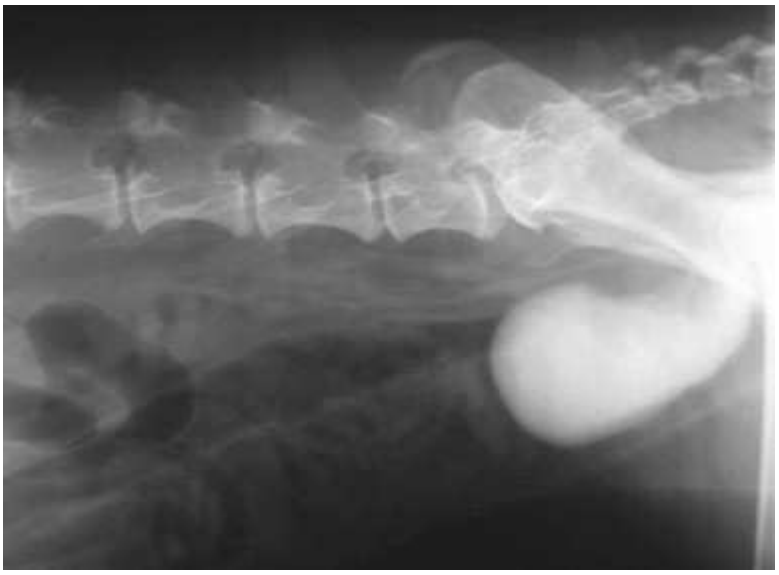
- Urinary bladder rupture
- Cystitis: hemorrhagic, emphysematous
- Bacterial contamination: iatrogenic UTI
- Bladder or urethral trauma
- Catheter kinking or knotting
- Positive-contrast media reaction (rare)
- Negative-contrast: possibility of air embolism with severe mucosal disease (rare)

PROCEDURE

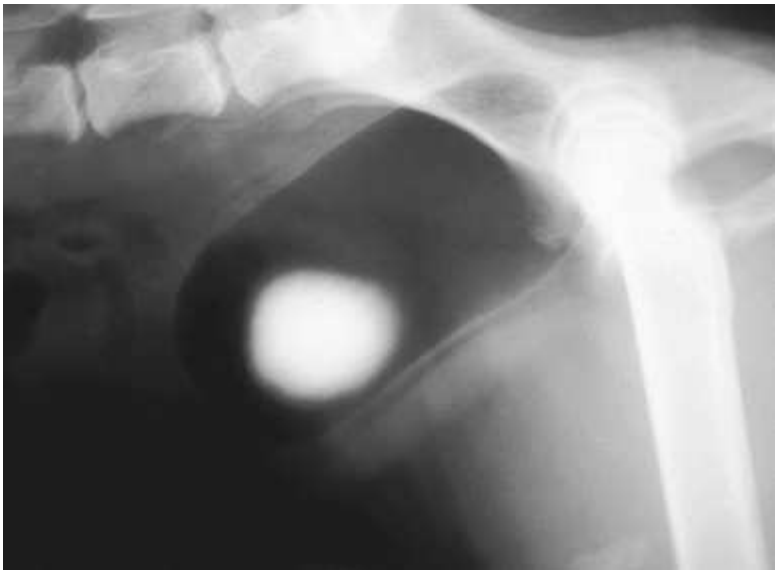
- Preliminary abdominal radiographs are made to determine adequate animal preparation and set radiographic technique.
- The kilovoltage peak (kVp) should be set between 65 and 75 to maximize contrast due to the photoelectric effect (K edge of iodine).
- Milliampere seconds (mAs) may need to be increased 25%-50% compared to settings for survey radiographs.
- The animal should be placed in left lateral recumbency.
- An assistant should extrude the penis in the male.
- The penis/vulva should be prepped with mild surgical scrub solution.
- Sterile lubricating jelly is placed on the Foley catheter.
- The catheter is then gently advanced into the urinary bladder (a stylet can be used with the Foley if necessary; see p. 1226).
- Inflate the catheter bulb with air, and then close the stopcock to maintain inflation.
- Attach a syringe onto the stopcock, and open the stopcock to this syringe.
- Remove as much urine as possible from the bladder (repeat as necessary to allow total emptying).
- Close stopcock to this syringe and discard syringe.
- Turn stopcock open to the contrast medium, and inject the dose of chosen agent.
- Palpate the bladder periodically to ensure it is not overdistended.



CYSTOGRAM Positive-contrast cystogram, lateral projection. Normal study.



CYSTOGRAM Positive-contrast cystogram, lateral projection. Large filling defect seen along caudodorsal aspect of urinary bladder later diagnosed as transitional cell carcinoma.



CYSTOGRAM Double-contrast cystogram, lateral projection. Normal study.

- Stop if back pressure is felt, if reflux is seen around the catheter, or if the bladder feels full.
    - Positive: once the contrast is in the bladder, images can be obtained.
    - Negative: once the contrast is in the bladder, images can be obtained.
    - Double: inject the positive contrast, then roll the animal to ensure good mucosal coating; follow this with injection of the negative contrast, then images can be obtained.
    - Note: If a double-contrast study is desired after a positive-contrast study, the majority of the positive contrast is removed from the bladder, leaving only a small puddle; then negative contrast is injected.
- Ventrodorsal and lateral radiographs are made immediately after injection.

POSTPROCEDURE

- Once the study is complete, the recoverable volume (majority) of contrast is withdrawn from the urinary bladder.
- Air should be removed from the catheter bulb before the catheter is withdrawn.
- If anesthesia used, expect a routine anesthetic recovery.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Plain abdominal radiographs: inexpensive means to survey the abdomen. Radiopaque cystic calculi can be visualized. Size and shape of the bladder often obvious.
- Abdominal ultrasound: noninvasive and readily available; excellent for visualization of bladder, especially wall thickness, luminal contents, and trigone region. Urinary bladder rupture not definitive with ultrasound.
- CT scan and MRI: provide excellent study of the bladder; however, these are costly and rarely performed for this indication.
- Urethrogram: see p. 1357

AUTHOR: LEEANN PACK

Cystocentesis

OVERVIEW AND GOAL

To obtain a sample of urine from the bladder

INDICATIONS

- Urinalysis
- Urine culture and sensitivity (C&S)
- Diagnostic evaluation of vaginal or preputial discharge or of discolored urine

CONTRAINDICATIONS

- Bleeding disorder
- Ascites
- Peritonitis
- Dyspnea, back/hip pain, or other conditions causing distress during dorsal recumbency
- Bladder neoplasia (tumor seeding in needle tract)

EQUIPMENT, ANESTHESIA

The procedure is generally performed awake, but sedation or general anesthesia does not preclude it. The following equipment should be available:

- A 22-gauge, 1½-inch (4 cm) needle
- A 12-mL syringe
- Cotton balls or gauze squares (e.g., 3 × 3 inches [8 × 8 cm])
- Isopropyl alcohol

ANTICIPATED TIME

<5 minutes

PREPARATION: IMPORTANT CHECKPOINTS

Identify contraindications on physical examination, and perform any diagnostic tests, including (as applicable) abdominal radiographs, abdominal ultrasound, CBC with platelet count, coagulation profile.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

The bladder is variable in its exact location from one individual to the next as well as in its degree of fullness in every individual. Therefore, it should be identified by palpation prior to cystocentesis.

CYSTOCENTESIS Ventral abdomen of a female dog in dorsal recumbency; cranial is to the right. A natural depression occurs on the ventral midline of the caudal abdomen of female dogs *(arrow)*, where isopropyl alcohol pools.

PROCEDURE

- The animal is placed in dorsal recumbency. The help of one or more assistants may be necessary to keep the animal in this position. In addition, a U-shaped trough may be used for keeping the animal comfortably recumbent. The examiner stands or kneels beside the animal (either side).
- The right-handed examiner palpates the animal's caudal abdomen with the left hand and holds the syringe—with needle attached—in the right hand.
- Landmarks:
    - General guidelines: ventral midline; cranial to the brim of the pelvis, caudal to the umbilicus
    - A commonly used landmark in female dogs, especially obese dogs, is the natural depression that forms on the caudal abdominal surface just cranial to the inguinal mammary glands on the ventral midline. Cystocentesis performed with the needle entering perpendicularly at this point is generally successful if the bladder is moderately or markedly full of urine.
    - In general, the urinary bladder is more easily palpated in cats than dogs and in thinner animals.
- With cystocentesis in male dogs, an assistant can retract the prepuce laterally. Alternatively, the prepuce may be drawn to one side by the examiner in the palm of the palpating hand.
- With the bladder encircled with the fingers of the left hand, the right-handed examiner cleans the overlying skin on the ventral midline with isopropyl alcohol–soaked gauze or cotton.
- With the right hand the examiner then introduces the needle through the overlying skin on the ventral midline, directed perpendicular to the skin (i.e., vertically downward when the dog is in dorsal recumbency). The examiner pulls back on the syringe plunger, creating negative pressure from the moment the needle is through the skin. Doing so helps identify penetration of the bladder as soon as it occurs.
- If no urine is obtained, it is important to NOT redirect the needle while it is in the abdomen; doing so could cause laceration of abdominal structures with the needle tip. When no urine is obtained, the needle may be withdrawn until only the needle tip remains (2-3 mm in the skin), redirected to a new angle, and then readvanced.
- Once urine flows into the syringe, the examiner withdraws the desired amount of urine and then withdraws the needle and submits the sample for analysis.

POSTPROCEDURE

No discomfort, gross hematuria, or other abnormality is expected after a properly performed cystocentesis.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Free-catch: atraumatic, but the sample is contaminated with urethral, preputial/vulvar, and cutaneous bacteria.
- Urethral catheterization: minimally invasive; may be more uncomfortable than cystocentesis in many animals and is not

practical for urine sampling in cats.

- Ultrasound-guided cystocentesis: useful when the bladder is small, when the animal is very obese, or when there is ascites or any mass lesion in the caudal abdomen.

CYSTOCENTESIS U-shaped foam trough used for comfortably maintaining an animal in dorsal recumbency.

AUTHOR: ETIENNE CÔTÉ

Cross-Match and Blood Typing

SYNONYMS

- Blood typing: determines the presence or absence of antigens on the red blood cell (RBC) membranes of the recipient and donor. Of major clinical interest are the blood types DEA 1.1 in dogs and the AB system in cats.
- Major cross-match: evaluates for antibodies in the recipient's plasma against the donor's RBCs, which is of greatest clinical significance.
- Minor cross-match: evaluates for antibodies in the donor's plasma against the recipient's RBCs.

OVERVIEW AND GOALS

- Cross-matching and/or blood typing eliminates most immunologic transfusion reactions.
- Maximize longevity of posttransfusion RBCs

INDICATIONS

- Blood typing: performed prior to administering a blood transfusion on all donors and recipients to minimize sensitization and avoid severe hemolytic transfusion reactions (i.e., AB mismatch in cats)
- Cross-match: performed prior to a whole-blood or packed RBC transfusion on animals that received a transfusion more than 4 days previously (even if blood typed) or have an unknown transfusion history:
    - First-time transfusions to dogs are considered safe without prior crossmatching, as dogs do not possess clinically significant naturally occurring antibodies.
    - Pregnancy does not appear to sensitize dogs to RBC antigens; consequently, dogs with prior history of pregnancy can safely be used as blood donors and can safely receive a first transfusion without a crossmatch as long as they are properly blood typed.
    - Ideally recommended in all cats, even with first transfusion, as cats have naturally occurring antibodies to the AB system and newly identified Mik red blood cell antigen. Transfusing cats without prior blood typing and/or cross-matching is dangerous; an AB mismatch can be lethal to a type B recipient. AB blood typing will not detect Mik-related incompatibilities.

EQUIPMENT, ANESTHESIA

Blood typing:

- Commercially available canine DEA 1.1 and feline AB system blood-typing cards (DMS Laboratories, Flemington, New Jersey)
- Approximately ≥ 0.4 mL EDTA anticoagulated (purple-top tube) whole blood

Cross-match:

- 1 mL EDTA-anticoagulated (purple-top tube) blood from recipient and donor (or cross-match segments from units of blood being considered)
- Tabletop centrifuge
- 3-mL test tubes (red-top tubes can be used)
- 0.9% saline
- Disposable pipettes or 1-mL syringes
- Test tube rack

ANTICIPATED TIME

- Blood typing: 2 minutes
- Major and minor cross-match: 40 minutes

PREPARATION: IMPORTANT CHECKPOINTS

- The stability and expiration of components of blood typing kits vary: ensure proper storage and check expiration dates.
- EDTA blood samples should be blood typed or cross-matched within 2-3 days of collection, as the physical integrity of the

RBCs is essential for correct results.
- Breed and geographic prevalence of blood types for dogs and cats are listed online (see web tables: Blood Type Frequencies, Dogs and Blood Type Frequencies, Cats).

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Dogs or cats that are autoagglutinating due to underlying disease (e.g., immune-mediated hemolytic anemia) cannot be accurately blood typed (false positive) and will always appear incompatible on cross-match.
- A patient cannot be accurately blood typed following recent blood transfusion using in-house blood-typing cards.
- Severely anemic cats or dogs (<10% hematocrit) may not show agglutination when using blood-typing cards (prozone effect). After a brief centrifugation, some of the plasma is withdrawn to concentrate the RBCs before adding a drop to the test cards.
- Feline blood-typing cards may not detect type AB cats.

PROCEDURE

Blood typing: commercially available blood-typing cards (see package inserts) **Cross-match:** Recently a gel-based major cross-match test kit (DMS Laboratories, Flemington, New Jersey) was commercialized for in-practice use (see figure), which may decrease the subjectivity of interpreting results, although no published data are available at this time (see package inserts).

STANDARD CROSS-MATCH (MAJOR AND MINOR):

Step 1:

- Collect 1-2 mL of donor blood in an EDTA tube, or use an equivalent 1-2 mL of cross-match segments from unit of blood being considered.
- Collect 1-2 mL of recipient blood in an EDTA tube.
- Centrifuge both donor and recipient blood in separate labeled tubes for 5 minutes (1000 *g*).
- Remove plasma using a pipette and save in separate labeled tubes for later use (use different pipettes for donor and recipient).
- Wash the remaining packed RBCs three times by filling tubes with 0.9% saline, gently resuspending, centrifuging (1000 *g)* for 5 minutes, and decanting off the saline (discard the saline).
- After a third wash, add 0.2 mL of washed packed RBCs from the donor red-top tube to 4.8 mL of 0.9% saline (in a separate tube), and gently mix to obtain a 3%-5% RBC solution (bright cherry red). Make a similar 3%-5% RBC solution with the washed recipient RBCs.

Step 2:

In a test tube:

- Mix 2 drops of recipient plasma and 1 drop of donor RBC suspension (major cross-match).
- Mix 2 drops of donor plasma and 1 drop of recipient RBC suspension (minor cross-match).
- Mix 2 drops of recipient plasma and 1 drop of recipient RBC suspension (auto-control).
- Incubate at 37°C (ideally, but room temperature is acceptable) for 15-20 minutes.
- Centrifuge for 30 seconds.
- Observe the plasma for hemolysis. Gently resuspend the RBC button by tapping the tube, and examine for agglutination clumps.
- Hemolysis or agglutination indicates incompatibility.

POSTPROCEDURE

- Administer type-specific blood to the patient. DEA 1.1+ dogs can receive DEA 1.1+ or DEA 1.1-blood, but DEA 1.1-dogs should only receive DEA 1.1-blood.
- When the recipient autocontrol shows hemolysis or agglutination (common in IMHA cases), the cross-match cannot be interpreted. In such cases, use DEA 1.1-blood or “universal blood” (determined by extensive blood typing), or use hemoglobin-based oxygen carriers (i.e., Oxyglobin).
- If all available units are incompatible, the least reactive unit may need to be administered.
- Cats that show a positive result in both wells of blood-typing cards should be retested in a reference laboratory for the rare AB blood type.

ALTERNATIVES AND THEIR RELATIVE MERITS

An EDTA-collected blood sample can be sent to commercial laboratories for extensive blood typing of dogs and cats: advised for

blood donors. Consultation with the laboratory is advised because different labs test for different canine erythrocyte antigens.

CROSS-MATCH BLOOD-TYPING Gel-based major cross-match test kit. (DMS Laboratories, Flemington, NJ)

AUTHORS: SØREN R. BOYSEN & MARIE-CLAUDE BLAIS

Computed Tomography Scan

SYNONYMS

CT Scan, CAT Scan, computed axial tomography

OVERVIEW AND GOALS

Computed tomography (CT) is a method of cross-sectional imaging that involves ionizing radiation. When compared to radiography, CT allows improved evaluation of areas of complex anatomy by avoiding superimposition of multiple structures, and it provides improved contrast resolution of tissues. CT can be used for assessing any area of the body. In veterinary medicine, common uses include assessment of the head (brain and nasal cavity) and thorax. It is also often used for surgical and radiation therapy planning.

INDICATIONS

- Disease of the central nervous system
- Disease of the nasal cavity/upper airway
- Determine the extent of tumor involvement for surgical planning
- Radiation therapy planning (used with specialized planning software)

CONTRAINDICATIONS

- Inability to tolerate general anesthesia
- Presence of large metallic implants in the area of interest. This does not contraindicate the procedure, but the information offered by the study will be limited by the presence of artifact.

EQUIPMENT, ANESTHESIA

- CT scanner
- Anesthesia equipment:
    - General anesthesia is required. CT studies are relatively brief, and either gas anesthesia or a constant rate infusion of intravenous anesthetic agent—generally propofol—can be used for the study. The equipment needed will be determined by the type of anesthesia used:
        - Gas anesthesia:
            - Endotracheal tube and laryngoscope for placement
            - Anesthesia machine: no special requirements (unlike MRI)
        - Constant rate infusion:
            - Endotracheal tube and laryngoscope for placement
            - Infusion pump
    - Monitoring equipment
    - Pulse oximeter
    - Electrocardiogram (ECG)
    - Emergency kit: as with any procedure performed under general anesthesia, the equipment and drugs necessary for emergency resuscitation of the patient should be immediately available.
    - Intravenous contrast agent:
        - Iodinated contrast agent labeled for intravenous use (i.e., diatrizoate/metrizoate compounds such as Renografin 60, iohexol [Omnipaque], iopamidol [Isovue])
    - Intravenous fluids (optional)
    - Heating pad/blankets (optional)

ANTICIPATED TIME

The time required to perform the study will depend on the CT scanner used and the study to be performed and is therefore quite variable. Most scans will be completed in 30 minutes or less.

EXAMPLE: CT scan of the brain:

- Two scans are performed, one prior to contrast injection and one following contrast injection.
- The time for each of these studies may vary from 5-10 minutes (older, single-slice translational scanners) to less than 30

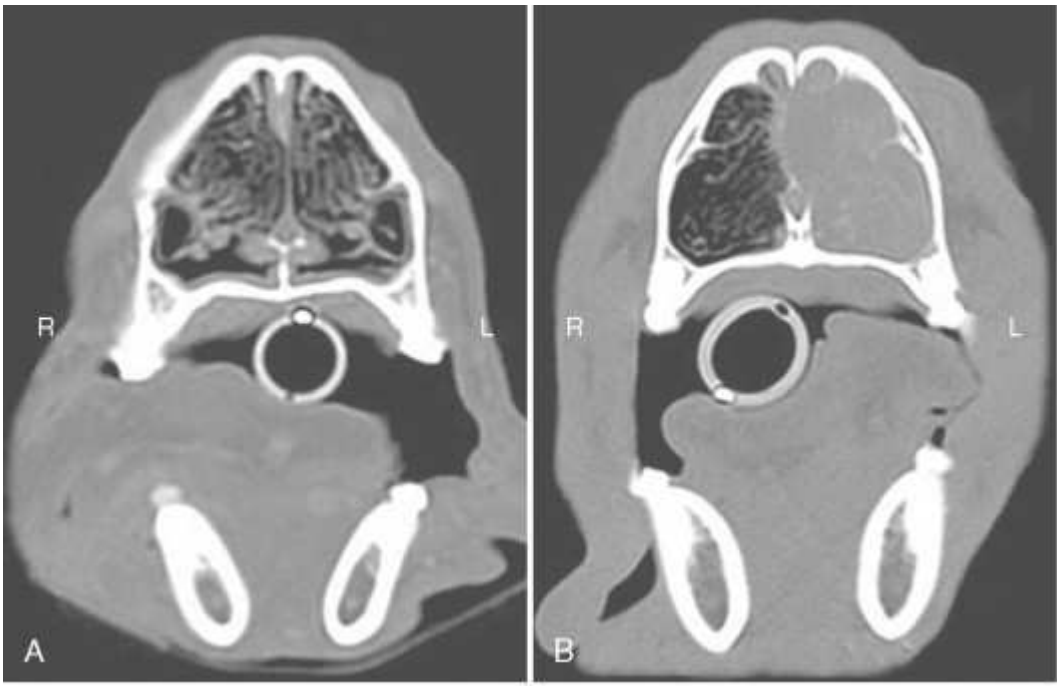
seconds (new multislice helical scanners).

Complex scans of large areas (abdomen or entire body for example) may require a pause in the scanning to allow the x-ray tube to cool. Generally this pause is relatively short (e.g., 2-3 minutes), but it must be considered when estimating the total general anesthesia time for the patient.

PREPARATION: IMPORTANT CHECKPOINTS

Preparation for general anesthesia:

- Routine preanesthetic fasting
- Place IV catheter: when placing the catheter, the anticipated position of the patient within the CT gantry must be considered, and the catheter should be placed to allow easy access to it during the procedure. For example, in patients undergoing CT scan of the head, it is convenient to have the IV catheter placed in the saphenous vein, although the forelimb can be extended caudally for ease of access if the catheter is in a cephalic vein.
- Make sure all needed equipment is available and functional. This is especially important if the study is to be performed at an outside (nonveterinary) facility.



COMPUTED TOMOGRAPHY SCAN NASAL CAVITY CT images from a normal **(A)** and abnormal **(B)** canine nasal cavity. CT is based on the principle of differential attenuation of tissues and, as in radiographs, bone appears white, air appears black, and soft tissues are intermediate in appearance. The term *density* is used for describing the appearance of tissues in CT images. In the normal patient, the nasal turbinates and nasal septum are present and surrounded by air. In the abnormal patient, the left half of the nasal cavity is filled with material of soft-tissue density, and there is loss (destruction) of the nasal turbinates. The nasal septum is thinned and deviated to the right. The right half of the nasal cavity is normal in appearance. This appearance is considered evidence of an aggressive process within the left half of the nasal cavity. Differentials for aggressive processes include neoplasia and fungal rhinitis. In this case, neoplasia is considered likely based on the mass effect within the nasal cavity.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Complications associated with general anesthesia
- Complications associated with the administration of intravenous contrast agent (rare in animals)

PROCEDURE

- Anesthetize the patient.
- Position the patient within the CT gantry; positioning depends on the area of interest and, in some cases, the size of the patient:
    - Connect IV fluids, place heating pad or blankets, and so forth.
- Scan

- Inject intravenous contrast agent: 600-800 mg iodine/kg of body weight as a bolus:
    - The concentration of iodine varies with the contrast agent used.
    - Sample calculation: 20-kg patient using a dosage of 700 mg iodine/kg:
        - Total dose = 14,000 mg iodine:
            - Renografin 60 (292.5 mg iodine/mL) = 14,000 ÷ 292.5 = 47.9 mL
            - Omnipaque 240 (240 mg iodine/mL) = 14,000 ÷ 240 = 58.3 mL
- Re-scan
- Briefly review images:
    - Rarely, the images obtained will identify an additional area of concern that should be scanned before the patient is allowed to recover from general anesthesia.

POSTPROCEDURE

No additional considerations beyond routine monitoring of the patient during recovery from general anesthesia

ALTERNATIVES AND THEIR RELATIVE MERITS

Magnetic resonance imaging (MRI): Advantages:

- Far superior contrast resolution
- No beam-hardening artifact (this artifact occurs in CT and severely limits evaluation of structures surrounded by dense bone such as the brainstem)

Disadvantages:

- Longer imaging times (and therefore, longer time under general anesthesia)
- Poor imaging of bone
- If available, MRI is the preferred imaging method for evaluation of the central nervous system.

AUTHOR: PATRICIA L. ROSE

EDITOR: ETIENNE CÔTÉ

Chest Tube Placement

SYNONYM

Thoracostomy tube placement

OVERVIEW AND GOALS

To provide means for frequent or continuous drainage of fluid or air from the pleural cavity

INDICATIONS

- Pyothorax
- Rapidly forming pleural effusion
- Recurring pneumothorax requiring repeated thoracocentesis
- Tension pneumothorax
- Postoperative thoracotomy management

CONTRAINDICATIONS

Severe bleeding disorder

EQUIPMENT, ANESTHESIA

- General anesthesia with intubation (ideally) or sedation
- Clippers
- Surgical scrub
- #11 scalpel blade
- Local anesthetic (e.g., 2% lidocaine, 0.2-0.5 mL/kg, SQ; maximum 7 mL)
- Small surgical pack or sterile hemostats
- Suture material (e.g., 2-0 to 4-0 nylon)
- An assistant (if possible)
- Thoracostomy tube
- Catheter adapter
- Three-way stopcock
- Injection caps
- ± Continuous drainage device
- 20-gauge orthopedic wire or plastic zipties
- Wire twister and cutter if using orthopedic wire

ANTICIPATED TIME

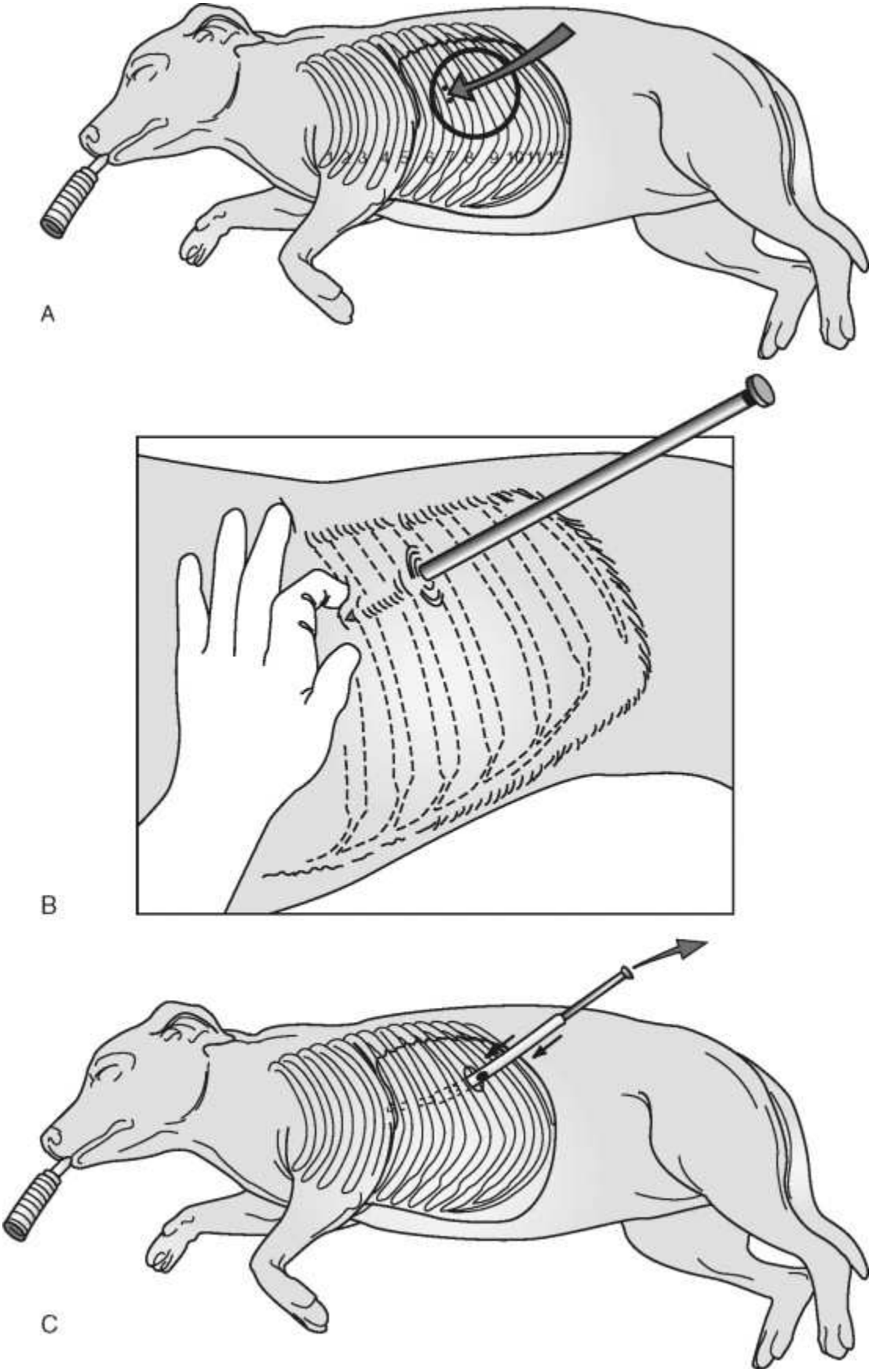
About 15-45 minutes

PREPARATION: IMPORTANT CHECKPOINTS

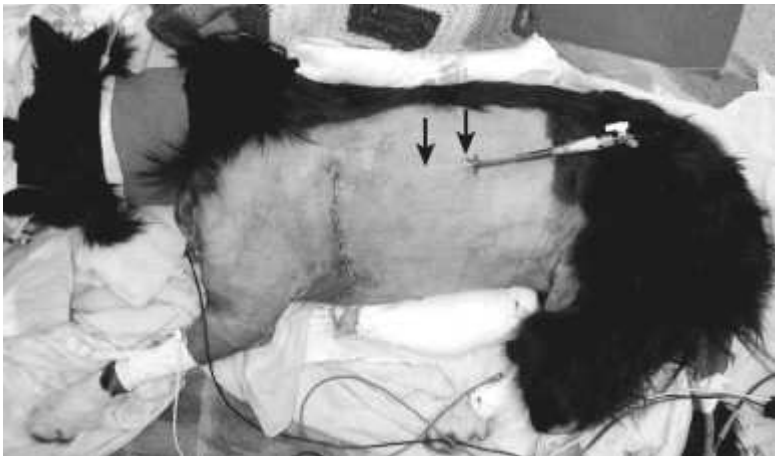
- Make 3-5 extra drainage holes in chest tube with scalpel blade if thick or purulent fluid is present in pleural space (< 50% of the diameter of tube). Be sure not to compromise the integrity of the tube with extra holes.
- Monitor animal's oxygenation with pulse oximetry during anesthesia and placement.
- If tension pneumothorax is present, continuous evacuation of pleural space by thoracocentesis until chest wall is opened will help stabilize animal.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Improper (SQ) placement of tube
- Impaling the heart or lungs with the tube's stylet/trocar
- Pulmonary contusions



CHEST TUBE PLACEMENT A, For placement of a chest tube, animal is in lateral recumbency, and an incision is made in the skin at least two intercostal spaces (ICS) caudal to planned site of entry into thorax. **B**, Chest tube and trocar within it are tunneled together SQ to the appropriate ICS, and chest is entered with the tube. **C**, Tube is then advanced off the trocar *(small arrows)* such that all side holes of the chest tube are within the pleural space, and trocar has not advanced farther into chest. Trocar is then withdrawn *(larger arrow)*, and chest tube is capped and secured.



CHEST TUBE PLACEMENT Chest tube in place after lateral thoracotomy for a penetrating wound. Tube enters skin at approximately the tenth intercostal space (ICS) *(large arrow)*, tunnels under skin for three rib spaces, and enters thorax *(small arrow)* through seventh ICS. Note "Chinese finger trap" suture pattern to secure tube and use of wire to secure tube-to-adapter and adapter-to-stopcock connections.

- Placement of the tube into the abdominal cavity, with abdominal organ trauma
    - Aforementioned complications are more common with the trocar method
- Tube migration or premature removal of tube by animal
- Development of life-threatening pneumothorax if tube becomes open to atmosphere

PROCEDURE

- General anesthesia (preferable); can be done with sedation for an emergency case
- Lateral recumbency
- Clip hair from lateral thorax, extending from axilla cranially to the last rib caudally, and from dorsal spine to ventral midline.
- Aseptically prep and drape area.
- Using scalpel blade, make a small stab incision in the skin over the highest point of the thorax at the ninth or tenth intercostal spaces (ICS).
- The assistant then pulls the skin cranially several centimeters and holds the skin in that position. The chest tube will be placed into the thorax via seventh or eighth ICS. When the skin is released after placement of the tube, there will be an SQ tunnel of 2-3 ICS over the tube. This helps prevent air or fluid leakage around the tube.
- Lidocaine can be injected into intercostal muscle at the tube insertion site, or an intercostal block can be performed, injecting lidocaine just ventral and caudal to the transverse processes of the thoracic vertebrae/head of ribs one space cranial and caudal and at the site of insertion. Before injecting, aspirate back to determine that needle is not in the intercostal artery or vein.
- If the patient is anesthetized, stop manual ventilation while actually inserting tube into thorax to deflate lungs and decrease risk of trauma to lungs.
- With the skin still drawn cranially, hemostats are used for bluntly dissecting vertically into the pleural space, spreading the jaws wide enough for the tube to snugly fit through the opening. The tube is inserted and advanced cranially and ventrally along the chest wall, making sure that all side holes in the tube are well within the thorax. The distance the tube is advanced can be measured with the stylet. The tip of the tube should be at the second or third ICS.
- Connect tube to a three-way stopcock and injection caps or a pleural drainage system.
- Secure to skin with a purse-string suture around the tube at the entry site and a "Chinese finger trap" suture pattern to reduce sliding of the tube.
- Place sterile dressing and light bandage.
- Tube connection sites can be secured with orthopedic wire in figure-eight patterns or plastic zip ties.

Alternate method, trocar technique:

- Sedation or anesthesia should be provided if possible.
- Initial prep as previously described
- Tube and trocar/stylet within it are tunneled SQ by 2-3 rib spaces and then positioned perpendicular to the chest wall and grasped tightly 1-2 inches from distal tip.
- Top of the tube will be hit bluntly with the palm of other hand, popping the tube through into pleural space; the other hand, grasping tube and trocar 1-2 inches from the distal tip, acts as a guard to prevent the tube from entering the thorax excessively.
- Tube is slid off the trocar/stylet cranially and ventrally, then connected and secured as described previously.
- This very rapid placement technique is only recommended in dogs in emergency situations, owing to increased risk of

iatrogenic trauma, and is never recommended in cats because of their very compliant chest walls.

POSTPROCEDURE

- Thoracic radiographs (lateral and ventrodorsal or dorsoventral) to check tube(s) placement
- Bandage to secure tube(s)
- Pain management: injectable opioids versus intrathoracic bupivacaine (both modalities can be used for optimal pain control).
    - Bupivacaine can be given at a dose of 1.5 mg/kg through tube every 6-8 hours.
- Continuous monitoring as long as the chest tube is in place because of the risks of disconnection and development of pneumothorax.

ALTERNATIVES AND THEIR RELATIVE MERITS

Repeat thoracocentesis: may become difficult to manage animal if pleural evacuation is needed frequently.

AUTHOR: LORI S. WADDELL

Cerebrospinal Fluid Collection

SYNONYMS

Spinal tap, CSF tap

OVERVIEW AND GOALS

- To safely collect an uncontaminated sample of cerebrospinal fluid (CSF) from an animal with suspected central nervous system (CNS) disease.
- CSF analysis is the single most valuable diagnostic test for evaluating inflammatory CNS disorders and it aids in the diagnosis of other encephalopathies and myelopathies.

INDICATIONS

- Clinical signs consistent with CNS or nerve root dysfunction
- Monitoring treatment efficacy of confirmed inflammatory CNS disease
- Intrathecal administration of contrast material (myelography)

CONTRAINDICATIONS

Absolute:

- Increased intracranial pressure (depressed mental status, bradycardia, hypertension, miosis, anisocoria)
- Any condition in which general anesthesia is contraindicated

Relative:

- Advanced imaging results identifying a noninflammatory disease process, which explains the animal's clinical signs

EQUIPMENT, ANESTHESIA

- General anesthesia and endotracheal intubation
- A few 20- or 22-gauge, 1½-inch spinal needles (2½ - or 3½-inch needle may be needed for large dogs or for lumbar approach).
- Hair clippers
- Surgical scrub solution, isopropyl alcohol, and gauze
- Sterile surgical gloves
- Sterile collection tubes (do not use tubes containing EDTA [lavender-top tubes])
- An assistant to position the animal and stabilize the animal's head and neck
- Level stationary or locked table

ANTICIPATED TIME

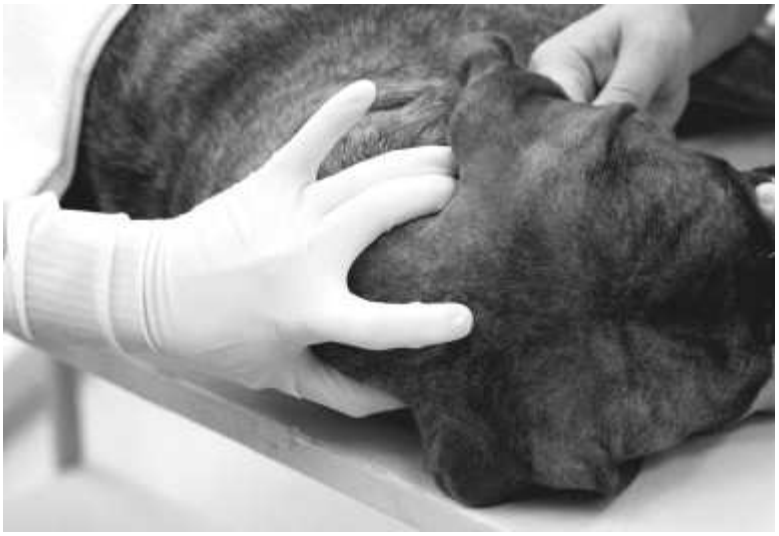
About 30 minutes of anesthesia

PREPARATION: IMPORTANT CHECKPOINTS

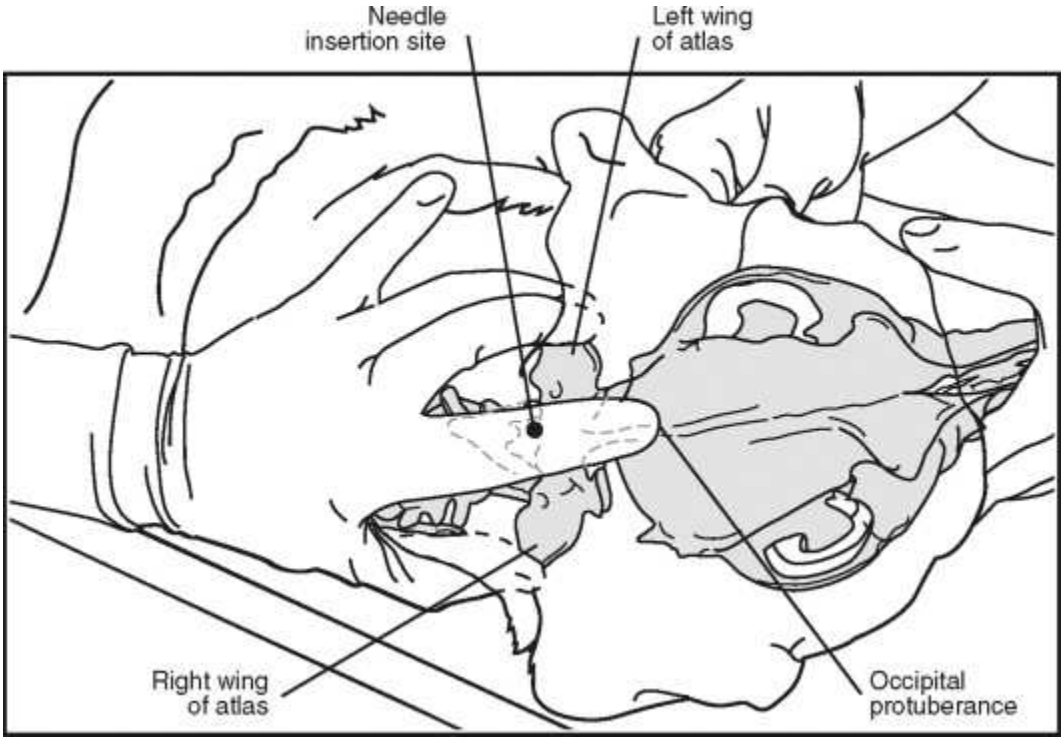
- Performed preferably after advanced imaging has ruled out both noninflammatory processes (neoplasia, malformation, vascular) and obvious increased intracranial pressure (coning and caudal displacement of the cerebellum, flattening of gyri, loss of sulci).
- Make arrangements for laboratory transport within 30 minutes of collection, or have in-house analysis equipment prepared and calibrated.
- If immediate analysis of the CSF is not possible, special preservation techniques may be required (prior laboratory consultation is recommended).
- Warn owners of hair clipping and low risk of complications. Complications associated with the procedure, although rare, can be fatal.

PROCEDURE

- General anesthesia and intubation
- Preparation and positioning for centesis from the cerebellomedullary cistern (preferred for ease and lower risk of blood contamination):
    - Shave and surgically scrub the skin from the occipital protuberance rostrally to the dorsal spine of C3 caudally and to the base of each pinna laterally.
    - Sterile gloves are worn, but the field is not usually draped.
    - Lateral recumbency: right lateral for the right-handed clinician and left lateral for the left-handed clinician.
    - An assistant holds the head flexed at a 90° angle to the neck and parallel to the table. Care must be taken to not overflex the neck, which could result in obstruction of the endotracheal tube or compress the jugular veins and increase intracranial pressure. For the head to be parallel to the table, the assistant must hold the nose slightly elevated from the table.
    - The assistant positions the dorsal aspect of the neck at the edge or slightly over the edge of the table.
    - The clinician should sit on a stool or kneel to be at eye level with the animal's head.
- Landmarking and puncture:
    - The right-handed clinician places the left thumb on the right wing of the atlas and the left ring or middle finger on the left wing of the atlas.
    - The left index finger is used for identifying the midline by palpating the occipital protuberance and the dorsal spine of C2, drawing an invisible line between these points.
        - Many cats and toy-breed dogs do not have a well-defined occipital protuberance. In these cases, the dorsal spine of C2 should be used as the sole landmark for identifying the midline.
    - The orientation of the needle's path will be parallel to the table's surface and toward the angle of the animal's mandible.
    - For dogs, using the right hand, the needle with stylette in place is inserted through the skin along the midline just cranial to the wings of the atlas.
    - In cats, the skin is tough, and the distance between the skin and subarachnoid space is very small. Therefore, although the same point of insertion is identified, the skin should be tented prior to inserting the needle through the skin into the subcutaneous tissues.
    - The needle is directed through subcutaneous fat and muscle toward the subarachnoid space, taking care to avoid lateral, caudal, or cranial deviation of the spinal needle.
    - Occasionally a loss of resistance to the needle insertion is felt as the needle passes through the fascial planes of the muscle and, eventually, the dorsal atlantooccipital membrane; this so-called pop is not reliable and should not be used as an indicator of appropriate depth of the needle.
    - While maintaining a grip on the hub of the needle with the right hand, the clinician uses the left hand to grasp the needle near its insertion into the skin.
    - The stylette is withdrawn with the right hand, and the hub of the needle is examined for the presence of CSF.
    - If no CSF is present, the needle is first withdrawn a few millimeters while watching for the appearance of CSF to ensure the needle has not been inserted too deep (into nervous tissue), and then the needle is advanced. The stylette need not be replaced at this point. (Although advancing the needle without the stylette creates a slight risk of creating a tissue plug in the needle, it decreases the risk of advancing the needle too deeply, as CSF will appear as soon as the subarachnoid space is entered.)
    - As the needle is advanced one of three things will happen:
        - CSF appears in the hub of the needle and will begin to drip out. The needle should then be advanced 1 mm to place the entire bevel in the cerebellomedullary cistern, and the needle is grasped firmly against the skin. The slight advancement and firm hold on the needle reduce the risk of blood contamination from meningeal vessels.
        - The needle hits bone. This is usually the occipital bone, and the needle should be redirected caudally to enter the cerebellomedullary cistern; if it strikes the atlas, the needle must be redirected cranially. The needle may be walked along the bone to find the cistern, bearing in mind that it will be only millimeters deeper, but this may result in blood contamination from trauma to the periosteum.
        - Frank blood appears in the hub. This most likely indicates that the needle is off midline and has punctured a venous sinus. In this case, the needle is removed and discarded, gloves are changed, the surgical prep is repeated, and the procedure is started again. Note: If blood is encountered, it is typically from a location outside the subarachnoid space and does not limit the ability to obtain an uncontaminated sample when the procedure is repeated.
    - Once CSF begins to drip from the hub, it is collected into two plain, sterile red-top tubes. Ideally, an assistant collects the sample, and the examiner does not release the needle during collection.
    - In general, 1 mL of CSF is required for assessment of the white blood cell (WBC) count, protein determination, and cytologic examination (1 mL/5 kg of body weight can be obtained safely).
    - If the animal weighs more than 5 kg, additional CSF can and should be collected for possible culture or ancillary diagnostics, such as infectious titers or immunoglobulin indices.



CEREBROSPINAL FLUID COLLECTION Landmarks. Dog is in right lateral recumbency, head pointing to right of photo. Right-handed clinician is using left hand to identify the occipital protuberance (index finger) and wings of the atlas (right wing of atlas: thumb; left wing of atlas: middle and ring fingers). Patient's neck is appropriately flexed (90°), and nose is elevated by an assistant so muzzle is parallel to table surface.



CEREBROSPINAL FLUID COLLECTION Diagram of same dog, showing bony landmarks and site of needle insertion.

CEREBROSPINAL FLUID COLLECTION Same animal. While clinician holds the needle, an assistant collects the cerebrospinal fluid.

  - Once the appropriate amount of CSF has been collected, the needle is removed.
  - Note: If during the procedure the heart rate acutely decreases or if fluid streams rather than drips from the hub when the subarachnoid space is entered, the needle should be removed and the procedure aborted.
- Preparation and positioning (for centesis from the lumbar subarachnoid space) is technically more difficult, yields less fluid, and is more likely to involve blood contamination but is more sensitive for focal thoracolumbar lesions:
  - The skin is shaved and surgically scrubbed over the dorsal midline from L3 cranially to the midsacrum caudally and the wings of the ilium laterally.
  - Sterile gloves are worn, but the field is not usually draped.
  - The animal is positioned in lateral recumbency with the hindlimbs and lumbar spine flexed (“tucked” posture).
- Landmarking and puncture:
  - The needle enters the L5-L6 or L6-L7 interspace in dogs, or the L7-S1 interspace in cats.
  - Except in very small or thin animals, the L6 dorsal spine is typically the most caudal and can be palpated just cranial to the wings of the ilium.
  - If the L7 dorsal spine is palpable, it is usually much smaller than that of L6 and lies between the wings of the ilium.
  - Radiographs can demonstrate individual differences in anatomy.
  - The needle is inserted into the skin just caudolaterally to the caudal dorsal spine of the space to be entered (i.e., caudolaterally to L6 for puncture between L5 and L6).
  - The needle is directed craniomedially to puncture the interarcuate space between the vertebrae.
  - If bone is encountered, the needle is redirected (usually cranially) until the space is identified.
  - If the needle is inserted to the hub and no bone is encountered, the needle is either too short or directed too far laterally.
  - Fluid can be collected from the dorsal subarachnoid space, but more often the needle is passed through the nervous tissue to the floor of the vertebral canal.
  - The stylette is removed, and if CSF is not recovered, the needle is withdrawn slightly to enter the ventral subarachnoid space while the examiner watches for the appearance of fluid in the hub of the needle.
  - CSF typically flows much more slowly from this site compared with the cerebellomedullary cistern.

POSTPROCEDURE

- Routine postanesthetic monitoring
- Monitor for neurologic deficits due to iatrogenic trauma (respiratory difficulty or vestibular ataxia with puncture from the cerebellomedullary cistern; paresis and proprioceptive ataxia with lumbar puncture).

ALTERNATIVES AND THEIR RELATIVE MERITS

MRI or CT scan (see pp. 1302 and p1233):

- Advanced imaging superior for the diagnosis of structural lesions
- May be strongly suggestive of inflammatory disease
- Typically used in addition to CSF analysis to fully evaluate disorders of the CNS

Serum infectious titers:

- Systemic disease not necessarily reflective of CNS disease
- For most inflammatory nervous system diseases, no infectious agent is identified.

AUTHOR: GREG KILBURN

Central Venous Pressure Monitoring

OVERVIEW AND GOALS

Central venous pressure (CVP) is a measurement that reflects the ability of the heart, and specifically the right side of the heart, to accept and pump blood through the circulatory system. The CVP reflects the interaction of the heart, vascular tone, and blood volume. Monitoring of CVP allows a better understanding of the circulatory status of the body and of the impact of fluid therapy.

INDICATIONS

- Monitoring the administration of large volumes of fluids in animals that are in shock or have impaired urine production
- Diagnostic help in difficult-to-diagnose right heart failure cases (e.g., constrictive pericarditis)

CONTRAINDICATIONS

Only those of jugular catheter placement (e.g., hypercoagulable or hypocoagulable states, skin infection over jugular site; see p. 1293)

EQUIPMENT, ANESTHESIA

- IV jugular catheter (Mila or Arrow double-lumen catheters)
- Sterile 500-mL saline bag with IV drip set
- CVP set (Universal CVP set [Abbott Laboratories]). Alternatively, if a purpose-made kit is not available, use the following: a sterile three-way stopcock, sterile IV fluid-type tubing, and a ruler (centimeter grading and at least 30 cm long). The sterile tubing is taped to the ruler, and it is held vertically, creating a simple pressure manometer.

ANTICIPATED TIME

- About 15 minutes to install the set
- About 2 minutes for each CVP reading

PREPARATION: IMPORTANT CHECKPOINTS

- The prerequisite is the placement of an IV jugular catheter (see p. 1293):
  - The distal tip of this catheter should be in the cranial vena cava, just cranial to the right atrium, which allows accurate measurement of CVP without inducing premature atrial contractions. Confirm position radiographically.
  - Mila or Arrow catheters are the most commonly used because their double lumen allows CVP measurement and/or blood sampling through one port and fluid delivery through the other.

PROCEDURE

Before connecting CVP set to patient's jugular catheter:

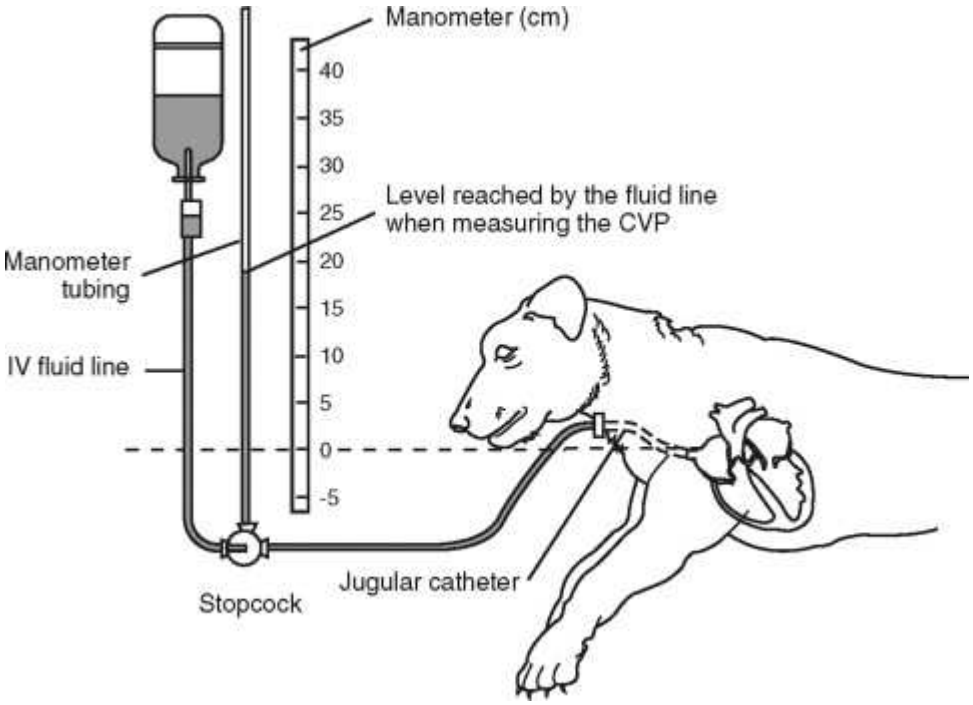
- One end (female end) of the CVP set goes to a suspended IV fluid bag. The line on that end should be closed using a clamp.
- A second end connects to tubing that is fixed to a scale (e.g., manometer scale or ruler). This line also should be closed using a clamp.
- The manometer tubing is pressed into the scale groove:
  - If using individual materials, tape the sterile IV fluid-type plastic tubing to the ruler.
- Using adhesive strips, fix the manometer on a vertical surface, such as the wall of a cage or a vertical stand, next to the animal and at a height such that the 0 on the scale of the manometer/ruler is at the level of the animal's heart (right atrium).
- Unclamp the fluid line coming from the fluid bag:
  - Fluid should run through the line until the line contains only fluid and no air.
- Then unclamp the manometer tubing and turn the three-way stopcock such that flow exists between the fluid line from the fluid bag and the fluid line of the manometer.
- Fill the manometer line with fluid to within 3 cm of its extremity.

Connecting CVP set to patient:

- Next, connect the remaining end (male end) of the CVP set to the jugular catheter. The stopcock is usually integral to the set.
    - If using individual materials rather than a purpose-made set, connect the male end of the three-way stopcock directly to the jugular catheter.
- Finally, turn the stopcock so that a column of fluid exists between the jugular catheter and the manometer.
- The fluid in the manometer will fall until it reflects the CVP (measured in centimeters of water).

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- One must allow fluid to flow frequently through the IV line to avoid plugging of the catheter by a blood clot. Periodic flushing with heparinized saline is desirable.
- Cardiac function needs to be factored in when interpreting results. For example, animals with tricuspid regurgitation may have elevated CVP irrespective of intravascular volume loads.
- The CVP level represents mostly loading conditions of the right side of the heart (right ventricular preload), not afterload.



CENTRAL VENOUS PRESSURE MONITORING CVP monitoring. Dashed line represents the level of the right atrium, the zero point for setting the manometer. The stopcock is closed to the IV fluid line; the jugular catheter and manometer tubing are in continuity. The dog's CVP reading is markedly elevated at 19 cm H2O.

(Reprinted with permission from Sattler FP: Shock. In Kirk RW, editor: Current veterinary therapy III, Philadelphia, 1968, Saunders.)

INTERPRETATION

- Normal CVP: variable; oscillates between -1 and +5 cm H2O.
- Values between +5 and +10 cm H2O are borderline.
- Values above +10 cm H2O may indicate too much blood volume expansion. IV fluids should no longer be administered.
- Values above +15 cm H2O may indicate right-sided congestive heart failure.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Blood pressure (BP) monitoring: easier to use and represents another way to monitor cardiovascular status and the impact of IV fluids. This is the best alternative to CVP monitoring. It does not require an IV jugular catheter.
- Weight: can be used for documenting rehydration; excessive weight gain could be a signal to slow/stop IV fluids.
- Packed cell volume/total solids (PCV/TS): a drop in the PCV/TS may indicate hemodilution.
- Urine specific gravity: a drop in the specific gravity could document successful restoration of plasma volume but is very dependent on kidney function.
- Pulmonary capillary wedge pressure/Swan-Ganz catheterization: accurately measures left-sided heart pressures, which CVP does not; however, this technique is much more technically demanding.

AUTHOR: ERIC DE MADRON

Catheterization, Urethral

SYNONYM

Urinary catheterization (see p. 1355 for catheterization of cats)

OVERVIEW AND GOAL

To pass a sterile catheter from the urethral orifice into the urinary bladder to obtain a urine sample or to evacuate the bladder

INDICATIONS

- Urine sample for urinalysis/urine culture
- Temporary management of urinary retention syndromes

CONTRAINDICATIONS

- Urethral pain
- Preputial/vulvar mass
- An animal that might otherwise be eligible for renal transplantation can be eliminated from the transplant list on the basis of prior urethral catheterization.

EQUIPMENT, ANESTHESIA

- Sterile polypropylene or red rubber-type catheter (or Foley catheter if indwelling); size ranges from 5-14 Fr, depending on the animal's size.
- Sterile lubricant
- Sterile syringe (3-20 mL)
- Sterile gloves
- ± Sterile tubing and urine collection bag (if indwelling catheter)

ANTICIPATED TIME

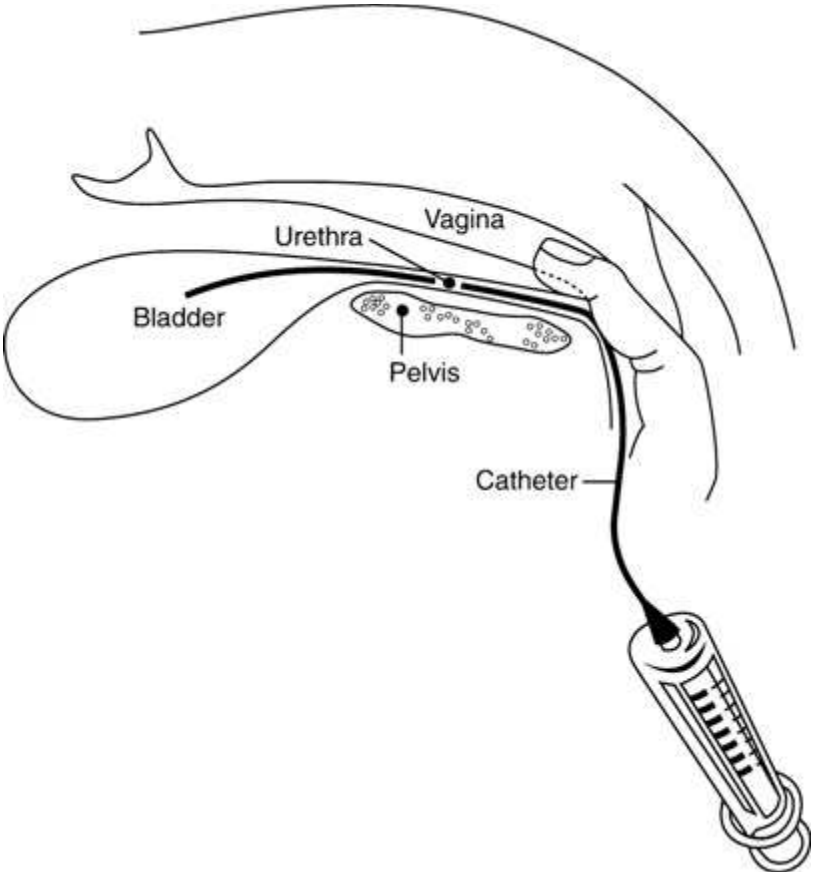
About 10 minutes

PREPARATION: IMPORTANT CHECKPOINTS

Rectal palpation is indicated as part of the physical examination of any adult dog, particularly prior to passing a urethral catheter (identify masses, sources of pain, or other factors that would affect passage of the catheter).

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Incorrect orientation (female): to enter the vulva, the directing (index) finger must be oriented dorsally, not cranially.
- Incorrect catheter position (female): clitoral fossa externally and vagina internally must be avoided in catheterizing female dog.
- Forceful advancement of the catheter: catheter should pass with no resistance and no discomfort. Otherwise, consider free catch, cystocentesis, or sedation/anesthesia (if placing indwelling catheter).



CATHETERIZATION, URETHRAL Cross-sectional anatomy of the female urogenital tract, demonstrating the proper position of catheter and index finger.

- Excessive advancement of the catheter: risks include bladder perforation and catheter looping/knot formation (requiring laparotomy).

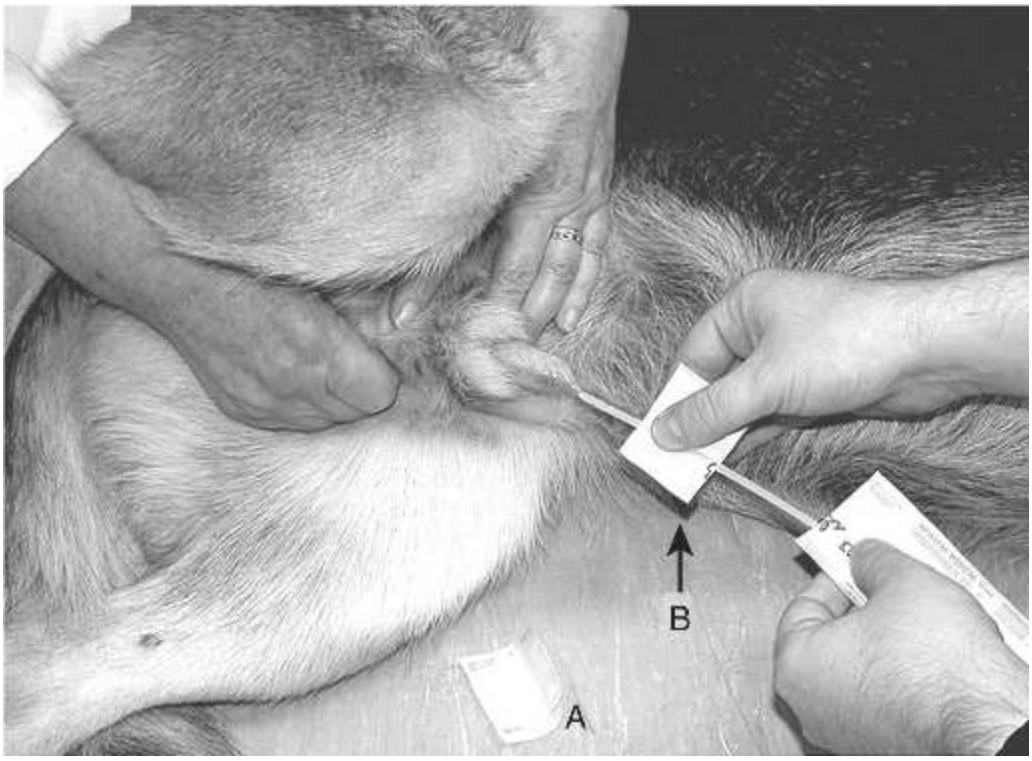
PROCEDURE

Female:

- The dog stands on an exam table or on the ground (giant-breed dogs). The procedure is also easily performed on the laterally recumbent (e.g., anesthetized) dog.
- While an assistant holds the dog's head, the examiner opens the sterile catheter wrapper, applies sterile lubricant to the catheter tip, and ensures that the catheter remains in a sterile field (e.g., the opened catheter wrapper).
- The right-handed examiner puts on sterile gloves, lubricates the right index finger, and takes the urinary catheter under his or her right index finger (palmar surface of finger), catheter tip at fingertip.
- The examiner lifts the dog's tail with the left hand and places the index finger on the vulva, pointing dorsally, and then enters the vulva by gently everting the vulvar lips and pressing cranially.
- The examiner advances the index finger and catheter directly dorsally (i.e., toward the ceiling in the standing dog) to a narrowing, which is the vestibulovaginal junction. The ischial arch also is palpable cranially.
- The urethral opening is on the cranial/ventral surface in this region, immediately adjacent to the ischial arch. Therefore, the catheter is advanced under the index finger such that the index finger blocks off the vestibulovaginal route and directs the catheter ventrally into the urethra. There should be no palpable resistance when advancing the catheter.
- Once urine flows from the catheter, it is advanced 2-3 cm (small dog) to 10-15 cm (large dog) into its final position.

Male:

- An assistant positions himself or herself dorsal to the laterally recumbent dog, elevates the dog's nondependent leg, and retracts the prepuce to expose the penis (see figure). A second assistant is usually needed to restrain the dog's head.
- The sterile catheter is kept within its sterile wrapper except for the distal end of the wrapper, which is cut off.



CATHETERIZATION, URETHRAL Urethral catheterization of the male dog. **A,** Distal end of wrapper cut off. **B,** Segment of sterile wrapper functioning as a sliding cuff for advancing the catheter.

- The next 3-5 cm of sterile wrapper is then cut and left overlying the catheter; it will serve as a sliding sterile cuff for advancing the catheter out of the wrapper and up the urethra, while keeping the clinician from touching the catheter directly with the fingers. This approach minimizes contamination without requiring sterile gloves.
- The catheter is placed into the urethral opening and is advanced until urine is obtained. Minor resistance may be felt at the ischium or prostate, but the procedure should be aborted if force seems necessary or if the animal seems uncomfortable.

POSTPROCEDURE

If an indwelling system is used, the catheter is fixed in place, and the extension tubing and collection bag are connected to the catheter.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Free-catch urine sample: simple and noninvasive but contaminates sample with urethral and genital bacteria and cells
- Cystocentesis: more invasive but may be less uncomfortable than catheterization; avoids urethral contamination

AUTHOR: ETIENNE CÔTÉ

Cardiopulmonary Cerebral Resuscitation

SYNONYMS

Cardiopulmonary resuscitation, CPCR, CPR

OVERVIEW AND GOALS

Cardiopulmonary cerebral resuscitation (CPCR) is instituted for cardiorespiratory arrest or near arrest. The goal is return of spontaneous and effective circulation (ROSC) and, ultimately, unassisted ventilation and appropriate cerebral function.

INDICATIONS

Cardiopulmonary arrest or near arrest; signs of impending arrest may include bradycardia, hypoventilation, hypothermia, hypotension, and progressive obtundation. These indicate that action should be taken to ensure continued effective circulation and ventilation. There are four cardiac rhythms that enter the definition of cardiac arrest: asystole, ventricular fibrillation, pulseless ventricular tachycardia (VT) or ventricular flutter (VF), and other pulseless electrical activity.

EQUIPMENT

- Endotracheal tube and laryngoscope
- Ambu-Bag, Bain Circuit, or mechanical ventilator
- Blood pressure (BP) measuring device (Doppler preferable)
- Electrocardiogram (ECG) (monitor preferable to printer)
- Defibrillator; internal and external paddles
- End-tidal carbon dioxide monitor
- Pulse oximetry
- Oxygen source
- Fluids: crystalloids (e.g., lactated Ringer's solution, 0.9% NaCl) and colloids (e.g., Hetastarch)
- Blood products (e.g., whole blood, packed red blood cells, polymerized bovine hemoglobin)
- Lubricant for eyes
- Point of care testing for blood glucose, electrolytes, packed cell volume, total solids, lactate, blood gases
- Other items that should be nearby: lidocaine jelly, suction tubing and means of generating suction, IV and urethral catheters, thoracotomy tubes, laceration packs
- Items for doing open thoracic cardiac massage and vascular cutdown procedures, self-retaining retractors
- Sterile gloves, means of warming fluids

The data collection sheet for record keeping should include:

- Date and time of arrest and institution of CPCR
- Animal name and medical record number, body weight, signalment and underlying disease, as well as assumed cause of the arrest
- A table or another quick and clear way to list which drugs are given, at what time they are given and at what dosage, and their effects
- Listing of fluid type and volume administered
- Time and energy of any defibrillation
- Pertinent laboratory results as tests are run during the procedure
- Personnel present during the event
- Time of return to spontaneous circulation or ending CPCR efforts
- Outcome
- Data that should be noted as well include size of endotracheal tube, time and settings if mechanical ventilation is instituted, changes in status of mentation, presence or absence of urine output, and BP measurement results.

PREPARATION: IMPORTANT CHECKPOINTS

- The owners of any critically ill animal should be consulted at the time of the animal's admission regarding their resuscitation wishes for the pet. In many cases of advanced or aggressive disease, advanced age, and financial limitations of the family, CPCR may not be appropriate, and the pet should be allowed to pass away peacefully.
- Successful CPCR is a team effort. The team consists of the clinician leading the arrest and individuals who are keeping a record of the event, acquiring the requested drugs or materials, administering the drugs and therapies, providing the chest compressions, and communicating with the animal's family. The team may contain any number of people, from few to many, with some having multiple roles.
- A senior knowledgeable individual must take charge in fostering a calm environment during CPCR, directing the other team members in their tasks, and keeping the team informed of progress. One responsible team member should be in communication with the owners to keep them apprised of progress and inform the team of changes in the family's wishes.
- Team members must be fully trained and prepared ahead of time concerning their responsibilities.
- All of the equipment that was previously listed (e.g., endotracheal tubes, breathing circuits, IV catheters, defibrillation paddles, sterile gloves, etc.) should be available in sizes appropriate for a wide variety of animals.
- Drug boxes should be checked weekly at least to ensure all drugs are available and have not reached their expiration dates.
- Equipment should be checked regularly for malfunctions and cleaned immediately after each use so that each piece is ready to be used again without notice.
- Data sheets should be kept nearby so that events, drug administration, animal information, and responses to treatments can be recorded in a timely and accurate fashion.
- After every CPCR event, the team should review the process to assess whether changes in plan, arrangement, or protocols are necessary for improvement of efforts in the future.

Emergency Drugs

Aminophylline: 25 mg/mL

Atropine*1: 0.54 mg/mL

Calcium gluconate*: (10% = 100 mg/mL [calcium: 27.2 mg/mL or 1.36 mEq/mL])

Dextrose*: 5% (50 mg/mL) or 50% (500 mg/mL)

Dobutamine*: 12.5 mg/mL

Dopamine*: 40, 80, 160 mg/mL

Doxapram: 20 mg/mL

Epinephrine*1: 1 : 1000 (1 mg/mL) or 1 : 10,000 (0.1 mg/mL)

Esmolol: 10 mg/mL

Furosemide*: 5% (50 mg/mL)

Lidocaine*: 2% (20 mg/mL)

Magnesium sulphate*: 10% (100 mg/mL, 0.8 mEq/mL), 12.5% (125 mg/mL, 1 mEq/mL), 50% (500 mg/mL, 4 mEq/mL)

Mannitol*: 5% (50 mg/mL, 275 mOsm/L), 10% (100 mg/mL, 550 mOsm/L)

Norepinephrine*1: 1 mg/mL

Phenylephrine: 10 mg/mL

Procainamide*: 100 mg/mL

Sodium bicarbonate*: 8.4% (1 mEq/mL)

Glucocorticoids:

Dexamethasone: SP (4 mg/mL)

Prednisolone sodium succinate: (10 or 50 mg/mL)

Methylprednisolone sodium succinate: (62.5 mg/mL)

Reversal Agents*:

Flumazenil: 0.1 mg/mL Naloxone: 0.4 or 1 mg/mL

Atipamezole: 5 mg/mL

Yohimbine: 2 mg/mL

Sample concentrations are listed; it is essential to check the actual concentration of available product.

* Indicates drugs that should be in all basic emergency kits. The others may be beneficial, and their use is dependent on clinician knowledge and familiarity.

1 Indicates that the drug can be administered intratracheally using a long catheter, generally at double the dose and followed by several deep breaths.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Inaccurate drug dosage administration
- Hyperventilation
- Inadequate fluid resuscitation
- Incorrect assessment of ECG, especially false interpretation of bad contact between ECG machine and animal as “ventricular fibrillation”
- Inadequately trained personnel
- Delayed defibrillation. The success of defibrillation in an experimental setting approaches 100% when instituted within 1 minute of onset of fibrillation and falls precipitously to virtually 0% after 10-15 minutes.
- Inadequate/infrequent monitoring of electrolytes, blood glucose, and physiologic parameters
- Malfunctioning or unavailable equipment
- Delayed decision to perform open-chest CPR in a patient for which it is appropriate
- Acute renal failure, diarrhea, liver dysfunction, and altered mentation and reflexes are common sequelae to inadequate oxygen delivery and tissue perfusion. Organ function must be closely monitored to take preemptive action should parameters deteriorate.

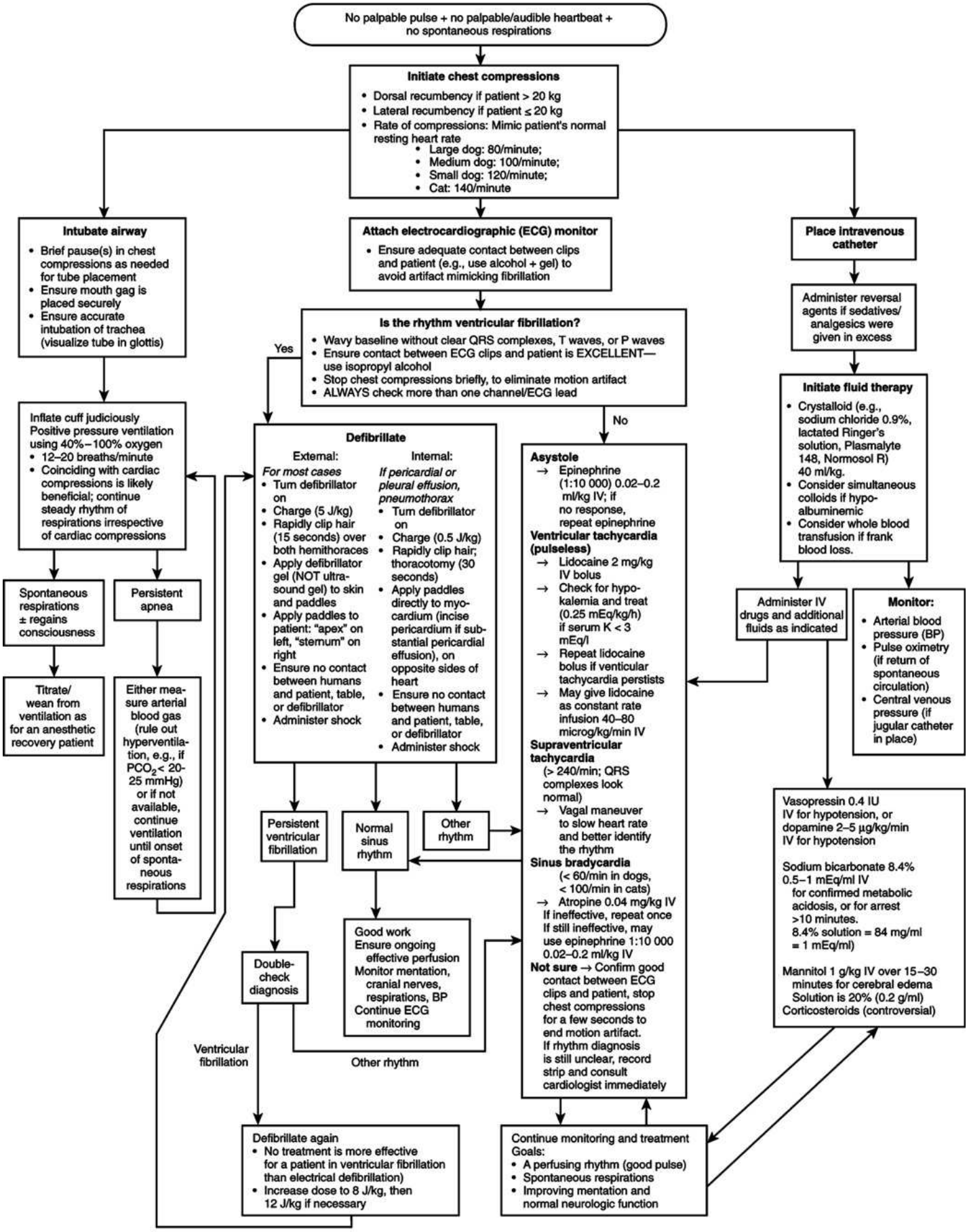
Prognosis overall is guarded to grave depending on the underlying disease process, age, and overall state of debilitation of the animal. The number of successful resuscitations (i.e., survive to discharge) may approach approximately 4% in dogs and possibly greater than 4% in cats; however, the fact that they occur with good critical care management means that every effort should be made to resuscitate animals when appropriate.

PROCEDURE

Most of the initial tasks listed here should be occurring simultaneously:

- Identify lack of effective spontaneous circulation and ventilation.
- Initiate chest compressions at 80-100 compressions/minute, compressing approximately 30% of chest diameter, with a 1:1 ratio of compression to relaxation. Hands should be placed over the widest part of the chest for patients > 10 kg. Hands should be placed over the heart for patients < 10 kg. Interruption of chest compressions should be minimized to <10 seconds until ROSC occurs.
- Intubate the airway, and place ECG leads on limbs.
- Begin assisted ventilation with 100% inspired oxygen at 10-12 breaths/minute, higher if pulmonary disease preventing effective oxygen transfer exists, or the patient was already hypoxemic.
- Identify cardiac rhythm if any.
- Establish vascular access (IV catheter) if not already established.
- If anesthetized, turnoff inhalant anesthetics, and reverse any injectable drugs that have reversal agents.

CARDIOPULMONARY CEREBRAL RESUSCITATION



- If thoracic compromise exists (e.g., pleural effusion, pneumothorax) or arrest is due to pericardial effusion, open-chest CPR must be instituted immediately. With pericardial effusion, open the pericardium ventral to the phrenic nerve to improve diastolic function of the heart and remove effusion.
- Fluid administration: IV (or intraosseous [IO], especially in pediatric animals). Shock rate administration (90 mL/kg in dogs, 45 mL/kg in cats, with constant monitoring and adjustments as needed) is appropriate if the patient was hypovolemic prior to the CPA. Otherwise, consider an initial bolus of 20 mL/kg in dogs, 10 mL/kg in cats if the patient was euvolemic; use caution with cardiac or renal disease. Hypertonic saline can also be considered (4-6 mL/kg of 3% saline IV slowly over 5 minutes).
- Administer epinephrine (low dose: 0.02 mg/kg IV; high dose: 0.2 mg/kg IV). Consider starting with the low dose, repeat with high dose if initial dose is unsuccessful.
- Vasopressin (0.2-0.8 U/kg IV) can be considered instead of or in combination with epinephrine.
- Defibrillate electrically (e.g., starting with 2-5 J/kg if closed chest, 0.2-0.5 J/kg if open chest) if ventricular defibrillation is present. Repeat defibrillation if ventricular fibrillation persists.
- Additional medications to consider to treat arrhythmias: atropine (0.04 mg/kg IV) followed by epinephrine again if asystole unresponsive to initial epinephrine; amiodarone (5 mg/kg IV or IO over 10 minutes) for refractory ventricular fibrillation, atrial fibrillation, supraventricular tachycardia (SVT), ventricular tachycardia (VT); lidocaine (2-3 mg/kg IV in dogs) for ventricular tachycardia or flutter; atropine for persistent bradycardia; magnesium (0.15-0.3 mEq/kg IV slowly over 10 minutes) for refractory ventricular arrhythmias.
- Start vasopressors (e.g., dopamine 2-10 mcg/kg/min IV) if BP not adequate once appropriate fluid resuscitation is administered.
- Assess metabolic condition with repeated blood gas analysis and electrolyte and blood glucose monitoring: treat abnormalities accordingly.
- Use ETco2 and Doppler transducer on the cornea to assess efficacy of CPCR attempts.
- Monitor body temperature, cranial nerve reflexes.

POSTPROCEDURE

MONITOR, MONITOR, MONITOR: ideally continuously; otherwise very frequent intermittent monitoring is required. A majority of critically ill animals that have been resuscitated will arrest again within a few hours. Clinicians should monitor the following:

- BP
- Ventilation
- Oxygenation
- Cranial nerve reflexes
- Mentation
- Blood gases
- Organ-specific chemistries
- Urine output
- Electrolytes
- Blood glucose
- Central venous pressure
- Lactate
- Packed cell volume (PCV)
- Coagulation deficits
- Body temperature

Clinicians should also consider the following during the monitoring period:

- Administration of mannitol at 1-2 g/kg IV over 30 minutes is useful to reduce cerebral edema secondary to hypoxic brain injury, as well as to support renal perfusion and improve circulation to tissues.
- Until the animal is conscious and mobile, recumbent animal care protocols must be used. Frequently turning the animal, lubricating its eyes, keeping it clean of eliminations, and keeping the oropharynx clean and/or suctioning the endotracheal tube are imperative. Monitor for pressure-induced sores and blood flow impairment.
- If postarrest recumbency lasts hours or more, passive range-of-motion exercises may help with improving ultimate recovery as well as helping assess the progress of the animal's muscle strength.

ALTERNATIVES AND THEIR RELATIVE MERITS

There are many approaches to and controversies associated with CPCR. Many books and/or articles list different drug dosages and indications or contraindications. The reader is advised to be prepared by reading multiple sources and generating a customized flow chart that takes into consideration the personnel, drugs, and equipment available at a particular practice. If the animal is stable to move, post-resuscitation management should ideally be handled in a well-staffed 24-hour facility.

SUGGESTED READING

ECC Committee, Subcommittees and Task Force of the American Heart Association. 2005 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation 112:IV1–IV203, 2005.

Hackett TB: Cardiopulmonary cerebral resuscitation. Vet Clin North Am Small Anim Pract 31:6, 1253–1264, 2001.

Plunkett SJ, McMichael M: Cardiopulmonary resuscitation in small animal medicine: an update. J Vet Intern Med 22:9–25, 2008.

AUTHOR: LILLIAN GOOD

1ST EDITION AUTHOR: SHARON DRELLICH

Diagnostic Peritoneal Lavage

SYNONYMS

Abdominal lavage; DPL

OVERVIEW AND GOAL

Instillation and subsequent evacuation of lavage fluid to evaluate suspected intraabdominal disease

INDICATIONS

Animals with suspected abdominal disorders for which other noninvasive/less invasive testing has been inconclusive or unavailable. Animals that might benefit from diagnostic peritoneal lavage (DPL) include those with:

- Abdominal trauma
- Acute abdomen
- Sepsis with no source identified
- Shock with no source identified

CONTRAINDICATIONS

- Cardiovascular/respiratory compromise that may be exacerbated by lavage fluid administration
- Coagulopathy
- Recent abdominal surgery
- Diaphragmatic hernia

EQUIPMENT, ANESTHESIA

- Minimum of two assistants
- Sedation may be necessary; local anesthesia and manual restraint may be sufficient for some animals.
- Hair clippers
- Surgical scrub solution
- Isopropyl alcohol
- Sterile gauze for scrubbing skin
- Local anesthesia (2% lidocaine)
- Sterile drape
- Sterile surgical gloves
- Sterile needle holders
- Sterile scissors
- A #11 blade for stab incision of skin
- Sterile drainage catheter—various devices can be used:
    - Peritoneal dialysis catheter (recommended)
    - Over-the-needle large-gauge IV catheter: may be prone to kinking
    - Abdominal drainage catheter
    - Red rubber feeding tube
- Sterile collection system consisting of “Christmas tree” adapter, three-way stopcock, IV drip set, and collection bag
- 2-0 or 3-0 nylon suture to anchor the catheter to the skin
- Bandage material:
    - Nonadhesive absorbent sterile pad
    - Cast padding
    - Kling-type bandage roll
    - Protective outer layer (Vet-wrap, etc.)
- Elizabethan collar
- Lavage fluid (typically lukewarm saline) and administration supplies that depend on the volume of lavage infused (syringe/needle versus fluid bag with drip set, 22 mL/kg)

ANTICIPATED TIME

About 15-40 minutes for placement. Additional time required for drainage depends on type of catheter selected, degree of flow obstruction encountered, and variation between animals.

PREPARATION: IMPORTANT CHECKPOINTS

- Ensure adequate manual or chemical restraint. Excessive struggling by the animal may result in contamination of the sterile field or increased risk of abdominal trauma during catheter placement.
- Maximize cardiovascular stability prior to the procedure.
- Receive owner approval for invasive procedure.
- Perform all abdominal imaging prior to the procedure, because lavage fluid instillation will affect future imaging interpretation.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Care must be taken during placement to avoid internal organ damage. Possible traumatic injury includes:
  - Vessel or organ laceration leading to hemoabdomen
  - Gastrointestinal (GI) tract perforation leading to septic peritonitis
  - Urinary tract laceration leading to uroabdomen
- Obstruction of catheter drainage holes with omentum is a frequent occurrence and can limit complete retrieval of lavage fluid. Repositioning the animal and flushing the catheter may help relieve the obstruction. Use of commercially available peritoneal dialysis catheters with numerous (50-100) small-diameter side holes may minimize complete omental plugging. Cutting additional side holes (never more than one-third the circumference, because tube breakage may occur) into a nonperitoneal dialysis-specific catheter can be performed to decrease plugging of a single distal opening.
  - If sufficient lavage fluid cannot be retrieved, complications such as animal discomfort, cardiovascular or respiratory compromise, or overhydration may ensue.
- Subcutaneous or external leakage of lavage fluid may occur, especially if the body wall incision is large. Tunneling the catheter at least 2 cm through the subcutaneous space will help minimize external leakage. Keep the body wall and skin incisions small; the tube should be inserted with a snug fit through the incisions.
- Ascending infection into the peritoneal cavity is infrequent but possible. Sterile technique must be maintained during placement and when manipulating the lavage materials. A bandage should be maintained over the catheter site, and the catheter should be removed when the procedure has been completed.

PROCEDURE

PATIENT PREPARATION:

- Sedate the patient if it is fractious or likely to struggle, or if the clinician's ability to maintain a sterile technique throughout the procedure is questionable.
- Empty urinary bladder through catheterization or manual expression (decreases potential for bladder trauma or laceration during catheter placement).
- Place in dorsal recumbency. (Left lateral recumbency is also possible but not preferred.)
- Clip hair from abdomen, from xiphoid to pubis.
- Surgical scrub
- Determine catheter insertion sites for the skin and body wall:
  - Recommended skin insertion site is 1-2 cm to the right of the umbilicus.
  - Recommended body wall insertion site is 1.5-3 cm caudal to the skin insertion site.
- Administer lidocaine injection at skin and body wall insertion sites, penetrating all tissue layers to be incised. Note: Pain with lidocaine injection can be minimized by mixing lidocaine with one-tenth the volume of 8.4 mEq/L sodium bicarbonate (adjusts to a more neutral pH) and by warming to body temperature (e.g., once filled, keep syringe tucked in clinician's axilla).
- Repeat surgical scrub.
- Wear sterile gloves.
- Drape sterile field.

PLACEMENT: The technique will vary depending on the chosen catheter device.

- Trocar-type peritoneal dialysis catheter:
  - Incise skin using a #11 blade: incision should be no larger than the catheter diameter.
  - Tunnel the catheter through the subcutaneous space to the desired body wall entry site.
  - Insert trocar and catheter through the body wall at a 45° angle, directed caudally.
    - A turgid abdomen allows easier placement.
    - With a flaccid abdomen, insertion may be facilitated by grasping and “tenting” the abdomen with one free hand while advancing the catheter with another hand.
  - After passage through the body wall, advance the catheter off the trocar to minimize the potential for trauma with the sharp trocar.

    - Final catheter placement should be within the abdominal cavity, along the ventral midline adjacent to the urinary bladder.
- Seldinger-type peritoneal dialysis/abdominal drainage catheter:
    - Insert using the same anatomic markers.
    - Use the Seldinger technique of initial guide wire placement, dilation, and subsequent catheter insertion along the guide wire.
- Over-the-needle IV catheter:
    - Make 2-4 additional side holes < 30% of the diameter of the catheter using a #10 blade.
    - Insert using the same anatomic markers, and advance the catheter off the stylet once the body wall has been fully penetrated.
- Red rubber feeding tube: see p. 1192.

ANCHORING:

- Anchor the catheter in place using 3-0 or-2-0 nylon suture. A purse-string suture should be placed in the skin, followed by a Roman-sandal/Chinese-finger-trap suture pattern.
- Attach the sterile collection system to the catheter port.
- Apply a sterile dressing at the insertion site, followed by a bandage.
- Caution: An Elizabethan collar should be used if the animal is left unsupervised at any time with the tube in place.

LAVAGE:

- Instill 22 mL/kg of warm saline into the abdominal cavity through the three-way stopcock. Closely monitor the cardiovascular and respiratory status of the animal during infusion for early detection of deterioration, warranting termination of the procedure. Place a sterile male adapter into the port when completed to maintain a closed system.
- Gently rock the animal from side to side, and gently massage the abdomen to promote fluid dispersion. Reduce or avoid this step if the patient's abdomen is painful.
- Attach a 6- to 20-mL syringe (dependent on body size and fluid volume instilled), and slowly (to avoid omental plugging) aspirate to obtain the fluid sample for analysis. Replace male adapter when completed.
- Open stopcock to the collection system, and allow gravity to drain the remaining lavage fluid. Incomplete retrieval is likely owing to partial absorption and ineffective retrieval. Maximum retrieval should be attempted.

REMOVAL:

- Cut the purse-string suture and remove the catheter.
- Place a skin suture if the incision > 5 mm.
- Maintain a sterile dressing and bandage over the incision site for 12-24 hours.

ANALYSIS:

- Evaluate color: clear fluid is not expected when peritonitis exists. Flocculent fluid indicates possible peritonitis. Red fluid indicates hemoabdomen. Green fluid likely contains bile.
- Perform packed cell volume (PCV) count: > 5% indicates significant hemoabdomen.
- Perform white blood cell (WBC) count: normal is approximately 1000 cells/mm^3.
- Perform cytologic examination of fluid for degenerative neutrophils, toxic change, intracellular bacteria, bilirubin crystals, neoplastic cells, and other such abnormalities.
- Consider aerobic/anaerobic culture if septic peritonitis is suspected.
- Consider chemistry evaluation of lavage fluid, with comparison to peripheral blood:
    - Elevated creatinine in lavage fluid indicates ruptured urinary tract.
    - Elevated bilirubin indicates ruptured biliary tree.
    - Elevated amylase indicates pancreatitis.

POSTPROCEDURE

- Monitor recovery from sedation/anesthesia.
- Supportive care as indicated for condition.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Percutaneous needle abdominocentesis (see p. 1194):
    - Technically easier to perform
    - Requires less equipment
    - Higher probability of a negative tap with small fluid volumes or pocketed areas of disease

- Abdominal ultrasonography:
  - Noninvasive
  - Allows visualization of the entire abdomen and detection of small or pocketed areas of fluid accumulation
  - Ultrasound-guided aspiration allows fluid collection without risk of side effects secondary to instillation of lavage fluid.
  - Diagnostic accuracy is operator dependent.
  - Not available at all veterinary facilities
- Abdominal CT scan (see p. 1233) or MRI (see p. 1302):
  - High diagnostic accuracy rate
  - Typically requires anesthesia
  - Limited to referral institutions
  - Expensive
- Laparoscopy (see p. 1298):
  - High diagnostic accuracy rate
  - Requires anesthesia
  - Expensive
  - Not available at many veterinary facilities
- Exploratory laparotomy:
  - High diagnostic accuracy rate
  - Requires anesthesia
  - Highly invasive

AUTHOR: LILLIAN I. GOOD

Dermatologic Diagnostic Procedures

SYNONYMS

Diagnostic techniques in dermatology, diagnostic testing in dermatology

OVERVIEW AND GOALS

- Tests that are performed to confirm a diagnosis and/or to rule out differential diagnoses for skin lesions
- The most common diagnostic procedures in dermatology are examination of the haircoat and skin with a good light source and magnifying lens, flea combing, acetate tape preparation, skin scrapings, skin cytologic examination, Wood's lamp examination, fungal culture for dermatophytes, and skin biopsies.

INDICATIONS

- Skin scrapings: used primarily to find mites and occasionally nematode infestation
- Skin cytologic examination: extremely useful diagnostic procedure indicated in almost every dermatology case. It can rapidly and inexpensively detect the presence of inflammation, infection (bacteria, fungi), autoimmune disease (acantholytic keratinocytes in pemphigus), or neoplasia.
- Wood's lamp examination: useful screening tool when dermatophytosis caused by *Microsporum canis* is suspected
- Dermatophyte culture: indicated when a dermatophytosis is suspected. In fact, it is indicated in virtually any cat with undiagnosed skin disease.
- Trichography is the microscopic examination of forcefully plucked hairs. This test is most useful for finding ectoparasites (particularly louse ova and *Demodex),* identifying hair shaft fracture, and finding large melanin clumps (macromelanosomes) causing hair shaft distortion in color dilution alopecia and black hair follicular dysplasia. It can be a useful tool in evaluating alopecic dogs, but normal anagen/telogen ratios have not been established for most breeds.
- Skin biopsies: performed to confirm a diagnosis or to provide direction (without always receiving a definitive diagnosis). Skin biopsies are recommended with any neoplastic or suspected neoplastic lesion, any persistent or unusual lesion, any vesicular dermatosis, and any undiagnosed alopecia.

CONTRAINDICATIONS

Virtually none

EQUIPMENT, ANESTHESIA

Simple equipment is required to perform veterinary dermatologic tests. Standard equipment and materials consist of:

- Biopsy kit, including biopsy punches
- One or two dull #10 scalpel blades
- Glass microscope slides and coverslips (20 × 40 or 22 × 50 mm)
- Mineral oil
- Cotton-tipped applicators
- Acetate tape (clear adhesive tape)
- Microscope
- Hemostat
- Handheld magnifying lens
- Flea combs
- Otoscope and several otoscopic cones
- Cytologic examination stain
- Wood's lamp
- Dermatophyte test media
- Sterile toothbrushes
- Syringes
- A few 22-, 23-, and 25-gauge needles
- Biopsy kit
- Local anesthetic (e.g., lidocaine 2%)
- Biopsy jars containing 10% neutral buffered formalin

ANTICIPATED TIME

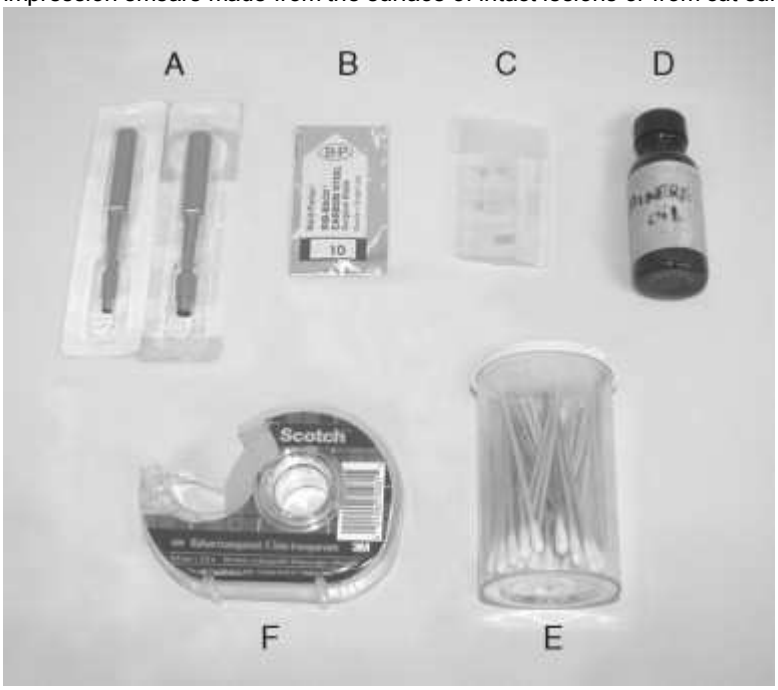
The procedure takes a few minutes.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Skin scrapings: to avoid false-negative results, it is important to clip hair before performing skin scrapings. However, it is preferable to use scissors when surface mites such as *Cheyletiella* are suspected, because they can be lost if electric clippers are used. Note: A positive scraping allows the clinician to find and identify a parasitic infestation, but its sensitivity in ruling out a diagnosis depends on the parasitic disease and the aggressiveness of sampling.
- Skin biopsies: do not scrub—or wipe or rub with alcohol or antiseptic—the surface of a biopsy site prior to performing punch biopsies; pathologic changes on the skin surface, which often are critical in making a diagnosis, may be altered or removed. For the same reason, do not shave the area of interest; gently clip the hair with scissors if necessary.

PROCEDURE

- Skin scrapings:
  - Apply a few drops of mineral oil to the area of skin selected for scraping or coat the dull scalpel blade that is used for performing the scraping with mineral oil. Broad superficial scrapings that collect scales and crusts should be performed when looking for mites living on the surface *(Cheyletiella)* or in the superficial layers of the skin *(Sarcoptes, Notoedres).* Deeper skin scrapings must be performed when suspecting the presence of deep-dwelling mites *(Demodex).* In the latter case, the skin must be squeezed to help extrude the mites from the hair follicles first, and the scrapings should be deep enough to create capillary oozing.
  - The skin scraping material that is collected on the scalpel blade is then smeared on a glass slide; additional mineral oil is added, and a cover slip is applied. The specimen is then examined with 40× *(Cheyletiella, Sarcoptes, Notoedres)* or 100× *(Demodex)* magnification.
  - *Demodex* mites are part of the skin's normal flora, but it is extremely rare to find them on skin scrapings. If one or a few mites are found, more deep skin scrapings should be taken to confirm the diagnosis of demodicosis. Conversely, numerous negative skin scrapings from appropriate areas should reliably eliminate demodicosis and notoedric mange. In addition, in areas that are difficult to scrape, hair can be plucked and the proximal ends examined under a microscope for the presence of *Demodex* mites.
  - Negative skin scrapings (even if several are performed) do not eliminate the possibility of sarcoptic mange or cheyletiellosis.
- Skin cytologic examination:
  - Allows microscopic examination of fluid or material collected from nodules, tumors, cysts, plaques, draining tracts, ulcers, pustules, vesicles, papules, and surface of the skin or ears. Several techniques may be used for obtaining samples. Specimens may be collected by:
    - Impression smears made from the surface of intact lesions or from cut surfaces of surgically



DERMATOLOGIC DIAGNOSTIC PROCEDURES Materials used for performing dermatologic diagnostic tests.

A, Biopsy punches. **B**, #10 scalpel blades. **C**, Glass microscope slides. **D**, Mineral oil. **E**, Cotton-tipped applicators. **F**, Acetate tape (clear adhesive tape).

excised lesions, such as nodules or tumors
- Impression smears made after lancing pustules or papules
- Fine-needle aspiration (FNA) of cells or material from lesions
- Smears made by rolling the cotton-tipped applicator across a glass slide (particularly useful for ear specimens)
- Scrapings of superficial epithelial cells with a dry, dull scalpel blade. This cellular material is then pressed firmly onto a glass slide.

- After the specimen has dried, the slide is stained with a modified Wright's stain (e.g., Diff-Quik) and examined microscopically. When a drop of mineral oil is put on the stained dried specimen and then covered with a large coverslip (22 × 40 or 22 × 50 mm), visualization of cells and most microorganisms at 400× is enhanced, so there is no need to perform an examination under oil immersion (1000×) in most cases.

- Wood's lamp examination:
  - This ultraviolet light's wavelength of 253.7 nm is temperature dependent, and the lamp should be turned on for 5-10 minutes before use. Certain dermatophytes (mainly *Microsporum canis* in veterinary medicine) may cause infected hairs (not scales or crusts) to fluoresce an apple green color. This occurs in about 50% of cases with *M. canis*.
  - It is a fast and inexpensive screening tool for dermatophytosis. False positives are unfortunately frequent. Glowing hair should be plucked and the proximal end further examined with the Wood's lamp or used for culture or direct examination for fungal elements under microscope. A negative examination does not rule out dermatophytosis.
- Dermatophyte culture (see p. 292):
  - Generally performed in clinics on commercial dermatophyte test medium (DTM), available in either glass jars or flat plates. The culture medium consists of Sabouraud's dextrose agar, antibacterial and antifungal agents to inhibit growth of contaminants, and phenol red (pH indicator).
  - Select hairs and scales for culture along the edge of newly developing lesions. Broken or frayed hairs and those that fluoresce with Wood's lamp are the best specimens. The plucked hairs should be firmly pressed onto the surface of the medium. Alternatively, vigorous brushing of the animal's haircoat with a sterile toothbrush or a small piece of sterile carpet can be used for collecting hairs and scales (more useful to identify carriers not showing obvious lesions). This material can be removed from the toothbrush with a sterile hemostat and placed into the culture medium. Alternately, if plates are used, the DTM is inoculated by gently embedding or repeatedly dabbing the toothbrush into the medium.
  - Ideally, the culture medium should be incubated at 22○C-30○C (72○F-86○F) and at about 30% of relative humidity for 2-3 weeks, and it should be checked daily for fungal growth. Desiccation hinders growth. It is recommended to keep the culture medium for up to 3-4 weeks in animals with antifungal pretreatment or suboptimal culture environment fungal growth.
  - A red color change with visible mycelial growth (typically cream color) is seen with dermatophytes on DTM. Contaminants (environmental molds) will eventually turn the media red; however, colony growth is usually well established before any color change appears in the medium. In addition, most saprophyte colonies are pigmented. Nonetheless, identification of the fungi is essential if a suspected dermatophyte is grown on culture.
  - Macroconidia must be collected from the mycelial surface by gently applying the sticky side of clear acetate tape to the aerial surface. The tape with sample is then pressed onto a glass slide over a drop of methylene blue or lactophenol cotton blue stain and examined under microscope for characteristic macroconidia.
- Skin biopsies:
  - The biopsy technique selected (punch biopsy, wedge biopsy, excisional biopsy) varies according to the type of lesions.
  - Site selection is crucial. Choose several representative lesions that may represent various stages of the same pathologic process or multiple problems, with emphasis on primary lesions if possible (e.g., pustules, vesicles).
  - Punch biopsy specimens (usually 6 mm) can be obtained under local anesthesia (1 mL of 2% lidocaine per site, injected subcutaneously beneath the specimen; do not exceed 1 mL per 5 kg of body weight). If a papule, pustule, vesicle, or any small lesion is selected, the lesion should be centered in the biopsy specimen. The biopsy punch should be rotated in only one direction to minimize shearing artifact. Handle the specimen carefully. The forceps should grasp either the hairs of the biopsy sample or its deepest surface (e.g., subcutis), never the core of the biopsy sample itself. The specimen must be put rapidly in 10% neutral buffered formalin. Skin biopsy punch sites can be sutured with one or two interrupted sutures.
  - Skin biopsies, along with a detailed history and animal description, should be submitted to a veterinary dermatopathologist.

ALTERNATIVES AND THEIR RELATIVE MERITS

Therapeutic trials (e.g., antiparasitic, antimicrobial) are frequently performed in veterinary dermatology and represent very useful diagnostic tools. For example, therapeutic trials with acaricidal agents such as macrocyclic lactones are often required when sarcoptic acariosis or cheyletiellosis is suspected but skin scrapings are negative.

AUTHOR: MANON PARADIS

Dental Radiography, Basic

OVERVIEW AND GOAL

To obtain diagnostic images of the teeth and surrounding structures using x-rays.

INDICATIONS

- Diagnosis, treatment planning, and postoperative assessment of treatment efficacy for various dental, oral, and maxillofacial conditions
- Dental radiographs should be obtained prior to tooth extraction to evaluate alveolar bone health and variations in root anatomy, and to determine the presence of dentoalveolar ankylosis or root replacement resorption that could potentially complicate the extraction procedure. They are essential when performing endodontic procedures.

Specifically, to diagnose and monitor:

- Regressive changes of the dentition including: caries, attrition, abrasion, and tooth resorption
- Dental (change in number or shape of teeth) and jaw size anomalies, including malocclusion, supernumerary teeth, and developmentally missing teeth
- Infection and inflammation of teeth, alveolar bone, and maxillofacial bones, including periodontitis, endodontic disease (pulp necrosis), periapical disease (apical granuloma, cyst or abscess, condensing osteitis, osteosclerosis), and osteomyelitis
- Oral and maxillofacial cysts and tumors
- Oral and maxillofacial trauma
- Disorders of joints of the head: mandibular symphysis separation; temporomandibular joint osteoarthritis, luxation, fracture, and ankylosis; open-mouth jaw locking
- Diseases of bone with manifestation in the jaws: craniomandibular osteopathy, calvarial hyperostosis, secondary hyperparathyroidism, fibrous osteodystrophy
- Diseases of the nose, orbit, and ear
- Partial or full-body imaging studies in small mammals and exotics

CONTRAINDICATIONS

Because dental radiography requires chemical restraint, it is contraindicated in patients that cannot undergo sedation or general anesthesia.

EQUIPMENT, ANESTHESIA

- Sedation or general anesthesia
- Radiolucent positioning and film-holding devices (e.g., bite blocks, foam rolls, syringe cases, gauze pads, paper towels, rubber bands) to keep the mouth open and the dental film packet in position without superimposition of maxillary and mandibular dental arches
- Dental x-ray machines:
  - Either handheld, stand-supported, or (more commonly) wall-/ceiling-mounted
  - Extension arm allowing vertical, horizontal, and rotational movement of the tube head without changing the patient's position
  - Adjusting exposure time based on patient size and tissue thickness to be imaged (between 0.1-0.6 seconds for teeth and jaws when using non-screen dental films and 1/10 of that time when using digital sensors)
- Dental x-ray films:
  - Nonscreen (providing greater detail than screened film used with standard x-ray machines)
  - Sizes 0, 1, 2, 3 and 4 (0, 2 and 4 most commonly utilized). Most jaw lesions can be satisfactorily assessed with size 2 and 4 dental film and intraoral imaging techniques.
  - Dot in corner of packet and also on the film: convex (raised) surface facing x-ray beam during exposure; after developing, dimple is used for distinguishing right side of mouth from left.
  - Contents of moisture resistant dental film packet:
    - Outer plastic wrap
    - Black paper on either side of the film
    - Layer of lead foil located at back of packet next to tab opening (protecting film from secondary radiation, which may cause fogging)
    - X-ray film
  - Types of film:
    - Ultra-speed (group D): most commonly utilized
    - Ekta-speed (group E): faster (reducing patient exposure and radiation), but image of slightly lesser quality than that obtained with ultra-speed film
  - Dental x-ray films can also be used with standard x-ray machines, using a technique of 100 mA, a film focal distance of 12 to 16 inches, and an exposure time of 1/10 second, with the kVp varying from 60 to 70 dependent on patient size.
- Other equipment:
  - Chairside darkroom (or automatic film processor) with small containers for the following solutions (from left to right): rapid developer, water, rapid fixer, and again water (or fixer, dependent on number of radiographs obtained)
  - Film clips and hangers
  - Dental view box
  - Envelopes or other storage system
- Digital imaging:
  - Most modern dental x-ray machines compatible with most digital hardware and software packages
  - Sensor pads (sizes 0 and 2) or photostimulable phosphor plates (size 4 also available) transferring images to a computer
  - Less radiation required to produce images
  - Digital image improvable with software programs

ANTICIPATED TIME

Obtaining a full-mouth dental series:

- Cats (8-10 films): 10-15 minutes

- Dogs (10-14 films): 15-20 minutes

Processing a full-mouth dental series:

- Cats: 5-10 minutes
- Dogs: 10-15 minutes

PREPARATION: IMPORTANT CHECKPOINTS

- Observe radiation safety guidelines:
  - Be protected against three sources of radiation: primary beam, secondary radiation emitted from the patient, and radiation leakage from the machine housing.
  - Wear film badges that monitor occupational exposure to radiation.
  - Keep amount of radiation exposure to a minimum.
  - Have x-ray machine accurately collimated and equipped with an accurate exposure timer.
  - Leave the room when radiographs are obtained.
  - If leaving the room is not possible, wear protective lead-lined gear, use a protective barrier, or stand at least 6 feet from the x-ray source and at an angle of 90°-135° to the central ray of the x-ray beam when the exposure is made.
- Film-processing solutions (rapid developer and fixer) should be disposed of properly in accordance with regional/local law, and lead foil from film packets should be separated and stored for recycling.
- Patient positioning varies; lateral recumbency allows for easy rotation of the head if needed and is a good starting position for obtaining most dental radiographs in cats and dogs.
- A full-mouth dental series may contain the following views:
  - Right maxillary premolars and molars
  - Right maxillary canine (lateral or lateral oblique view)
  - Right and left maxillary canines and incisors (occlusal view)
  - Left maxillary canine (lateral or lateral oblique view)
  - Left maxillary premolars and molars
  - Left mandibular premolars and molars
  - Left mandibular canine (lateral or lateral oblique view)
  - Right and left mandibular canines and incisors (occlusal view)
  - Right mandibular canine (lateral or lateral oblique view)
  - Right mandibular premolars and molars

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO BE AVOIDED

POSITIONING ERRORS:

- Elongation: abnormally long teeth due to tube angle too perpendicular to apico-coronal axis of teeth when bisecting angle technique is used
- Foreshortening: abnormally short teeth due to tube angle too perpendicular to film when bisecting angle technique is used
- Superimposition: summation effect due to tube head aligned too far in rostral or caudal direction
- Clear circular perimeter: cone cut
- Blurred image: movement of patient, tube head, or film during exposure
- Image distortion: excessive bending of film during positioning
- White crescents or lines: sharp bend or pressure on film prior to exposing
- Dark crescents or lines: sharp bend or pressure on film after exposing but before processing
- Area of interest not on image: tube head misaligned
- Blurry, magnified image: film too far from subject to be imaged
- Stipple pattern on light film: film placed backward

EXPOSING ERRORS:

- Dark film: overexposed
- Light film: underexposed
- Double image: double exposure

PROCESSING ERRORS:

- Entire film clear: emulsion detached from film or unexposed film
- Clear area along one edge: processing solution level too low
- Incomplete variable processing: paper stuck to film during processing
- Dark film (not overexposed): overdeveloped
- Light film (not underexposed): underdeveloped
- Black spots: contamination of film with developer prior to processing
- Yellow or brown stains: inadequate fixation, inadequate rinsing (incomplete removal of fixer)
- White spots: contamination of film with fixer before processing
- Green discoloration: films in contact during processing
- Fingerprints: film touched with contaminated fingers
- Frosted film surface: inadequate rinsing (incomplete removal of fixer)
- Small white circles: bubbles in processing solutions
- Thick white lines: scratched emulsion during processing
- Streaks: inadequate processing, solution contamination, contaminated hanger clips
- Mottled areas (too light or too dark): poorly mixed processing solutions, with temperature variances (too low or too high)
- Fogged film: light contamination or overprocessing

PROCEDURE

OBTAINING DENTAL RADIOGRAPHS:

- Parallel technique:
  - Film placed parallel to apico-coronal axis of the teeth
  - X-ray beam directed perpendicular (90○) to the film and the teeth
  - Used for imaging the molars and caudal premolars of the mandible and the nasal cavity
- Bisecting angle technique:
  - Film placed as close to the teeth as possible
  - Angle formed by the apico-coronal axis of the teeth and the plane of the film bisected by an imaginary line, with the tube head (x-ray beam) positioned perpendicular to this imaginary line
  - Used for imaging all maxillary teeth and the rostral premolars, canines, and incisors of the mandible
  - Peculiarity in cats: radiographs of the maxillary premolars and molars utilizing the bisecting angle technique results in superimposition of the zygomatic arch over the root apices of the teeth. To eliminate this superimposition:
    - An extraoral technique may be utilized; *or*
    - Premolars and molars may be intentionally elongated slightly when using the intraoral technique to eliminate the superimposition of the zygomatic arch by decreasing the vertical angulation of the tube head.

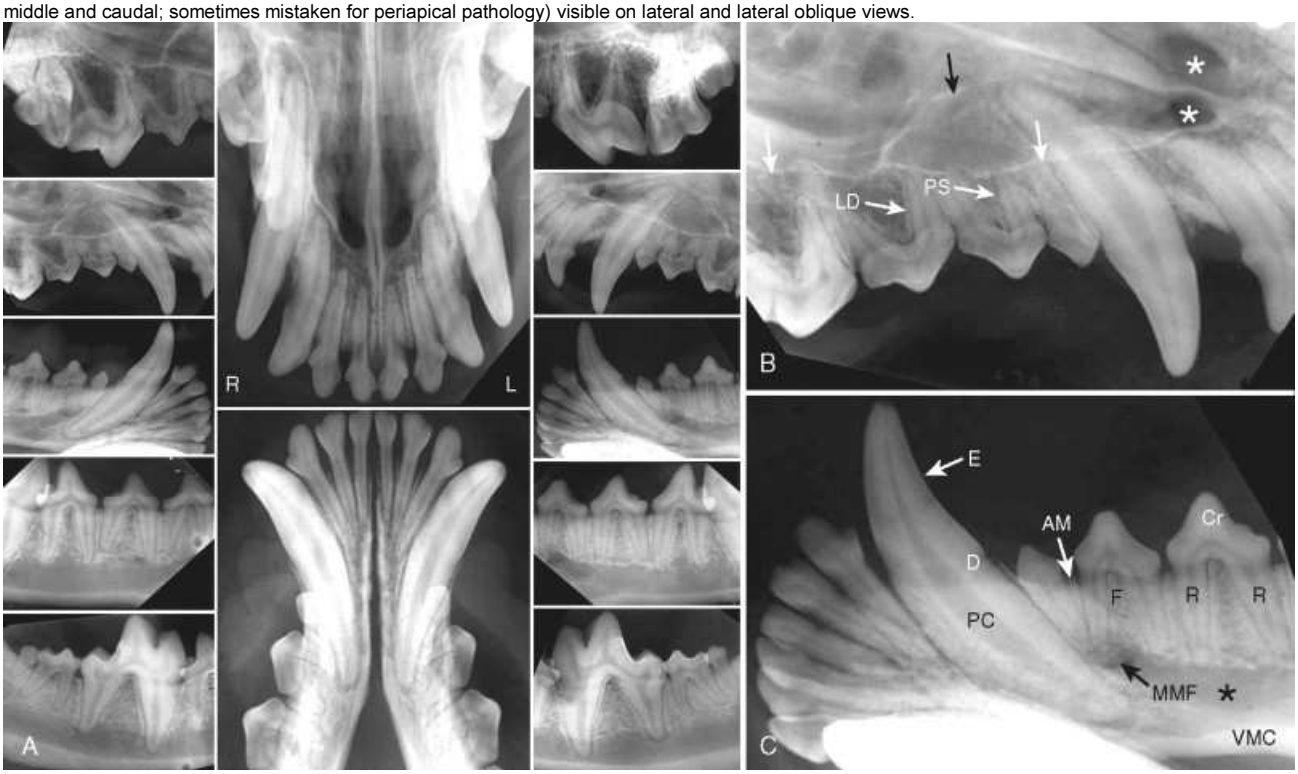
PROCESSING EXPOSED FILMS:

- Chairside darkroom:
  - Close lid of the chairside darkroom.
  - Hold film packet in one hand and a film clip in the other.
  - Slide both hands through front sleeves into the chairside darkroom.
  - Remove exposed x-ray film from packet, and place it in film clip.
  - Place film first into developer for about 30 seconds.
  - Briefly (few seconds) rinse in water.
  - Then place film into fixer for at least 60 seconds before viewing.
  - After a final water rinse, view film using a dental view box to make a diagnosis.
  - After viewing, place film for another 15 minutes into fixer, followed by thorough rinsing in water for 20 minutes and air drying.
  - Store completely dry films in a labeled envelope (or other storage system), and keep as part of the patient's medical record.
- Automatic processor:
  - Automatic processors designed for dental films can deliver processed film in a fully fixed, dried condition within 5 minutes.
  - Dental film can also be processed if taped to a larger film that serves as a leader by dragging the dental film through a large automatic processor.

POSTPROCEDURE

INTERPRETING PROCESSED FILMS:

- Labial mounting:
  - Place processed film on view box so that raised dot is projecting toward the viewer.
  - Determine if image is of upper or lower jaw.
  - Rotate film so that maxillary tooth crowns point downward and mandibular tooth crowns point upward.
  - View image as if one is looking from outside at a closed mouth whose maxillary and mandibular teeth are made visible after raising upper and lower lips.
- Radiographic landmarks:
  - All three-rooted teeth are located in the upper jaw.
  - Palatine fissures are also located in the upper jaw.
  - Upper jaw will often have white lines visible on lateral and lateral oblique views that are superimposed on teeth (indicating maxillary conchal crest and line of conjunction between body and palatine process of the maxilla).
  - Lower jaw will often have ventral mandibular cortex, mandibular canal (radiolucent tubular structure in the mandible), and mental foramina (rostral, middle and caudal; sometimes mistaken for periapical pathology) visible on lateral and lateral oblique views.



DENTAL RADIOGRAPHY, BASIC A, Full-mouth dental radiographic series in a 2-year-old dog with complete permanent dentition: radiographs are arranged in labial mounting (with raised dot facing the viewer). Maxillary tooth crowns point downward, and mandibular tooth crowns point upward. *L,* Left side; *R,* right side. **B**, Lateral radiographic view of right maxillary incisors, canine, and premolars in a dog (labial mounting). Note the palatine fissures *(asterisks)*, the line of conjunction between the body and palatine process of the maxilla *(large white arrows)*, and the conchal crest *(large black arrow)*. *LD,* Lamina dura; *PS,* periodontal space. **C**, Lateral radiographic view of left mandibular incisors, canine, and premolars in a dog (labial mounting). Note the mandibular canal *(asterisk)*. *AM,* Alveolar margin; *Cr,* crown; *D,* dentin; *E,* enamel; *F,* furcation; *MMF,* middle mental foramen; *PC,* pulp cavity; *R,* root; *VMC,* ventral mandibular cortex.

(Copyright Dr. Alexander M. Reiter.)

- Components of the tooth and its supporting structures:
  - Crown and root(s)
  - Enamel (covering the crown) and dentin (core hard tissue of the tooth)
  - Cementum (covering the root), periodontal space (containing the periodontal ligament), and lamina dura (cortical bone extending into the alveoli)
  - Pulp cavity (pulp chamber in crown and root canal in root)
  - Furcation (area where two roots meet at the crown)
  - Alveolar margin (most coronal extension of the alveolar bone)

ALTERNATIVES AND THEIR RELATIVE MERITS

The largest dental films (size 4) may also find use for radiographic evaluation of the nasal cavity, orbit, zygomatic arch, mandibular ramus, temporomandibular joint and tympanic bulla in cats and small dogs and for partial or full-body imaging studies in small mammals and exotics.

AUTHOR: ALEXANDER M. REITER

Dental Prophylactic Treatment

SYNONYMS

Dental cleaning and polishing, dental prophylaxis

OVERVIEW AND GOALS

- Complete oral examination
- Removal of calculus and plaque buildup on teeth to create a healthier dentogingival environment
- Polishing teeth surfaces to make them less prone to calculus accumulation

INDICATIONS

- Accumulation of bacterial plaque (soft) or dental calculus (hard) on the dental surface
- Treatment of gingivitis
- Prevention of periodontal disease
- Annual dental examination
- Part of the maintenance phase in the treatment of periodontitis

CONTRAINDICATIONS

- Established periodontitis: animal should receive more involved diagnostic and treatment procedures rather than prophylactic treatment. Diagnosis includes dental examination, periodontal probing and full-mouth intraoral radiographic examination. The first stage of treatment is aimed at controlling the infection; it includes dental cleaning and polishing, root planing, dental extractions and antimicrobials as needed. It is followed by a period of maintenance with home care and reevaluation. The second stage of treatment, periodontal surgery, is done a month later once the periodontium has healed, if the level of compliancy of the owner with home dental care is adequate and if the periodontium still needs to be restored to help prevent reinfection.
- When general anesthesia is contraindicated because of systemic illness
- Old age is not a contraindication.
- Note: Dogs with mitral valve endocardiosis have not been shown to have a greater risk of dental procedure–associated bacterial endocarditis than dogs with normal heart valves.

EQUIPMENT, ANESTHESIA

- General anesthesia and tracheal intubation
- Hand instruments:
  - Scalers (H 6-7)
  - Curettes (Gracey 3/4, Gracey 13/14, Mini-five 1/2)
  - Dental explorer and periodontal probe (XP-17/0W)
  - Dental mirror
  - Instrument tray
  - Ceramic sharpening stone
- Power instruments:
  - Ultrasonic (magnetostrictive with metal stack, magnetostrictive with ferrite rods, or piezoelectric) or sonic scaler
  - One tip for removal of gross and moderate calculus buildup
  - One perio (or universal) tip for removal of subgingival calculus and debris. The energized water spray at the end of the tip also kills bacteria with what is referred to as the *cavitation effect.*
  - Dental unit, either air or electric powered, with low-speed handpiece and contra-angle attachment. Since the speed of the prophy cup should be around 4000 rpm, a contra-angle-attachment with a 4:1 gear ratio is usually necessary with air-driven units.
  - Prophy head, multi-use or single-use
  - Rubber prophy cups; prophy paste (jars or unidose cups) or flour pumice medium grit
- Chlorhexidine solution 0.12%
- Good lighting conditions, magnifying glasses
- Dental chart

ANTICIPATED TIME

About 20 minutes for a cat and 45 minutes for a dog

PREPARATION: IMPORTANT CHECKPOINTS

Operator protection:

- Surgical mask, gloves, eye protection, scrub top or gown
- Instill 0.12 % chlorhexidine solution in the animal's mouth before starting the procedure to reduce bacterial counts in the aerosols generated during power scaling.

Animal protection:

- Keep the animal warm because of the cooling effect of the water spray during power scaling. Protect the eyes (lubrication, towel), and sterilize the instruments. Appropriately inflate the cuff of the endotracheal tube, and use lubricating gel.
- Administer antibiotics only if animal is immunosuppressed, has an internal prosthesis, or has a severe infection: 20 mg/kg ampicillin IV 1 hour prior to the procedure; or clindamycin, 5 mg/kg, or clavulanic acid-amoxicillin, 13.5 mg/kg, PO 12 hours prior to the procedure.
- Place cotton gauze in the oropharynx to catch pieces of calculus that could otherwise enter the trachea after extubation.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Forgetting to remove the cotton gauze in the oropharynx before extubation
- Causing thermal damage to the dental pulp by staying too long over a tooth during power scaling or polishing or inadequate water spray during power scaling
- Damaging the tooth surface by being heavy-handed during scaling and polishing or by using burs (Rotosonics) to remove calculus
- Dental cusp (tip) fracture caused when using extraction forceps to chip away the calculus (not recommended)
- Power instrumentation: use the lowest effective intensity (power) setting; use a light touch; work with the last 3 mm at the end of the tip; keep the tip moving, with adequate water spray. Use a gauge to check tip wear, and replace when 2 mm has been lost (50% loss of efficacy).

PROCEDURE

- The anesthetized, intubated animal is placed in lateral recumbency, and all stages of the procedure described here are performed on the lingual side of the teeth on the recumbent side and the labial side of the teeth on the non-recumbent side. Then the animal is turned over, and the procedure can be repeated (avoids turning the animal multiple times).
- Remove very heavy calculus deposits with a dental scaler or hoe.
- Remove gross and moderate supragingival calculus using hand instrumentation (dental curette, scaler) or power instrumentation (sonic or ultrasonic with a heavier tip at moderate- to high-intensity setting).
- The working surface of the power scaler should be held parallel not perpendicular to the tooth surface.
- Remove light supragingival and subgingival calculus with hand instrumentation (dental curette) or power instrumentation (sonic or ultrasonic with slim perio or universal tip at low-to moderate-intensity setting).
- A disclosing solution can be used for checking for the presence of dental plaque, or an air spray from an air/water syringe for the presence of calculus.
- The teeth are polished with prophy paste or flour pumice.
- Dental examination with dental explorer; periodontal examination with periodontal probe. Chart all the findings.
- Flush the gingival sulcus with an atraumatic needle and saline to remove the prophy paste or flour pumice, calculus debris, and bacteria.
- Perform final rinse with 0.12% chlorhexidine.

POSTPROCEDURE

- Discuss home oral care with owners, and find appropriate regimen.
- Provide the owner with information about the postoperative treatment plan, including the date of the next dental appointment.

ALTERNATIVES AND THEIR RELATIVE MERITS

- The wrong alternative to preventing periodontal disease with dental prophylactic treatment and home dental care is to wait until periodontal disease has progressed, and periodontal treatment is necessary to help control disease progression. This is

obviously not an option that benefits the animal or owner.
- Brushing the teeth will not remove existing calculus.
- Dental prophylactic treatment performed without general anesthesia provides some cosmetic improvement but no long-term benefit.

AUTHOR: YVAN DUMAIS

Dental Preventive (Home) Care

Client Education Sheet Available on Website

OVERVIEW AND GOALS

A regimen of home dental care is designed to help keep the periodontium healthy in between professional oral prophylactic or therapeutic treatments.

INDICATIONS

- Accumulation of bacterial plaque (soft) or dental calculus (hard) on the dental surface
- Prevention of gingivitis and periodontal disease
- Part of the maintenance phase in the treatment of periodontitis

CONTRAINDICATIONS

- When the animal needs professional dental prophylactic treatment (gingivitis, calculus, or plaque buildup) or periodontal treatment (periodontitis, loss of dentogingival attachment)
- Oral hygiene complements and does not replace professional dental care.

EQUIPMENT, MATERIAL

- Soft-bristle toothbrush; pet toothpaste
- Food that is specially designed to reduce dental plaque or calculus formation
- Oral rinses to help reduce dental plaque formation
- Chew toys

ANTICIPATED TIME

The home dental care regimen is discussed during regular visits or as part of a comprehensive oral prophylactic treatment or periodontal treatment. Once the regimen is well accepted by the pet and the owner, it is a daily routine that takes only 1 or 2 minutes.

PREPARATION: IMPORTANT CHECKPOINTS

- The home dental care regimen should be selected after considering the animal's needs; the will, availability, and dexterity of the owner; and the compliance of the animal.
- The implementation may require some form of training or behavior positive reinforcement before the pet associates home dental care with something fun.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- The desire to achieve thorough oral hygiene right at the beginning is often a deterrent for the owner and the animal. Most pets will not tolerate more than 20 seconds of toothbrushing and will not allow brushing the aspect of the teeth facing the palate or the tongue.
- In pets that have minimal calculus buildup, an annual thorough dental examination/cleaning under anesthesia often is not recommended. As a result, these animals may end up having severe dental or periodontal problems for an extended period of time before the problem gets noticed. It is sad that after investing a lot of effort in home dental care for prevention, these owners are not getting the success they were expecting because the recommendation for professional dental care was never made until it was clinically obvious that a problem was present. Pets, just as humans, need both: home dental care and professional dental care.
- Many chew toys have a round cross-sectional shape and are so hard that the carnassial teeth are prone to break when the pet bites down on them.
- There are so many products on the market and so many claims, most unsupported by credible independent research, that it is difficult to choose what to recommend to clients. A credible and independent source of information on the efficacy of dental products is the Veterinary Oral Health Council website (www.vohc.org), and products bearing the council's seal are recommended.

PROCEDURE

Training for toothbrushing; instructions for the owner:

- Start with a bare finger and apply pet toothpaste on the rostral (front) teeth.
- Massage the gingiva for a few seconds. Repeat many times a day.
- As the pet gets used to it, go farther caudally in the mouth until the pet tolerates the procedure being done up to and including the molars.
- Once the pet is comfortable with the procedure, start using a toothbrush with soft bristles, and apply the toothpaste again on the rostral teeth, brushing for a few seconds.
- Go farther caudally as the pet tolerates the procedure. Give praise and rewards immediately after. Brush daily.
- Movement: for the incisors, brush from the gingiva toward the tip of the teeth. For the other teeth, brush with a circulatory movement with the bristles slightly oriented toward the gingiva of the upper jaw, then lower jaw, so that the action is focused on the area next to the gingival margin. With the mouth closed, the last teeth of the lower jaw are hidden behind the teeth of the upper jaw; however, the area next to the gingiva can still be brushed.

Other alternatives:

- Food specially designed to prevent calculus or plaque formation either mechanically (fibers) or chemically. Fibers help clean the caudal teeth.
- Rinses: chlorhexidine 0.12% for treatment and prevention of gingivitis (not for periodontitis, because it is ineffective on organic material, cannot reach bottom of periodontal pockets); zinc and ascorbic acid, mainly for their action on epithelium and connective tissue post treatment.
- Products containing enzymes that enhance the antimicrobial action of saliva and leukocytes
- Products that stimulate oral exercise, production of saliva, and removal of plaque and calculus

POSTPROCEDURE

Professional dental care once a year to allow complete oral examination, removal of plaque and calculus in areas where they still build up despite home dental care, and tooth polishing

ALTERNATIVES AND THEIR RELATIVE MERITS

In absence or ineffectiveness of home dental care, the frequency of professional dental care is adjusted to prevent or control periodontal disease.

AUTHOR: YVAN DUMAIS

Dental Extraction

SYNONYM

Exodontics

OVERVIEW AND GOALS

- Removal of a tooth in a way that ensures complete removal of the root(s) and rapid healing of the dental alveolus and oral soft tissue
- Simple extraction is indicated for simple rooted teeth, except canine teeth or any tooth that has already lost most of its attachment. Canines and multirooted teeth usually require surgical extraction.

INDICATIONS

- Nonvital (dead) teeth; teeth with exposure or contamination of the endodontic system
- Moderate to severe periodontal disease
- Nonrestorable dental lesions: dental resorptions, dental fractures
- Persistent primary teeth, retained roots or impacted teeth, some teeth involved in jaw fracture
- Dental malocclusions
- Oral surgery, removal of oral tumors, oral cysts

CONTRAINDICATIONS

- When general anesthesia is contraindicated because of severe uncontrolled metabolic disease
- Animals with a bleeding disorder
- Animals undergoing chemotherapy or radiotherapy

EQUIPMENT, ANESTHESIA

- General anesthesia, preemptive pain control, and regional or local anesthesia are utilized as needed.
- Simple extraction:
  - Dental radiograph (see p. 1246)
  - A #11 or #15 scalpel blade
  - Dental elevator(s)
  - Dental forceps
- Surgical extraction: as above, plus:
  - Periosteal elevator
  - Dental unit with high-speed handpiece and FG dental burs (No. 699-701, regular, long shank, and surgical lengths)
  - Bone rongeurs or bone rasp
  - Bone curette
  - Sterile saline with syringe and atraumatic needle
  - Soft-tissue scissors (LaGrange)
  - Tissue forceps
  - Needle holder, 4-0 resorbable suture material with swaged-on needle

ANTICIPATED TIME

About 5 minutes for most simple extractions and 20 minutes for most surgical extractions

PREPARATION: IMPORTANT CHECKPOINTS

Dental radiographs: check for the number of roots, their shape, and their structural integrity (root resorption); the condition of the surrounding bone; and the presence or absence of a periodontal ligament with possible root ankylosis.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Oronasal fistula: if occurs, should be closed with a mucoperiosteal flap, either at the time the extraction is done or as a delayed surgery if the gingival tissue is so inflamed that its capacity to hold sutures is questionable.
- Root fracture:
    - Most easily prevented by examination of the preoperative radiographs and proper treatment planning. If the root is in advanced stage of resorption, is ankylosed, and has no evidence of periodontal or endodontic infection, it could be left in place for continued resorption.
    - Although the clinician should try to remove as much root material as possible in an animal with root fracture, the risk of damaging surrounding tissue should be weighed against the benefit of finding the last piece of root material.
    - When a root fragment is left in situ, the owner should be informed of that aspect of the surgery, and follow-up radiographs should be included in the treatment plan. The risk of causing an abscess is higher when the root fragment has been mobilized and its blood supply severed during its attempted extraction.
- Jaw fracture: usually the result of a blind attempt at extracting a tooth on the mandible without preoperative dental radiographs and appropriate treatment planning. Small-breed dogs with severe periodontal disease of the first lower molars and cats during extraction of the mandibular canines are the most likely to be at risk for jaw fracture during dental extraction.
- Root fragments in the nasal cavity or the mandibular canal should be retrieved.

PROCEDURE

Simple extraction:

- Incision of the gingival attachment around the tooth with a scalpel blade
- Mobilization of the tooth with dental elevators using first-class lever, wheel-and-axle, or wedge types of forces:
    - The tip of the elevator is used circumferentially as a wedge between the root and the bone to stretch the periodontal ligament, or as a wheel and axle with the side of the blade engaged under the enamel bulge mesial or distal to the tooth, to elevate the tooth out of the alveolus.
    - Use light forces over a longer period (at least 10 seconds each time) to break the attachment without fracturing the root.
    - Extend the index finger (of the hand holding the elevator) along the shaft of the elevator to protect deeper structures in case of slippage.
- Extraction with dental forceps once the tooth is mobile. Light rotation force may help.
- Check that extraction is complete; perform a postoperative radiograph if needed.
- Brief digital pressure to help hemostasis, reduce expansion of the alveolar wall caused by the extraction, and approximate the gingival margins
- Suture if needed

Surgical extraction:

- Incision of the gingival attachment around the tooth with a scalpel blade
- Elevation of a mucoperiosteal flap with a periosteal elevator
- With a dental bur, buccal cortical bone and alveolar bone is removed to expose the root surface up to half its length.
- On a multirooted tooth, the crown is sectioned between the roots.
- Each individual root with its attached piece of crown is elevated.
- Check that the extraction is complete.
- Smooth the edge of the alveolar bone with a bone rongeur or rasp; curette and flush debris out of the alveolus.
- Trim the border of the soft tissue if needed (LaGrange scissors).
- Suture with a simple suture pattern.
    - After a surgical extraction, the gingiva is sutured back in place, even in the case of an abscess.
    - It is important to cover the bone exposed during elevation of the soft tissue.

POSTPROCEDURE

- Surgical extractions: pain medication for 4 days, soft food for 10 days
- Antibiotics are used if the animal shows systemic clinical signs (fever, loss of appetite, etc.) or if the condition has progressed to osteomyelitis.
- Recheck in 10-14 days.

ALTERNATIVES AND THEIR RELATIVE MERITS

Endodontics, periodontics, and orthodontics are other alternative treatments. They have the advantage of preserving the teeth and are often a better option when the owner is interested in doing the necessary aftercare and home dental care.

AUTHOR: YVAN DUMAIS

Defibrillation, Electrical

OVERVIEW AND GOALS

Electrical defibrillation is the treatment of choice for cardiac arrest characterized by ventricular fibrillation. It consists of application of an electric shock to the heart, causing massive depolarization; when defibrillation is successful, this massive depolarization is immediately followed by spontaneous resumption of sinus rhythm.

INDICATIONS

Ventricular fibrillation

CONTRAINDICATIONS

- Conscious animal
- Normal cardiac rhythm but electrocardiographic (ECG) artifact mimics ventricular fibrillation
- Poor or inappropriate contact between defibrillation paddles and animal
- Inability to electrically isolate animal from surrounding animals or humans (e.g., in contact with same pool of water/urine/other conductive medium)
- Ventricular fibrillation > 10 minutes' duration

EQUIPMENT, ANESTHESIA

- Clippers for hair
- Defibrillator; ideally, combined defibrillator-electrocardiograph to avoid risk of electrical damage to stand-alone ECG machine
- Defibrillation coupling gel

ANTICIPATED TIME

About 1 to 10 minutes

PREPARATION: IMPORTANT CHECKPOINTS

- Is it ventricular fibrillation?
  - ECG shows coarse or fine patternless electrical activity with no synchronized activity (no QRS complexes) when ventricular fibrillation is present.
  - If the animal is conscious, the rhythm is not ventricular fibrillation.
  - If a pulse is palpable, the rhythm is not ventricular fibrillation.
- Is the animal prepared correctly?
  - Dorsal or lateral recumbency on a dry, insulated surface (e.g., foam mat or linoleum floor)
  - Hair clipped from both hemithoraces over heart (fourth through sixth intercostal spaces [ICS], right and left)

Note: The limbs of the animal will flail when the shock is administered, and any objects (e.g., monitoring instruments, drug bottles, etc.) in their trajectory must be removed prior to shock delivery.

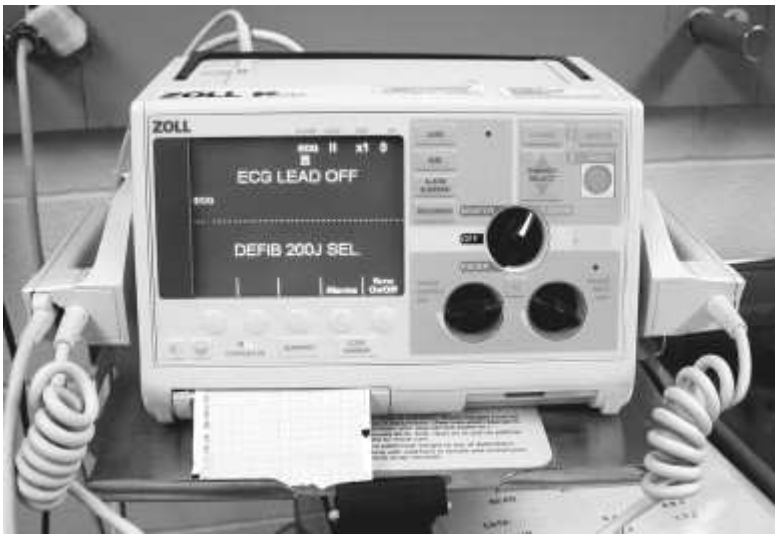
POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Electric shock can be transmitted to bystanders. Note: This complication can cause cardiac arrest in human or animal onlookers. This result is best avoided by ensuring that no one is in contact with the animal or anything the animal is touching before delivering a shock. It is also important to ensure that no indirect contact from urine, saline, or any other fluids that may be trickling from the animal is occurring between the animal and the shoes of surrounding individuals. Shouting "clear" is not enough, since most people do not know what to do in response.
- Defibrillation is too late. The success of defibrillation approaches 100% when it is performed within the first minute of ventricular fibrillation, then decreases by 10%-15% per minute. Defibrillation is the most important treatment when there is ventricular fibrillation, and some have suggested revising the "ABCs" of resuscitation to the "DABCs," with *D* for defibrillation.
- Poor application of paddles on animal
  - Paddles must be set widely apart (i.e., one on each side of the thorax); if too close, an electric arc between them can cause severe skin burns and operator injury.

- Defibrillator gel must be applied between the defibrillator paddles and the animal's skin. Note: Any facility that owns a defibrillator must also own a tube of defibrillator gel, because alternatives are inadequate: ultrasound gel is contraindicated (nonionic/nonconductive), alcohol is flammable, and bare skin without a coupling agent can be burned by electric arcs.

PROCEDURE

- The animal is placed in lateral or dorsal recumbency.
- Rapid clip of hair over the left and right precordia (area of chest overlying the heart): 20 seconds.
- The ECG diagnosis of ventricular fibrillation is confirmed:
  - Animals with ventricular fibrillation are always unconscious (nonperfusing rhythm) and pulseless.
  - Alcohol or gel must be present at all points of contact between the ECG wires/clips and the animal (to rule out poor connection artifact/"pseudofibrillation").
  - Click from leads I to II and then to III on the ECG monitor to check for organized electrical cardiac activity in any lead. If present, defibrillation is contraindicated.
- The defibrillator is charged: 5 J/kg.
- Defibrillator gel is smeared on the surface of both paddles.
- The paddles are applied to the thorax: paddle marked "Left" or "Apex" is on left hemithorax, and paddle marked "Right" or "Sternum" is on the right.
- All onlookers and assistants must stand back and be neither in direct nor indirect contact with the animal. The only contact point between the animal and the person administering the shock is the paddles.
- The shock is delivered.
- The ensuing ECG rhythm is assessed immediately.



DEFIBRILLATION, ELECTRICAL Typical defibrillator. Paddles are clipped to side of unit, and screen displays both electrocardiographic (ECG) information and defibrillation charge (at 200 J in image). Controls for energy selection, charging, and shock administration on front panel are also present as finger controls directly on the paddles (not shown).

DEFIBRILLATION, ELECTRICAL Tube of defibrillator gel.

POSTPROCEDURE

If the rhythm still appears to be ventricular fibrillation, it should be quickly confirmed (check other ECG leads on the monitor, and

ensure ECG connection between animal and machine is good); if confirmed, defibrillation is immediately warranted once again at 8 J/kg. Up to 12 J/kg may be administered. When the rhythm is any other than defibrillation, standard cardiopulmonary resuscitation procedures are followed (see p. 1223).

ALTERNATIVES AND THEIR RELATIVE MERITS

- Precordial thump (physical blow to the chest): theoretically delivers physical “equivalent” of electrical shock; unproven value, many potential drawbacks, and never preferred over electrical defibrillation.
- Pharmacologic defibrillation (bretylium, potassium chloride/calcium chloride, etc.): unproven and not known to be widely successful in the clinical setting.

AUTHOR: ETIENNE CÔTÉ

Excretory Urogram

SYNONYMS

IVP, intravenous (IV) pyelogram, IV urogram

OVERVIEW AND GOALS

When the kidneys are difficult to assess by plain-film radiography or when qualitative renal functional information is needed, an excretory urogram could be performed. On survey abdominal radiographs, the renal silhouette may not be visualized in animals that have decreased abdominal detail (young, thin, peritoneal fluid).

INDICATIONS

- Identify kidneys (if poor abdominal detail)
- Mass lesions of kidneys (or mass in region of kidney)
- Qualitative assessment of renal function
- Patency, continuity of urinary tract
- Prior to nephrectomy
- Abnormal renal size, shape
- Persistent hematuria
- Suspected renal or ureteral calculi
- Suspected hydronephrosis
- Suspected ureteral ectopia, ureterocele
- Suspected ureteral rupture
- To evaluate the urinary bladder when it cannot be catheterized
- Postoperative assessment of urinary tract (patency, strictures, leakage)

CONTRAINDICATIONS

- Dehydration
- Previous reaction to iodinated contrast medium (a nonionic medium should be used)
- Caution should be used in animals with the following conditions:
    - Diabetes mellitus
    - Multiple myeloma
    - Congestive heart failure
    - Hypertension
    - Concurrent drug administration (cardiac glycosides)
    - Severe debilitation

EQUIPMENT, ANESTHESIA

- Many recommend the use of general anesthesia or heavy sedation; however, an excretory urogram can be performed in an unanesthetized animal.
- IV catheter
- Hair clippers
- Surgical scrub solution, rubbing alcohol, and gauze/sponges for prepping skin where catheter is placed
- Tape/releasing elastic (Vetrap-type) bandage
- Iodinated contrast medium (sodium iothalamate, sodium diatrizoate)
- Nonionic contrast medium (iohexol, iopamidol) if clinically warranted
- Syringe
- Heparin/saline for flush
- Enema set
- Antianaphylactic agents (e.g., diphenhydramine, 2-4 mg/kg for IM injection)
- Oxygen and a drug cart to address any possible complication during the procedure.

ANTICIPATED TIME

Approximately 1 hour

PREPARATION: IMPORTANT CHECKPOINTS

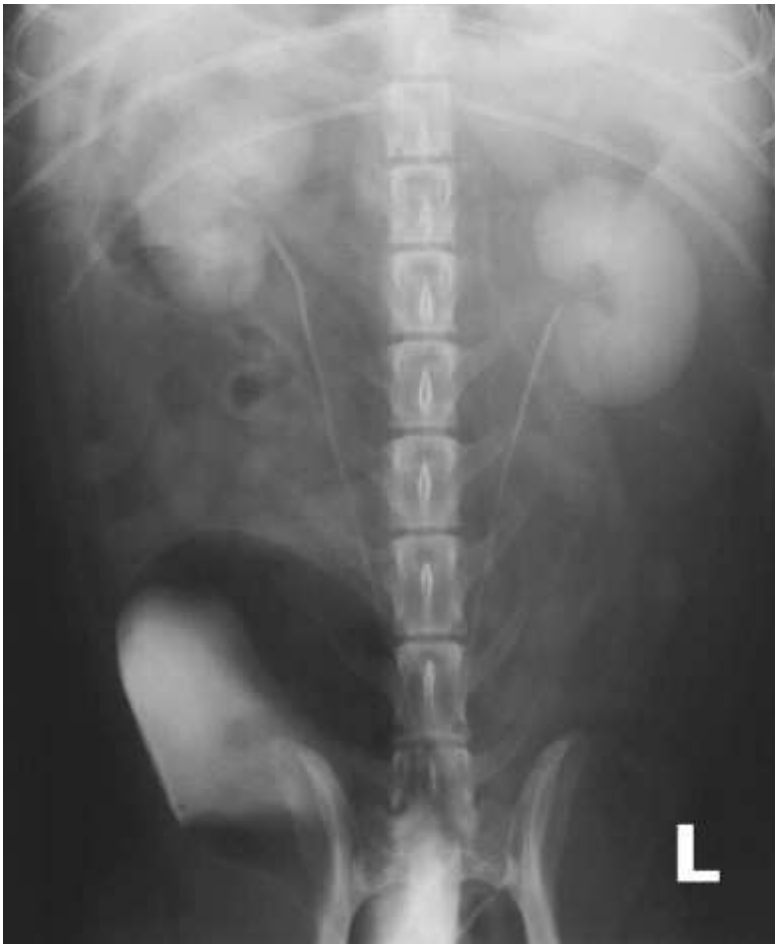
- The owner should be advised that hair will be removed from the site of IV catheter placement.
- Animal should have fasted 24 hours.
- Water given ad libitum
- Enema given at least 2 hours prior to study to remove a maximum of the fecal material from the colon to allow visualization of kidneys and ureters
- Assess hydration: proceed only if normal.
- Clip the hair where the IV catheter is to be placed.
- The site for the catheter placement should be prepped with surgical scrub solution, rubbing alcohol, and gauze sponges.
- Place an IV catheter in a cephalic or jugular vein; it is imperative that the catheter be properly placed.
- Secure the catheter in place with tape or releasing elastic (Vetrap-type) bandage.
- Add 900 mg iodine per kg body weight contrast material into syringe.
- Add an appropriate amount of heparin/saline flush into syringe.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

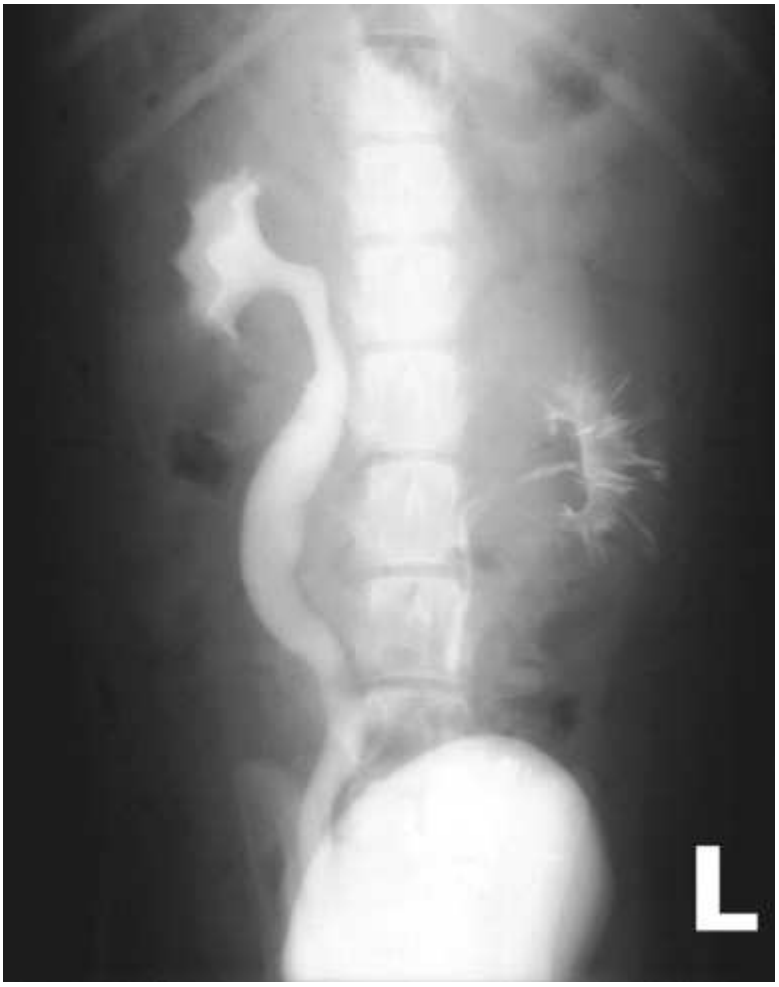
- Vomiting: this often occurs immediately after injection of the contrast medium. If the animal is muzzled, the muzzle should be removed immediately to avoid aspiration.
- Systemic hypotension, bradycardia
- Anaphylaxis (airway edema, vascular collapse, bronchospasm)
- Perivascular injection may result in sloughing of surrounding tissue.
- Contrast media–induced renal failure
- The administration of iodinated contrast media may affect urine specific gravity, urine sediment, and urine culture results for 24 hours following administration.
- Blood values (blood urea nitrogen [BUN], creatinine, prothrombin time [PT], partial thromboplastin time [PTT], activated partial thromboplastin time [APTT], thromboplastin time [TT], and hematocrit) might also be affected for up to 24 hours after contrast administration.

PROCEDURE

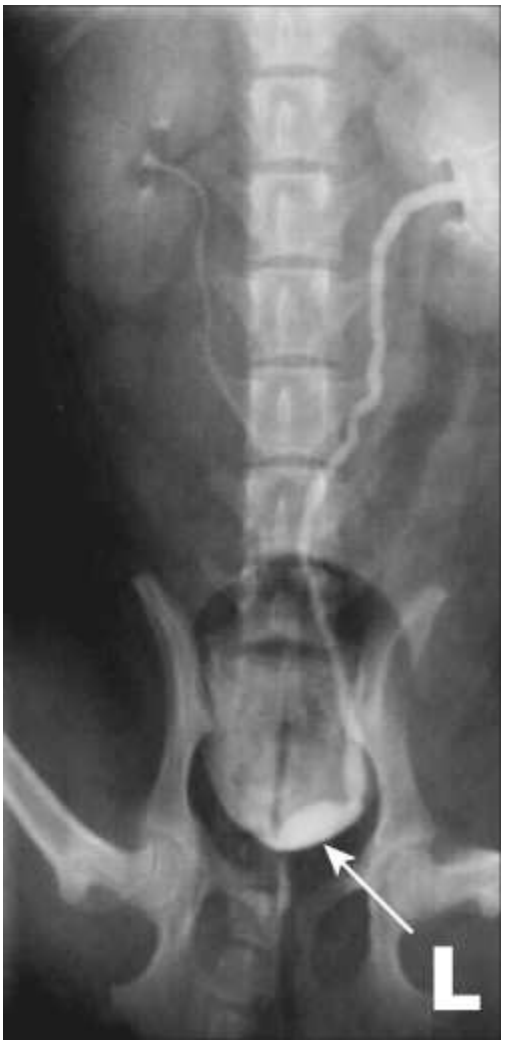
- Preliminary abdominal radiographs are made to determine adequate animal preparation and to set radiographic technique.



EXCRETORY UROGRAM Excretory urogram, ventrodorsal view. Normal study. Both kidneys and both ureters are clearly seen; contrast material is also seen in urinary bladder (right of midline). *L*, Left.



EXCRETORY UROGRAM Excretory urogram, ventrodorsal view. Ectopic ureter (left side), normal ureter (right side). Ectopic ureter is diffusely enlarged (hydroureter), especially distally where it inserts in an ectopic location *(arrow)*. *L*, Left.



EXCRETORY UROGRAM Excretory urogram, ventrodorsal view. Pyelonephritis (right side). Right-sided hydronephrosis and severe hydroureter are apparent. *L*, Left.

- The kilovoltage peak (kVp) should be set between 65 and 75 to maximize contrast due to the photoelectric effect (K-edge of iodine).
- Flush the catheter to again ensure patency.
- Inject contrast material rapidly as a bolus.
- Flush the catheter of residual contrast material.
- A ventrodorsal view is obtained at 20 seconds.
- Ventrodorsal and right lateral views are obtained at 5 minutes, 20 minutes, and 40 minutes.
- Oblique views are obtained at 5 minutes to visualize ureteral termination at the urinary bladder.

POSTPROCEDURE

- If anesthesia is used: routine anesthetic recovery
- Maintain adequate hydration.
- The IV catheter should remain in place for at least 15-20 minutes after the study is completed. The port for venous access might be necessary should a contrast media adverse reaction occur.
- Remove the catheter > 20 minutes after the procedure.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Plain abdominal radiographs: inexpensive means to survey the abdomen. Radiopaque renal or ureteral calculi can be visualized. Size and shape of the kidneys can be assessed if abdominal detail is adequate and fecal material is not obscuring their visualization.
- Abdominal ultrasound: excellent potential for visualization of kidneys, especially in animals that show poor radiographic abdominal detail. Renal size, shape, position, and echogenicity relative to the liver and spleen can be assessed. The size of the renal pelvis can also be evaluated. The internal architecture of the kidneys can be assessed. Ultrasound can determine if

masses are solid or cystic in nature. Resistive index can be calculated.

- CT scan: provides excellent detail of the size, shape, and margination of the kidneys. IV contrast media can also be used to enhance findings in the kidneys and or ureters. This imaging modality can also be used for assessing renal vascular anatomy when screening feline renal transplant donors. CT scans, however, are more costly to perform than other studies already listed and require general anesthesia.
- Nuclear scintigraphy:
    - Diethylenetriaminepentaacetate (DTPA): to determine global and individual kidney glomerular filtration rates; to evaluate the animal's response to treatment; to evaluate function of contralateral kidney prior to surgery and possible removal of diseased kidney; to identify and determine the severity of subclinical renal disease in an animal receiving nephrotoxic agents; and to examine renal perfusion by obtaining rapid serial images during first pass circulation
    - Mercaptoacetyltriglycine (MAG3): to determine global and individual kidney effective renal plasma flow

AUTHOR: LEEANN PACK

Ethanol Ablation of Thyroid and Parathyroid Tumors

SYNONYMS

Percutaneous ethanol injection, PEI, chemical ablation

OVERVIEW AND GOALS

Ethanol ablation, under ultrasound guidance, has been used most commonly in veterinary medicine for the minimally invasive treatment of parathyroid tumors. Additional reported uses of this procedure include benign thyroid tumors in cats, as well as other tumors, and renal, liver, and pancreatic cysts. The goal of this procedure is to eliminate the detrimental secretory function of a benign endocrine tumor in a minimally invasive fashion.

INDICATIONS

For parathyroid ablation in cases of primary hyperparathyroidism (PHPT). For thyroid ablation, consider in cases of feline unilateral hyperthyroidism or feline thyroid cysts.

CONTRAINDICATIONS

- There are few contraindications to percutaneous ethanol injection (PEI) therapy in hyperparathyroid dogs. Successful therapy does require a large enough nodule (typically over 3-4 mm in diameter), a skilled ultrasonographer, and advanced ultrasound equipment. It should not be attempted if these criteria are not met.
- It should also not be attempted in multiple nodules at the same time, especially bilaterally, for fear of transient laryngeal swelling and dysfunction after the injection.
- PEI has not worked well in cats with bilateral thyroid disease and should also never be performed bilaterally in cats. It can be considered as an alternative to surgery, radioiodine therapy, or methimazole in cats with unilateral hyperthyroidism.

EQUIPMENT, ANESTHESIA

- Intravenous or inhalant general anesthesia
- High-quality ultrasound equipment with a high-frequency probe (at least 10 MHz) and an ultrasonographer experienced at evaluating cervical structures and aspirating small nodules in an accurate fashion
- 96% ethanol
- At least one 2.5- to 3-mL syringe
- Low-flow extension set
- 25- to 27-gauge 1½-inch needles

ANTICIPATED TIME

The procedure itself lasts seconds once the needle has been properly inserted into the parathyroid nodule. Depending on the experience and expertise of the ultrasonographer, the size of the nodule, and the ultrasound equipment, 30 minutes to an hour are a reasonable time frame for completion of the procedure.

PREPARATION: IMPORTANT CHECKPOINTS

- The diagnosis of primary hyperparathyroidism should be confirmed utilizing ionized calcium and PTH testing and by ruling out other causes of hypocalcemia.
- The dog's neck should then be examined ultrasonographically, and the parathyroid nodule should be definitively located and measured.
- The dog should then be anesthetized and placed in dorsal recumbency for the procedure, with the ventral aspect of the neck clipped.
- 1 mL of 96% ethanol should be prepared with no air bubbles and attached to a 25- to 27-gauge 1½-inch syringe, and a low-flow extension set should be placed between the needle and syringe and primed with ethanol prior to injection.
- In the case of a hyperthyroid cat, unilateral hyperthyroidism should be confirmed based on hormonal testing and nuclear scintigraphy. Once confirmed, the preparation is identical to dogs with PHPT.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO BE AVOIDED

Possible errors include:

- Not offering owners surgery as an alternative to injection. This is especially true if there is concurrent urolithiasis or another reason to have surgery.

- Attempting to inject a nodule that is too small, without the right equipment, experience, or expertise and without proper anesthesia or sedation
- Not properly identifying the parathyroid nodule and differentiating it from the carotid artery, which can look very similar in a cross-section ultrasonographic view of the cervical region. The nodule must be round or elliptical in the longitudinal plane as well and ideally should also be documented to have no laminar flow using color-flow Doppler.
- Assuming the tip of the needle is in the nodule and the injection will be successful without a proper test injection. Once the area has been infiltrated with a large amount of ethanol around the nodule, it becomes very hard to visualize the nodule or the needle, and the attempt often must be aborted.

PROCEDURE

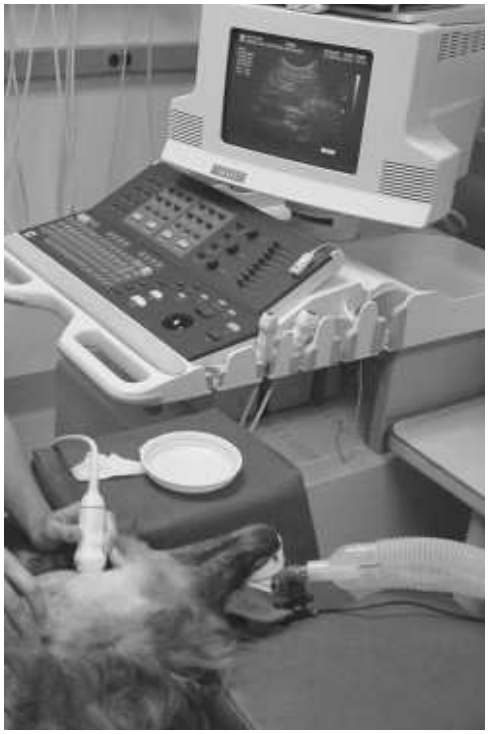
- The parathyroid or thyroid nodule is definitively identified and differentiated from the carotid artery.
- A 25- or 27-gauge needle attached to an extension set and syringe and filled with 96% ethanol is carefully advanced into the nodule under ultrasound guidance.
- Once the tip of the needle is thought to be in the center of the nodule, a small test dose of alcohol (less than 0.1 mL) is given. This should produce a small, white, hyperechoic "cloud" within the nodule that should not be seen dispersing rapidly along tissue planes. If there is a doubt that the tip is not in the nodule, the needle should be removed from the nodule and repositioned and the test dose repeated.
- If the tip of the needle appears to be within the nodule, the ethanol should be injected until all parts of the nodule become hyperechoic. This may require slight repositioning of the needle in a large nodule.
- Within approximately 10 minutes, the injected area will become hypoechoic, so the decision whether the nodule has been completely filled with ethanol or not must be done within that time frame after starting the injection.
- When the filling is complete, the needle is removed, and the animal can be recovered.

POSTPROCEDURE

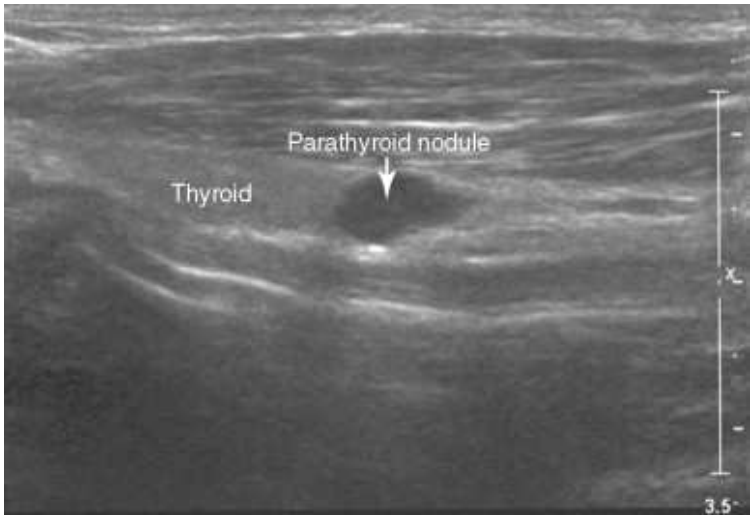
No life-threatening or persistent complications have ever been observed following this procedure in dogs. Transient unilateral laryngeal swelling/paresis and Horner's syndrome can occur and tend to resolve within 1-4 days. Bilateral injections should not be attempted due to the risk of bilateral postprocedure laryngeal swelling. Dogs with PHPT should be monitored closely for 5-10 days after ablation for signs of hypocalcemia and should be supplemented as necessary with calcium and vitamin D. Clinical decision-making regarding calcium and vitamin D supplementation, as well as postinjection calcium monitoring, is the same as when surgical parathyroidecto mies are performed for the definitive treatment of PHPT.

ALTERNATIVES AND THEIR RELATIVE MERITS

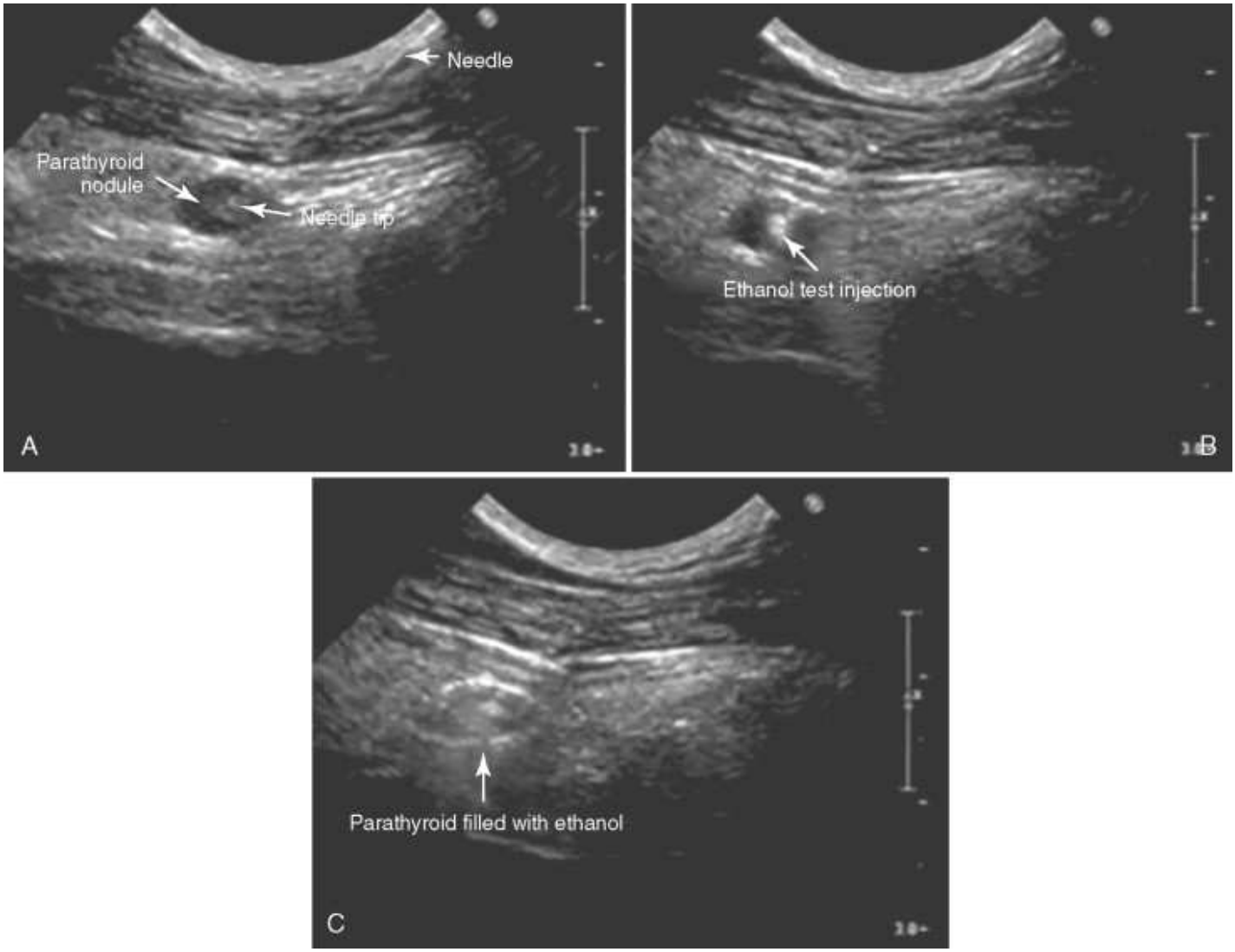
PEI is only one way to definitively treat PHPT. Alternatives are surgical removal of the parathyroid nodule or nodules and percutaneous heat ablation, which is performed in a similar fashion to PEI, but heat rather than ethanol is used to necrose the tissue via the inserted needle. Surgery is still the gold standard and should always be offered as such to the owner. Heat ablation may be superior to ethanol ablation in terms of fewer transient effects of the leakage of ethanol into the surrounding tissue but does require additional specialized equipment. The advantages of both heat ablation and PEI over surgery include shorter anesthetic time, a more rapid recovery, and less surgical healing or scar formation. Their disadvantage, in addition to the occasional transient local side effects of PEI, is the potential to fail, meaning the needle will not be properly inserted or the nodule will not be completely destroyed. Another disadvantage to the two less invasive options is that no tissue is obtained; hence the tumor cannot be classified histologically. Since almost all parathyroid tumors behave in a benign fashion regardless of their histopathologic features, this is not as severe a disadvantage as it would be in the case of other neoplasms.



ETHANOL ABLATION OF THYROID AND PARATHYROID TUMORS Anesthetized dog properly positioned in dorsal recumbency and prepared for percutaneous ethanol injection.



ETHANOL ABLATION OF THYROID AND PARATHYROID TUMORS Ultrasound image of a parathyroid nodule, with the thyroid gland, in a dog with primary hyperparathyroidism.



ETHANOL ABLATION OF THYROID AND PARATHYROID TUMORS Ultrasonographic images of percutaneous ethanol injection (PEI) therapy in a dog with primary hyperparathyroidism. **A**, Needle entering the parathyroid nodule, with tip clearly visible within the nodule. **B**, Test dose of ethanol being injected, and hyperechoic material remaining within the nodule. **C**, Parathyroid nodule has been completely infiltrated with ethanol immediately following successful PEI therapy.

SUGGESTED READING

Goldstein RE, Long C, Swift NC, et al: Percutaneous ethanol injection for treatment of unilateral hyperplastic thyroid nodules in cats. J Am Vet Med Assoc 218(8):1298–1302, 2001.

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Schaefer C, Goldstein RE: Canine primary hyperparathyroidism. Compend Contin Educ Pract Vet 31(8):382–390, 2009.

AUTHOR: RICHARD E. GOLDSTEIN

Epidural Analgesia/Anesthesia

SYNONYM

Extradural blockade

OVERVIEW AND GOALS

Administration of drugs into the epidural space to provide decreased sensory and sympathetic pain transmission modulation (analgesia) and/or complete motor blockade (anesthesia). Drugs can be administered in one dose (single shot) repetitively or by continuous infusion:

- Epidural analgesia: injection of an opioid a phencyclidine an alpha-agonist or a nonsteroidal antiinflammatory drug (NSAID)
- Epidural anesthesia: injection of a local anesthetic

INDICATIONS

Caesarean section thoracostomy pelvic or hind limb orthopedic manipulations amputations (forelimb and hind limb) abdominal procedures tail or perineal procedures diaphragmatic repair pancreatitis peritonitis intervertebral disk disease (IVDD) thoracic trauma Advantages:

- Lengthy quick-onset analgesia
- Few systemic side effects for acute/chronic medical or surgical pain
- Reduced requirements for parenteral and inhalant drugs
- Alternative to general anesthesia for animals at high risk (American Society of Anesthesiologists III IV V E categories; see p. 1372)
- Adjunct to balanced anesthesia regimes

CONTRAINDICATIONS

Absolute contraindications:

- Coagulopathy/bleeding disorder
- Localized infection/inflammation over entry to epidural space
- Increased intracranial/intraspinal pressure (head trauma space-occupying mass)
- Risk of or present severe respiratory depression (phrenic nerve injury tentorial herniation)

Relative contraindications (requires alteration of dose frequency drugs or placement site):

- Urinary retention
- Meningitis encephalitis diskospondylitis
- Severe anatomic/neurologic disturbance or obesity at landmarks
- Inexperienced administration

Contraindications for use of local anesthetics in epidurals:

- Uncorrected hypovolemia
- Vasodilatory shock
- Severe clinical cardiac disease or liver impairment (third-spaced fluid disease ascites)
- Acute renal failure
- Sympathetic disturbance (e g autonomic disease dysautonomia)
- Use of potent systemic vasodilators

EQUIPMENT, ANESTHESIA

Most animals that receive an epidural are heavily sedated or under general anesthesia at the time of administration. Premedication with both anxiolytic and analgesic drugs (opioid, alpha-agonist) is recommended even if continued progression into general anesthesia is not anticipated, owing to the pain of positioning, approach, and administration of epidural agents. Equipment:

- Hair clippers
- Surgical scrub solution, isopropyl alcohol or saline, gauze/sponge

- Epidural or spinal needle (Quincke, Husted, or Tuohy needles); 22- to 20-gauge, 1½- to 3½-inch small hypodermic needles (22 gauge, ½-1½ inch) can also be used for tiny animals.
- Sterile gloves
- Sterile saline
- "Test syringe" for saline and air mix
- Syringe for administration of combination of local and/or opioid
- A few 20-gauge needles (used for withdrawing drugs from vials)
- Local anesthetics for epidural injection: 0.5% bupivacaine, 2% lidocaine, or 0.75% ropivacaine (all must be preservative- and epinephrine-free)
- Opioids for epidural injection: morphine, preferably preservative free (Duramorph, Astramorph, preservative-free morph), but parenteral morphine has been used for single-dose injection without complications anecdotally; buprenorphine, oxymorphone, hydromorphone, dexmedetomidine, and ketamine may also be utilized.
- A second operator (assistant) to allow strict attention to aseptic technique

For epidural catheterization, the following will also be required:

- Blunt-tipped, lateral-faced opening needle with curved bevel (Tuohy needle)
- Continuous or indwelling epidural catheter
- Injection port with screw or lock fitting to avoid inadvertent disconnection
- Sterile scissors to tailor-cut the catheter to proper length
- Microfilter
- Sterile covering for site and/or part/total catheter (Tegaderm)
- Suture material (3-0 nylon or other monofilament, nonabsorbable suture)
- Needle holders
- Suture scissors

ANTICIPATED TIME

- Experienced operator: 3-5 minutes
- Inexperienced operator, anatomic/animal positioning issues, dermatologic uncleanliness: 20 minutes

PREPARATION: IMPORTANT CHECKPOINTS

- Base doses on lean body weight.
- Review anatomy for placement of entrance needle: most epidurals are performed at the lumbosacral junction because the cord terminates cranial to this area in dogs and near this area in cats; however, epidurals can be administered at any intervertebral space if lumbosacral (LS) access is limited.
- Consider ratio of each component: opioid, local anesthetic, alpha agent, ketamine, and/or others.
- Positioning of animal: sternal with hind legs pulled fully cranially under body or else flexed and stable under pelvis ("frog-legged"). Aged, debilitated, or traumatized animals may be uncomfortable in either position, so lateral positioning is also used. Obese animals are best placed in sternal, not only because of ease in identifying LS space but also because oxygenation and ventilation may be optimal.
- Premedication:
    - Medetomidine, 0.005-0.01 mg/kg (5-10 mcg/kg) IM or IV
    - Can also instead use a combination of anxiolytic plus analgesic: anxiolytic (acepromazine, 0.02-0.05 mg/kg IM or IV; or midazolam, 0.2-0.5 mg/kg IM or IV), plus analgesic (hydromorphone, 0.1 mg/kg IM or morphine 0.5-2 mg/kg IM)

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO BE AVOIDED

- The following can be seen with technical difficulty in prepping or identifying (finding) the epidural space: infection, hemorrhage, spinal or nerve root trauma.
- The following can be seen with use of certain agents: respiratory depression, urinary retention, pruritus, nausea and vomiting (opioids), motor paralysis, systemic vasodilation (lidocaine or high doses of bupivacaine/ropivacaine).
- Subarachnoid injection frequently results in superb analgesia but can cause respiratory and cardiac arrest or seizures with cranial advancement of drugs.

PROCEDURE

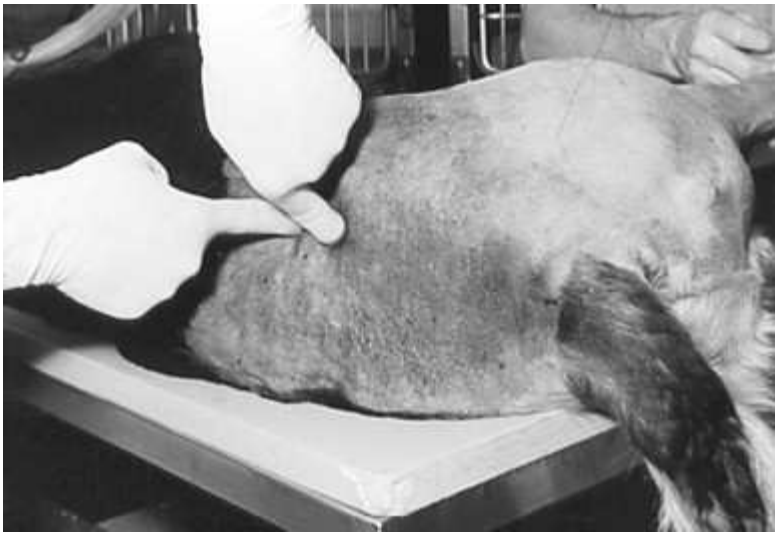
- The lumbosacral space is identified by palpating the most cranial dorsal aspects of each ilial wing, drawing an imaginary line between wings, and palpating the spinous process of L7 caudal to this line. The spinous process of L7 is smaller and shorter than that of L6 and, as such, is often more difficult to find. Staying directly on midline, the site of entry (LS space) is identified by placing a fingertip on the spinous process of L7 and gently rocking the finger caudally into the depression behind the process. The needle entry site is within this depression.
- The animal is positioned appropriately, the approximate LS area clipped, then aseptically prepped three times using

alternating chlorhexidine scrub and saline.

- Sterile gloves are unwrapped, and the paper sleeve is used as a sterile field; syringes, needles, and instruments are opened on the sleeve around the gloves.
- Epidural drugs are aseptically drawn into a syringe; dosages: some clinicians prefer combined local anesthetic bupivacaine, 0.1-0.3 mg/kg (motor sparing at 0.5%), with morphine, 0.02-0.1 mg/kg, for canine patients. This combination can be diluted to a total volume of 0.1-0.15 mL/kg with saline if advancement of the solution into the thoracic area is needed (thoracotomy, forelimb amputation, diaphragmatic repair, etc.). Total volume rarely exceeds 6 mL of saline, local, and opioid combined for canine patients for an injection made from the lumbosacral space. Injections made more cranially are reduced in volume by 25% per four to five vertebral bodies. Saline addition to the mixture is dictated by need for cranial spread of the agents.
- For cats, 0.02-0.1 mg/kg morphine is diluted with saline to a total volume of 0.1-0.2 mL/kg. Local anesthetic is rarely used because of the propensity to administer this into the subarachnoid space and the increased toxicity potential in this species.
- Both species: 0.5-2 mL saline with 0.5-2 mL of air are drawn into another syringe, which will act as an epidural space “tester” or identifier.

TECHNIQUE OF EPIDURAL INJECTION:

- Clinician approaches the patient from behind (facing in the same direction as the patient) if sternal recumbency, or from either behind or dorsal (the side of the table/hip against the patient's back, facing caudally) when the patient is in lateral recumbency.
- Brace the hand holding the needle on the patient's back. Use the other hand to identify the LS space as outlined above.
- The needle is then advanced transcutaneously at a 90○ angle to the skin surface over the LS site.
- The primary source of resistance is the dorsal spinous ligament, the ligamentum flavum. This is the hardest layer to penetrate and millimeter depth pushes are required to realize first, entry into the ligament, and second, the classic “loss of resistance” or “pop” as the epidural space is entered ventral to the ligament. Many clinicians will remove the stylet from the needle once ligamentum resistance is palpated, and add a small amount of saline to the hub of the needle in order to ascertain entry below the ligamentum.
- Once the ligamentum is penetrated, the hub of the needle is inspected for presence of blood or cerebrospinal fluid (CSF):
    - If blood is seen, the needle tip is partially redrawn and redirected.
    - If CSF is encountered, the needle is probably within the subarachnoid space, and should be withdrawn slightly.
    - If no blood or CSF is seen, assurance of epidural space is made by:
        - Loss-of-resistance technique: the syringe containing the saline and air is attached to the hub of the needle. The syringe plunger is then depressed. If there is no increase in resistance to pushing the plunger, the needle is correctly positioned in the epidural space. If the air bubble in the syringe is compressed or pushed against the saline as the plunger is depressed, the needle tip lies in the paraligamentous tissue, and the placement is incorrect.
        - Hanging drop technique: when the ligamentum flavum is encountered—the first sign of resistance—the stylet is withdrawn and the hub is filled with saline so the liquid forms a meniscus. As the space is entered, the normally negative pressure will cause aspiration down the needle shaft, and the fluid and meniscus will disappear.
- Once the correct positioning is confirmed, the injection proceeds over a 30-60 second time frame. Often, respiratory and cardiac rate increase during injection.



EPIDURAL ANALGESIA/ANESTHESIA Lumbosacral region of dog in left lateral recumbency. On the dorsal midline, the caudal-most dorsal spinous process, L7, is palpated (clinician's left hand). This process, shorter and smaller than that of L6 (clinician's right hand), is located caudal to an imaginary line that joins the most cranial dorsal aspects of both iliac crests. The point of epidural entry is the lumbosacral space, which is directly caudal to the dorsal spinous process of L7.

TECHNIQUE OF EPIDURAL CATHETERIZATION:

- Once the needle enters the space, the bevel of the needle must face cranially.
- The catheter is then threaded down the needle.
- Catheter advancement should proceed without resistance. The catheter should never be withdrawn into the needle because of the possibility of shear/breakage.
- Once the catheter is advanced to the appropriate space, the needle is then withdrawn over the catheter.
- A section of skin adjacent to the site of entry is then penetrated with the needle. The needle is tunneled parallel to the surface of skin for 1.5-2 cm and then exits the skin.
- The catheter's free end is then fed retrograde up the needle.
- The needle is then withdrawn, and the catheter is effectively “tunneled” away from the epidural site. This provides for decreased chances of bacteremia/infection in the epidural space.
- Excess catheter length is cut from the catheter, using sterile scissors.
- The filter and injection port are secured.
- The epidural medications are then administered through the catheter, with the amount reduced to accommodate for placement of catheter tip.
- The catheter cap and filter are secured with suture. A protective sterile covering is placed over the catheter and LS space.

POSTPROCEDURE

- Onset of analgesia varies from immediate for lidocaine epidurals, to 30-60 minutes for bupivacaine epidurals, to 2-4 hours for morphine and oxymorphone epidurals.
- Duration of analgesia varies from 1 hour for lidocaine epidurals, to 3-6 hours for bupivacaine epidurals, to 12-15 hours for morphine epidurals.
- Pain of injection is severe with local anesthetics and ketamine. Some clinicians strongly suggest utilizing each as diluted solutions only and administering bupivacaine only if the animal is under the influence of heavy sedation/analgesia or is anesthetized.
- Vomition, nausea, and drooling are common when catheters are placed in the thoracic spinal canal, when heavy volumes or concentrated morphine is used, or when pain/sudden hypotension is sensed during an injection (“awake bupivacaine epidurals”).
- The injection cap, filter, and dressing should be replaced every 72-96 hours using aseptic technique in catheters that are routinely used (q 12 h to q 8 h treatments).
- Swelling or pain over the tunneled site or, more importantly, over the catheter entry site warrants removal of the catheter. Replacement should then be questioned; alternative analgesic methods are suggested instead.

ALTERNATIVES AND THEIR RELATIVE MERITS

- General inhalant anesthesia: cardiorespiratory depression; expense
- Systemic narcotic administration: side effects of gastrointestinal (GI) stasis, respiratory depression, and mild anxiety; expense
- Recent electrostimulation and ultrasound techniques have allowed placement of blockades very close to nerves, nerve roots, and plexi; these may afford safe, economical, and less technically challenging means to providing analgesia without sympathetic blockade, although they do frequently include motor blockade.

SUGGESTED READING

Hansen BD: Epidural catheter analgesia in dogs and cats: technique and review of 182 cases (1991-1999). J Vet Emerg Crit Care 11(2), 2001.

Valverde A: Epidural analgesia and anesthesia in dogs and cats. Vet Clin North Am Small Anim Pract 38(6), 2008.

www.vasg.org (veterinary anesthesia analgesia support group)

AUTHOR: ANDREA L. LOONEY

Enema: Scintigraphic (Radionuclide)

SYNONYMS

Nuclear portogram, per rectum portal scintigraphy, transcolonic portal scintigraphy

OVERVIEW AND GOAL

Portosystemic shunts (PSS) are a relatively common congenital disorder in dogs and cats. Scintigraphy provides a rapid, noninvasive screening test for this disorder.

INDICATIONS

- Confirm the presence of a macroscopic PSS
- Evaluate the effectiveness of previous surgical shunt vessel attenuation
- Provide limited information regarding the number (single versus multiple) and location (intrahepatic versus extrahepatic) of the PSS vessel(s)

CONTRAINDICATIONS

Critical animal condition precluding relative isolation necessary to comply with regulatory requirements

EQUIPMENT, ANESTHESIA

Gamma camera and either an analog recorder (microdot) or preferably a nuclear medicine computer are necessary for calculation of shunt fraction.

ANTICIPATED TIME

- Procedure time of 5 minutes
- Isolation time (varies by local regulatory agency) of 6-60 hours

PREPARATION: IMPORTANT CHECKPOINTS

Animal:

- No animal preparation is required.
- Ideally, animals are fed the morning of the procedure.
- Discontinuation of oral lactulose for 36 hours prior to procedure may improve rectal uptake.
- Evacuation enemas are encouraged as a form of preparation by some clinicians but may not be routinely used by other clinicians.

Radionuclide setup:

- Prepare a dose of sodium ^{99m}T-pertechnetate (37-74 MBq/kg) in a small volume (<1 mL) in a shielded syringe case.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Delivery of isotope into transverse colon
- Poor positioning of animal on camera relative to location of radionuclide delivery in colon
- Inadequate radionuclide uptake

PROCEDURE

Technique, initial:

- Position the animal in right lateral recumbency on a Plexiglas table positioned over the gamma camera.
- Place the lubricated end of a pediatric feeding tube or IV extension set into the distal rectum (with the tip just inside the anal sphincter).
- Connect a three-way stopcock to the end of the delivery tubing.

- Connect a syringe containing 5-10 mL of air to the three-way stopcock.
- Connect the shielded syringe containing the sodium ^{99m}T-pertechnetate dose.

Technique, main:

- Introduce dose into feeding tube.
- Begin dynamic image acquisition.
- Flush dose into colon using room air flush.

Dynamic image acquisition parameters:

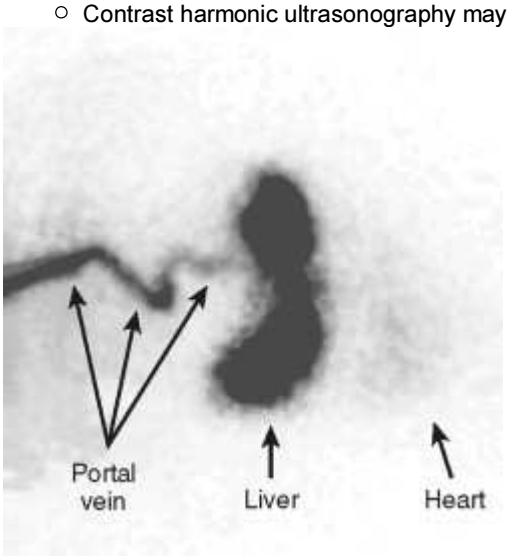
- Analog (microdot): 16 dynamic images of 5-second duration
- Digital (computer): 100 dynamic images of 2-second duration using 128 × 128 matrix

POSTPROCEDURE

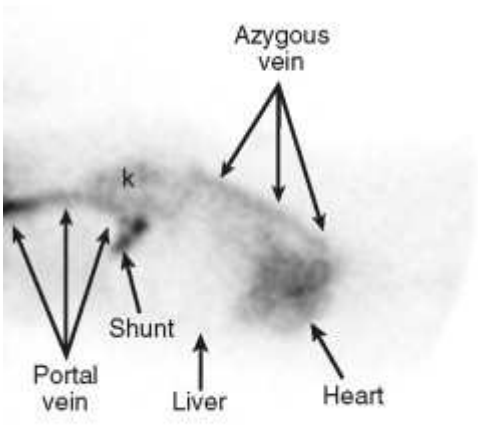
Isolation of animal in a radiation safety area is required until animal monitoring consistent with local release criteria. Collection of animal waste produced during isolation; the waste is treated as radioactive and typically held for decay before disposal.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Transsplenic portal scintigraphy:
  - Requires sedation or anesthesia
  - Requires concurrent use of ultrasound for guidance of splenic injection
  - Overcomes poor rectal absorption that occurs sporadically in some patients
  - May produce false negative results for portosystemic shunting occurring caudal to the portal vein
  - Increased count density is possible, allowing more accurate characterization of the morphology of the PSS vessel.
- Ultrasound:
  - More readily available
  - Very operator dependent
  - Good success for diagnosis of intrahepatic shunts, limited by overlying ribs and lungs
  - Limited success for diagnosis of extrahepatic shunts, owing to interference by adjacent gas-filled intestines
  - Contrast harmonic ultrasonography may reduce operator dependence.



ENEMA, SCINTIGRAPHIC (RADIONUCLIDE) Composite image of early phase of a scintigraphic enema in a normal dog. Lateral projection; cranial is to right. Note clear visualization of portal vein and liver, with incomplete visualization of heart.



ENEMA, SCINTIGRAPHIC (RADIONUCLIDE) Composite image of early phase of a scintigraphic enema in a dog with a surgically confirmed portoazygous shunt. Same orientation as in other figure. Note visualization of portal vein, shunt vessel at level of right kidney (k), and visualization of azygous vein. Minimal visualization of liver is due to reduced portal blood flow.

- Helical CT scan contrast portography:
  - Requires anesthesia
  - More expensive
  - Provides global perspective of entire abdomen with excellent anatomic detail
  - Generally used in cases of confirmed PSS when additional anatomic information is desired prior to surgical intervention
- MRI angiography:
  - Least available
  - Requires anesthesia
  - More expensive
  - Provides global perspective of entire abdomen, with excellent anatomic detail
  - Generally used in cases of confirmed PSS when additional anatomic information is desired prior to surgical intervention
- Intraoperative mesenteric portography:
  - Generally considered the gold standard for diagnosis of PSS
  - Requires anesthesia
  - Invasive
  - Expensive
- Liver biopsy:
  - Requires anesthesia
  - Invasive
  - Unable to confidently distinguish between macroscopic shunt and intrahepatic microvascular dysplasia (otherwise known as portal vein hypoplasia)

SUGGESTED READING

Daniel GB, Bright RM, Ollis P, et al: Per-rectal portal scintigraphy using ^{99m}technetium pertechnetate to diagnose portosystemic shunts in the dog and cat. J Vet Intern Med 5:23–27, 1991.

Koblik PD, Hornof H: Transcolonic sodium pertechnetate Tc99m scintigraphy for diagnosis of macrovascular portosystemic shunts in dogs, cats, and potbellied pigs: 176 cases (1988-1992). J Am Vet Med Assoc 207:6, 1995.

Koblik PD, Komtebedde J, Yen CK, et al: Use of transcolonic ^{99m}technetium pertechnetate as a screening test for portosystemic shunts in dogs. J Am Vet Med Assoc 196:6, 1990.

AUTHOR: MICHAEL R. BROOME

Enema (Evacuation, Retention)

OVERVIEW AND GOALS

Emptying of colonic content (evacuation) and/or colorectal administration of substrates (retention)

INDICATIONS

Evacuation enema:

- Treatment of colonic impaction/constipation
- Preparation of the animal for colonoscopy

Retention enema:

- Treatment of severe hepatic encephalopathy

CONTRAINDICATIONS

Painful anus, rectal mass/obstruction

EQUIPMENT, ANESTHESIA

- Enema solutions:
  - Warm tap water or isotonic saline (5-10 mL/kg)
  - Docusate (emollient enema promoting water penetration within the feces)
  - Mineral oil (lubricant enema; 5-10 mL for small dogs and cats, 10-20 mL for medium-sized dogs, 20-30 mL for larger dogs)
  - Lactulose (hyperosmotic laxative; 5-10 mL for cats)
- Preparation of the animal for flexible colonoscopy: to perform a successful colonic examination, thorough preparation of the animal is mandatory. Enema administration alone is often not enough to obtain a fully clean colon. Therefore, the following should also be performed in those animals to ensure a successful colonoscopy:
  - The animal should be fasted for 24-36 hours preceding colonoscopy.
  - The use of an oral gastrointestinal (GI) isosmotic lavage solution such as Golytely, Colopeg, or Colyte is recommended two times, a few hours apart, in the afternoon preceding colonoscopy:
    - Dogs: 30 mL/kg through an orogastric tube
    - Cats: 30 mL/kg through a nasoesophageal tube
  - One or two enemas is/are administered the afternoon before and the morning of the colonoscopy until the animal is evacuating watery fluid. Often “larger” quantities of water are necessary to obtain an adequately cleaned colon (dogs > 20 kg: 1 L; dogs > 40 kg: 2 L). Use a funnel and a large tube.
- Treatment of severe acute hepatic encephalopathy:
  - First perform a cleansing enema to evacuate all remaining colonic content.
  - Retention enema (total amount of 15 mL/kg): allows the delivery of fermentable substrates or colonic pH modification:
    - Lactulose (1:2 dilution with water)
    - Neomycin in water (10-20 mg/kg)
    - An alternative is to use diluted povidone iodine (1:10, rinse thoroughly after 15 minutes).
- See also Hepatic Encephalopathy, p. 501.

ANTICIPATED TIME

About 15-30 minutes

PREPARATION: IMPORTANT CHECKPOINTS

- Fluid therapy is an essential part of the management of colon impaction.
- Animals should be well hydrated.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Some enemas, such as docusate, can promote GI water loss and should be used with caution if the animal is dehydrated.
- If enemas are administered too quickly, they can lead to discomfort and vomiting.
- Enemas should be administered after they are warmed to body temperature.
- Do not administer mineral oil with docusate.
- Do not administer sodium phosphate enemas to small dogs or cats, because such enemas can induce dehydration, neurologic signs, and severe hyperphosphatemia, hypernatremia, and hypocalcemia.
- If the animal has much anal or rectal pain, enemas should be replaced by an extra administration of an oral GI lavage solution.
- If the animal is not cooperative, sedation or general anesthesia can be necessary.

ENEMA (EVACUATION, RETENTION) Enema tube that is well lubricated before going into the anus. Distal end of tube must be smooth and rounded and not have sharp edges. It is generously lubricated, passed into the anus, and advanced to a maximum point that corresponds to the distance from the anus to the last rib.

ENEMA (EVACUATION, RETENTION) Large volumes of fluid instilled using gravity, a funnel, and tube. This procedure is performed either for preparation for colonoscopy or as a treatment for constipation.

PROCEDURE

- Slowly insert a very well-lubricated catheter or feeding tube through the anus (10-14 Fr). In cats, a 60-mL syringe and a urinary catheter can be used.
- Enema solution should be warmed and administered slowly. It may be administered by syringe, or larger volumes may be instilled more easily using a funnel and gravitational flow.
- When there is no resistance, the tube is inserted for a total length equal to that from the anus to the last rib (pre-measure the tube).

POSTPROCEDURE

- Animals usually have diarrhea.
- If enema administration was unsuccessful, animals with colon impaction may require manual extraction of impacted feces (under anesthesia).
- After the administration of an oral GI lavage solution, the animal should be kept quiet in a cage to avoid the potential risk of developing gastric dilatation/volvulus.
- Dogs should be regularly walked on a leash to allow defecation.

ALTERNATIVES AND THEIR RELATIVE MERITS

Pediatric suppositories (dosage is 1 to 3, according to body weight [cat/small dog to large dog]) such as glycerol, docusate (Colace), or bisacodyl (Dulcolax) can be used as an alternative to enemas. These are safer than the use of phosphate enemas, especially for cats or smaller dogs.

AUTHOR: SYLVIE DAMINET

Electroretinogram

SYNONYM

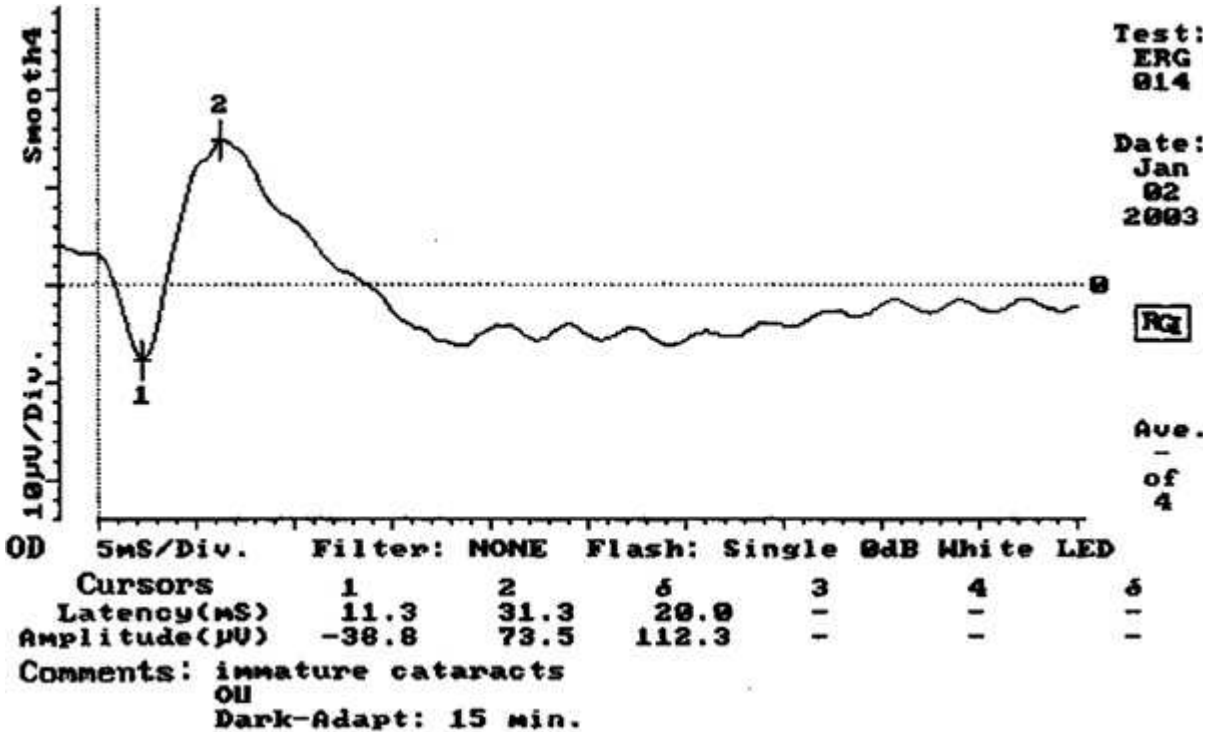
ERG

OVERVIEW AND GOALS

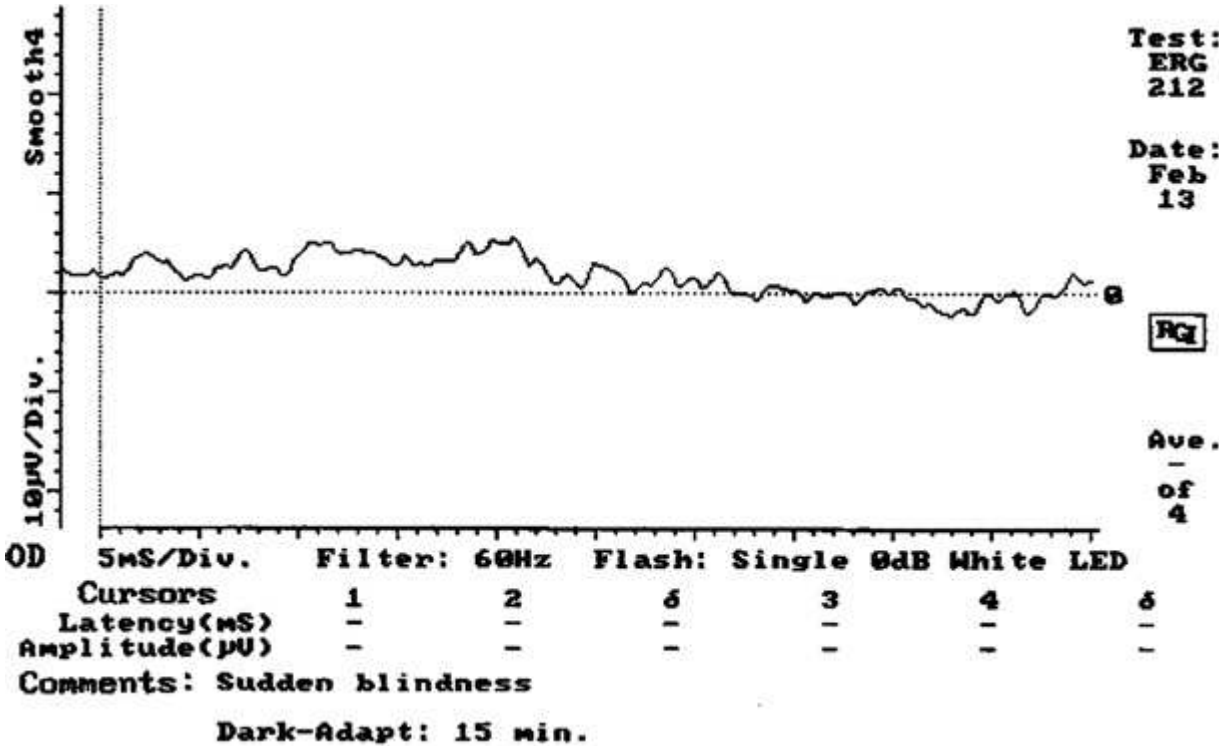
- Evaluation of retinal function (quantitative or qualitative) through measurement of the electrical response generated after the photoreceptors receive a light stimulus
- An electroretinogram (ERG) by itself does not determine whether an animal can see; the retina is only one part of the visual system.

INDICATIONS

- Differentiation of causes of sudden blindness (i.e., sudden acquired retinal degeneration syndrome [SARDS] and optic neuritis)
- Evaluation of retinal function to determine cataract surgery suitability
- Identifying inherited retinal disease (i.e., progressive retinal atrophy [progressive rod-cone degeneration] or progressive rod-cone dysplasias) at an early age well before clinical signs and gross retinal changes occur
- Evaluation of damage incurred by glaucoma or toxic effects of drugs
- Evaluation of the effects of optic nerve hypoplasia on retinal function



ELECTRORETINOGRAM Normal ERG. The number 1 marks the nadir of the a-wave, and the number 2 marks the peak of the b-wave.



ELECTRORETINOGRAM ERG from dog with SARDS. No normal waves are detectable.

CONTRAINDICATIONS

- Panuveitis
- Corneal ulcer
- Any contraindication for general anesthesia or sedation

EQUIPMENT, ANESTHESIA

Equipment:

- Gold-foil contact lens electrode or an atraumatic wire electrode (placed in conjunctival cul-de-sac). Contact lens electrodes are used most often.
- Reference and ground electrodes
- Standardized light source for light stimulus
- “Safe” light, red light, or small red penlight
- Timer for dark adaptation
- Conducting agent to facilitate electrical contact between the contact lens electrode and the eye; methylcellulose (Gonak) or GenTeal Tear Gel
- Table; if stainless steel, cover with nonconducting material (rubber padding).
- Optional: head rest for elevation and positioning of head; this may be made of foam, rolled-up blankets, or sandbags.

Anesthesia or sedation:

- General anesthesia or sedation; some animals will tolerate the procedure with topical anesthesia only (and contact lens electrode), but the risk of artifact is increased.
- General anesthesia prevents animal movement (artifact source) and allows more precise direction of the light stimulus into the eye via fixation of the eye.
- Sedation; one of these three protocols can be considered:
  - Acepromazine (0.03 mg/kg IV) and hydromorphone (0.05 mg/kg IV):
    - Observe precautions/contraindications, especially with acepromazine.
  - Diprivan (propofol) 4-6 mg/kg IV to effect (low doses will be sufficient in most cases).
  - Medetomidine (0.005-0.01 mg/kg [dogs, cats] IM) combined with butorphanol (0.2 mg/kg [dogs, cats] IM)
- Other anesthetic or sedation protocols may be employed; be consistent to aid in correct interpretation of the recordings.
- General anesthesia and sedation depress the ERG response.
- Butorphanol is the sedative most likely to depress ERG response.
- Topical anesthetic (i.e., proparacaine)

Personnel (two people):

- One to monitor anesthesia or sedation, position the animal's head, ensure that light stimulus is directed into the eye during the flash, cover the fellow eye, and check to see that all electrodes are in position during test
- One to run the computer program during the test

ANTICIPATED TIME

About 1-1½ hours, including time for pupillary dilation

PREPARATION: IMPORTANT CHECKPOINTS

- Knowledge of retinal physiology
- Familiarity with ERG equipment
- Control of inflammation; especially important in a precataract surgery evaluation. Lens-induced uveitis will decrease ERG amplitudes.
- Dilation of pupils
- Bleaching of retinal pigments in rods by exposure to bright light before dark adaptation
- Dark adaptation (4 minutes minimum, 20 minutes desirable)
- Lock room to avoid inadvertent exposure to light and necessity of starting procedure again.
- Use grounded outlet to decrease/eliminate 60-cycle interference.
- Take off wristwatch to decrease 60-cycle interference.
- Set up computer, supplies, equipment before dark adaptation.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

POSSIBLE COMPLICATIONS:

- Corneal ulcers, especially in diabetics with decreased corneal sensitivity and increased risk of corneal ulceration
- Hypoxemia or death due to failure to monitor animal during general anesthesia

COMMON ERRORS:

Preparation errors:

- Failure to dilate pupils fully Procedural errors:
- Failure to direct light stimulus directly into eye
- Failure to prevent “light spill” into fellow eye while recording “first” eye; this decreases amplitude of “second” eye by bleaching retinal pigments.
- Error in labeling which eye is which on recordings
- Lack of standardized protocol for specific model of equipment on premises
- Lack of standardized anesthesia/sedation, leading to difficulty in interpretation of results
- Excess noise due to failure to use signal averaging and filters
- Excess muscle fasciculations in eyelids due to inadequate sedation, leading to excess noise in the readings. The use of an eyelid speculum exacerbates muscle activity due to muscle stretching.
- Dull electrode needles
- Gap in gold-foil electrode ring on contact lens electrode, leading to inaccurate reading or artifact
- Expulsion of contact lens or reference electrodes during procedure, leading to artifact or inaccurate reading
- 60-cycle interference caused by lights, appliances in same room, using a non-insulated table
- “Stray” light stimulus from computer monitor during procedure, leading to lower amplitude readings

Animal-derived errors:

- Eyes are closed, leading to very low amplitude readings.
- Blinking during light stimulation, leading to low amplitude readings
- Third eyelid is prolapsed, expelling the contact lens or leading to very low-amplitude readings due to the failure of light to reach retina.

Interpretation errors:

- Misinterpretation of findings due to lack of knowledge of retinal physiology and basis of the test

PROCEDURE

- Dilate pupils with short-acting mydriatic (i.e. tropicamide) 30 minutes before sedation.
- Sedate or induce general anesthesia as necessary.
- Place reference electrode in skin over ipsilateral zygomatic arch, 5 cm distal to lateral canthus.
- Place ground electrode in skin over top of muzzle. If dog must be muzzled, place ground electrode in skin on forehead. If electrode needles do not go into skin easily, discard and use new electrodes to avoid discomfort to animal and increase accuracy of reading.
- Dark adapt patient for minimum of 4 minutes, optimum of 20 minutes.
- Place topical anesthetic in eye.
- Place conducting gel on concave surface of contact lens.
- Place contact lens in eye, ensuring that the lens is centered on the cornea and not on top of the nictitating membrane.
- Perform standardized protocol. Protocols are available in ERG units' software. To determine rod function, important in progressive rod-cone degeneration, a blue filter under scotopic conditions must be used.
- Use signal averaging. This produces an averaged response after a predetermined number of flashes (5-10) and enhances the signal-to-noise ratio.
- Use band-pass filters to screen out unwanted frequencies.
- A normal ERG consists of a low-amplitude negative a-wave 10-12 msec after the light stimulus, followed by a large positive b-wave. In some tracings, the c-wave (a third wave) is seen as a positive deflection.
- The a-wave is produced by the photoreceptors and the b-wave by movement of potassium in and out of Müller cells and indirectly by bipolar cells.

POSTPROCEDURE

- Remove electrodes from eye and skin.
- Soak contact lens electrode in distilled water; do not rub the inside surface of the lens to clean it, because this action will remove the gold-foil circle, rendering it useless.
- Flush eye with sterile eye wash and stain for corneal ulcer.
- Partially reverse butorphanol sedation with naloxone, or recover from general anesthesia.
- Measure amplitude of recordings, the amplitude from the nadir (lowest point) of the negative a-wave to the peak of the positive b-wave.
- Record findings on a separate disc or CD for a backup copy, and print hard copy for animal's record.

ALTERNATIVES AND THEIR RELATIVE MERITS

Genetic testing for inherited retinal disease:

- Many tests are available for specific dog breed–related inherited retinopathies but not for all breeds.
- Only requires blood test, so simpler than ERG

Maze test under photopic and scotopic conditions:

- May be gross screening test for retinal atrophy
- Unable to determine anatomic source of defect in sudden blindness cases

SUGGESTED READING

Komaromy AM, Brooks DE, Dawson WW, et al: Technical issues in electrodiagnostic recording. Vet Ophthalmol 5(2):85–91, 2002.

Mentzer AE, Eifler DM, Montiani-Ferreira F, et al: Influence of recording electrode type and reference electrode position on the canine electroretinogram. Doc Ophthalmol 111(2):95–106, 2005.

Sims MH: Electrodiagnostic evaluation of vision. In Gelatt KN, editor: Veterinary ophthalmology. Baltimore, 1999, Lippincott, Williams & Wilkins, pp 484–504.

AUTHOR: NANCY B. COTTRILL

Electromyography (EMG) and Motor Nerve Conduction Velocity (NCV)

SYNONYMS

Electrodiagnostics; EMG, NCV

OVERVIEW AND GOALS

- Integral component of diagnostic evaluation of animals suspected of having neuromuscular disorders (neuropathy, myopathy, neuromuscular junctional disease).
- May confirm and characterize the presence of nerve, neuromuscular junction, or muscle disease in these animals.
- If the EMG is abnormal, a neuromuscular disease is present but a normal EMG does not rule out the possibility of a neuromuscular disease.
- Useful for differentiating denervation from disuse atrophy.
- Is very sensitive but not very specific.
- Generally part of a diagnostic workup that may also involve nerve and muscle biopsy, cerebrospinal fluid (CSF) analysis, laboratory testing (serology, endocrine testing, measurement of metabolites), radiographs and advanced imaging (MRI or CT).

INDICATIONS

- Animals with clinical signs and neurologic examination suggestive of neuromuscular disease (diffuse or focal).
- Animals with peripheral nerve injuries.
- May help confirm the presence of endocrine disease (hyperadrenocorticism-pseudomyotonia).

CONTRAINDICATIONS

Electrodiagnostics require general anesthesia, so relative contraindications include megaesophagus or severe weakness (hypoventilation).

EQUIPMENT, ANESTHESIA

- General anesthesia and tracheal intubation are required. For sensory nerve conduction studies in which paralysis with atracurium is required, a ventilator is needed.
- Should ideally be performed in electrically shielded room to minimize background noise.
- Differential amplifier, computer with appropriate software for labeling and calculations, needle electrodes for stimulating and recording impulses (concentric needle electrode preferred for electromyography [EMG]), isopropyl alcohol, and measuring tape.
- Surgical pack: often, muscle and nerve biopsies (see p. 1305) are done following electrodiagnostics.
- In some cases, percutaneous endoscopic gastric (PEG) tube placement (see p. 1270) is beneficial while animal is anesthetized (providing nutritional support, administering medications, etc.).

ANTICIPATED TIME

- EMG: 10–20 minutes
- EMG + nerve conduction velocity (NCV): 40-60 minutes

PREPARATION: IMPORTANT CHECKPOINTS

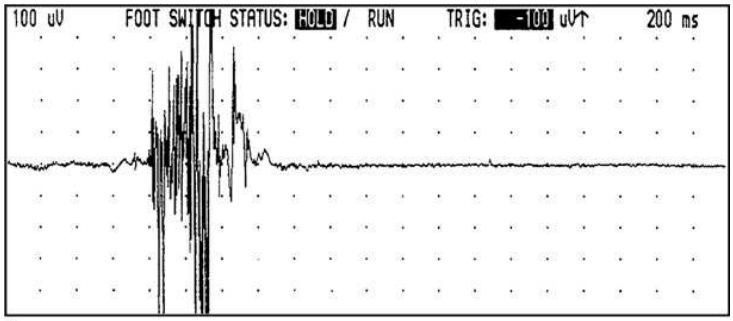
- Monitor body temperature and prevent hypothermia, which prolong nerve conduction times (1.8 m/s drop for every 1°C drop in limb temperature).
- Draw blood for chemistries prior to procedure, as EMG will cause a transient increase in CK.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Complications related to anesthesia
- Regurgitation and aspiration pneumonia in animals with megaesophagus/ esophageal dysfunction or dysphagia

PROCEDURE

- Animal is premedicated, anesthetized, intubated, and then maintained with inhalational anesthetic (isoflurane, sevoflurane).
- Placed in lateral recumbency
- EMG:
  - Needle electrodes are used for recording electrical activity in major muscle groups in appendicular muscles and in epaxial and masticatory muscles; rarely esophageal, laryngeal muscles, and tongue.
  - Evaluation is performed both by listening for characteristic sounds of electrical potentials and visually examining the waveforms produced by the potentials on the monitor.
  - Sensitivity is greatly increased by increasing the number of “passes” through the muscle (by continually redirecting the needle within the muscle) and by increasing the number of muscles sampled, as denervation potentials may be present in only a few areas.
  - A short burst of electrical activity occurs during needle placement is normal due to temporary disruption of muscle fibers (insertional activity). Other normal electrical potentials called miniature end plate potentials and endplate spikes may occur as a result of spontaneous depolarization of part or all of a myofiber.
  - Normal healthy muscle is otherwise electrically silent at rest.
  - Other spontaneous electrical discharges in resting muscle (i.e., anesthetized animal) are abnormal and indicate neuromuscular disease.
  - Abnormal EMG activity includes fibrillation potentials, positive sharp waves, complex repetitive discharges, or myotonic discharges. In general, the type of waveform is not specific for neuroanatomic location (nerve versus muscle) or pathophysiologic mechanism of disease.
  - Abnormal EMG activity confirms the presence of neuromuscular disease and helps localize which muscle groups are affected; however, abnormal EMG activity cannot differentiate between myopathic or neuropathic disease.
  - EMG changes due to denervation may not be detected for 5 to 10 days after initial injury.
  - Severity of clinical signs does not always correlate with severity of EMG changes.
- Motor NCV:
  - Using stimulating needle electrodes, a nerve is stimulated at various accessible points along its anatomic pathway.
  - Needle or surface electrodes within or over a muscle innervated by the nerve record a compound muscle action potential (CMAP), which results in a simple biphasic waveform.
  - Measurements made include the nerve conduction velocity (NCV), as well as the CMAP, amplitude, duration and area
  - Nerves commonly tested in domestic animals include the sciatic, peroneal, cranial tibial, radial, musculocutaneous, and median.
  - The recurrent laryngeal, facial nerve, and trigeminal nerves are rarely tested.
  - Nerve conduction velocity along various segments of axon may be determined by measuring the distance between points of stimulation (ideally at least 100 mm to decrease the effect of human measurement error) and difference in latency of waveforms (velocity [meters per second] = Ddistance/D time).
  - The amplitude of the waveform is proportional to the number of available axons. Axonal disease results in a decreased number of axons and decreased CMAP amplitude and may also cause secondary EMG changes due to denervation.
  - Nerve conduction velocity measures the speed at which action potentials travel down the axon.
  - Decreases in NCV may be due to demyelination or due to loss of the large, fastest conducting axons.
  - Demyelinating diseases, in addition to causing decreases in NCV, cause a widening and distortion of the CMAP waveform, and temporal dispersion or distortion of the waveform over the time axis.
  - Many peripheral nerve diseases result in both axonal loss and demyelination, causing decreased amplitude, temporal dispersion, and decreased conduction velocity in addition to abnormal EMG activity due to denervation.
  - Measuring nerve conduction velocity is helpful in determining whether disease is demyelinating, axonal, or both, as well as whether the nerves are more affected proximally or distally. It is also helpful in determining which nerves are affected.
  - Pathophysiologic mechanism of disease cannot be determined using NCV.
  - Nerve and muscle biopsies are often necessary to determine the etiology of disease, although EMG and nerve conduction velocity help determine the nature of disease (demyelinating versus axonal versus myopathy) and optimal biopsy sample site.



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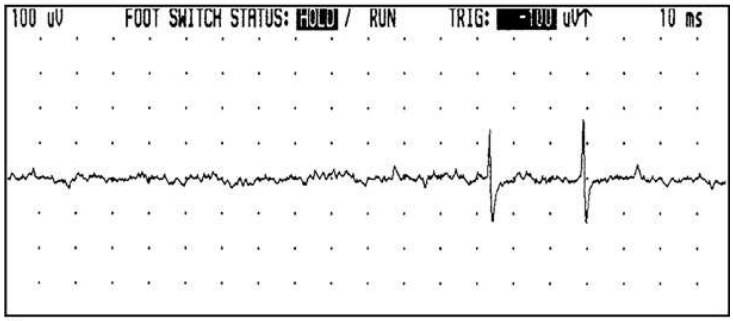

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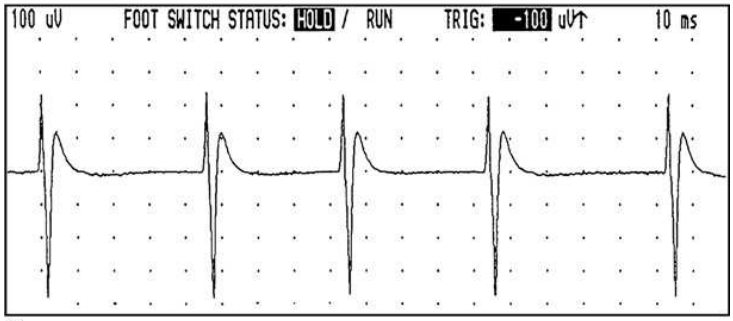
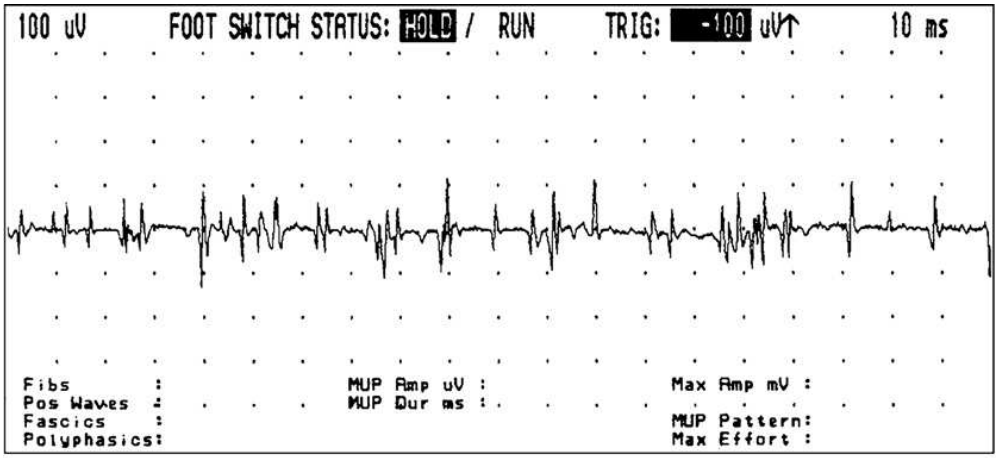


C

ELECTROMYOGRAPHY (EMG) AND MOTOR NERVE CONDUCTION VELOCITY (NCV) Types of electrical activity seen in normal muscle during electromyography evaluation. **A,** Insertional activity. Note abrupt onset and termination of activity associated with needle placement (100 mV/div; 200 msec/div). **B,** Miniature end-plate potentials with two end-plate spikes indicating close proximity of needle to an end plate (100 mV/div; 10 msec/div). **C,** Motor unit action potentials seen during voluntary muscle activity in an awake animal (100 mV/div; 10 msec/div).

(Reprinted with permission from Cuddon PA: Electrophysiology in neuromuscular disease, Vet Clin North Am Small Anim Pract 32:31-62, 2002.)



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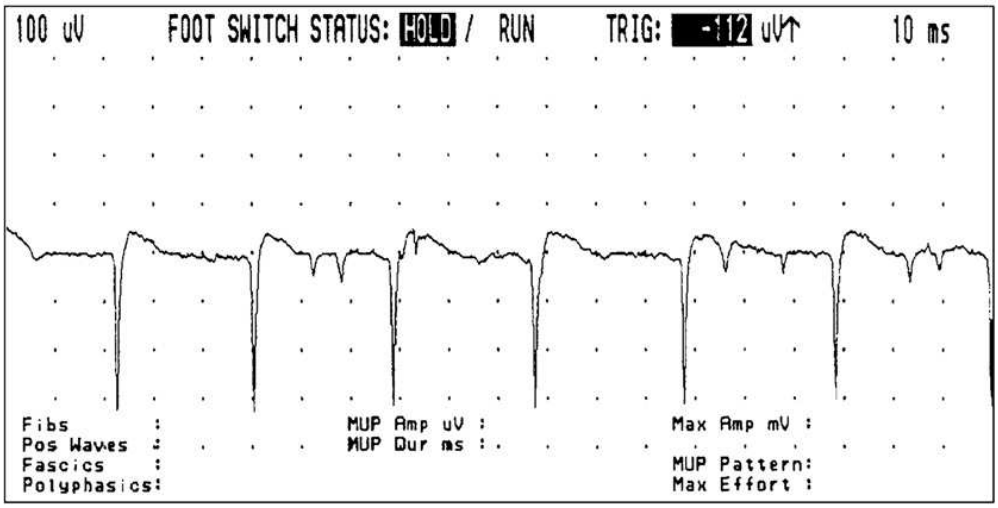
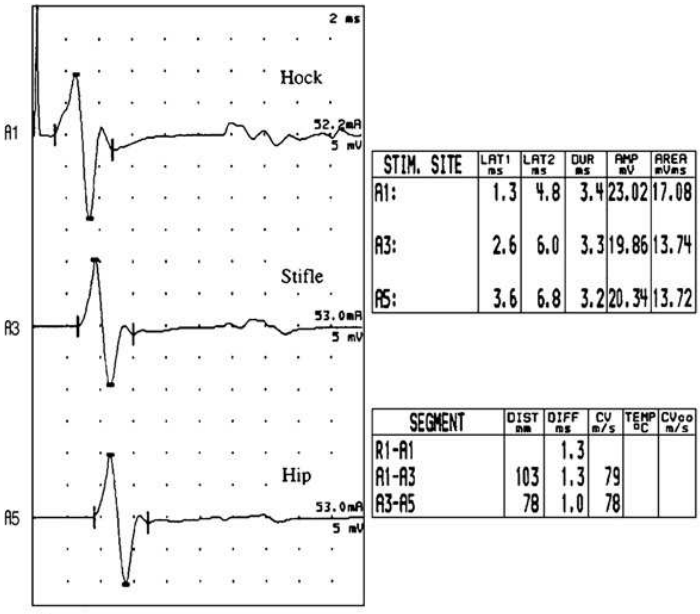


B

ELECTROMYOGRAPHY (EMG) AND MOTOR NERVE CONDUCTION VELOCITY (NCV) Electromyography: abnormal spontaneous electrical activity. **A,** Fibrillation potentials, moderate density (100 mV/div, 10 msec/div). Fibrillation potentials may be associated either with denervation secondary to axonopathy or with primary myopathy. Density and consistency of observed fibrillation potentials are accurate reflections of severity of muscle involvement. **B,** Spontaneous electrical activity in the form of positive sharp waves (100 mV/div; 10 msec/div).

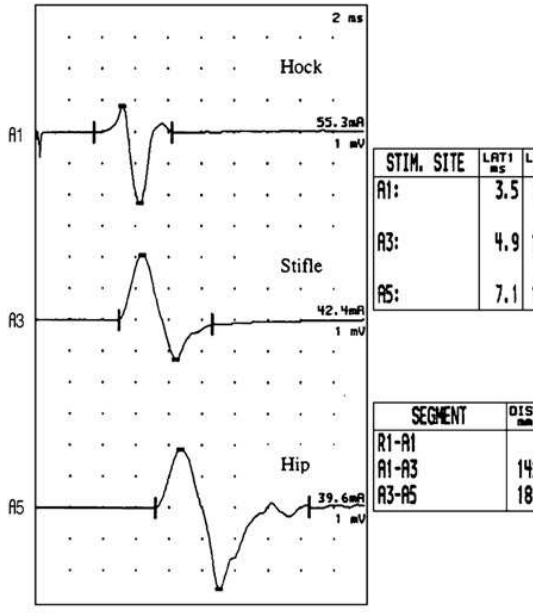
(Reprinted with permission from Cuddon PA: Electrophysiology in neuromuscular disease, Vet Clin North Am Small Anim Pract 32:31-62, 2002.)



STIM. SITE	LAT1 ms	LAT2 ms	DUR ms	AMP mV	AREA mVms
A1:	1.3	4.8	3.4	23.02	17.08
A3:	2.6	6.0	3.3	19.86	13.74
A5:	3.6	6.8	3.2	20.34	13.72

SEGMENT	DIST mm	DIFF ms	CV m/s	TEMP °C	CVoo m/s
R1-A1		1.3			
A1-A3	103	1.3	79		
A3-A5	78	1.0	78		

A



STIM. SITE	LAT1 ms	L
A1:	3.5	
A3:	4.9	
A5:	7.1	

SEGMENT	DIS mm
R1-A1	
A1-A3	14
A3-A5	18

B

ELECTROMYOGRAPHY (EMG) AND MOTOR NERVE CONDUCTION VELOCITY (NCV) Motor nerve conduction studies recorded from the plantar interosseous muscles following stimulation of the sciatic-tibial nerve at the hock, stifle, and hip in a normal dog **(A)** and in a dog with generalized muscle disease **(B)** (mitochondrial myopathy). Note marked generalized decrease in compound muscle action potential (CMAP) amplitudes (3.12, 3.37, and 4.51 mV) from all sites of stimulation in the myopathic dog when compared with the normal dog (23.02, 19.86, and 20.34 mV). Despite CMAP amplitude reduction, the dog with myopathy has normal MNCVs (101 and 85 m/sec). Generalized CMAP amplitude decrease can also be observed in prejunctional neuromuscular diseases such as botulism, as well as in primary axonopathies. (Recording parameters: **A,** 5 mV/div and 2 msec/div; **B,** 1 mV/div and

2 msec/div.)

(Reprinted with permission from Cuddon PA: Electrophysiology in neuromuscular disease, Vet Clin North Am Small Anim Pract 32:31-62, 2002.)

POSTPROCEDURE

- Monitor recovery from anesthesia.
- Nerve and muscle biopsies are often indicated after electrodiagnostic testing to determine the pathophysiology of disease (e.g., inflammatory, infectious, neoplastic, degenerative, toxic, endocrine).
  - See Muscle and Nerve Biopsy, .
  - For additional details, consult recommended methods for submission of samples in Shelton and Engvall, 2002.
- In some cases, PEG tube placement is indicated while the animal is anesthetized.

ALTERNATIVES AND THEIR RELATIVE MERITS

Muscle and nerve biopsies as already described

SUGGESTED READING

Cuddon PA: Electrophysiology in neuromuscular disease. Vet Clin North Am Small Anim Pract 32(1):31–62, 2002.

Sheldon GD, Engvall E: Muscular dystrophies and other inherited myopathies. Vet Clin North Am Small Anim Pract 32:103–124, 2002.

AUTHOR: GREG KILBURN

Electrocardiography

SYNONYMS

- Electrocardiogram: ECG, EKG
- Electrocardiograph: ECG machine

OVERVIEW AND GOALS

- To obtain a tracing that represents the rhythm of the heartbeat
- Electrocardiography is the diagnostic test of choice for evaluating cardiac arrhythmias.
- Electrocardiography may also provide some limited information regarding cardiac structure (sizes and proportions of waves and complexes sometimes indicate chamber enlargement) and systemic disturbances (e.g., hyperkalemia, hypoxemia).

INDICATIONS

- Evaluation of a cardiac arrhythmia noted during physical examination
- Part of routine cardiovascular monitoring during general anesthesia or intensive care
- Monitoring of a cardiac arrhythmia noted during anesthesia or hospitalization
- Evaluation of an animal with clinical signs suggesting syncope
- Evaluation of an animal with suspected or confirmed hyperkalemia

CONTRAINDICATIONS

Severe dyspnea contraindicates restraint in lateral recumbency for ECG.

EQUIPMENT, ANESTHESIA

- Electrocardiograph (ECG machine). Each ECG wire should end in an atraumatic clip that connects the machine to the animal's skin.
- A table with a waterproof foam-core pad on which the animal can lie comfortably (to reduce electrical interference emerging through the table)
- Isopropyl alcohol for improving contact between ECG clips and skin

ANTICIPATED TIME

- Basic tracing: 5 minutes
- Ongoing monitoring: any duration
- For prolonged monitoring, see Holter/Cardiac Event Monitoring, .

PREPARATION: IMPORTANT CHECKPOINTS

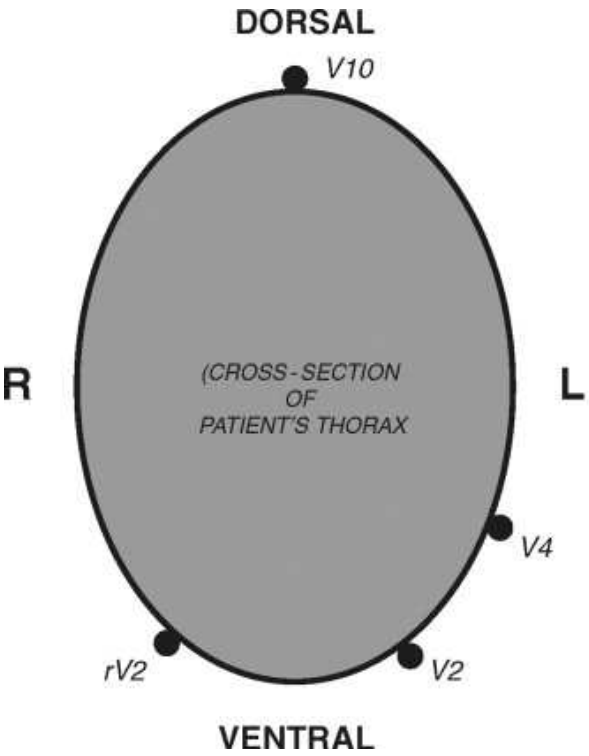
Check that the electrocardiograph has sufficient paper supply and is functioning. There is no ink in most electrocardiographs (heat-sensitive paper and thermal stylus).

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Animals that are in respiratory distress should not be restrained for electrocardiography; these animals should be assessed while they are standing (or in any other position in which they are not distressed), or the ECG should be postponed until dyspnea has improved or resolved.

- Artifact can be minimized by:
  - Using enough isopropyl alcohol at the point of contact between the skin clips and skin
  - Avoiding metal-on-metal contact between clips; often, with smaller dogs and cats, the wires need to be held apart by the person performing the ECG to avoid wire-to-wire or clip-to-clip contact during the procedure.
  - Choosing a quiet, comfortable environment to perform the tracing; a cold or stressful environment may trigger shivering (and motion artifact), whereas an excessively warm or stressful environment can induce panting in dogs (and motion artifact).
  - Replacing the ECG wire set every 5 years under all circumstances or annually with heavy use (e.g., used multiple times weekly) because the wires tend to fracture internally with age
  - Evaluating multiple ECG leads rather than just one lead; each lead provides a different perspective on the electrical activity of the heartbeat, and lead II is not necessarily the lead in which the clearest P waves, QRS complexes, T waves, and minimal artifact are seen.
- Overinterpretation of the dimensions of P waves and T waves as indicating cardiac chamber enlargement is a common pitfall; echocardiography is much more sensitive and specific than electrocardiography for assessing cardiac structure.
- Motion artifact may mimic abnormal cardiac activity and cause misdiagnosis.
- In-hospital monitoring that lasts for hours or more should involve the use of atraumatic or minimally traumatic skin clips: either (1) a small patch of skin can be shaved on each side of the thorax and stick-on, human ECG patches can be used or (2) loops of small-gauge steel suture may be passed through the skin in the usual locations on the four limbs, and the ECG wires are clamped to these loops instead of directly to the skin.

ELECTROCARDIOGRAPHY Patient is comfortably restrained in right lateral recumbency, with proximal long bones of the limbs perpendicular to long axis of body. Insulating (waterproof, foam core) pad and fleece blankets are under patient to reduce the influence of electrical interference.



AS WRITTEN ON CABLES (= HUMAN*)	VETERINARY TERMS (and previous vet nomenclature)	LOCATION ON THE PATIENT'S CHEST
V1	rV2 (CV5RL)	RIGHT 5TH INTERCOSTAL SPACE, JUST TO RIGHT OF STERNUM
V2	V2 (CV6LL)	LEFT 6TH INTERCOSTAL SPACE, JUST TO LEFT OF STERNUM
V3	V4 (CV6LU)	LEFT 6TH INTERCOSTAL SPACE, AT THE COSTOCHONRAL JUNCTION
V4	V10	DORSAL MIDLINE, DIRECTLY DORSAL TO V4 (APPROXIMATELY @ 7TH THORACIC VERTEBRA

* V5 and V6 are not used in veterinary medicine.

ELECTROCARDIOGRAPHY Placement and utility of precordial leads.

ECG Clip/Electrode Placement for Standard Limb Leads (I, II, III, aVR, aVL, aVF)

RA, white	Right forelimb; clip to skin just proximal to the olecranon (caudal triceps region).
LA, black	Left forelimb; clip to skin just proximal to the olecranon (caudal triceps region).
RL, green	Right hind limb; clip to skin just proximal to the stifle (cranial thigh); ground wire.
LL, red	Left hind limb; clip to skin just proximal to the stifle (cranial thigh).

PROCEDURE

- The procedure is the same for cats and dogs.
- Performing an ECG requires two people (clinician and assistant), unless animal restraint is not necessary (anesthetized or unconscious

animal).

- The assistant restrains the animal in right lateral recumbency. Sitting, sternal, and dorsal positions are equally acceptable; determination of the mean electrical axis from these other positions is inaccurate, but this has no effect on assessing the cardiac rhythm.
- The assistant stands or sits behind (dorsal to) the right-laterally recumbent animal and holds the animal's limbs perpendicular to the long axis of the animal's body. Note: For the humeri and femurs to be truly perpendicular to the long axis of the body, the assistant needs to extend the limbs sometimes quite substantially. Fore-limbs (at the level of the carpi) are held in the assistant's right hand and hind limbs (at the level of the tarsi) in the left.
- The clinician attaches the ECG clips (electrodes) to the appropriate points on the animal for the limb leads as well as the precordial leads.
- A standard ECG includes representative recordings from all six limb leads, usually 3-15 seconds each for I, II, III, aVR, aVL, and aVF, and will provide further information if precordial leads are also recorded.
- A standard ECG also includes a “rhythm strip,” which is a continuous tracing of the same lead for 12 seconds to 1 minute or more:
    - The most commonly used lead for the rhythm strip is lead II, but the lead that is chosen should be the one that shows the clearest P waves, QRS complexes, and T waves.
    - The duration of the rhythm strip depends on the reason for performing the ECG and can be as long as is needed (several minutes) when an intermittent arrhythmia is being sought.
- Generally, if an abnormality has not been detected over a period of 1-4 minutes of ECG recoding on paper, then the procedure is terminated. The tracing obtained thus far is reviewed meticulously, and if further ECG evaluation is needed, ongoing ECG monitoring either with an in-hospital display monitor (e.g., oscilloscope) or portable telemetry (see p.1287) can be used.

POSTPROCEDURE

The clips are carefully detached from the skin prior to releasing the animal's restraint.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Thoracic radiographs: provide some information on cardiac structure (e.g., chamber enlargement), but this information is limited by substantial overlap between normal and mild to moderate abnormalities. Also indicated when ST-segment elevation or depression is present (assess for pulmonary or airway lesions).
- Echocardiography: the clinical gold standard for assessing cardiac chamber size; indicated if cardiac enlargement is suspected based on ECG and/or radiographs
- Pulse oximetry/arterial blood gas measurement: if ST segment elevation or depression is noted in the absence of structural heart disease (e.g., cardiomyopathy, advanced valvular disease, congenital heart disease)
- Serum potassium measurement: if lack of P waves is noted, especially in an animal with a history and/or physical findings suggesting a reason for hyperkalemia (urgent)

AUTHOR: ETIENNE CÔTÉ

Echocardiography

SYNONYMS

Cardiac ultrasound; echo; transthoracic echocardiography

OVERVIEW AND GOALS

A complete echocardiographic study should:

- Reveal the pertinent acquired or congenital cardiac lesions
- Evaluate valvular function
- Quantify ventricular systolic and diastolic function
- Estimate the hemodynamic burden through quantification of chamber size (dilation, hypertrophy)

INDICATIONS

- Congenital or acquired cardiac disease (valvular, myocardial, pericardial), cardiac neoplasia, pulmonary hypertension, systemic hypertension, and pleural effusion or respiratory distress of uncertain etiology
- Limited echo studies can be useful in selected emergency situations (e.g., pericardial effusion, estimation of atrial size, or ventricular ejection fraction during initial stabilization if other initial diagnostic modalities are hazardous or nondiagnostic).

CONTRAINDICATIONS

- Animal should be stable enough to handle restraint.
- Animals with life-threatening problems (e.g., pleural effusion, pulmonary edema, and other causes of respiratory distress) need to be stabilized (limited echo study might be warranted or postponed).

EQUIPMENT, ANESTHESIA

- Scanning table with holes cut out because examination from beneath the animal improves image quality
- Ultrasonic transmission gel
- Isopropyl alcohol
- Hair clippers might be needed.
- Ultrasound equipment; sector-scanning transducers preferred:
    - For cats and small dogs (usually 7.0-8.0-MHz transducer), medium-sized dogs (5.0-MHz transducer), large dogs (2.5-3.5-MHz transducer)
    - It may be necessary to use two different probes during one examination.
- The echocardiography machine should have M-mode, two-dimensional (2D), Doppler (pulsed-wave, continuous-wave, and color-coded), and electrocardiogram (ECG) capabilities.
- Sedation/anesthesia is neither required nor desired except in very uncooperative animals.

ANTICIPATED TIME

Variable due to experience and case complexity (5-40 minutes).

PREPARATION: IMPORTANT CHECKPOINTS

- Dogs and cats usually require little preparation for echocardiographic examination.
- Fasting is not needed.
- Hair might be clipped over the right third to the sixth intercostal spaces (ICS) and left at the fourth to the seventh ICS (precordial transducer locations); however, in most dogs and cats, satisfactory images can be obtained by parting the haircoat, applying isopropyl alcohol liberally over area of interest, and finally applying transmission gel.

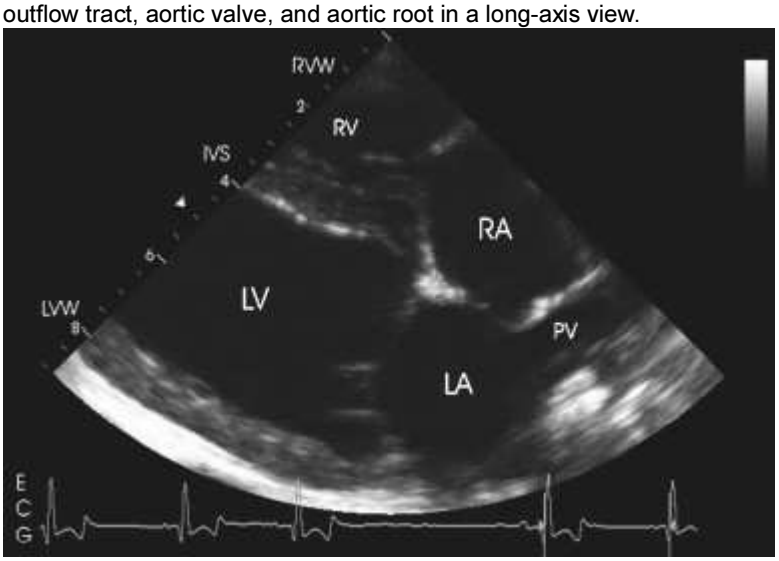
POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Although the technique has no known physical hazard, there are risks associated with the improper interpretation or use of the results of the ultrasound.
- Use high-frequency transducers to obtain quality images of near-field structures.
- Use low-frequency transducers for quality Doppler (color, pulse wave, continuous wave) signals.

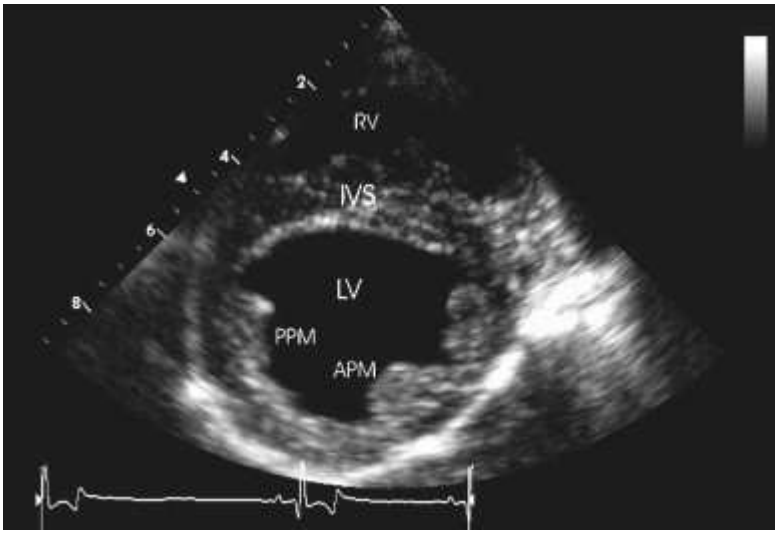
- Adjust depth of the real-time image to fill the field of view (reduce amount of lung field).
- Adjust gain to avoid producing a white, distorted image due to a high setting; too low a setting will produce a weak signal.
- Remember the concept of blue/away and red/toward (BART) for color-flow Doppler studies.

PROCEDURE

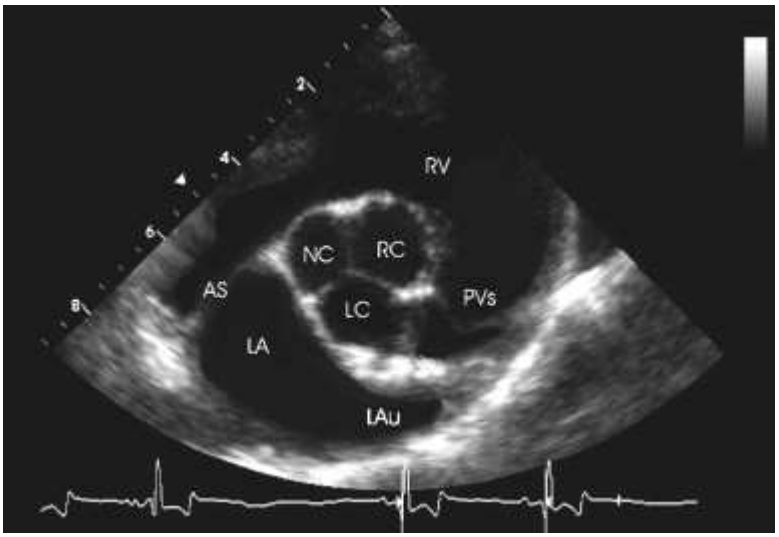
- Image quality is improved in lateral recumbency; however, dogs and cats may be examined in a standing, sitting, or sternal position.
- The ultrasound machine's ECG clips are attached to the legs as recommended by the manufacturer (ECG is used for measurements and timing within the cardiac cycle).
- Starting in right lateral recumbency (animal's legs toward the examiner), the right parasternal location (window) is between the right third and sixth ICS, between the sternum and costochondral junctions (landmark: palpate right precordial heartbeat and place transducer at this location to start). Attention is paid to having the assistant restrain the animal, with the forelegs drawn cranially to open the axilla/acoustic window.
- **Long-axis views**: The beam plane is oriented slightly clockwise from perpendicular to long axis of the body, parallel to the long axis of the heart, and with the transducer index mark pointing toward the heart base (craniodorsal, approximately toward the animal's shoulder). The following two views are obtained: first, a four-chamber view with the ventricles displayed to the left and the atria to the right; second, a view obtained by slight clockwise rotation of the transducer from the four-chamber view into a slightly more craniodorsal orientation revealing the left ventricular outflow tract, aortic valve, and aortic root.
- **Short-axis views:** Rotate the transducer about 90○ toward the sternum from the four-chamber view (keep probe in same position except for the rotation) such that the beam plane is oriented perpendicular to the long axis of the heart, with the transducer index mark now pointing cranially toward the animal's elbow (proper orientation identified by circular symmetry of the left ventricle or aortic root). There are five standard transverse images (left ventricle with papillary muscles, left ventricle at mitral chordae tendineae level, left ventricle at mitral valve level, heart base–aorta/left atrium level, and heart base–pulmonary artery) obtained from this position by pivoting the transducer from the apex to the base of the heart (caudal/ventral to cranial/dorsal).
- Turn animal over into left lateral recumbency, with the animal's legs still toward the sonographer.
- **Left caudal (apical) parasternal location:** The location is between the left fifth and seventh ICS, as close to the sternum as possible (landmark: palpable left apical heartbeat):
    - **Left apical two-chamber views:** The transducer index mark is pointing toward the heart base (dorsal), and the beam plane parallel to the long axis of the heart—the left side of the heart—is visualized (left atrium, left ventricle, and mitral valve). Slight rotation of the transducer into a craniodorsal to caudoventral orientation reveals left ventricle, outflow tract, aortic valve, and aortic root in a long-axis view.



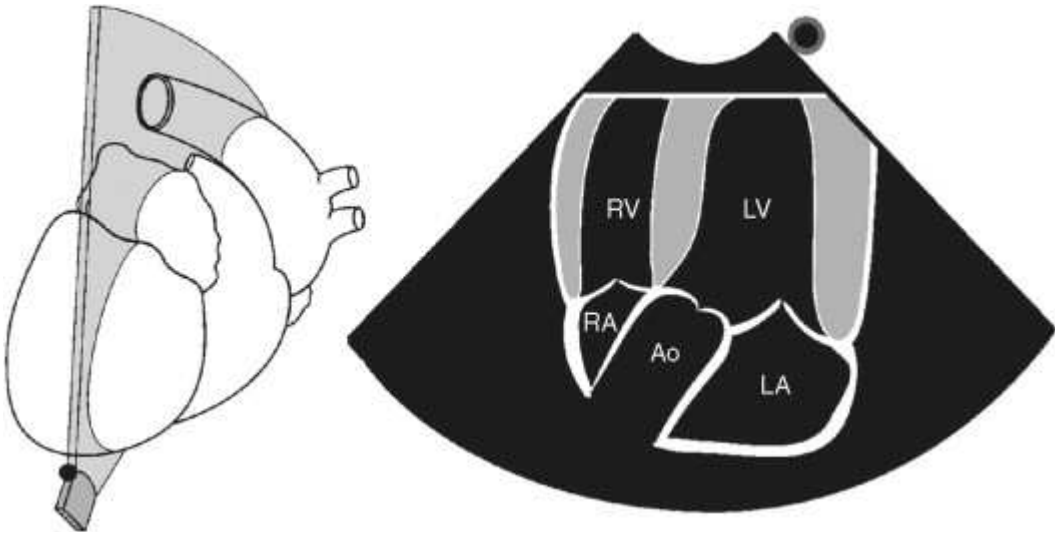
ECHOCARDIOGRAPHY Right parasternal four-chamber long-axis view in a normal dog (obtained without shaving). *IVS,* Interventricular septum; *LA,* left atrium; *LV,* left ventricle; *LVW,* left ventricular wall; *PV,* pulmonary vein; *RA,* right atrium; *RV,* right ventricle; *RVW,* right ventricular wall.



ECHOCARDIOGRAPHY Right parasternal short-axis view at the left ventricular papillary muscle level in same dog. From this view, gentle pivoting motion (caudal/ventral to cranial/dorsal) of the transducer beam toward the base will reveal the other four standard views obtained from this location. *APM,* anterior papillary muscle; *IVS,* interventricular septum; *LV,* left ventricle; *PPM,* posterior papillary muscle; *RV,* right ventricle.



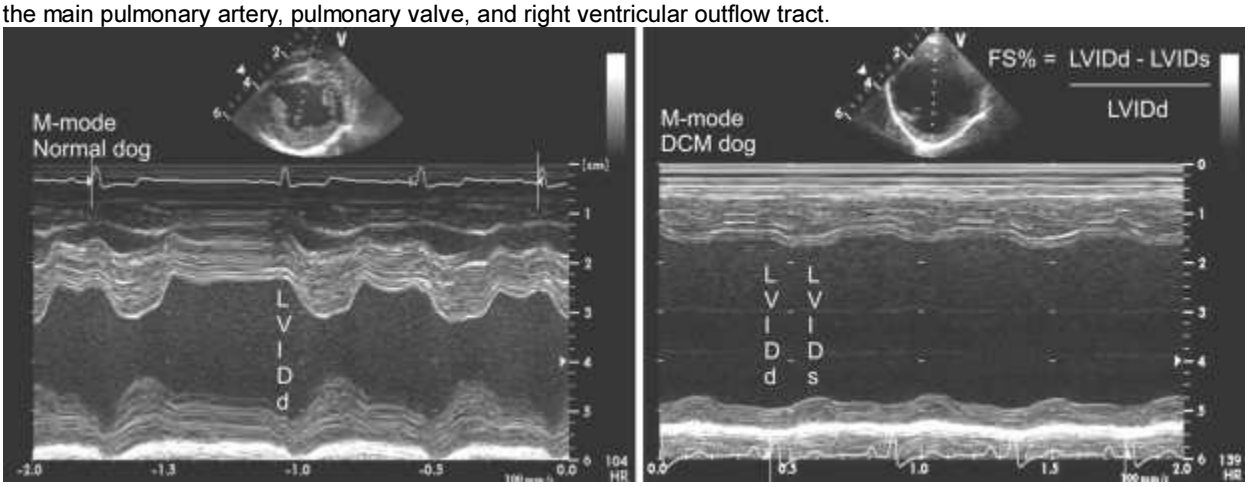
ECHOCARDIOGRAPHY Remaining in the same right parasternal window as the two previous views, gently pivoting toward the heart base, the right parasternal short-axis view at the left atrium/aorta level was obtained in the same dog. *AS,* atrial septum; *LA,* left atrium; *LAu,* left auricle; *LC,* left coronary cusp; *NC,* noncoronary cusp; *PV,* pulmonary vein; *PVs,* pulmonic valve; *RC,* right coronary cusp; *RV,* right ventricle.



ECHOCARDIOGRAPHY Five-chamber view is obtained at left apical parasternal location. Left apical parasternal location is the only time during echocardiographic examination when index mark on head of transducer is directed caudally. *Ao,* aorta; *LA,* left atrium; *LV,* left ventricle; *RA,* right atrium; *RV,* right ventricle.

- **Left apical four-chamber views:** This is the only view in which the transducer index mark is pointing to the left and caudally, opposite of all other views. Note: The transducer should be as far back toward the apex of the heart as possible, often around the seventh ICS, and tilted to point cranially. The beam plane is in a left-caudal to right-cranial orientation and then directed dorsally toward the heart base, revealing the ventricles in the near field closest to the transducer and the atria in the far field (heart is oriented vertically; left ventricle, mitral valve, and left atrium should appear to the right). Modest cranial tilting of the beam from the above view will bring the left ventricular outflow region into view (five-chamber view).

- **Left cranial parasternal location:** The location is between the left third and fourth ICS, between the sternum and costochondral junctions.
  - **Long-axis views:** With the transducer index mark pointing cranially and the beam plane oriented parallel to the long axis of the body and heart, a view of the left ventricular outflow tract, aortic valve, and ascending aorta is obtained (left ventricle will be displayed to the left and aorta to the right). From this position, angling of the beam ventral (toward the sternum) to the aorta brings out the right atrium/right auricle, tricuspid valve, and inflow region of the right ventricle (displayed to the right, while the left ventricle will be noted to the left). Finally, angling the transducer dorsally (transducer will almost be horizontal and parallel with the table) in relation to the ascending aorta produces a view of the main pulmonary artery, pulmonary valve, and right ventricular outflow tract.



ECHOCARDIOGRAPHY Two M-mode studies of left ventricle. *Left,* Normal dog shows vigorous excursions of the interventricular septum *(above)* and left ventricular free wall *(below)* from systole to diastole. The absolute diameter of the left ventricle is within normal limits. *Right,* Dog with dilated cardiomyopathy has visibly poor left ventricular systolic function (almost no difference between systole and diastole) and a very enlarged left ventricular diameter compared to normal.

LVIDd, left ventricular internal diameter in diastole; LVIDs, left ventricular internal diameter in systole; FS%, fractional shortening.

  - **Short-axis views:** Remain in the same location as for the cranial long axis, and rotate the transducer until the transducer's index mark is toward the thoracic spine (dorsally, about 90○ from the location of long-axis view; aorta should appear circular in the center of the image). The right ventricular inflow tract should be to the left, and outflow tract and pulmonary artery to the right.

POSTPROCEDURE

- Remove ECG clips.
- Wipe gel and alcohol from animal.

ALTERNATIVES AND THEIR RELATIVE MERITS

Transesophageal echocardiography:

- Semi-invasive procedure
- Requires general anesthesia in animals
- Provides superb clarity and resolution

SUGGESTED READING

Bonagura JD: Echocardiography. J Am Vet Med Assoc 204:516–522, 1994.

Oyama MA: Advances in echocardiography. Vet Clin North Am Small Anim Pract 34(5):1083–1104, 2001.

Thomas WP, Gaber CE, Jacobs GJ, et al: Recommendations for standards in transthoracic two-dimensional echocardiography in the dog and cat. J Vet Intern Med 7:247–252, 1993.

AUTHOR: ROBERT PROŠEK

Foreign-Body Removal, Esophageal (Endoscopic)

SYNONYM

Minimally invasive removal of esophageal foreign bodies

OVERVIEW AND GOALS

- Objects causing esophageal obstruction are most commonly found in one of three locations: at the thoracic inlet, at the level of the base of the heart, or immediately cranial to the gastroesophageal sphincter.
- About 90% of foreign bodies obstructing the esophagus can be removed without performing a thoracotomy. An attempt should be made to try to remove these foreign bodies via esophageal endoscopy in order to avoid surgery and its complications (e.g., difficult access, limited healing ability, and associated morbidity). Removal of these objects is achieved by making use of rigid or flexible endoscopes.
- If a foreign object cannot be removed via the oral route, an attempt can be made to pass the object through into the stomach using a large-bore stomach tube and copious lubrication, provided complications such as esophageal perforation (from a sharp-edged foreign body, esophageal wall devitalization, or overly aggressive forward pressure) are avoided. Objects passed from the esophagus into the stomach may then be removed via a gastrotomy or left to be digested (in the case of bones and other digestible objects).

INDICATIONS

Presence of foreign objects lodged in the esophagus (e.g., bones, fishhooks, needles, toys, partially regurgitated hair balls)

CONTRAINDICATIONS

Esophageal perforation is an absolute contraindication to minimally invasive approaches; thoracotomy is indicated in these cases.

EQUIPMENT, ANESTHESIA

- General anesthesia
- Cuffed endotracheal tube
- Mouth gag/speculum
- Rigid tube for esophageal dilation (optional); typical external diameters are 2 cm (cat, small dog), 3 cm (medium-size dog), and 4 cm (large dog). The end of the tube should have smooth edges (may heat with flame, then trim edges when cool before using).
- Rigid proctoscope or flexible fiberoptic endoscope
- Endoscopic basket or grasping forceps (recommended) or endoscopic biopsy forceps (second choice)
- Water-soluble lubricating jelly
- Polyethylene catheter or feeding tube (optional)
- Suctioning apparatus

ANTICIPATED TIME

Approximately 20-90 minutes, depending on size of object and ease with which it can be grasped, atraumatically dislodged, and retrieved

PREPARATION: IMPORTANT CHECKPOINTS

- Assess for location of foreign body, presence of signs of aspiration pneumonia, and evidence of esophageal perforation by performing survey and contrast radiography using low osmolality, nonionic contrast medium. Radiographs should be performed or repeated immediately prior to induction of general anesthesia to avoid anesthetizing an animal in which a foreign body has spontaneously passed into the stomach.
- Endoscopic evaluation of location of foreign body and state of esophageal mucosa
- Ensure adequate hydration and perfusion.
- Antibiotic therapy if indicated by complications (described in following paragraphs); often empirically at first (e.g., ampicillin, 22 mg/kg IV q 8 h; and enrofloxacin, 5 mg/kg diluted 1:1 in 0.9% saline and given slowly IV q 24 h [cats] or q 12 h [dogs]) and then guided by results of culture and sensitivity (C&S).

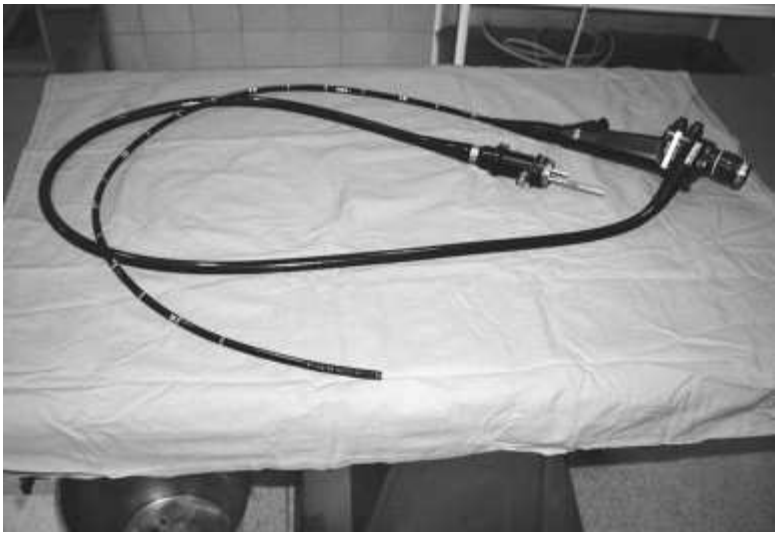
- Advise the owner of possible complications.
    - There may be a need for emergency thoracotomy if perforation occurs or if removal via the oral route is impossible; possible gastrotomy may result if the foreign body has to be pushed through into the stomach and is unlikely to be digested.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Esophageal mucosal trauma (erosion, ulceration)
- Esophageal perforation, pyothorax, pleuritis, mediastinitis
- Aspiration of esophageal contents and aspiration pneumonia
- Tension pneumothorax (associated with esophageal insufflation when using flexible fiberoptic endoscope)
- Bradycardia due to vagal stimulation
- Sepsis (due to aspiration or to esophageal rupture)
- Esophageal stricture (first clinical manifestations usually >2 weeks postoperatively)
- Bronchoesophageal fistulation (rare)
- Failure to radiograph immediately prior to induction (foreign body may have passed spontaneously)

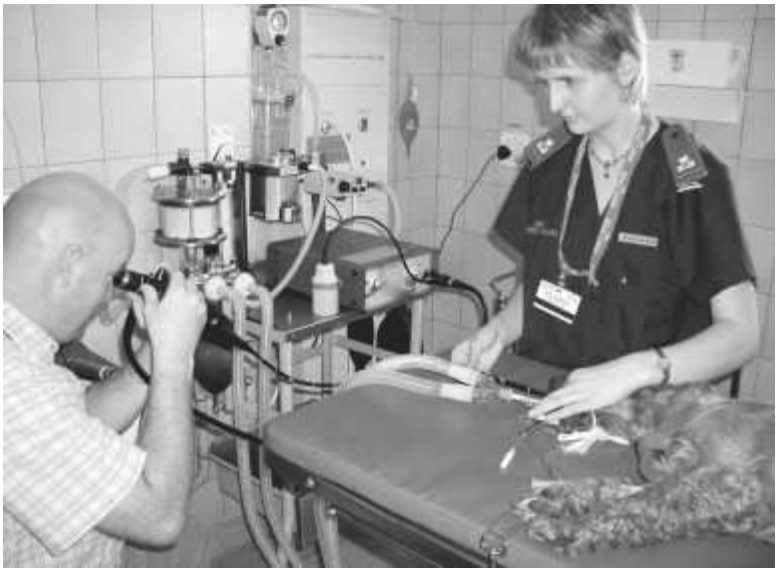
PROCEDURE

- General anesthesia
- Place endotracheal tube and inflate cuff to prevent aspiration of esophageal contents.
- Animal in sternal or left lateral recumbency (allows the esophagus to lie over the aorta)
- Examine the mouth (especially the sublingual region) for the presence of objects such as thread, needles, or fishhooks.
- Suction esophagus to remove any liquid contents and contrast medium.
- Insert mouth gag/speculum.
- Rigid proctoscope technique:
    - Lubricate proctoscope.
    - Pass the proctoscope orally and into the esophagus to the level of the foreign body, visualizing the foreign body and any evidence of perforation that would contraindicate further endoscopic manipulations.
    - Lubricant can be placed at the site of the foreign body, using a polyethylene catheter with the tip placed at the level of the foreign body, between the foreign body and esophageal mucosa.
    - Using grasping forceps, bring the foreign body close to the end of the proctoscope.
    - If the foreign body is small enough, it can be partially or entirely pulled into the lumen of the proctoscope.
    - The foreign body, proctoscope, and grasping forceps are pulled out together via the mouth by gentle manipulation and with adequate lubrication. Continuous visualization and gentleness of traction are essential through this process. This is to ensure that complications such as esophageal laceration or perforation are noticed immediately if they occur, that the retrieval can be stopped immediately, and that the foreign body be repositioned or the procedure be aborted in favor of thoracotomy if serious complications are noted.
    - If retrieval is not possible, an attempt should be made to gently push the foreign body through to the stomach using a well-lubricated stomach tube, provided no evidence of esophageal devitalization (e.g., deep mucosal lacerations and discolorations or other signs of possibly imminent perforation) are seen.
    - Careful examination of the esophageal wall after foreign body removal; any suspicion of possible esophageal perforation warrants close radiographic and clinical monitoring.
- Flexible fiberoptic endoscope technique:
    - For medium-size or larger dogs, a rigid tube can first be placed to assist in dilating the esophagus. The endoscope can then be passed through this tube.
    - Lubricate the endoscope.
    - Pass the endoscope to the level of the foreign body, visualizing the foreign body and assessing the integrity of the adjacent esophagus.



FOREIGN-BODY REMOVAL, ESOPHAGEAL (ENDOSCOPIC) A 1-m flexible fiberoptic endoscope. This endoscope is adequate for esophageal procedures in dogs and cats of all body sizes.

FOREIGN-BODY REMOVAL, ESOPHAGEAL (ENDOSCOPIC) Large *(top)* and two small *(below)* rigid proctoscopes, used for retrieving esophageal foreign bodies, and small proctoscopic stylet *(bottom)*. Stylet is placed into proctoscope for advancing into esophagus. Once desired degree of insertion is achieved, stylet is withdrawn, and glass port (seen in the open position in the large proctoscope, *top*) may be closed for most effective visualization.



FOREIGN-BODY REMOVAL, ESOPHAGEAL (ENDOSCOPIC) Operator *(left)* examines esophagus of an animal, using a flexible fiberoptic endoscope; assistant adjusts endoscope's insertion and rotation according to operator's instructions.

- Insufflation of air will allow dilation of the esophagus around the foreign body. This may also be useful in dislodging foreign bodies such as bones that are embedded in the esophageal wall.
- Lubrication can also be placed at the site of the foreign body, using a catheter or feeding tube as already described.
- Grasping forceps or biopsy forceps can be passed through the endoscope biopsy channel. The use of biopsy forceps is a last resort, because dulling and damage to the instrument are possible.
- Grasp the foreign body, and pull it close to the endoscope.
- The endoscope, forceps, and foreign body are gently pulled out together via the mouth while ensuring adequate esophageal dilation and lubrication.
- If the foreign body is lodged to the extent that it cannot be retrieved easily, an attempt could be made to either slightly push it aborally or to rotate it gently. If the maneuvers result in dislodging the object, another attempt can be made to retrieve it.
- If retrieval is not possible, an attempt should be made to push the foreign body through to the stomach.
- The esophageal mucosa is carefully examined endoscopically after removal of the foreign body.

POSTPROCEDURE

- If esophageal mucosa is damaged (e.g., suspected on endoscopic observation of darkened/discolored esophageal mucosa, deep mucosal lacerations, or after prolonged, difficult procedure; confirmation comes from intraprocedure or postprocedure radiographs):
  - Clean lacerations that do not extend through the full thickness of the esophageal wall can be left to heal by epithelialization.
  - Full-thickness tears and areas of esophageal necrosis require immediate surgical resection or repair.
- Withhold food and water for 24 hours.
- Maintain hydration and electrolyte balance.
- Pain management: antibiotics (as already described), prokinetic agents, corticosteroids, and/or gastric antacids may be indicated (see pp. 365 and p. 367).
- Gastrostomy feeding tube placed distal to the site of the foreign body if prolonged withholding of food is indicated (such as in cases of esophageal mucosal damage).
- Once the animal has recovered, first introduce liquids, followed by gruel if no adverse reactions are noted once liquids have been introduced.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Advancement of foreign body into stomach followed by gastrotomy:
  - If a foreign body is too large or awkward to grasp, an attempt could be made to gently push it through into the stomach. Digestible objects such as bones could be left in the stomach to digest, but sharp objects and objects such as toys should not be pushed into the stomach (risk of esophageal perforation). Follow-up radiography is advised to ensure that foreign bodies were either digested or passed through the digestive tract.
- For cases in which esophageal perforation and its complications have already developed (see p. 363), surgical removal of the foreign body via thoracotomy is the only alternative.

AUTHOR: MIRINDA NEL (VAN SCHOOR)

Fistulogram

SYNONYM

Positive-contrast fistulogram

OVERVIEW AND GOAL

Fistulograms are radiographic contrast procedures that may be utilized in the evaluation of a cutaneous draining tract.

INDICATIONS

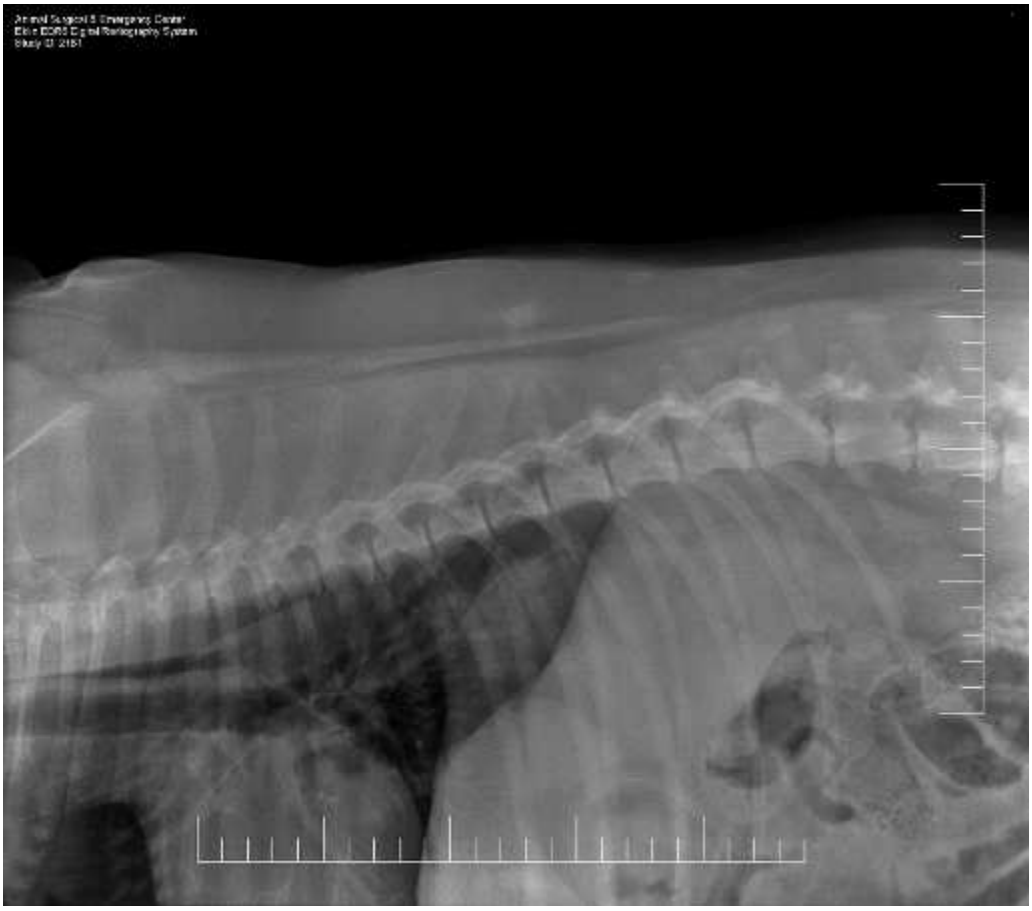
- Identify soft-tissue foreign bodies (e.g., splinters, plant awns, glass)
- Locate potential source of a draining tract (e.g., orthopedic implants, sutures)
- Identify communication of tract with body cavity or organ

CONTRAINDICATIONS

Known sensitivity to contrast media

EQUIPMENT, ANESTHESIA

- Contrast media:
  - Ionic or nonionic organic iodinated contrast agents
- Catheters:
  - Variable length and size depending on extent of lesion
  - Preferably semirigid without balloon tip, such as a tomcat catheter; no stylets
- Sedation/anesthesia may be required for fractious animals.



FISTULOGRAM Lateral radiographic projection of torso of a dog prior to contrast injection. There is a suggestion of minor radiopacity in dorsal body wall dorsal to location of a draining tract.

(Courtesy Dr. Phil Gill.)

ANTICIPATED TIME

About 5–20 minutes

PREPARATION: IMPORTANT CHECKPOINTS

- Sedation/anesthesia if required
- Hair clipped and area scrubbed/disinfected
- Survey radiograph of region

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

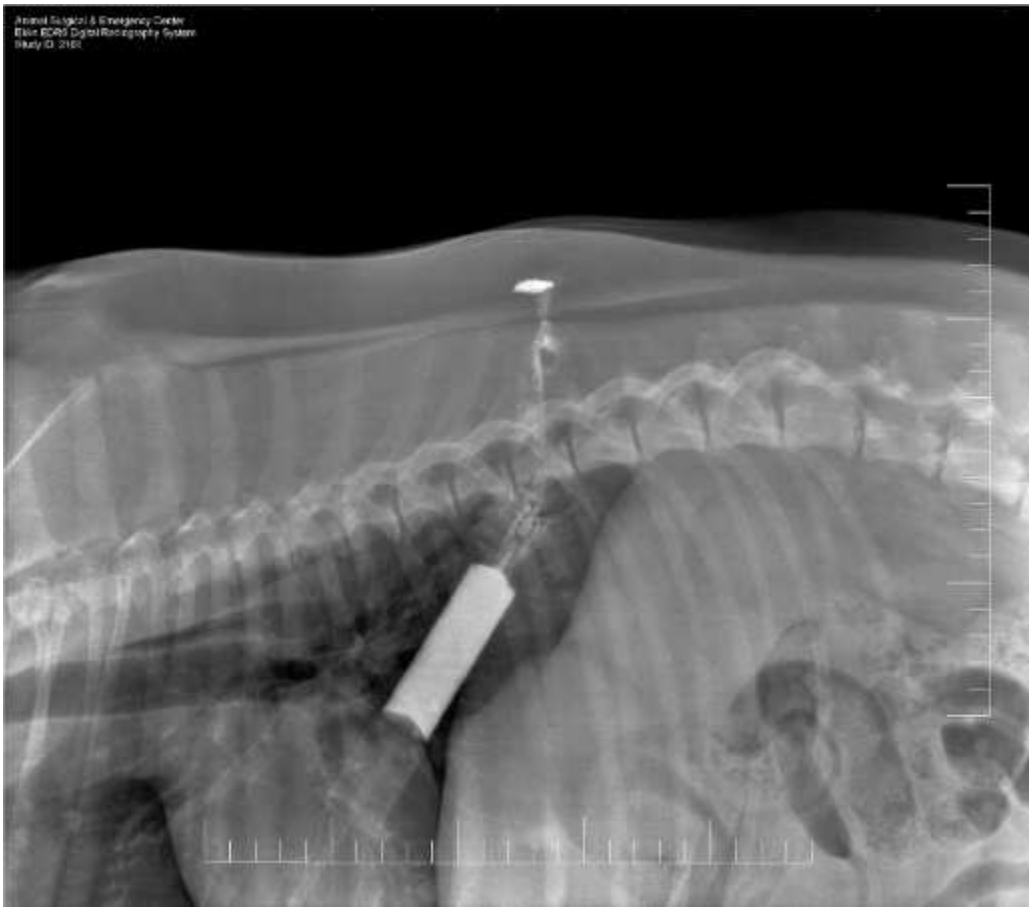
- Systemic reaction to contrast agents (rare)
- Local irritation from hypertonic contrast agents (rare; can dilute with saline or sterile water for prevention)
- Leakage of contrast into fascial planes leading to nondiagnostic study (common)
- Inability to follow full extent of draining tract (common)
- Masking of small foreign bodies by opacity of contrast agent (common)

PROCEDURE

- Catheter is placed retrograde into draining tract as far as possible.
- Injection (usually 1-12 mL) while catheter in place or while drawing it back out
- Appropriate radiographic projections; two views at right angles are usually sufficient.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Ultrasound:
  - Easy to perform
  - Variable information obtained; may detect foreign bodies
  - Difficult to follow extent of tract
- CT scan and MRI:
  - Expensive
  - Variable information obtained



FISTULOGRAM Lateral radiographic projection of same dog after contrast injection into a cutaneous draining tract on lateral thorax. Study shows extent of draining tract, with pooling of contrast media in dorsal body wall. Filling defect in contrast-filled tract created by catheter.

(Courtesy Dr. Phil Gill.)

AUTHOR: BRETT KANTROWITZ

Fine-Needle Sampling for Cytologic Analysis: Lung

OVERVIEW AND GOALS

Minimally invasive diagnostic tool with a good diagnostic yield for focal lesions. Good technique increases the diagnostic yield and reduces complications.

INDICATIONS

- Pulmonary masses and nodules
- Areas of pulmonary consolidation
- Lower diagnostic yield and greater risk to animal for diffuse (interstitial) pulmonary diseases

CONTRAINDICATIONS

Bleeding disorders (coagulopathy, thrombocytopenia, thrombocytopathia)

EQUIPMENT, ANESTHESIA

- A few sterile 22-gauge needles (1-3½" [2.5-9 cm])
- A 12-mL syringe
- A standard 33" (84-cm) flexible extension set for IV lines
- Glass slides
- Blow dryer
- Image guidance if possible (ultrasound, CT scan, fluoroscopy, radiology)
- General anesthesia is recommended to reduce risks of pulmonary lacerations and pneumothorax.

ANTICIPATED TIME

About 30 minutes

PREPARATION: IMPORTANT CHECKPOINTS

- Warn owners that hemorrhage and pneumothorax are possible complications, warranting intensive care and sometimes presenting a life-threatening situation.
- Rule out bleeding disorders.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Hemorrhage (pulmonary, pleural, airways)
- Pneumothorax
- Proceeding too slowly. While the procedure must be prepared for and carried out carefully, time is of the essence during fine-needle sampling. Tissue trauma activates coagulation, which can rapidly plug the needle or degrade the quality of the sample.
- Short and slow needle passes. A slow or timid back-and-forth motion does not detach a sufficient number of cells. The needle tip, however, must remain within the target tissue during this part of the procedure to avoid contamination by, or damage to, surrounding tissues.
- Changing directions while the needle is deep in the lesion causes shearing of tissue, lung lacerations, bleeding, and pain. The needle should always be withdrawn to the skin's surface (almost out but not quite) before being redirected.
- Aspiration. When aspiration is used in the lungs, air is aspirated as soon as the bevel enters an air-filled space, and the sample is lost in the syringe or extension set. A vigorous back-and-forth motion without aspiration is sufficient to detach cells, create mild bleeding, and fill the needle with a diagnostic sample.
- Multiple sites. An important point is to obtain three to five cellular biopsies of different areas of large lesions, because masses or large lesions may contain a mixture of necrotic, inflamed, hemorrhagic, neoplastic, and normal tissues.
- Nondiagnostic samples. With experience, a clinician can identify cellular smears with the naked eye. If the smear does not appear cellular, the procedure should be repeated. If there is any doubt, the sample can be evaluated immediately by in-house microscopic examination.

PROCEDURE

- Induce general anesthesia, including endotracheal intubation.
- Clip the hair from the sampling site(s), and prepare the site with surgical scrub.
- Connect extension set between syringe and needle.
- Fill syringe with 5-10 mL of air.
- The clinician hangs the syringe and extension tubing around his or her neck (like a stethoscope) and holds the needle like a pen to allow precise manipulations.
- Localize lesion with diagnostic imaging. Fine-needle procedures guided only by radiographs can be performed on large masses or when large areas of the lungs are affected. Note: Sonographic guidance works only if the mass, nodule, or consolidated lobe is in contact with the thoracic wall.
- Rapidly position the needle tip within the lesion. Avoid keeping the needle tip close to pleural surfaces, to reduce lacerations during respiratory motion.
- Move the needle rapidly back and forth using long needle passes (away from major blood vessels), and try staying within the lesion. Do not use negative pressure.
- Rapidly withdraw the needle.
- Immediately expel the sample on glass slides using the air-filled syringe.
- Make smear using the standard blood smear technique or a gentle squash technique.
- Immediately air-dry the smear with a blow dryer.
- Repeat the procedure to obtain two to three cellular smears of the lesion(s).

POSTPROCEDURE

Risks of pneumothorax are significantly reduced (5% versus 40%-50%) if the animal is kept in lateral recumbency (biopsy side down) for 30-60 minutes following the procedure. If the animal is stable, keep under anesthesia 15-20 minutes after the procedure. This simple precaution takes advantage of recumbency atelectasis to rapidly seal any lung perforations or lacerations.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Tru-Cut or core biopsy:
  - May be associated with more complications
  - May be more accurate for diffuse pulmonary diseases
- Bronchoscopy/bronchoalveolar lavage:
  - Minimally invasive: lowest risk of iatrogenic pneumothorax
  - Requires disease process that is exfoliating cells into the alveoli or airways (e.g., useful for lung consolidation due to pneumonia), so false negatives are possible.
- Surgical biopsy:
  - More costly
  - More invasive
  - Most definitive diagnostic sampling technique for diffuse (interstitial) pulmonary diseases

AUTHORS: MARC PAPAGEORGES, MICHÈLE MENARD

Fine-Needle Aspirate, Ultrasound-Guided

SYNONYM

Needle biopsy

OVERVIEW AND GOAL

Procedure to obtain small tissue or fluid samples using ultrasound guidance and real-time monitoring of needle placement

INDICATIONS

- Ultrasonographic evaluation of focal mass lesion or nodule
- Ultrasonographic evaluation of diffuse or focal parenchymal organ abnormalities
- Drainage of cysts, abscesses, or fluid

CONTRAINDICATIONS

- Cavitated mass: risk of hemorrhage
- Bleeding disorder: risk of hemorrhage
- Suspected transitional cell carcinoma: possibility of seeding tumor along needle tract

EQUIPMENT, ANESTHESIA

- A few 22- or 25-gauge standard sterile injection needles, 1½ inches (4 cm) in length:
  - Longer needle (3½ inch [9 cm]) required if using biopsy guide
- A few 6-mL syringes
- Glass microscope slides
- Hair clippers
- Surgical scrub, rubbing alcohol, gauze
- Sector or linear-array ultrasound transducer
  - Sector transducers allow sampling of deep structures
  - Linear-array transducers provide better resolution of superficial structures.
  - ± Biopsy guide: easiest method, but angle of needle insertion is fixed.
  - Sedation often not needed for fine-needle aspirate (FNA)
  - Occasionally, IV or gas anesthesia required (e.g., anxious animal, small structure in close proximity to large vessel)

ANTICIPATED TIME

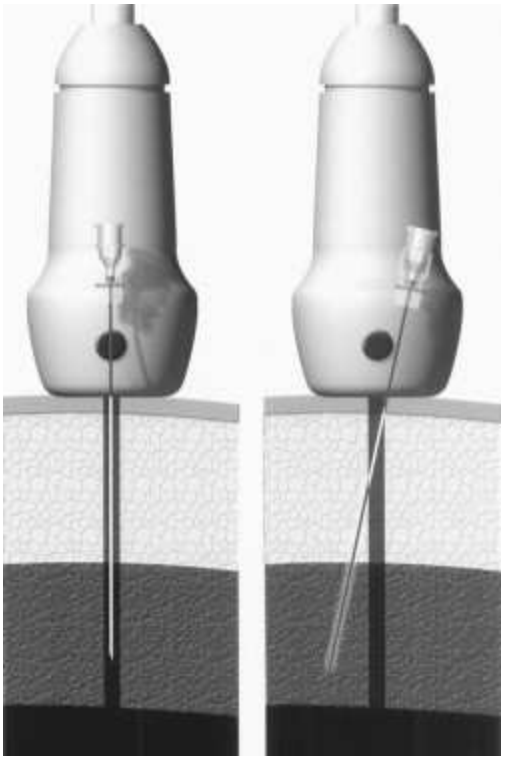
About 5-10 minutes

PREPARATION: IMPORTANT CHECKPOINTS

- Perform coagulation profile, platelet count, and arterial blood pressure (BP) measurement if animal is at an increased risk of bleeding.
- Determine if sedation is required; place IV catheter if needed.
- Ensure proper animal restraint.

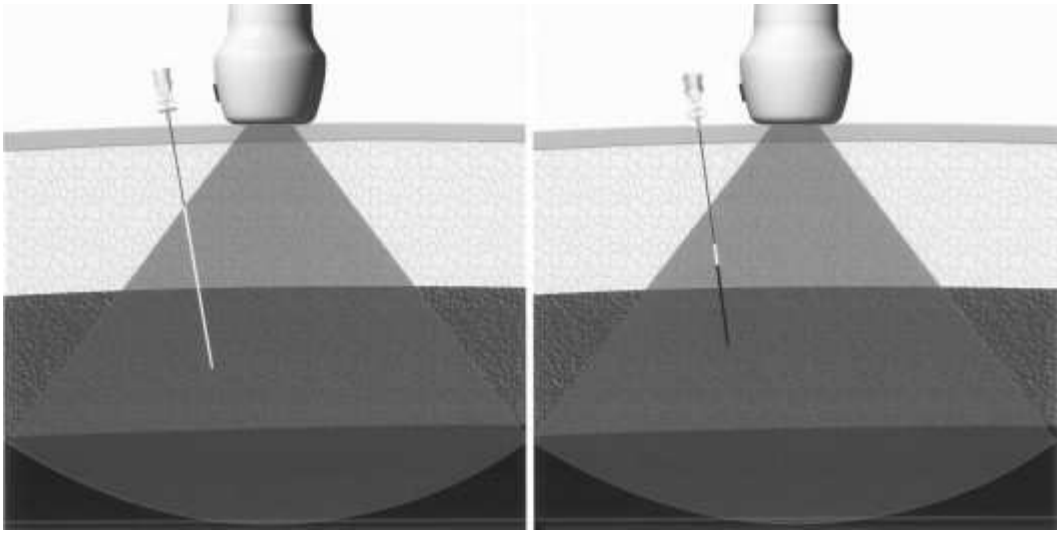
POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- To decrease hemodilution, avoid the suction method in sampling vascular organs (e.g., spleen).
- Identify and avoid large vessels within the organ being sampled or those adjacent to the structure (e.g., aorta adjacent to lymph node).
- Hemorrhage is uncommon if 22- or 25-gauge needle is used and the movement of the needle through the entire procedure is one-dimensional (in and out only, with no side-to-side motion).



FINE-NEEDLE ASPIRATE, ULTRASOUNDGUIDED Importance of correct alignment between needle and ultrasound probe. *Left*, Correct alignment is present, and full extent of needle is seen. *Right*, Needle is not aligned with ultrasound beam, and only proximal portion of needle is seen. Here, trauma to deeper tissues is possible because location of needle tip is unknown.

(Reprinted from Fife WD: Abdominal ultrasound: aspirations and biopsies. In Ettinger SJ, Feldman EC, editors: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders, pp 271-275.)



FINE-NEEDLE ASPIRATE, ULTRASOUND-GUIDED Views as seen on monitor of ultrasound machine, perpendicular to other figure. *Left*, Correct alignment produces complete visualization of needle. *Right*, Probe/needle malalignment underrepresents depth of needle.

- Do not move the needle side to side within an organ, because this will cause tissue trauma.
- If redirecting needle orientation, withdraw needle tip to subcutis and then reinsert. Redirecting with needle fully advanced is ineffective (position changes little or not at all) and dangerous (shearing of tissue with needle tip).
- Cells may dry and clot in the needle very quickly. Therefore, when the needle is withdrawn, the expulsion of needle contents onto a microscope slide and the slide smearing technique should all be completed within seconds.
- Avoid penetrating bowel lumen, especially with larger gauge needles, because of risk of peritonitis.
- Sample the left aspect of the liver when possible to avoid the gallbladder and hilar vessels on the right. If the liver is small or cranially located, consider an intercostal approach.
- With renal aspirates, sample the caudal cortex of the kidney to avoid the medulla and hilar vessels.

- In cases of bilateral renal abnormalities, the left kidney should be sampled owing to its more caudal location.
- Do not pass through an organ other than the one being aspirated.
- Avoid administering drugs that cause splenomegaly or panting (e.g., phenothiazines, some opiates).
- If aspirating an adrenal gland mass, be aware of possible BP alterations and severe hemorrhage in the case of pheochromocytoma.

PROCEDURE

- Restrain the animal in dorsal or lateral recumbency. A padded U-shaped trough can be used for the animal so that it is more comfortable when lying down (see p. 1236).
- Clip hair from the ventral abdomen.
- Thoroughly evaluate area of interest, characterize lesion, identify adjacent or internal vessels to be avoided, and determine least traumatic location and direction of needle placement.
- Prepare skin with surgical scrub.
- Obtain ultrasound image of area to be sampled.
- Ensure probe marker location on screen corresponds with desired needle course.
- Freehand technique: hold transducer in one hand, and insert needle with other.
- The suction technique is useful in aspirates of less vascular structures (e.g., lymph node) but often results in hemodilution when aspirating vascular organs like the spleen.
    - Without syringe suction:
        - Introduce a 22- or 25-gauge needle parallel to plane of ultrasound beam, visualizing needle as it is advanced.
        - Slowly fan transducer side to side to identify entire needle length to tip.
        - Advance and retract needle three to four times to fill needle shaft with tissue cells. If using a spinal needle, remove the stylet before beginning the advancing and retraction of the needle.
        - Withdraw needle from animal, and quickly attach a 6-mL syringe prefilled with 5 mL room air.
        - Expel contents onto microscopic slide(s) immediately, and lightly smear using standard blood smear technique.
    - With syringe suction:
        - Attach 6-mL syringe to 22- or 25-gauge needle.
        - Introduce needle parallel to plane of ultrasound beam, as already described.
        - Apply suction to syringe three to four times while gently advancing and retracting needle.
        - Disconnect syringe and withdraw needle from animal.
        - Retract plunger to fill syringe with air, and reconnect syringe to needle.
        - Expel contents onto microscopic slide(s) immediately, and lightly smear using standard blood smear technique.
- Multiple samples of each organ or lesion should be obtained.

POSTPROCEDURE

Scan to evaluate for hemorrhage (very uncommon with this procedure).

ALTERNATIVES AND THEIR RELATIVE MERITS

Tissue-core and surgical biopsy are more invasive but of greater diagnostic quality because of the ability to collect larger tissue samples.

SUGGESTED READING

Nyland TG, et al: Ultrasound-guided biopsy. In Nyland TG, Mattoon JS, editors: Small animal diagnostic ultrasound, ed 2, Philadelphia, 2002, WB Saunders, pp 30–48.

Penninck DG, Finn-Bodner ST: Updates in interventional ultrasonography. Vet Clin North Am Small Anim Pract 28:1017–1040, 1998.

AUTHOR: WENDY D. FIFE

Feeding Tube Placement: Percutaneous Endoscopic Jejunostomy (PEJ)

Client Education Sheet Available on Website

SYNONYMS

Percutaneous endoscopic-assisted placement of jejunostomy feeding tube; percutaneous gastrojejunostomy feeding tube

OVERVIEW AND GOALS

Placement of a jejunal feeding tube using endoscopic assistance, rather than laparotomy or laparoscopy, to provide postgastric enteral feeding to nutritionally deficient or debilitated animals. The jejunostomy tube is placed using a concurrent/existing percutaneous gastrostomy (PEG) tube. Use of percutaneous endoscopic jejunostomy (PEJ) is uncommon because of the relative cost and stocking of supplies, inexperience, and infrequency of needs that are not accommodated by surgical or laparoscopic-assisted placement of jejunal feeding tubes. Enteral feeding provides the advantage of improved overall metabolism and health of the intestinal tract. Enteral feeding reduces intestinal bacterial translocation, maintains glutamine synthesis, and improves and maintains gut immunologic barrier functions.

INDICATIONS

- Postgastric feeding is advised for animals with uncontrolled vomiting from any cause.
- Following gastric or biliary surgery
- Pancreatitis
- Disorders causing persistent gastroparesis (e.g., following intestinal surgery)
- Animals at increased risk of active or passive gastroesophageal reflux and aspiration (e.g., prolonged recumbency, pharyngeal dysfunction, laryngeal paralysis, altered mentation)

CONTRAINDICATIONS

- Unresolved peritonitis
- Anesthetic risks
- Large-volume peritoneal effusion

EQUIPMENT, ANESTHESIA

- General anesthesia is required, with endotracheal intubation.
- Postprocedural analgesia
- Mouth gag
- Sterile water-soluble lubricant for endoscope passage
- Supplies as needed to place percutaneous endoscopic gastrostomy (PEG) tube (see p. 1270)
- 2-0 monofilament suture material
- Iohexol as water-soluble radiographic contrast agent
- Flexible video or fiberoptic endoscope and ancillary equipment appropriate to size of animal (generally 7-9 mm diameter with 100 cm length is acceptable for most cases).
- Endoscopic snare or grasping forceps
- Vacuum source for endoscopic suction
- PEG tube that is 18-24 Fr in diameter, as a kit with PEJ or as a separate item (e.g., Pezzer mushroom-tip catheter)
- PEJ tube that is 6-12 Fr in diameter (e.g., Wilson-Cook Medical, Global Veterinary Products, Compat brand by Novartis) and 35-150 cm in length; PEJ kits with gastrostomy tubes are also available (e.g., Mila International Inc. Medical Instrumentation for Animals); variable diameters and lengths based on supplier and animal size; internally coated catheters have an internal lubricant that activates when flushed with sterile water; 1 mm = 3 Fr.
- Weighted PEJ tubes are less commonly used; they have a tungsten bulb at the tip that adds weight to help prevent migration of the tube back to the stomach; these are preferred by some endoscopists and not by others.
- A 0.021- to 0.037-mm (50-150 cm) flexible guide wire matched to selected PEJ feeding tube
- Fluoroscopy is preferred to be available, especially while staff is learning the technique. Flash (then saved) images on the preview monitor of digital radiographic equipment can help in identifying the location of the distal tip of the PEJ if fluoroscopy is not available.
- Elizabethan collar or other restraint to prevent patient's removal of PEJ or PEG tubes
- Orthopedic stockinette appropriate to size of animal to create a “sweaterlike” effect

ANTICIPATED TIME

About 40-80 minutes (including placement of PEG tube)

PREPARATION: IMPORTANT CHECKPOINTS

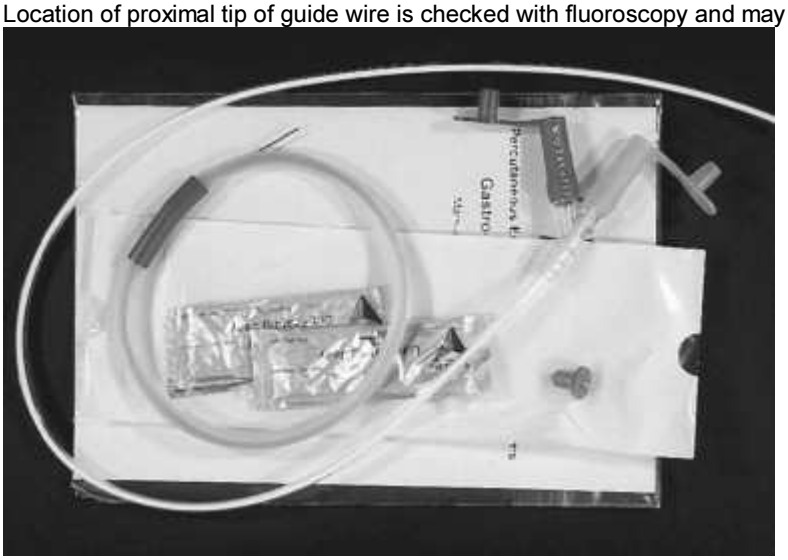
- Test or check integration of guide wire, PEG tube, and PEJ tube for compatibility of diameters and lengths.
- Plan for coordination of staff regarding anesthesia, endoscopy, and fluoroscopy/radiography.
- Discuss with client the potential that the PEJ tube may become occluded or may migrate back to stomach despite best efforts and cost of catheters.
- Check or estimate the fill volume of catheter prior to placement.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Stoma site infection
- Premature removal by animal of tube (teeth, rubbing on objects in environment)
- Peritonitis if adhesion of body wall to stomach breaks down
- Diarrhea induced by feeding enteral formula
- Reflux of enteral feeding product aborally
- PEJ tube migration back to the stomach and possible vomition of the tube aborally
- Complications occur with about the same frequency as with use of PEG tubes.

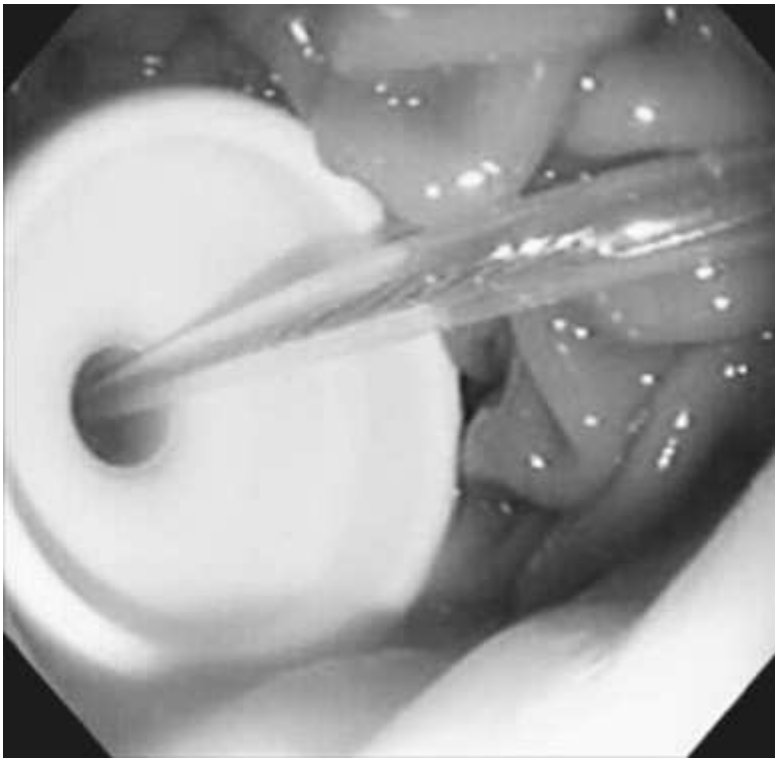
PROCEDURE

- Clip and prep left side of animal from approximately the eighth intercostal space (ICS) to just cranial to the stifle and from dorsal spinous process to ventral midline.
- General anesthesia, with endotracheal intubation
- Animal is positioned in right lateral recumbency.
- A PEG tube is placed (see p. 1270).
- Endoscope is passed to stomach from oral cavity.
- A snare or retrieval basket is passed via the gastrostomy (PEG) tube to the stomach.
- Endoscope is then maneuvered through the snare or basket.
- Pylorus is then visualized, and the endoscope is passed through to the mid-duodenum.
- Guide wire is passed via the operating channel of endoscope and continued forward blindly along the lumen of the small intestine until it is estimated that the tip is located in the proximal third of the jejunum.
- Guide wire is fed through the endoscope while the endoscope is slowly withdrawn from the body; the position of the guidewire in the body remains the same.
- Guide wire should then be in the center of the snare or basket. This is tightened and withdrawn via the gastrostomy (PEG) tube to the exterior so as to pull guide wire through the gastrostomy (PEG) tube (proximal tip is in jejunum, and distal end extends out the gastrostomy tube).
- Location of proximal tip of guide wire is checked with fluoroscopy and may be adjusted in position.



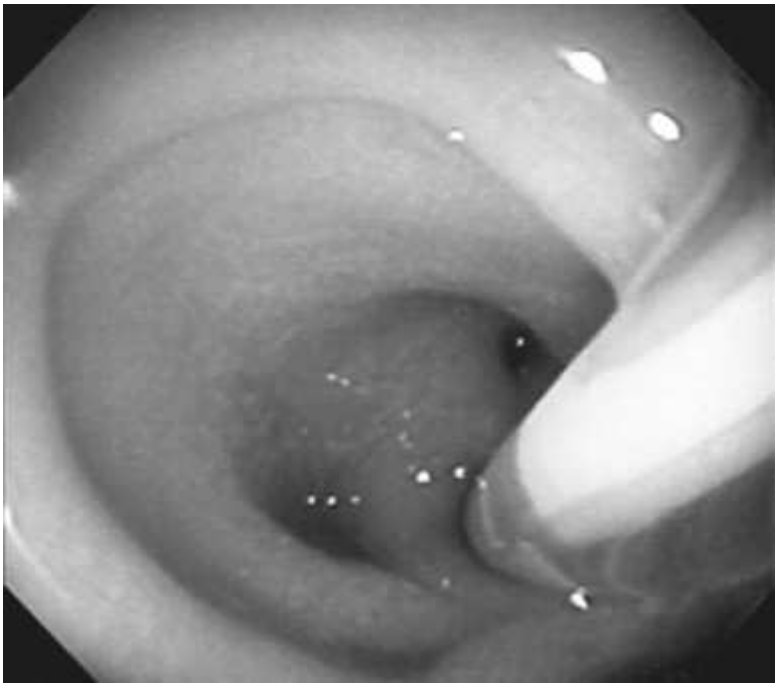
FEEDING TUBE PLACEMENT: PERCUTANEOUS ENDOSCOPIC JEJUNOSTOMY (PEJ) Endoscopic image. Luminal view of stomach, showing gastrostomy/PEG tube with jejunostomy/PEJ tube inserted.

(Courtesy Dr. Al Jergens.)



FEEDING TUBE PLACEMENT: PERCUTANEOUS ENDOSCOPIC JEJUNOSTOMY (PEJ) Gastrojejunostomy combined kit from Wilson-Cook.

(Courtesy Dr. Al Jergens.)



FEEDING TUBE PLACEMENT: PERCUTANEOUS ENDOSCOPIC JEJUNOSTOMY (PEJ) Endoscopic image. Luminal view of duodenum, showing jejunostomy/PEJ tube over the guide wire (guidewire not seen).

(Courtesy Dr. Al Jergens.)

- PEJ tube is flushed with copious amounts of water to activate lubricant.
- PEJ tube is passed over the guide wire until it extends a length adequate for the proximal tip to be in the proximal third of the jejunum.
- PEJ tube location is assessed with fluoroscopy or radiography with test infusion of a few milliliters of water-soluble contrast agent (iohexol); the PEJ tube may be repositioned as needed.

- Guide wire is removed slowly while the PEJ is held stable.
- PEJ tube is secured to animal's body or to the PEG tube as it exits the left side of the abdomen.

POSTPROCEDURE

- Place Elizabethan collar on the animal to prevent removal of both PEG and PEJ tubes.
- To protect tubes, place and adjust orthopedic stockinette “sweater” over animal's body, including two holes cut for the forelegs; this should be “comfortable” to reduce stimulus for premature removal by animal.
- Monitor recovery from anesthesia.
- Instill the volume of sterile water needed to fill tube every 2 hours to keep tube patent.
- Begin enteral nutrition via the PEJ tube 12 hours following PEG tube placement.
- Monitor stoma site; expect mild inflammation and swelling; discharge from stoma may appear serous or mildly purulent, but cytologic analysis should reveal no bacteria; cleanse stoma gently with sterile saline and gauze squares as needed; surgical scrub can be used if needed but should be rinsed off completely.
- PEJ tube may be used as long as it remains functional and needed; often used for days to many weeks.
- Enteral feedings, either as boluses or constant drip infusion, are started with goal of one-third of daily caloric requirements being given the first day, two-thirds the second day, and full feedings by the third day.
- After removal of the PEJ tube, the remaining gastrostomy (PEG) tube may be used for nutrition if appropriate.
- The gastrostomy tube is left in place a minimum of 10 days to ensure adequate adhesion of stomach to the abdominal wall.
- The gastrostomy tube is removed by gentle progressive traction in a caudal direction that is also directed slightly away from the body; the remaining stoma will often close over within 4 to 8 hours after tube is removed.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Nasojejunostomy tubes are placed with endoscopic or fluoroscopic assistance. These have the advantage of not requiring a gastrostomy tube. However, they have problems with nasal irritation, short duration of use (often a few days), difficulty in placing the tip distally enough in the jejunum, and problems with postprocedural retrograde migration back to the stomach or being vomited aborally.
- Laparoscopic-assisted jejunostomy tubes can be placed at the end of a diagnostic or therapeutic laparoscopy. This technique involves exteriorizing a loop of jejunum, which then is held with four stay sutures while a pursestring suture is placed in the antimesenteric side. The jejunostomy tube is placed through an incision in the center of the purse-string suture. This suture is tightened when the tube has been placed successfully (using fluoroscopy to confirm location and aboral direction). A box suture technique is used for creating an adhesion of the intestine to the body wall that secures the safe position of the jejunostomy tube. Problems can involve aboral migration or confusion in the direction for placement of the tube. Other complications include those that would be possible with surgically placed jejunostomy tubes.

AUTHOR: MARK E. HITT

Gastroscopy/Duodenoscopy

SYNONYM

Upper gastrointestinal (GI) endoscopy

OVERVIEW AND GOALS

Minimally invasive endoscopic method of visualizing the mucosal surface of the stomach and proximal duodenum. This procedure offers the possibility of retrieving foreign bodies, performing mucosal biopsies, and placing a gastrostomy or jejunostomy tube.

INDICATIONS

- Chronic or acute vomiting
- Gastric foreign body
- Suspicion of gastric or duodenal ulcer
- Suspicion of gastric or duodenal neoplasia
- Suspicion of inflammatory bowel disease
- Placement of percutaneous endoscopic gastrostomy (PEG) tube for enteral feeding

CONTRAINDICATIONS

- Food in stomach
- Large and/or sharp foreign body

EQUIPMENT, ANESTHESIA

- General anesthesia required
- Endotracheal intubation required
- Mouth gag/speculum
- Flexible fiberoptic or video endoscope with monocular or video display:
    - Diameter of 9-10 mm and length of 1000-1250 mm are sufficient for both gastroscopy and duodenoscopy of most medium- to large-sized dogs and for only gastroscopy of cats and small dogs.
    - A diameter of 5.5 mm or less is usually necessary to enter the duodenum of cats or small dogs. A length of 900-1000 mm is usually sufficient for cats and small dogs.
- Vacuum source for endoscopic suction
- Endoscopic biopsy forceps
- Endoscopic foreign body retrieval forceps, snares, or baskets
- Biopsy jar with 10% buffered formalin

ANTICIPATED TIME

- Usually 60-90 minutes anesthesia time (30-60 minutes endoscopy time)
- Complex foreign body retrieval may take >60 minutes.

PREPARATION: IMPORTANT CHECKPOINTS

- Animal should have fasted for 12 hours prior to the procedure if possible.
- Simpler, less invasive diagnostic procedures are performed prior to endoscopy (e.g., CBC, serum biochemistry profile, urinalysis, abdominal radiographs in all cases, abdominal ultrasound, fecal flotation, adrenocorticotropic hormone stimulation test, and others as indicated by the specific features of each case).

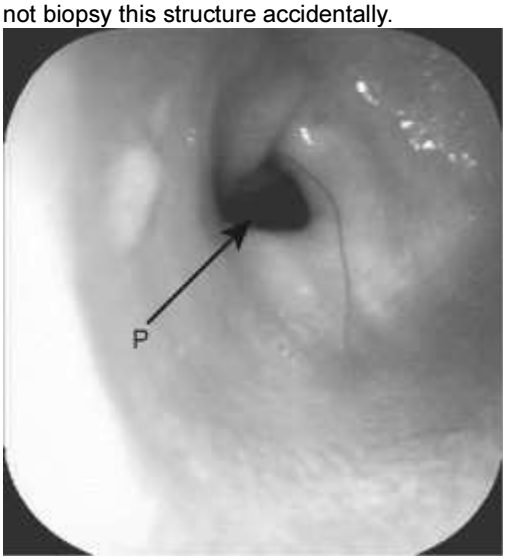
POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Narcotic analgesics (e.g., morphine, meperidine, and butorphanol) increase motility of the pyloric antrum and may make passage of the endoscope into the duodenum difficult.
- Gastric or duodenal rupture:

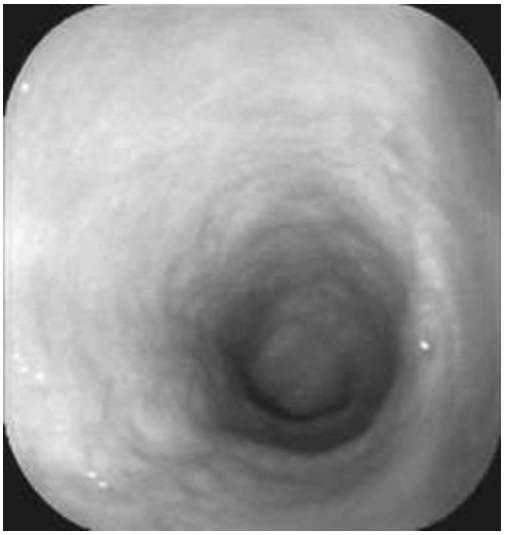
    - Usually only occurs when the wall is compromised by a deep ulcer or neoplasia.
- Overinsufflation, usually of the stomach, may cause potentially severe bradycardia due to abdominal compartment syndrome (see p. 4) and creates the risk of gastric rupture.
- Prior administration of barium may make visualization difficult, and aspirating it with suction through the endoscope may be damaging to the suction channel of the endoscope.
- Failure to recognize the major duodenal papilla as a normal structure (major and minor duodenal papillae in cats) could lead to inadvertent biopsy, which in turn presents the potential for fibrosis and obstruction of the pancreatic and common bile ducts.

PROCEDURE

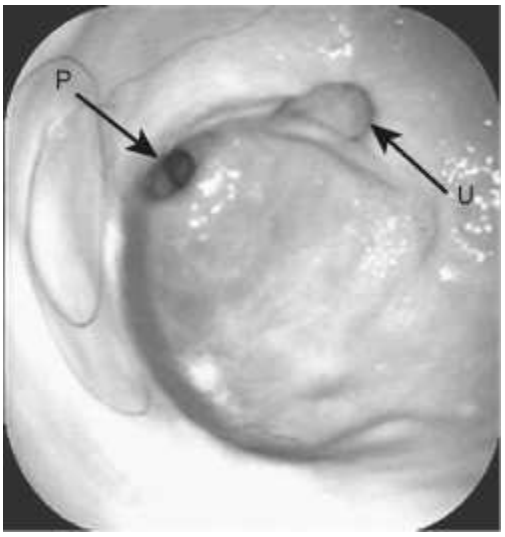
- Induce general anesthesia.
- Position the animal in left lateral recumbency. This is the position in which the pylorus is most easily entered.
- Place a mouth gag to keep the jaws open.
- Lubricate the endoscope with water-based lubricating jelly.
- Introduce the endoscope into the mouth, and feed it gently through the upper esophageal sphincter.
- Examine the esophageal mucosa as the scope is advanced down to the lower esophageal sphincter.
- Insufflate the esophagus with enough air to prevent the walls from collapsing on the scope and reducing visibility. An assistant may be required to gently occlude the upper esophagus by gently squeezing the cervical region externally, immediately cranial to the larynx, to prevent insufflated air from escaping out of the mouth. This will not be necessary once the tip of the endoscope is in the stomach.
- Whenever the scope is traveling down a tubular structure such as the esophagus or duodenum, it is important to keep repositioning the scope so the lumen of the tube is kept in the center of the screen. This maximizes visibility and minimizes trauma to the gut wall.
- Thread the scope through the lower esophageal sphincter by keeping the opening to the stomach in the center of the screen/view piece while gently advancing the scope.
- Once the distal end of the endoscope is in the stomach, insufflate the stomach with air to separate the walls and improve visibility. Insufflate until the rugal folds of the stomach are less prominent but still present. If the rugal folds are completely flattened, the stomach is so inflated that there is risk of compromising respiration or rupturing the stomach.
- If duodenoscopy is to be performed, it is best to proceed directly to the pylorus while it still may be relaxed. Prolonged insufflation or other activity in the stomach stimulates pyloric tone and motility, making threading the scope through the pylorus more difficult.
- Advancing the scope through the pylorus is usually the most difficult part of this procedure. The tone and degree of patency of the pylorus can be quite variable.
- If it is difficult to advance the scope to the opening of the pylorus (i.e., the scope is fed into the animal but advances no closer to the pylorus), suction some air out of the stomach—it may have been overinflated. This is common in large-breed dogs.
- If the pylorus is open, immediately advance the scope into the duodenum. If the pylorus is closed, maintain the opening to the pylorus in the middle of the screen while gently advancing the scope. If resistance is encountered, do not force the scope. Sometimes insufflating some air at the opening of the pylorus will stimulate it to open.
- If the pylorus is impossible to thread, try feeding a closed pair of endoscopic biopsy forceps through the pylorus. Use the threaded forceps as a stylet to feed the scope into the duodenum. If the scope still will not pass through the pylorus, consider using a smaller scope.
- Once the distal end of the endoscope is in the duodenum, advance the scope down to the limit of its length.
- Identify, if possible, the major duodenal papilla where the pancreatic duct and common bile duct empty into the duodenum. Do not biopsy this structure accidentally.



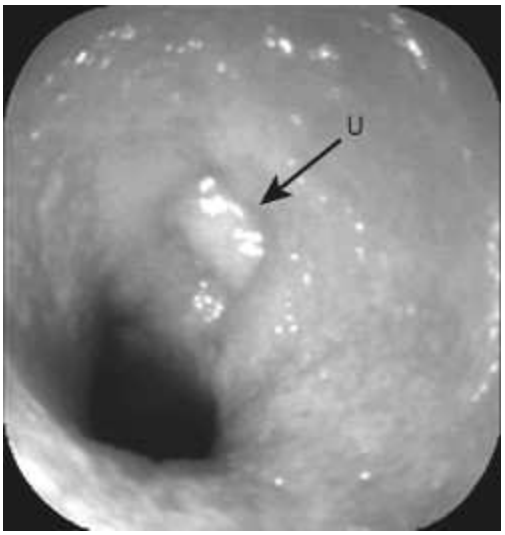
GASTROSCOPY/DUODENOSCOPY Endoscopic view of the normal pylorus (P).



GASTROSCOPY/DUODENOSCOPY Endoscopic view of the normal duodenum.



GASTROSCOPY/DUODENOSCOPY Endoscopic view of the pylorus (P) and a large craterlike gastric ulcer (U).



GASTROSCOPY/DUODENOSCOPY Endoscopic view of a duodenal ulcer (U).

- Examine and identify any irregularities to the duodenal mucosa and any foreign bodies.

- Obtain multiple (6-12) mucosal biopsies using biopsy forceps. Store these biopsies in 10% formalin. Any brushings or fluid samples for cytologic analysis or culture may be obtained now as well.
- Slowly withdraw the endoscope from the duodenum while obtaining mucosal biopsies and deflating the duodenum.
- Once the tip of the endoscope is back in the stomach, examine the entire stomach, including obtaining a retroflexed view to visualize the gastric cardia. This maneuver requires maximal flexion of the endoscope tip such that the endoscope itself is seen emerging through the cardia. Identify any mucosal irregularities, masses, ulcers, or foreign bodies.
- Obtain multiple (6-12) biopsies of any irregular structures and normal mucosa. Be cautious about taking a biopsy of deep gastric ulcers, because this could cause perforation of the stomach wall.
- Deflate the stomach before withdrawing the endoscope into the esophagus.
- Deflate the esophagus while slowly continuing to withdraw the endoscope from the esophagus. Suction any fluid in the esophagus, because it may be refluxed gastric acid that may ulcerate the esophagus if left behind.
- Take the scope out of the animal, remove the mouth gag, and recover the animal from anesthesia.

POSTPROCEDURE

- This procedure is minimally invasive, and the animal rarely requires analgesics after the endoscopy.
- Anesthetic recovery is usually routine.
- Clean the endoscope (internal and external surfaces) immediately before secretions and fluid have dried and are difficult to remove.

ALTERNATIVES AND THEIR RELATIVE MERITS

Exploratory laparotomy:

- Large, full-thickness biopsies may be taken from anywhere in the GI tract.
- All the abdominal organs may be visualized and biopsied if needed.
- Virtually any foreign body may be retrieved anywhere in the stomach or intestine.
- Serosal surfaces and wall thickness can be evaluated.
- Gastrostomy tube or jejunostomy tube may be placed.
- Tumors or abnormal tissue may be surgically excised.
- More invasive
- May be more costly
- May be more time consuming
- More painful for the animal/longer recovery time
- Greater risk of peritonitis and incisional dehiscence
- Unable to visualize the esophagus
- Unable to visualize the mucosal surface of stomach or intestines unless a gastrotomy or an enterotomy is performed

AUTHOR: PETER FOLEY

Gastric Intubation, Gavage, Lavage

SYNONYMS

Gastric decompression, orogastric feeding, orogastric intubation

OVERVIEW AND GOAL

Passage of a hollow tube into the mouth and through the oropharynx into the stomach to facilitate decompression of gas, removal of stomach contents (lavage), or administration of large volumes of liquid, food, or medication (gavage)

INDICATIONS

- Gastric intubation:
  - Preoperative stabilization of gastric dilatation/volvulus (GDV); allows evacuation of gas and fluid, resulting in an improved hemodynamic state
  - Relief of discomfort associated with gaseous dilatation (without torsion) of the stomach
- Gavage:
  - Administration of large volumes of liquid medication, including:
    - Activated charcoal after toxin ingestion
    - Barium for gastrointestinal (GI) contrast radiography
    - Hyperosmotic laxative agent prior to colonoscopy
  - Administration of formula to neonatal animals that are not nursing on their own
- Lavage:
  - Preoperative stabilization of GDV. Removal of stomach contents may help decrease the speed of gas reaccumulation while the animal is being prepared for surgery, thus slowing or preventing cardiovascular deterioration.
  - Removal of stomach contents with suspected intoxications

Note: Gastric lavage may not be indicated in all cases of toxin ingestion. Substance ingested, consistency, time since ingestion, and animal status will influence whether gastric lavage is appropriate.

CONTRAINDICATIONS

- Esophageal disease that could lead to tube-induced trauma or perforation. Conditions of concern include esophageal stricture, neoplasia, ulceration, megaesophagus, and recent esophageal surgery.
- Gastric disease that could lead to tube-induced trauma or perforation. Conditions of concern include neoplasia, ulceration, and recent gastric surgery.
- Any swallowing disorder (megaesophagus, esophageal motility disorder, etc.), pharyngeal disorder, or laryngeal disorder (paralysis, previous tie-back surgery, etc.) that could predispose a nonendotracheally intubated animal to aspiration.
- If even one of these conditions is present, the risk of the procedure versus its benefits must be considered (and will vary from case to case) before deciding whether to perform the procedure.

EQUIPMENT, ANESTHESIA

Gastric intubation:

- Two assistants (minimum)
- Flexible plastic tubing of various length and diameter. The distal end must be smooth and atraumatic; smoothing may be achieved by brief heating of the end of the tube over a flame, cooling, and trimming edges with a scalpel blade. One to three side holes may facilitate evacuation of stomach contents by minimizing obstruction of a single distal hole with gastric mucosa or ingesta.
- A roll of clinic-type white cloth tape
- Water-soluble lubrication jelly
- Mouth gag/speculum

If gastric lavage, all of the above, plus:

- Funnel or stomach pump
- Container (e.g., bucket) to collect stomach contents and lavage fluid

- Lavage fluid: usually warm (body temperature) water

ANTICIPATED TIME

Dependent on cooperation of animal; additional time may be needed for sedation or general anesthesia:

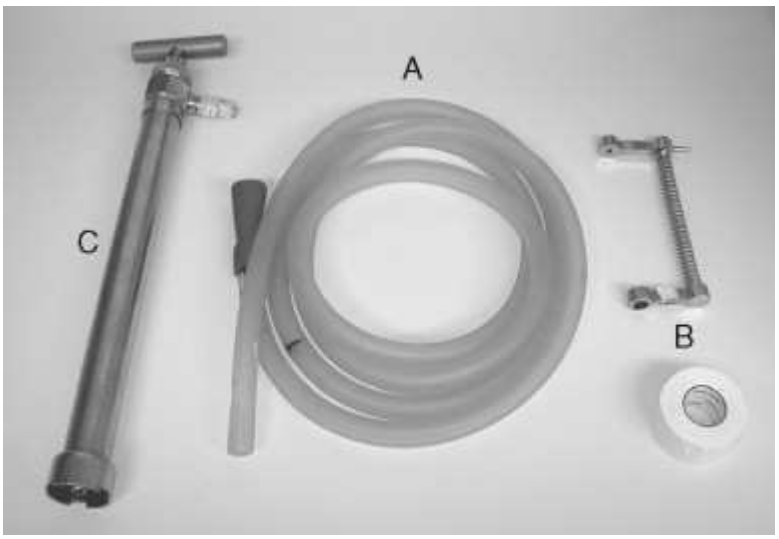
- Gastric intubation: 2-5 minutes
- Gavage: 3-10 minutes
- Lavage: 10-60 minutes

PREPARATION: IMPORTANT CHECKPOINTS

- Ensure that adequate manual or chemical restraint for the procedure is planned. Personal preference and animal stability may dictate the degree of sedation or anesthesia chosen. Note: Some clinicians prefer to ensure a patent and protected airway to minimize the potential for aspiration pneumonia through the use of general anesthesia and a cuffed endotracheal (ET) tube when gastric lavage is performed.
- Maximize cardiovascular stability prior to the procedure.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Inadvertent passage of the orogastric tube into the trachea can result in mild to severe complications:
  - Tracheal irritation leading to transient coughing or mucosal bleeding is possible.
  - Tracheal or bronchial placement of the gastric tube can result in airway obstruction until the tube is repositioned.
  - Tracheal or bronchial tearing can result in pneumomediastinum, pneumothorax, and death.
  - Tracheal or bronchial administration of gavage or lavage fluids can result in severe aspiration pneumonia and death.
  - See procedure (as explained in following paragraphs) for avoidance of this complication.
- Oral, pharyngeal, laryngeal, esophageal, or gastric trauma can result if excessive force is used for passing the gastric tube. Full-thickness tearing is possible, especially with a preexisting underlying disease.
- Inability to pass the tube into the stomach may be due to the choice of a tube with a diameter that is too large, esophageal obstruction (foreign body, stricture, neoplasia), torsion of the stomach, or excessive lower esophageal sphincter (LES) tone. Discontinuation of metoclopramide prior to elective gastric intubation is recommended to minimize LES tone.
- Inadequate sedation of an uncooperative animal will lead to longer procedure times and increased risk of injury to the animal and veterinary staff.
- Inability to effectively remove gastric contents through lavage may be related to excessive size or adhesive nature of gastric contents, gastric compartmentalization, or other factors.
- Regurgitation during lavage, gastric overfilling, or esophageal administration of large volumes of lavage fluid can result in aspiration if a cuffed ET tube is not in place.
- Excessive tube advancement can cause occlusion of the distal end of the tube against stomach mucosa. Palpation of the tube pressing against the stomach wall may indicate a need for partial retraction.



GASTRIC INTUBATION, GAVAGE, LAVAGE Materials and equipment used for gastric intubation and lavage. **A**, Orogastric tube. **B**, Metal speculum or roll of tape to be used as a mouth gag. **C**, Stomach pump for lavage.

PROCEDURE

- Manual restraint, sedation, or general anesthesia as indicated
- Position animal in sternal recumbency. If animal is uncomfortable, alternate positions may be better tolerated (sitting, standing, lateral, etc.).
    - Placement of the animal on an elevated surface will allow gravity-assisted efflux of stomach contents and lavage fluid once the tube is in place.
- Choose appropriate tube diameter for esophageal size and procedure planned. Example: A tube with an outer diameter of 1.5 inches (3.5 cm) is appropriate for most medium-sized dogs (45 lb [20 kg]). A larger tube size may be necessary for effective lavage versus gas decompression.
- Measure the length of tube necessary to pass from the nose to the xiphoid. Mark this distance on the tube with a piece of tape or nontoxic marker.
- Place a mouth gag (speculum) to prevent the animal from chewing on the tube.
    - A roll of 2-inch (5 cm)-wide clinic-type white cloth tape works well in many animals. The tube will pass through the hole in the tape roll. Place tape roll on top of the tongue and behind all 4 canine teeth.
    - Have an assistant hold the mouth closed around the mouth gag.
    - Avoid using a gag that will damage the teeth.
- Generously lubricate the distal portion of the stomach tube.
- Pass the tube into the mouth through the mouth gag.
- Advance the tube through the oropharynx and into the esophagus. Steps to promote and confirm esophageal and subsequent gastric intubation include:
    - Choice of a larger gastric tube size than appropriate ET tube size will lessen the possibility of tracheal intubation.
    - A neutral or very slightly ventro-flexed position of the head (i.e., avoiding extension of the neck) will reduce the opportunity for the tube to pass into the trachea.
    - In the awake animal, allow the swallowing reflex to facilitate tube passage through the pharynx.
    - If substantial coughing occurs, reassess placement, because the orogastric tube may be in the trachea.
    - Palpate the tube in the esophagus (separate from the tracheal rings).
    - Direct visualization of tube passage through the esophagus along the left side of the neck (lean, short-haired patients).
    - Small amounts of air infused into the stomach tube result in a gurgling sound when the stomach is ausculted.
    - Mild suction applied to the tube should reveal negative pressure, stomach contents, or odorous gastric gas with proper gastric intubation, whereas air flow and absence of negative pressure suggest that the tube is in the airways.
- Pass the tube up to the marked point that indicates where the tube should have entered the stomach. Relief of gas pressure can be assessed through auditory, tactile, and olfactory observations.
    - Certain conditions such as GDV may inhibit tube passage into the stomach. Choice of a smaller tube, gentle rotational pressure on the tube, repositioning of the animal, or percutaneous needle gastric decompression may facilitate passage.

DECOMPRESSION:

- Place the external portion of the stomach tube lower than the animal's head and body to allow gravity-assisted evacuation of stomach contents.
- Gentle massage of the stomach through the body wall may help to increase efflux.

GAVAGE:

- Using syringe, funnel, or stomach pump, instill the desired medication through the tube into the stomach.
- With administration of viscous materials, dilution with water may facilitate passage through the tube.
- Coughing, dyspnea, or cyanosis at any point suggests the tube may be in the respiratory tree. The procedure is terminated immediately, with kinking of the proximal tube (to avoid leakage of tube contents during withdrawal), tube removal, and animal care (physical examination, thoracic radiography as warranted, etc.).

LAVAGE:

- Using a funnel or stomach pump, instill approximately 5-10 mL/kg of lukewarm (body temperature) water into the tube.
- Acute onset of coughing, dyspnea, or cyanosis warrants immediate termination, as already described.
- Hold the tube higher than the animal's head to prevent efflux of the lavage fluid until desired.
- Gently massage the stomach to facilitate mixing of the stomach contents with the lavage fluid.
- Lower the stomach tube below the level of the head to allow the lavage fluid to efflux. Gentle manipulation of the tube forward or backward 1-3 cm may improve efflux.
- If the tube obstructs with stomach contents, flushing or manual breakdown may relieve the obstruction. If this is unsuccessful, the tube should be removed and the entire process repeated.
- Repeat lavage administration and efflux until the efflux is clear and the stomach contents have been removed.

REMOVAL:

- Kink the tube during removal to prevent laryngeal/pharyngeal contamination with liquid remaining in the tube lumen.
- Remove the mouth gag.

POSTPROCEDURE

- Monitor recovery from sedation/anesthesia.
- Supportive care as indicated for the condition.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Nasoesophageal/nasogastric intubation:
  - May be less stressful to the animal than orogastric intubation
  - Tube can be left in place for repeated aspirations/instillations.
  - Small tube diameter prevents administration of viscous substances and effective lavage. Withdrawal of large volumes of gastric contents is not possible.
- Percutaneous needle decompression/gastrocentesis:
  - May be easier to perform in a fractious animal
  - Allows gastric gas decompression when degree of torsion or another esophageal obstruction prevents tube passage
  - Potential for splenic puncture/laceration, gastric vessel or wall laceration, or other abdominal trauma
  - Ineffective for removing ingesta or large volumes of gastric contents
- Manual oral administration of medications or formula (pediatric animals):
  - Decreased chance of complications associated with orogastric intubation and gavage
  - Administration of large volumes to an uncooperative animal is labor intensive.
  - Risk of aspiration with force feeding
- Induced emesis to clear gastric contents:
  - Often more effective at removing stomach contents than lavage
  - Risk of aspiration, especially with decreased mentation or laryngeal/pharyngeal dysfunction
  - Not indicated with caustic ingestions
  - Not effective in all animals

AUTHOR: LILLIAN I. GOOD

Holter/Cardiac Event Monitoring

Video Available on Website

SYNONYMS

Ambulatory electrocardiography, cardiac telemetry

OVERVIEW AND GOALS

Goal: to assess the cardiac rhythm during an extended period of time. The monitor may record the cardiac rhythm continuously for 24-48 hours (Holter monitor) or only when triggered to record over a period of days to weeks (event monitor). With both devices, the pet is able to be in their home environment, and the owner is able to observe pet behavior.

INDICATIONS

- Syncope
- Episodic clinical signs of uncertain type but that might represent syncope
- Screening of breeding or at risk animals (boxers, Dobermans) for latent arrhythmia (arrhythmia not causing overt clinical signs)
- Monitoring of antiarrhythmic drug effects (Holter monitor only)

CONTRAINDICATIONS

- Animal thought to be likely to damage a portable monitor
- Animal that will be bathed or will be swimming
- Animal too small to carry monitor (monitoring may still take place, but animal stays mainly in pet carrier or cage for recording period)

EQUIPMENT, ANESTHESIA

- Clippers for hair
- Isopropyl alcohol
- Gauze squares or cotton balls
- Cardiac electrode adhesive patches (cutaneous)
- Ultrasound gel
- Bandage material: roll gauze, Esmarch-type bandage material (e.g., Vetrap), stretch adhesive-type cotton bandage (e.g., Elastikon, Elastoplast), 2-inch white medical tape, +/− cast padding
- Holter or event monitor, including wires to connect to animal, new batteries, and a blank digital card (Holter only), +/− Holter vest
- Interpretation system and printer or access to such a system

Note: Monitors are expensive systems not routinely owned by general practices. They are available for rental from many sources, including www.labcorp.com, www.vetheart.com, www.idexx.com, and www.pdsheart.com. Additionally, many veterinary college cardiology services have mail-out Holter programs. Veterinary sources are preferred because knowledge of common veterinary diseases (boxer dogs with arrhythmogenic right ventricular cardiomyopathy [ARVC], miniature schnauzers with sick sinus syndrome [SSS]), normal veterinary findings (sinus arrhythmia, sinus tachycardia, sinus pauses during daytime rest), and common veterinary artifacts (purring, panting, shaking) are important parts of interpretation. The monitor itself is sent by courier to the hospital for placement on the animal. Instructions for placement and patient daily diaries are usually sent with the monitor. When the monitoring period is over, the monitor is mailed back or transmitted via transtelephonic signal (event monitor), and findings and interpretations are reported back. Some mail-out programs (mostly veterinary colleges) will also provide consultation on the case as part of the service, along with the written Holter/event monitor report.

ANTICIPATED TIME

- Installation: 10 minutes (event monitor) or 20 minutes (Holter)
- Monitoring period: 24 or 48 hours (Holter); 7-30 days (event monitor, longer if battery is replaced; weeks to many months for surgically implanted event monitors)

PREPARATION: IMPORTANT CHECKPOINTS

If the reason for using cardiac monitoring is the occurrence of sporadic clinical signs, a complete medical evaluation is usually indicated first:

- CBC, serum biochemistry panel, urinalysis: all cases, hypoglycemia, hypocalcemia
- Serum preprandial and postprandial bile acids (if consistent with case): hepatic encephalopathy
- Electrocardiogram (ECG; standard, in-hospital): all cases; the diagnosis may be apparent without the need for Holter or cardiac event monitoring.
- Thoracic radiographs, echocardiogram: all cases; assessment of cardiac structure, presence or absence of signs of congestive heart failure.

The monitor itself is checked for proper function before preparing to install it on the animal. These instructions are usually sent with the monitor. Discussion of care of the monitor with the owner: the monitor must stay dry, clean, intact, and undamaged. It is customary to have the owner leave a deposit in the sum of the replacement cost of the monitor before leaving the hospital with the machine.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Wet monitor: no swimming or bathing during the recording period. In the rain, a plastic bag should be placed over the monitor by the owner.
- Damaged/chewed monitor or wires: if the owner observes the animal damaging the monitor, an immediate recheck is warranted. The equipment can be examined, and subsequently the monitor may simply be more heavily wrapped to prevent damage, or the monitoring period may be terminated and the monitor removed.
- Unstuck electrode patches: prevented by cleaning and preparing the skin with isopropyl alcohol prior to patch placement. Although not routine, in very active patients, a small amount of tissue glue can be used to prevent this.
- Poor electrode patch contact with skin: prevented by cleaning and preparing the skin with isopropyl alcohol prior to patch placement and adding a small amount of ultrasound gel to the center of the patch before applying it to the skin (see following paragraphs).
- Monitoring period is inexplicably shorter than expected: prevented by using new batteries every time. In addition, for audiotape Holter monitors, it is important to be sure that the audiotape is not put into the monitor backwards.
- Poor triggering of event button (Holter) or record button (event monitor): prevented by carefully showing the owners how to trigger the event and record buttons on the monitor at the time of installation.
- Letting batteries run out, causing the captured events to be deleted (event monitor): clients need to return 1 day prior to expected end of battery life to replace battery.

PROCEDURE

HOLTER MONITOR:

- The animal's apex beat (heartbeat on the thorax) is palpated on both the right and left side of the chest. These will be the sites of electrode patch placement.
- The hair is clipped over these areas bilaterally, starting close to the sternum and working upwards ensuring a generous clip: There must be room for the electrode patches and a few centimeters of space separating them.
- The hairless skin is wiped clean with isopropyl alcohol–soaked gauze or cotton and allowed to dry before placing the electrodes. Technician Tip: The patient should be standing during the application of the Holter or event monitor to ensure proper positioning of the leads and for taping purposes.
- Some cardiologists prefer to attach the patches to the wires of the monitor prior to placing the patches on the animal, which is acceptable. The following method will describe the alternative approach.
- Patch preparation: a very small dollop of ultrasound gel is placed on the center of each electrode patch. For very active patients, a tiny amount of tissue glue (<1 full drop) can be placed on opposite ends of the adhesive band of each electrode patch.
- The patches are attached to the animal's skin: three patches on the left (starting just left of the sternum) and two patches on the right, leaving a half inch to an inch between each electrode. For taping ease, make sure electrode snaps are all facing in the same direction.
- Secure electrodes with either 1-inch or 2-inch white tape. Wrap the tape all the way around the chest, covering the electrodes on both sides but leaving snaps exposed.
- The leads are attached to the patches according to the color scheme usually shown in the inside of the Holter recorder or within the instructions. Pressing the wire attachments directly onto the patches on the thorax can be painful to the animal and is not recommended. Rather, after the patch is attached to the skin, the patch and underlying skin are elevated with the finger, and the electrode is pressed in using thumb and forefinger.
- Once the leads are connected, the wires are gathered on top of the spine, with the cable exiting to the right side (most Holter vests have the recorder pocket on the right side) and taped with 2-inch tape to the tape around the chest. The only wire now left exposed is the cable that attaches to the recording system. This should come out over the left side of the patient's spine.
- The monitor is attached to the animal as follows:

    - The monitor is held in a dorsal midline location and 2-inch tape is wrapped around the chest, incorporating the wires and monitor such that they emerge at the dorsal midline.
    - Gauze is then wrapped over the tape, around the thorax, as well as cranial to the shoulders in a figure-eight pattern, creating a “vest” of bandage material. The monitor is included in this layer.
    - Esmarch-type (e.g., Vetrap) is then wrapped over the gauze in a similar fashion.
    - Occasionally, elastic cotton adhesive (Elastikon-type) bandage material is used along the cranial and caudal borders of the Vetrap to secure to the animal.
    - The Vetrap and Elastikon can be replaced with the use of a dog backpack (available in stores that sell equipment for outdoor activities) or a purpose-made Holter vest for dogs (see online video for description of application).
    - The monitor's event button should still be visible and accessible to the owner, but connections onto the thorax, loops of wire, and the rest of the monitor itself should be protected.
- If a clock setting can be adjusted on the monitor, it is set to the current time. If not, the times at which the battery was installed and the recording began are noted as time zero in the medical record.
- Instruct the owner to keep a diary of the dog's activities, including the time of the observed activity. This includes both normal activities and events thought to be of clinical relevance. They also may press the event button on the monitor if an episode of apparent significance (e.g., collapse) occurs; it will be flagged on the Holter recording.

After the recording period (24-48 hours):

- The bandage material, monitor, wires, and electrode patches are removed without the use of scissors. The entire system is unwrapped to avoid cutting of the leads and wires. Removal of the skin patches may be facilitated with isopropyl alcohol.
- The cassette or digital card is analyzed or sent back for analysis along with the recorder.

EVENT MONITOR:

- Animal preparation and patch preparation are the same as for Holter monitors (as already described).
- There are only two wires/electrodes and therefore only two electrode patches. The right-sided electrode (white) is connected to the electrode patch on the right hemithorax, and the left-sided electrode is connected to the patch on the left, as described previously.
- The monitor is wrapped onto the animal also as described above. It is essential to leave the record button visible and accessible.
- When the animal has an episode, the owner must press the record button. Doing so captures the ECG preceding and following the time the button was pressed. Typically, the monitors are set to store the preceding 45-second time period of ECG and the subsequent 15 seconds, for a total of 1 minute of ECG spanning the clinical episode.
- Event monitors typically have a total memory of 5 minutes (i.e., five 1-minute episodes), though newer models can store 18 minutes or more.
- Newer models can also be programmed to automatically store events if the owner is not present to witness the event. For example, the monitor can be programmed to record any heart rate lower than 40 bpm or higher than 200 bpm.

After the recording period (anywhere from 6 days to 8 weeks!):

- The bandaging, wires, and monitor are removed. The monitor is either returned to the supplier or in some models, the stored information can be transmitted transtelephonically to the receiving station. If this is not done very soon after a recorded event, the batteries continue to be drained, and the information eventually will be lost.

ALTERNATIVES AND THEIR RELATIVE MERITS

- In-hospital ECG: less motion artifact but generally shorter and under artificial conditions
- Holter monitor instead of event monitor: for screening for occurrence of latent arrhythmia; for antiarrhythmic drug monitoring
- Event monitor instead of Holter monitor: for long-term (days) monitoring; for smaller animals; for transtelephonic transmission of recorded information
- Implantable event monitor (Reveal Plus [Medtronics]): Allows an extended period of monitoring (up to 10 months). Devices are very small (size of a cigarette lighter), and implantation is achieved with a subcutaneous pocket and local anesthesia in many cases. Devices are now donated to a veterinary cardiology group (CANPACERS) and are inexpensive. Access to a Medtronic programmer is necessary, however, to retrieve the stored information.

AUTHOR: AMARA ESTRADA

Hemodialysis

SYNONYMS

Blood purification, renal replacement therapy

OVERVIEW AND GOALS

Hemodialysis is a blood purification procedure used for correcting azotemia and normalizing the fluid, electrolyte, and acid-base imbalances resulting from kidney disease. In this procedure, the animal's anticoagulated blood circulates through an artificial kidney (hemodialyzer) and is exposed to an electrolyte solution (dialysate) across a semipermeable membrane. Metabolic waste products, exogenous toxins, and excess water are removed from the bloodstream by diffusion (concentration gradient) and convection (hydrostatic gradient) through the dialysis membrane. The combination of these two basic blood purification principles define different treatment modalities, including hemodialysis (HD: diffusion), hemofiltration (HF: convection), and hemodiafiltration (HDF: combined diffusion and convection).

In acute uremia, hemodialysis restores metabolic stability and is provided for a finite period of time to allow animals to use their potential of recovery from acute kidney injury. Hemodialysis itself has no direct effect on renal recovery. Although hemodialysis can also be used for indefinite renal replacement in end-stage chronic kidney disease, chronic kidney disease is rarely a true indication because of the associated costs and the limited availability.

INDICATIONS

- Acute uremia: worsening azotemia and clinical signs of uremia despite adequate conventional therapy, anuria, fluid overload, severe refractory hyperkalemia, severe azotemia (blood urea nitrogen [BUN] > 100 mg/dL, creatinine > 10 mg/dL)
- Chronic kidney disease: acute decompensation, preanesthetic stabilization, pretransplant conditioning, chronic renal replacement
- Miscellaneous: fluid overload, acute poisoning, drug overdose (small-molecular-weight toxins or drugs with minimal protein binding capacity)

CONTRAINDICATIONS

- Small animal size (<2 kg) (relative contraindication)
- Severe pulmonary or cerebral hemorrhage (due to required anticoagulation)
- Cardiovascular instability and hypovolemia (should be corrected first)

EQUIPMENT, ANESTHESIA

Sedation/anesthesia: required for the placement of a vascular access but not for the hemodialysis procedure itself.

- Vascular access: short-term, temporary large-bore double-lumen catheter (7 Fr for cats and small dogs; up to 14 Fr for larger dogs); long-term, permanent double-lumen or twin-lumen catheter with subcutaneous tunneling; typically placed surgically in the external jugular vein
- Hemodialysis delivery system (hemodialysis machine)
- Disposable extracorporeal circuit and dialyzer (artificial kidney)
- Water purification system: particulate filter, carbon sorbent, water softener, deionization bed, and reverse osmosis
- Dialysate concentrates
- Replacement fluids for convective therapies (HF, HDF): on-line preparation or specific hemofiltration replacement fluids
- Monitoring equipment: blood pressure (BP) monitor, coagulation timer (e.g., activated clotting time [ACT]), in-line blood volume and oxygen saturation monitor (e.g., Critline), electrocardiogram (ECG)
- Emergency cart: cardiopulmonary resuscitation drugs, oxygen, endotracheal tube
- Protamine (for excessive heparinization and active hemorrhage)
- Physical restraint (i.e., harness and table straps)

ANTICIPATED TIME

- Acute treatments: depending on the degree of azotemia and the selected therapeutic schedule, initial treatments can be provided as intermittent (treatment of 1-8 h) or continuous therapy; treatments are provided daily until normalization of azotemia; a schedule of three times a week is then maintained until recovery of renal function.
- Chronic treatments: 4-5 hours, three times a week
- Every treatment necessitates 2 additional hours for setup, animal preparation, and completion.

PREPARATION: IMPORTANT CHECKPOINTS

- Initial database for animal evaluation and formulation of the dialysis prescription: body weight, physical exam, body temperature, heart rate, BP, hematocrit/total solids, serum chemistry profile (especially BUN, creatinine, electrolytes, Tco2 [$Hco3^-$]), coagulation time (e.g., ACT)
- Adequacy of vascular access: should deliver between 15 and 50 mL/min in cats and very small dogs and 200-500 mL/min in large-breed dogs
- Preparation of the dialysis system: alarm testing, priming and refreshing of the extracorporeal circuit
- Dialysis prescription: type and size of dialyzer and extracorporeal circuit, total volume of blood to be processed, duration of the treatment, ultrafiltration (fluid removal), dialysate composition and profiling (Na^+, K^+, bicarbonate, additives), dialysate flow rate and temperature, anticoagulation (type, prime, infusion rate), type of fluid used to prime the extracorporeal circuit (crystalloid, colloid, blood), and special procedures (e.g., single-needle operation, bypass time)

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Intradialytic complications: hemorrhage, hypotension, vomiting (hypovolemia, dialyzer reaction), dialysis disequilibrium (osmotic fluid shift into the intracellular compartment due to rapid correction of the azotemia; cellular edema can progress to cerebral edema and death), malfunction of vascular access, clotting of the extracorporeal circulation.
- Interdialytic complications: hemorrhage, delayed dialysis disequilibrium, catheter complications (thrombosis, vascular stenosis, infection, chylothorax)
- Other complications: related to severe uremia (i.e., uremic pneumonitis, encephalopathy, ulcers), its treatment (i.e., fluid overload, drug toxicity), or to the underlying etiology precipitating the renal failure (i.e., sepsis, hypovolemic shock)

PROCEDURE

Establishment of vascular access:

- A temporary or permanent dialysis catheter is placed aseptically in the external jugular vein, with the tip reaching the cranial vena cava or the right atrium. Permanent catheter placement requires general anesthesia for venotomy and subcutaneous tunneling. Proper placement is confirmed by adequate blood flow and thoracic radiographs. The dialysis catheter is strictly dedicated to dialysis therapy, and it is never used for other indications. It is prepared and handled aseptically for each use.

Anticoagulation:

- Animals require anticoagulation for extracorporeal circulation, typically with unfractionated heparin (initial bolus of 50 U/kg IV, followed by a constant rate infusion [CRI] of 50 IU/kg/h). Target: doubling of coagulation time (e.g., ACT 160-190 seconds).
- Alternative protocols have been established for animals with hemorrhagic risk: regional anticoagulation with citrate, special filters with anticoagulant membrane, and other modifications to provide low-heparin or heparin-free therapy.

Initiation of dialysis therapy:

- The dialysis machine is equipped with appropriate disposables (extracorporeal circuit, hemodialyzer), and its function is tested according to the manufacturer's protocols. Animals are equipped with a harness and strapped to the table to loosely restrain their activity.
- The catheter is connected to the extracorporeal circuit using aseptic techniques, and the extension lines are secured to the animal's body to avoid accidental catheter removal. The extracorporeal circulation is established under close monitoring of cardiovascular and respiratory status, and it is progressively increased to reach the prescribed blood flow.

Monitoring:

- Cardiovascular parameters (heart rate, BP, venous oxygen saturation, relative blood volume change), general condition (mentation, pupillary light reflexes), anticoagulation (ACT), and machine function (extracorporeal blood flow, dialyzer clearance) are monitored and recorded every 15-30 minutes for the duration of the treatment.
- Initial dialysis treatments commonly necessitate additional monitoring, including ECG and pulse oximetry.

End of therapy:

- The blood circulating in the extracorporeal circuit is returned to the animal, and the disposables are discarded.
- The dialysis catheter is locked with a solution of concentrated heparin (50-500 U/mL in cats; 500-5000 U/mL in dogs) and protected with a neck bandage until the next treatment.

POSTPROCEDURE

- Monitor for hemorrhage and dialysis disequilibrium (neurologic changes).
- Because of the persistent effect of systemic heparinization: no needle stick (IV, IM, SQ), no placement or removal of IV or arterial catheters, and no procedure that could potentially cause mucosal or internal hemorrhages up to 12 hours following discontinuation of dialysis.
- Assessment of dialysis adequacy: treatment adequacy implies global control of all the individual problems of renal failure, of which dialysis only addresses a few directly. Nutrition; pain control; treatment of renal hyperparathyroidism, anemia, and metabolic acidosis; and further supportive care are critical for successful therapy and are not corrected by hemodialysis. Blood volume processed, time on dialysis, convective fluid removal (ultrafiltration), normalization of chemistry parameters, and reduction ratios of urea and creatinine are commonly used for describing treatments. However, dialytic adequacy is more accurately described using kinetic modeling of urea removal and generation. The insight gained into the nutritional adequacy of the animal renders this analysis central for the global assessment of animals undergoing dialysis.
- Maintenance of the dialysis equipment is critical for adequate operation and safety of the procedure: Before each treatment, dialysate is controlled for traces of residual chlorine; at the end of each treatment, the machine is rinsed with acid and bleach to remove bicarbonate and protein deposits, respectively. At the end of every dialysis day, the machine is disinfected with a chemical or heat cycle. A quantitative bacteriologic culture of the dialysate water is scheduled once a month and a chemical water analysis for trace elements once a year.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Continuous renal replacement therapy (CRRT): a slower but extended form of dialysis therapy with more gradual correction of hydration and metabolic imbalances; lower blood and dialysate flow rates imply fewer treatment interruptions and alarms and, potentially, a technically less demanding form of therapy. Safe treatment still requires a thorough understanding of renal pathophysiology and dialysis technology, especially when used for treating severely uremic animals. After initial correction of the azotemia, maintenance of uremic animals with CRRT is hampered by the low efficiency of the treatments and the need for continuous therapy. The requirement for continuous anticoagulation may also be a relative contraindication in some uremic patients.
- Renal transplantation: offers the potential of long-term replacement of all renal functions when recovery can no longer be expected; however it requires surgical expertise and experience with the management of the long-term immunosuppression to avoid graft rejection; its availability is limited.

SUGGESTED READING

Cowgill LD, Francey T: Hemodialysis. In DiBartola SP, editor: Fluid, electrolyte, and acid-base disorders in small animal practice, ed 3, St Louis, 2006, Saunders-Elsevier, p 650.

AUTHOR: THIERRY FRANCEY

Intubation, Endotracheal

SYNONYM

Placement of a tube into the tracheal lumen via an oral approach

OVERVIEW AND GOAL

Endotracheal intubation is performed routinely in dogs and cats undergoing general anesthesia and is also a fundamental technique in emergency/critical care situations.

INDICATION

- To establish and maintain airway patency in animals under general anesthesia
- To protect respiratory tract from aspiration of foreign material during anesthesia
- To facilitate delivery of supplemental oxygen and volatile inhalant anesthetic agents
- To minimize exposure of hospital personnel to waste anesthetic gases
- To minimize anatomic dead space and optimize respiratory efficiency
- To facilitate delivery of positive-pressure ventilation

CONTRAINDICATIONS

Oral approach may not be possible with mandibular/maxillary trauma, temporomandibular disorders, oropharyngeal lesions, or oropharyngeal surgery where endotracheal tube placement would interfere with the surgical field.

EQUIPMENT, ANESTHESIA

Primary equipment:

- Appropriate endotracheal tube
- Adequate lighting
- Roll gauze to secure tube

Supplemental equipment:

- Laryngoscope
- Local anesthetic
- Stylet or guide tube
- Sterile water-soluble lubricant
- Mouth speculum

ANTICIPATED TIME

- Routine: <30 seconds in an adequately anesthetized animal
- Difficult airway: <3-4 minutes

PREPARATION: IMPORTANT CHECKPOINTS

- Adequate anesthetic depth required to provide good muscle relaxation and inhibit airway reflexes
- Preoxygenation indicated in select animals
- Measurement of tube length and trimming if necessary (see Procedure, below)

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Laryngospasm
- Trauma to larynx/trachea
- Vagal reflex activity

- Unrecognized esophageal intubation
- Bronchial intubation
- Postextubation upper airway obstruction

PROCEDURE

- Place anesthetized/unconscious animal in sternal recumbency.
- An assistant opens the animal's mouth by placing one finger and thumb behind the maxillary canine teeth. Lips are pulled upward and out of oral cavity. The animal's head and neck are extended to form a straight line.
- Do not support or put pressure under animal's neck.
- Grasp the animal's tongue, and use gentle pressure to extend it rostrally and ventrally. Excessive traction on the tongue should be avoided.
- With laryngoscope: place tip of blade at base of tongue underneath epiglottis, and exert downward (ventral) pressure. This disengages the epiglottis from the soft palate and directs it rostrally, allowing the laryngeal opening to be visualized. Note: Do not place laryngoscope blade on top of epiglottis.
- Without a laryngoscope: use the endotracheal tube to disengage the epiglottis from the soft palate and expose laryngeal opening.
- If local anesthetic is used for desensitizing the larynx, apply it to vocal folds using spray dispenser, cotton swab, or hypodermic needle and syringe for topical application.
- Advance endotracheal tube between the vocal folds into trachea. In cats, wait until the folds separate during inspiration before attempting to advance tube.
- Do not force tube. If resistance is encountered, back out slightly, maneuver tip of tube's bevel between the vocal folds, and gently rotate tube while advancing.
- Ensure that distal portion of tube lies at level of thoracic inlet and proximal end terminates at level of animal's incisors. Tubes may need to be shortened to appropriate length before placement.
- Tie piece of roll gauze tightly around tube, without constricting lumen, at a point caudal to animal's incisor teeth. Secure gauze around maxilla or back of animal's head.
- Connect endotracheal tube to breathing system, and begin delivery of oxygen.
- Close pop-off valve, and gently squeeze reservoir bag until a pressure of 20 cm H^2O is reached in breathing system, while listening for sound of leaking air exiting oral cavity around tube. Incrementally inflate cuff on tube using an “air syringe” until sound of leak is terminated. Avoid cuff overinflation, and remember to open pop-off valve once cuff is inflated.

INTUBATION, ENDOTRACHEAL Intubation of an anesthetized dog. An assistant extends the dog's neck and retracts the lips. The right-handed clinician is holding both a laryngoscope and the dog's tongue in the left hand and is placing the endotracheal tube using the right hand.

- Correct tube placement may be confirmed by:
  - Palpation of single tubular structure in cervical region (as opposed to two tubes, representing an intubated esophagus alongside a trachea that is not intubated)
  - Movement of reservoir bag corresponding to thoracic wall movements associated with animal inspiration/expiration
  - Auscultation of good breath sounds bilaterally during positive-pressure ventilation
  - Detection of carbon dioxide in animal's exhaled gases and evidence of normal capnographic tracing

POSTPROCEDURE

- Extubate when animal's oral/pharyngeal reflexes have returned.
- In brachycephalic animals, endotracheal tube should be left in place as long as possible during recovery.
- In animals undergoing procedures associated with accumulation of blood/fluid in oral cavity, cuff may be left partially inflated during extubation.

ALTERNATIVES AND THEIR RELATIVE MERITS

Tracheostomy or pharyngostomy: oral approach preferred in routine cases (no tissue trauma and technically simple to perform)

AUTHOR: LEIGH A. LAMONT

Intravenous Catheter Placement

SYNONYM

Peripheral venous catheterization. Jugular venous catheter placement is discussed separately (see p. 1293)

OVERVIEW AND GOAL

To obtain intravenous (IV) access for the administration of fluids, medications, anesthetic agents, and blood products

INDICATIONS

- Fluid resuscitation (dehydration, shock)
- Seizures
- Renal failure
- Cardiopulmonary cerebral resuscitation (CPCR)
- General anesthesia
- Chemotherapy
- Anemia

CONTRAINDICATIONS

- Injury or infection at site of catheter placement

EQUIPMENT, ANESTHESIA

- Sedation usually not required but dependent on disposition and health of animal
- IV catheter (type selected depends on size and location of vein, patient requirements, cost):
    - Winged infusion set (“butterfly” catheter)
    - Over-the-needle catheter (most commonly used for peripheral catheterization)
    - Through-the-needle catheter
    - Over-the-wire-guided catheter
- Clipper with No. 40 blade
- White tape
- Surgical scrub
- Alcohol
- Gauze sponges
- Syringe with heparinized saline
- T set/injection cap
- Bandaging material (required for long term catheter):
    - Roll gauze
    - Cast padding
    - Bandage wrap (e.g., Vetrap)
    - Bandage scissors

ANTICIPATED TIME

5-10 minutes

PREPARATION: IMPORTANT CHECKPOINTS

Determine site of catheter placement:

- Usually placed in the cephalic and lateral saphenous (canine) or medial saphenous (feline)
- Other sites include the accessory cephalic vein (distal to the carpus), dorsal common digital vein (over the metatarsals), auricular, jugular, and femoral veins.

Determine the type and size of the catheter required:

- Butterfly catheters are best used for blood collection and short-term infusion of nonirritating drugs or fluids.
- Use the largest bore catheter possible if needing to give a large amount of fluids rapidly.
- To avoid trauma to the vein in patients requiring multiple catheterizations, choose the smallest-gauge catheter possible.

A full/mini cutdown may be required in emergencies where the vessel cannot be visualized. Specifically, animals with tough skin or that are dehydrated may require a small 1- to 2-mm skin incision with a 20-gauge needle to prevent crimping or burring of the catheter.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

Complications:

- Phlebitis
- Thrombosis
- Sepsis
- Extravasation resulting in edema/necrosis at the catheter site
- Blood loss (catheter becomes disconnected from fluids/T set)
- Catheter embolism

Common errors:

- Avoid using the saphenous vein in animals with diarrhea or polyuria, and the cephalic vein in vomiting animals, due to risk of contamination.
- Catheter is placed too proximal on the limb, and flow is occluded when leg is flexed.

PROCEDURE

For over-the-needle catheters:

- Clip area and prepare aseptically.
- Occlude the vein, and insert the catheter at a 15-30○ angle, with bevel facing up.
- Advance the catheter until you see a flash of blood in the catheter hub. To get the catheter tip fully into the vein, advance the catheter an additional 1-3 mm; otherwise, only the stylet tip, and not the catheter itself, is in the vein. If blood flow stops, back the catheter out to a point where there is blood flow, and reattempt to seat the catheter in the vein.
- With the hand that is holding the leg, stabilize the hub of the needle; with your other hand, advance the catheter over the needle. (If the catheter does not advance smoothly, do not reinsert the needle into the catheter while in the leg. Further attempts can be made more proximal or at a different site.)
- Have the assistant apply pressure over the tip of the catheter to prevent blood from contaminating the site. Attach the injection cap or T set/T port.
- Dry the site with gauze and secure the catheter in place with tape.
- Flush the catheter with saline. If the catheter is properly placed, the flow of fluid in the vein can be palpated above the tip of the catheter, and blood can be aspirated.
- Wrap catheter with bandage material.

POSTPROCEDURE

- Inspect bandage and catheter site daily and monitor for pain, inflammation, edema, and infection.
- Flush catheter with heparinized saline every 4-6 hours if not administering an infusion.
- Apply an Elizabethan collar or catheter guard if necessary to avoid self-trauma.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Central venous catheter: used for administering total parenteral nutrition, monitoring central venous pressure, and obtaining repeated blood samples
- Intraosseous catheter placement: useful in neonates or in patients where IV access attempts have failed
- Subcutaneous fluid administration: inexpensive and convenient but only useful in stable patients with good peripheral perfusion

AUTHOR: ELAINE REVELER

Intraosseous Catheter Placement

OVERVIEW AND GOALS

- Insertion and maintenance of a patent catheter in the marrow cavity of a long bone for purposes of administering parenteral fluids, drugs, blood, or virtually any other agent that is routinely given IV.
- The technique is most commonly used in debilitated neonatal and pediatric animals, in which peripheral veins may be very small and difficult to access but also in which the bone is soft and entered fairly easily.

INDICATIONS

- Urgent fluid replacement in a severely dehydrated/hypovolemic kitten or puppy (most common indication)
- Plasma or blood transfusion in an animal that has poor peripheral or jugular venous access
- Administration of drugs when IV access is not available

CONTRAINDICATIONS

- Osteopenia (nutritional or metabolic bone disease) or fracture affecting the target bone
- Infection of the overlying soft tissues
- Sepsis is a relative contraindication. The benefit of fluid administration must be felt to outweigh the risk of osteomyelitis.

EQUIPMENT, ANESTHESIA

Sedation or general anesthesia is necessary for animals that are otherwise well. However, intraosseous catheters are often placed in severely debilitated animals; local anesthesia with 2% lidocaine (typical kitten/puppy dose: 0.25 mL) is sufficient for these animals, provided all tissue layers are intiltrated (subcutis, muscle, periosteum).

- Clippers for hair
- Isopropyl alcohol, surgical scrub supplies, and sterile gauze squares
- Spinal needle: typically 20 gauge, 1½ or 2½ inches (4-6 cm) long
- T-port-type injection cap with side connector
- Sterile gloves
- Tissue glue
- Heparinized saline flushes
- Bandage material: roll gauze, cast padding, stretch and release bandage (e.g., Vetrap), white medical tape
- Suture scissors and bandage scissors
- ± Splint material (e.g., wooden tongue depressor in pediatric patients) to protect the spinal needle after placement

ANTICIPATED TIME

About 20 minutes

PREPARATION: IMPORTANT CHECKPOINTS

- Review anatomic landmarks.
- Consider alternatives (e.g., IV catheter).

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Damage to nerves (especially sciatic) or vessels. Risk is minimized by manipulating the limbs as described in the following paragraphs.
- Spinal needle kinking, causing obstruction; common. Minimized by using a needle that is not excessively long, that is not overly thin (a 22-gauge needle should probably be the smallest used in even the smallest animals), and by bandaging the proximal/protruding part of the needle in a way that reduces the lateral forces applied to it when the animal bumps against the cage wall, lies down, or rolls over.
- Using a regular 18-gauge needle (hypodermic/injection-type) instead of a spinal needle has been described, but this approach is not recommended. The procedure involves “coring out” a path by placing an 18-gauge needle in the appropriate place, immediately removing it (since, without a stylet, it will be plugged with bone), and placing a second, new 18-gauge

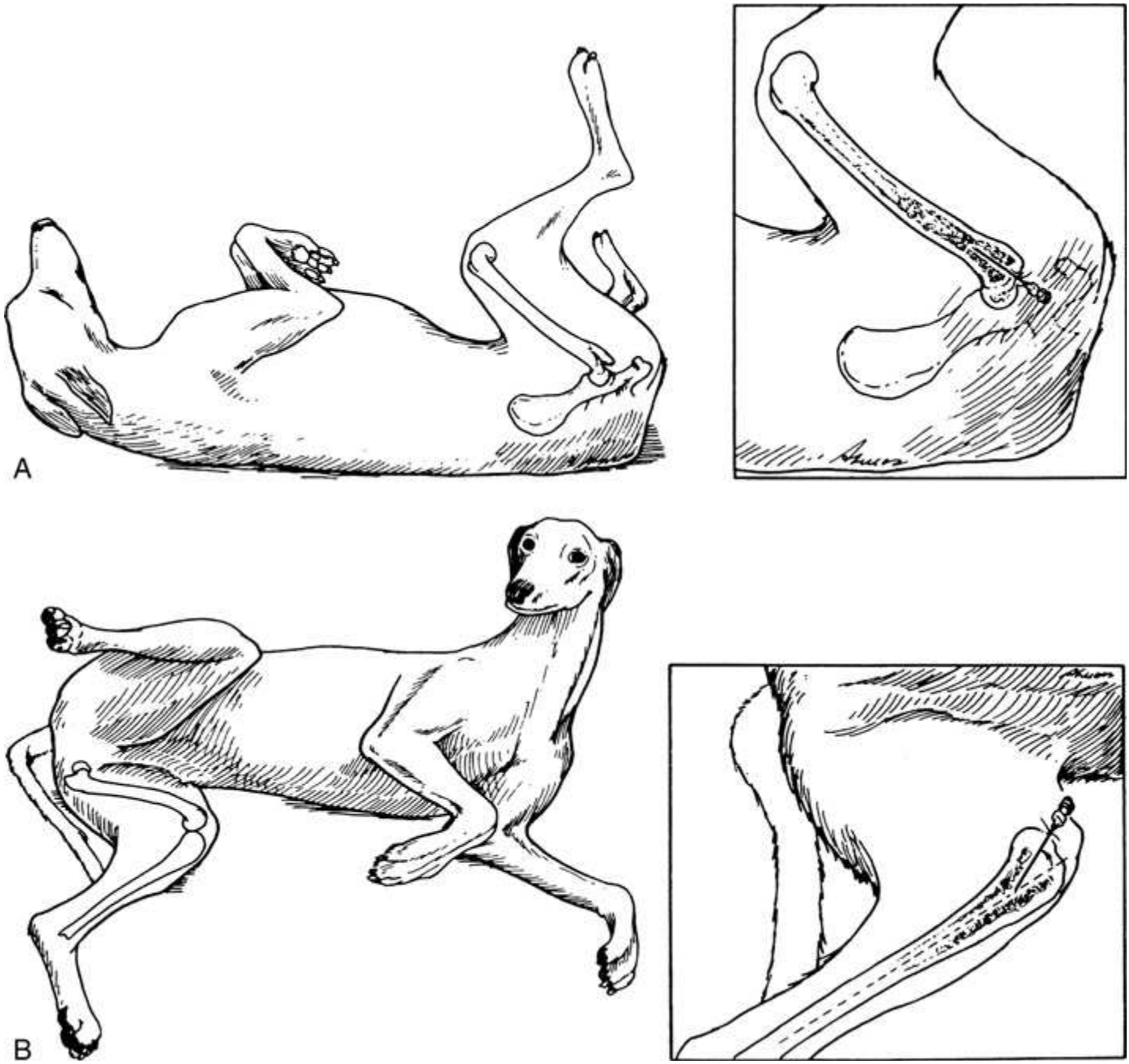
needle in the tract just created by the previous needle. Complications, including replugging with bone in the second needle, inability to find the hole when placing the second needle, and leakage of fluid around the needle, are extremely common. Therefore, only spinal needles (with stylets) should be used, not regular hypodermic needles.

PROCEDURE

FEMORAL APPROACH:

- Sedation/general anesthesia is administered if deemed necessary based on animal parameters (e.g., mentation, extent of illness, vital signs).
- The animal is placed in lateral recumbency, and the nondependent leg is used.
- The clinician palpates the hip; the greater trochanter of the femur is the outer/lateral landmark, and the trochanteric fossa medial to the greater trochanter is the target.
- The overlying skin is clipped of hair and aseptically prepped.
- If no sedation or general anesthetic has been administered, local anesthetic is infiltrated into the trochanteric fossa at this time.
- A 2-mm stab incision is made in the skin overlying the trochanteric fossa.
- The femur is rotated internally and adducted and is held in this position during needle placement to reduce the risk of traumatizing the sciatic nerve.
    - The sciatic nerve courses medial to the trochanteric fossa, dorsal to the acetabulum. Therefore, entering the trochanteric fossa from its lateral-most aspect minimizes the risk of sciatic nerve damage.
- The spinal needle is placed through the stab incision in the skin and onto the greater trochanter (lateral to target). It is then moved gradually in a medial direction until it enters the trochanteric fossa.
- Once in the trochanteric fossa, the needle is advanced parallel to the long axis of the bone, with the hub of the needle held firmly to allow a burrowing, clockwise-counterclockwise rotating motion to facilitate advancement of the needle. A mild loss of resistance is usually felt when the needle reaches the marrow cavity. NOTE: It is important not to advance the needle the length of the entire bone and into the distal cortex, because this could block flow through the needle.
- When the needle is sufficiently advanced, the stylet is withdrawn. The T-port is filled with heparinized saline, fitted onto the spinal needle hub, and flushed with heparinized saline.
- The spinal needle is sutured in place (to prevent migration outward) using a Chinese-finger-trap suture pattern. This may be further solidified by applying tissue glue to the suture as it courses over the hub of the spinal needle and the T-port.
- Cast padding, roll gauze, and bandage material are rolled around and over the needle hub and T-port in a way that protects the needle from becoming kinked or damaged with the animal's movements. Wooden tongue depressors or other splint materials can be useful for protecting the part of the needle that protrudes from the femur.
- The T-port can be connected to an IV fluid set, a blood transfusion set, or other, based on the animal's needs.
- There should be no outward signs of discomfort; if there are, nerve damage or other complications should be suspected, and the spinal needle may need to be withdrawn.

INTRAOSSEOUS CATHETER PLACEMENT Different views of two 20-gauge, 2½-inch spinal needles used for intraosseous catheterization.



INTRAOSSEOUS CATHETER PLACEMENT Intraosseous catheter placement. **A,** Femoral approach. **B,** Tibial approach.

(Reprinted with permission from Otto CM, Crowe DT Jr: Intraosseous resuscitation techniques and applications. In Kirk RW, Bonagura JD, editors: Kirk's current veterinary therapy XI, Philadelphia, 1992, Saunders, pp 107–112.)

TIBIAL APPROACH:

- The preparation is as described for the femoral approach, but the target area is the medial proximal tibia.
- The spinal needle enters the tibia on the medial surface of the tibial tuberosity and is directed laterodistally, as shown.
- The protocol is otherwise the same from the removal of the stylet to the end of the procedure.

POSTPROCEDURE

- Catheter care includes flushing with 0.2-0.4 mL sterile saline every 6-8 hours if an infusion is not being administered through the needle. It is important not to overflush the system in small animals, causing systemic heparinization.
- Catheter obstruction is a common problem. Most cases are prevented by proper placement (not too deep in the bone, causing blockage from the distal cortex), and proper securing and protection of the spinal needle so the animal does not bend it; prevention also is possible by regular flushing or infusion to keep the catheter patent.

- If the spinal needle becomes obstructed or bent and needs to be replaced, a different bone should be chosen for intraosseous catheter placement because a minimum of 24-48 hours are needed for the bone to heal. Otherwise, leakage from the original needle site of entry and subcutaneous pooling of the administered fluid/blood/drug commonly occur.
- The spinal needle can usually be removed without sedation or general or local anesthesia and without eliciting signs of pain from the animal.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Venous cutdown for peripheral or jugular catheter: acceptable alternative but more invasive, possibly with a greater risk of local infection.
- Intraperitoneal administration: acceptable in mildly/moderately ill pediatric animals, including for blood transfusion. Lack of direct access to the circulation is a substantial drawback compared to intraosseous catheterization.

AUTHOR: ETIENNE CÔTÉ

Inhalant Medication Administration

OVERVIEW AND GOAL

To deliver medication to the respiratory tract with maximal efficacy and minimal side effects

INDICATIONS

Virtually any disease of the respiratory tract for which oral or injectable corticosteroids are indicated:

- Lymphocytic-plasmacytic rhinitis
- Allergic rhinitis
- Laryngeal edema secondary to laryngeal paresis/paralysis or mass
- Reverse sneeze
- Chronic bronchitis
- Asthma
- Eosinophilic pneumonia

Any disease of the respiratory tract for which oral or injectable bronchodilators are indicated:

- Asthma
- Chronic bronchitis (occasional)
- Bronchial compression secondary to left heart enlargement (occasional)

CONTRAINDICATIONS

Prior known sensitivity to inhaled medications

EQUIPMENT, ANESTHESIA

- Face mask: specific to species and size of animal's muzzle
- Spacer: specific to size of animal
- Metered dose inhaler (MDI)

ANTICIPATED TIME

- Inhalation time is usually 7-10 seconds, q 24 h to q 12 h or as needed (bronchodilator).
- Preparation time for animal may be a matter of seconds if animal is trained and comfortable with the device or may last weeks if training is required.

PREPARATION: IMPORTANT CHECKPOINTS

- Approximately 90% of dogs and 65% of all cats will tolerate the placement of the mask and spacer apparatus the very first time.
- Animals that will not tolerate this device initially still can be trained to acceptance. This usually takes a few days to a few weeks.
- Approximately 5% of dogs and 20% of cats will not accept this form of medication delivery even after weeks of training.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Some animals cough immediately after inhaling the medications. No treatment for this is required.
- Mild conjunctivitis occasionally occurs if the top of the mask is in contact with the lower conjunctival lid margins.
- Contact dermatitis of the muzzle occasionally occurs.
- “Thrush,” a yeast infection within the posterior pharynx, is a frequent complication in humans. This has not been reported in dogs or cats using inhaled corticosteroids.
- Growth retardation is a potential concern in children using inhaled corticosteroids. This has not been reported in dogs and cats.
- Cats with respiratory distress due to bronchoconstriction will very quickly benefit from inhalation of bronchodilator drugs. The

temporary restraint required to administer these drugs has not been reported to result in clinically significant complications in this setting.
- Some cats will hold their breath. If this occurs, it is essential to wait until the animal begins breathing for 7-10 breaths.
- Some dogs and cats have nasal congestion that prevents inhalation by this method. In these cases, it is useful to instill a drop of a topical nasal decongestant (e.g., phenylephrine drops [Neo-Synephrine]) into either or both nostrils and wait 10-15 minutes before using the inhaled medications.

INHALANT MEDICATION ADMINISTRATION Spacer device connected to a face mask.

PROCEDURE

Technique, initial:

- Shake MDI three to five times vigorously.
- Attach MDI to spacer.
- Position the animal for gentle restraint and to prevent side-to-side movement.

Technique, main:

- Place the mask over the animal's nose (cats) or muzzle (dog). If right-handed, use left hand to place mask.
- Use right hand to actuate (spray) medication, one puff into spacer.
- MDI for albuterol comes as one dose only (90 mcg/actuation).
- MDI for fluticasone comes as 44, 110, and 220 mcg/actuation.
- Watch animal breathe for 7-10 breaths by watching the chest wall/abdomen.
- Alternatively, count 7-10 condensations of breath within the plastic mask.
- If an animal is resistant and in respiratory distress, it is usually safe to administer the medication with two people involved to temporarily restrain the animal. This is true even in the case of respiratory distress due to asthma.

POSTPROCEDURE

- Wipe patient's face/muzzle with washcloth.
- Maintain cleanliness of spacer according to manufacturer's recommendations.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Nebulization does not offer superior drug-delivery results compared to the simple mask/spacer combination.
- Long-acting corticosteroids cannot be administered by inhalation.
- Oral prednisone/prednisolone should be considered when the animal requires immediate antiinflammatory treatment. Inhaled corticosteroids may take 7-10 days to reach full effect. In these cases, prednisone/prednisolone should be administered for the first week concomitantly with the inhaled corticosteroid.
- Parenteral bronchodilators can be used (e.g., terbutaline, subcutaneously [SQ]) if an animal is fractious and cannot be easily restrained.
- Topical medications: no current or prior objective data that document the effectiveness of transcutaneously-administered corticosteroids or bronchodilators in the treatment of respiratory disorders in dogs or cats.

- Alternative therapies: many unproven alternative, evolving, and experimental approaches to treating respiratory disease in the canine and feline species.

AUTHOR: PHILIP PADRID

INHALANT MEDICATION ADMINISTRATION Spacer connected to a metered dose inhaler (MDI) and a self-sealing mask of the type commonly used for induction of anesthesia. Spacer acts as a reservoir for inhaled medication, so animal breathes the drug into its airways whenever it breathes through the face mask.

Jugular Catheter Placement and Management

OVERVIEW AND GOALS

Jugular venous access is essential in small-animal critical care and general medicine for a variety of therapeutic and diagnostic reasons.

- The duration of catheter patency and function tends to be longer with jugular catheters compared to peripheral catheters.
- Higher osmolar solutions (parenteral nutritional solutions, glucose solutions) may be administered more safely through these catheters compared to peripheral venous catheters.
- Jugular venous catheters allow for easier through-the-catheter blood sampling and are necessary for measuring central venous pressure.
- Jugular catheter sites are less likely to be contaminated from vomit and diarrhea in animals with those problems.

INDICATIONS

- When multiple/serial blood samples are required (e.g., diabetic ketoacidotic animals)
- Measuring central venous pressure (CVP)
- Constant rate infusions of hyperosmolar solutions (e.g., dextrose solutions > 5%)
- Total/partial parenteral nutrition (T/PPN) administration
- In animals with severe vomiting and diarrhea that require IV access

CONTRAINDICATIONS

- Hypercoagulable states (e.g., protein-losing nephropathy)
- Increased intracranial pressure (holding off jugular vein may increase intracranial pressure)
- Hypocoagulable states (e.g., liver failure, rodenticide anticoagulant intoxication)
- Thrombocytopenia
- Thrombocytopathia
- Skin infection over site of jugular catheter placement

EQUIPMENT, ANESTHESIA

- Sedation generally not necessary in critically ill animals but may be needed in fractious animals
- Clippers
- Sterile surgical gloves
- Surgical scrub soap
- Gauze squares for surgical prep of site
- Heparinized saline flushes
- Suture material
- White cloth-type tape
- Bandaging material (e.g., roll gauze, cast padding, and Elastikon/Elastoplast-type adhesive roll bandage)
- Injection cap
- Triple-antibiotic ointment
- Guide-wire technique: the following four items are available in kits manufactured by Cook, Mila, and Arrow:
    - Hypodermic needle
    - Guide wire
    - Dilator
    - Polyurethane IV catheter
- Other materials:
    - A #11 scalpel blade
    - Suture material (e.g., 2-0 to 4-0 nylon)

ANTICIPATED TIME

About 20 minutes

PREPARATION: IMPORTANT CHECKPOINTS

Check coagulation profile (prothrombin time [PT], partial thromboplastin time [PTT], platelet count, platelet function)

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

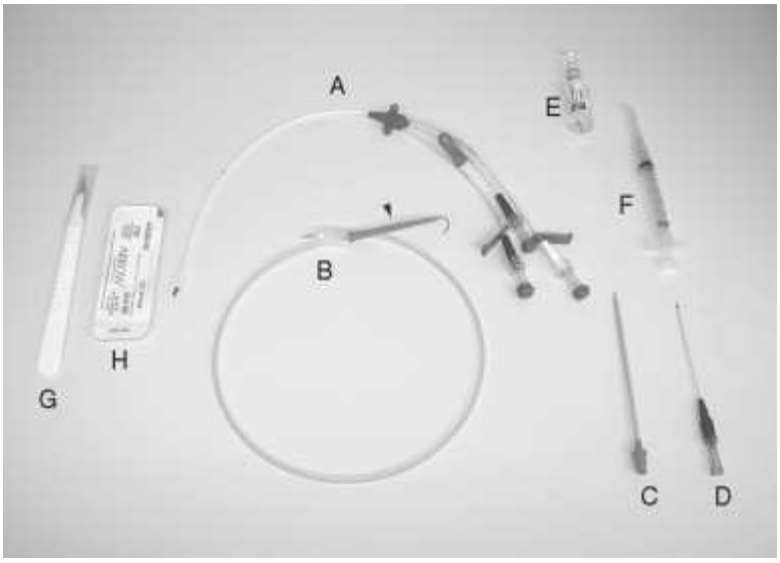
- Do not use leashes that go around the neck (neck leads) when a jugular catheter is in place.
- Place needle guard when using through-the-needle catheters before removing the stylet. Otherwise, the needle can lacerate or transect the catheter.
- Avoid excessively tight neck bandaging.

PROCEDURE

- Catheter placement should always be done aseptically.
- Animal should be in lateral recumbency, with the nonrecumbent side being the side with the jugular to be catheterized.
- Clip hair from site. Centered over the jugular furrow, the clip and aseptic prep extend approximately as follows:
    - From slightly beyond the ventral midline of the neck ventrally to halfway between the ventral and dorsal midlines dorsally
    - From the thoracic inlet caudally to the angle of the mandible cranially
- Prepare site aseptically with complete surgical scrub.

GUIDE-WIRE TECHNIQUE:

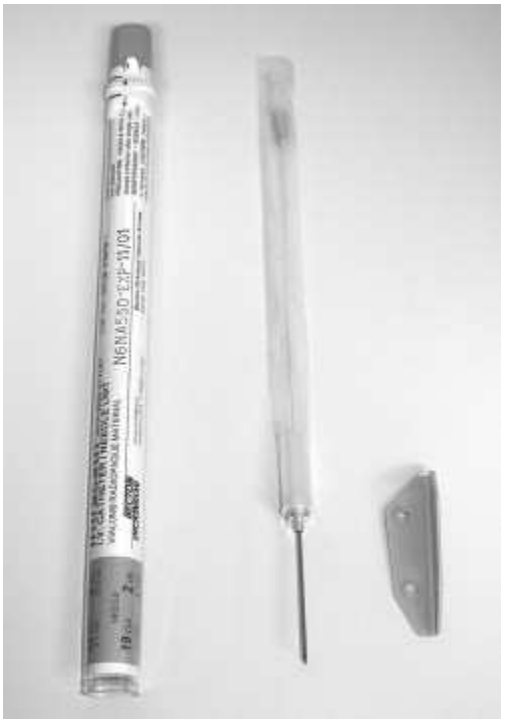
- Use sterile surgical gloves when placing the catheter.
- Drape site with sterile drape.
- Check that catheter or needle about to be used for venipuncture can accept guide wire (compatible diameters).
- Insert needle in vessel (jugular venipuncture):
    - Catheter (generally needs to be larger than 20-gauge) may used in place of needle.
    - In thick-skinned animals, a two-step approach may be better:
        - Raise the jugular vein.
        - Lift (tent) the skin overlying the jugular vein.
        - Enter only the skin with the needle/catheter, or make a small stab incision in the skin with a sterile scalpel blade.
        - Gently return the skin to a normal position (keeping the needle in place in the skin).
        - Advance the needle into the raised jugular vein.
- Place guide wire into vessel through needle or catheter, J-tip (not straight tip) first. To do so, the guide wire is retracted into the J-tip straightening device (a small, tapered sleeve), and the device with the straightened J-tip is placed into the catheter. The guide wire may then be advanced easily through the catheter and into the jugular vein, with the J shape emerging from the peripheral catheter in the jugular vein to avoid trauma from a straight guide wire tip.
- After advancing the guide wire a few cm into the jugular vein (4-10 cm, depending on the patient's size), do not move the guide wire for the rest of the procedure until the catheter is in place.
- While holding the guide wire firmly with one hand (guide wires are Teflon-coated and slippery), remove needle or catheter from vessel and off the wire while ensuring the guide wire stays in the vessel.
- Maintain digital pressure over the catheter placement site to minimize hemorrhage.
- Measure length of guide wire protruding from skin; it should be a few cm greater than the length of the dilator (withdraw guide wire slightly as needed).
- Place dilator over the wire into the vessel (this dilates the vessel insertion site so the catheter can be placed more easily into the vessel). Expect some bleeding around the site, which should be controlled with direct pressure. Some jugular catheter kits have a combined catheter-dilator configuration, which allows the dilation step and the catheter placement step to occur simultaneously.
- While holding the guide wire firmly in place, remove the dilator back over the wire, making sure that wire stays in the vessel. Apply pressure over the site to minimize hemorrhage.
- Thread IV catheter over the wire, and advance catheter into the vessel.
- Remove wire, making sure the catheter stays in place.
- Remove air in the catheter line with the use of a 3-mL syringe that contains heparinized saline.
- Flush catheter with heparinized saline without administering air to animal.
- Suture catheter to skin.
- Cover site with nonadhesive bandage.
- Bandage catheter in a stable position (neck wrap).



JUGULAR CATHETER PLACEMENT AND MANAGEMENT Guide wire–type jugular catheter kit. **A**, Triple-lumen jugular catheter. **B**, Flexible Teflon-coated stylet with J-tip straightening sleeve *(arrowhead)*. **C**, Vessel dilator. **D**, Peripheral IV catheter (large-bore needle may be used instead, but guide wire must fit through it). **E**, Local anesthetic. **F**, Syringe for injecting anesthetic. **G**, Disposable scalpel for making skin incision. **H**, Suture material.

THROUGH-THE-NEEDLE CATHETER TECHNIQUE:

- Insert needle into vessel. The two-step technique may help (as just described).
- Advance catheter through the needle into the vessel.
- Lock catheter into needle hub.
- Withdraw needle from vessel and skin (i.e., withdraw needle by 3-4 cm, ensuring catheter remains well in the jugular vein), and place the needle guard over needle.
- Remove stylet from catheter.
- Cap catheter and flush catheter with heparinized saline.
- Suture catheter to skin.
- Cover site with nonadhesive bandage.
- Bandage catheter in a stable position (neck wrap).



JUGULAR CATHETER PLACEMENT AND MANAGEMENT Through-the-needle jugular catheter. Inside the kit *(left)* are the catheter *(center)* and needle guard *(right)*. Note plastic sheath of catheter, which allows catheter to be advanced through needle into

the patient without wearing sterile gloves; also note large needle that remains with the patient and must be covered with needle guard.

POSTPROCEDURE

- Assess tightness of bandage around animal's neck after each layer is placed. A finger should easily pass between skin and bandage.
- For walks, leashes should be placed around shoulders, or use a harness.
- If using multiple-lumen catheters, be sure animal cannot chew lumen lines.
- When using multiple lumens, designate one for TPN (usually the most distal).
- Flush line(s) with heparinized saline every 6 hours to maintain patency.

ALTERNATIVES AND THEIR RELATIVE MERITS

Peripheral catheter: technically simpler and cheaper but does not allow jugular catheter functions as already described.

AUTHORS: ELISA A. PETROLLINI ROGERS, KENNETH DROBATZ

Luxation Reduction (Closed): Shoulder, Elbow, or Hip

SYNONYMS

Coxofemoral luxation (hip); dislocated shoulder, elbow, hip; scapulohumeral luxation (shoulder)

OVERVIEW AND GOALS

- Severe joint trauma can cause ligament/joint capsule damage, resulting in displacement of the bones of a joint.
- Closed reduction aims to restore the normal alignment of the joint without surgical intervention, and to maintain stability until these soft tissues heal.

INDICATIONS

- Traumatic luxation of normal shoulder, elbow, hip joints
- Acute luxation (<5 days)

CONTRAINDICATIONS

- Luxation associated with severe ligament damage or avulsion fractures that impede normal joint function and/or leave the joint unstable after closed reduction
- Failure of closed reduction due to interposed soft tissue, hematoma, or recurrent luxation necessitates open (surgical) reduction
- Chronic luxation (>5 to 7 days)
- Dysplastic joint:
    - Glenoid dysplasia
    - Total hip replacement may be a better option in cases of severe hip dysplasia.
- Femoral head and neck ostectomy (FHO) may be an acceptable alternative to closed/open hip reduction in a small dog or cat.

EQUIPMENT, ANESTHESIA

- General anesthesia
- Rope or leash to provide counterpressure (hip luxation)
- Assistant
- Bandage material

ANTICIPATED TIME

About 10-30 minutes

PREPARATION: IMPORTANT CHECKPOINTS

- Advise owner of aftercare and possible drawbacks:
    - Recurrence
    - Degenerative joint disease
    - Decreased range of motion
    - Possible need for open reduction
    - Postreduction bandage care
    - Postreduction exercise restriction

After anesthetic induction:

- Minimum of two views of the joint to confirm luxation versus fracture
- Animal in lateral recumbency, affected limb up (affected limb on the nonrecumbent side)
- Hanging the affected limb can be useful (elbow luxation) for 5-10 minutes: secure the carpus, and hoist the limb vertically with traction. Be sure to secure the limb proximal to the metacarpi, and use a thick, soft rope (or roll gauze) in a double-loop technique, rather than single loop, to distribute pressure evenly on the distal limb. These measures reduce the risk of

iatrogenic damage.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- If there is excessive instability following closed reduction, open reduction should be performed.
- Failure to critically evaluate plain radiographs to assess joint anatomy or damage, avulsion fragments, and intraarticular debris
- Trying to reduce a luxation with sedation alone
- Failure to appropriately bandage the luxation
- Removal of bandage too soon
- Inadequate patient exercise restriction
- When hanging the forelimb to help with elbow luxation reduction: be sure to secure the limb proximal to the metacarpi, and use a thick, soft rope (or roll gauze) in a double-loop technique to distribute pressure evenly on the distal limb. These measures reduce the risk of iatrogenic damage.

PROCEDURE

All luxation reductions are performed with the animal under general anesthesia and in lateral recumbency, affected side up (nondependent).

- Shoulder:
  - Forelimb held in extension (in a ventral direction perpendicular to the long axis of the body, as in the standing animal)
  - For lateral luxation of the humeral head, apply medial pressure to the head at the same time as lateral pressure on the scapula.
  - Check range of motion and stability.
  - Place leg in a Spica splint.
  - For medial luxation of the humeral head, apply lateral pressure to the head at the same time as medial pressure on the scapula.
  - Check range of motion and stability.
  - Place the leg in a Velpeau sling.
  - Splint or sling can be removed after 2 weeks.
  - Passive range-of-motion exercises can begin after bandage removal, but restricted exercise is essential for another 2-4 weeks.
- Elbow:
  - Radius and ulna are usually luxated laterally relative to the distal humerus.
  - With the elbow in flexion, inwardly rotate the antebrachium.
  - Combined with elbow flexion, this movement enables the anconeal process of the ulna (caudal-most extent of the trochlear notch in the ulna) to hook into the olecranon fossa of the humerus. This maneuver is followed by careful extension of the elbow.
  - Hook the anconeal process of the ulna between the humeral condyles, and carefully extend the elbow. With this part of the maneuver, the joint should now be reduced.
  - Passive range-of-motion exercises can begin after bandage removal, but restricted exercise is essential for 4-6 weeks, followed by 2 weeks of leash exercise only.
- Hip:
  - Assistant stands on opposite side of animal, holding the ends of a padded rope or leash placed in the animal's groin to provide counterpressure.
  - Craniodorsal hip luxation (more common):
    - The tarsus is grasped and externally rotated while the femur is pulled caudally.
    - The head of the femur rides up (moves laterally and then caudally) and over the dorsal acetabular rim.
    - Internal rotation while maintaining distal traction on the femur, together with direct pressure on the greater trochanter, will seat the head in the acetabulum.
    - Place hip in an Ehmer or modified Ehmer sling for 2 weeks.
  - Caudoventral luxation:
    - The femur should be abducted and externally rotated to seat the femoral head in the acetabulum.
    - Hobbles may be applied for 10-14 days.
  - Medially-directed pressure can be applied to the reduced proximal femur as the hip is passively flexed and extended in an attempt to drive debris from the acetabulum.

POSTPROCEDURE

- Radiograph to evaluate the reduction.
- Toes should be accessible or visible to monitor for heat, cold, swelling, or pain.
- Bandage needs to be protected from moisture and kept clean and dry.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Open reduction:
  - Requires surgical intervention
  - Greater cost
  - Carries a higher rate of success than closed reduction for the shoulder, elbow, and hip
- FHO may be worth considering for cats and small dogs, as the possibility of hip reluxation is eliminated.
- Arthrodesis can provide pain relief for a chronically unstable joint. Aside from cost, complications include nonunion, stress fractures, implant failure and infection.
- Excision glenoid arthroplasty for the shoulder joint. There are few reports of glenoid arthroplasty, but an abnormal gait is to be expected.
- Amputation

AUTHOR: NICHOLAS J. TROUT

Local and Regional Anesthesia

SYNONYM

Local blocks

OVERVIEW AND GOALS

- *Local anesthesia* and *regional anesthesia* refer to a broad range of techniques that utilize local anesthetic agents delivered to a discrete anatomic area (as opposed to systemic delivery).
- With these techniques, the local anesthetic agent inhibits pain by blocking transmission of noxious input (and other types of sensory input) before it ever reaches the brain. The animal's level of consciousness is not affected.
- This contrasts with general anesthesia, during which nociceptive processing continues to occur, but the animal is not able to perceive pain owing to the unconscious state.

INDICATION

- Infiltrative anesthesia:
  - Incisional block: supplemental analgesia for a variety of surgical procedures (e.g., abdominal wall incisions, total ear canal ablation incisions)
- Peripheral nerve blocks:
  - Dental nerve block: supplemental analgesia for tooth extractions, maxillary/mandibular surgeries
  - Brachial plexus block: supplemental analgesia for surgical procedures involving the forelimb distal to shoulder
  - Distal radial, ulnar, and median nerve blocks: supplemental analgesia for feline onychectomy or any surgical procedure involving the distal forepaw
  - Intercostal nerve blocks: supplemental analgesia after lateral thoracotomy or desensitizing area around isolated rib fractures
- Epidural anesthesia/analgesia:
  - Lumbosacral injection of local anesthetic: indicated for caudal procedures/injuries only (e.g., involving hind limb, tail, perineum, caudal abdomen)
  - Lumbosacral injection of opioid: hydrophilic opioids (i.e., morphine) indicated to supplement analgesia for a variety of procedures (e.g., hind limb, tail, abdominal, forelimb, thoracic, cervical procedures)
- Other regional techniques:
  - Intraarticular anesthesia/analgesia: supplemental analgesia for procedures involving the joint space (stifle most common)
  - Interpleural anesthesia: supplemental analgesia for thoracic and cranial abdominal pain (especially pancreatitis)
  - IV regional anesthesia: desensitization of a distal limb to facilitate surgery

CONTRAINDICATIONS

- Infiltrative anesthesia, peripheral nerve blocks, others:
  - Injection into infected tissue
- Epidural anesthesia/analgesia (see p.1260):
  - Injection into infected tissue (at lumbosacral junction)
  - Coagulopathy
  - Septicemia
  - Uncorrected hypotension (especially with local anesthetics)
  - Significant trauma/lesion at lumbosacral junction

EQUIPMENT, ANESTHESIA

- Infiltrative anesthesia:
  - Incisional block:
    - Hypodermic needle (22, 25 gauge), syringe, sterile gloves, local anesthetic
    - Dosages (total per animal): lidocaine, ≤5 mg/kg (dog), ≤3 mg/kg (cat); bupivacaine, ≤2 mg/kg (dog), ≤1 mg/kg (cat)
    - Animal is usually under general anesthesia, and block is done either before incision is made or at the end of the surgery prior to complete closure.
- Peripheral nerve blocks:

- Dental nerve block:
  - Hypodermic needle (22, 25 gauge), syringe, local anesthetic
  - Dosages (total per animal): lidocaine, ≤5 mg/kg (dog), ≤3 mg/kg (cat); bupivacaine, ≤2 mg/kg (dog); ≤1 mg/kg (cat)
  - Animal is usually under general anesthesia.
- Brachial plexus block:
  - Hypodermic needle (22 gauge) or spinal needle (22 gauge, 2-3 inches [5-8 cm]), syringe, local anesthetic
  - Dosages (total per animal): lidocaine, ≤5 mg/kg (dog), ≤3 mg/kg (cat); bupivacaine, ≤2 mg/kg (dog), ≤1 mg/kg (cat)
  - Specialized insulated needle (22 gauge, 3 inches) required if a nerve locator is to be used.
  - Animal is usually sedated or under general anesthesia.
- Distal radial, ulnar, median nerve blocks:
  - Hypodermic needle (22, 25 gauge), syringe, local anesthetic
  - Dosages (total per animal): lidocaine, ≤5 mg/kg (dog), ≤3 mg/kg (cat); bupivacaine, ≤2 mg/kg (dog), ≤1 mg/kg (cat)
  - Animal is usually under general anesthesia, and block is done prior to surgical procedure.
- Intercostal nerve block:
  - Hypodermic needle (22, 25 gauge), syringe, local anesthetic.
  - Dosages (total per animal): lidocaine, ≤5 mg/kg (dog), ≤3 mg/kg (cat); bupivacaine, ≤2 mg/kg (dog), ≤1 mg/kg (cat)
  - Animal is usually sedated or under general anesthesia.

- Epidural anesthesia/analgesia (see p.1260):
  - Spinal needle (18, 20, 22 gauge; Quincke or Huber point, 1½-3½ inches [4-9 cm]), syringe, sterile gloves, local anesthetic (preservative-free lidocaine, bupivacaine), ± opioid (preservative-free morphine)
- Other regional techniques:
  - Intraarticular anesthesia/analgesia:
    - Hypodermic needle (22 gauge), syringe, sterile gloves, local anesthetic (lidocaine, bupivacaine) ± opioid (morphine)
    - Dosages (total per animal): lidocaine, ≤5 mg/kg (dog), ≤3 mg/kg (cat); bupivacaine, ≤2 mg/kg (dog), ≤1 mg/kg (cat)
    - Animal is usually sedated or under general anesthesia.
  - Interpleural anesthesia:
    - Butterfly catheter (22 gauge) or through-the-needle catheter (20 gauge, 2 inches); preplaced chest tube or commercial interpleural anesthesia tray, syringe, sterile gloves, local anesthetic
    - Dosages: lidocaine, ≤5 mg/kg (dog) q 2-4 h; ≤3 mg/kg (cat) q 4h. Bupivacaine, ≤2 mg/kg (dog) initially, then ≤1 mg/kg q 6 h; ≤1 mg/kg (cat) initially, then ≤0.5 mg/kg q 6 h
    - Animals are usually sedated or under general anesthesia.
  - IV regional anesthesia:
    - Cling-and-release bandage material (e.g., Vetrap), IV catheter (22 gauge), tourniquet, hypodermic needle (22 gauge), syringe, local anesthetic (lidocaine)
    - Dose: lidocaine, 2.5-5 mg/kg (dog only)
    - Animal is usually sedated.

ANTICIPATED TIME

This time period does not include clipping of hair and preparation of the site where indicated.

- Infiltrative anesthesia:
  - Incisional block: <1-2 minutes
- Peripheral nerve blocks:
  - Dental nerve blocks: <1-2 minutes
  - Brachial plexus block: <5-10 minutes
  - Distal radial, ulnar, median nerve blocks: <1-2 minutes
  - Intercostal nerve blocks: <1-2 minutes
- Epidural anesthesia/analgesia: <5-10 minutes
- Other regional techniques:
  - Intraarticular anesthesia/analgesia: <1-2 minutes
  - Interpleural anesthesia: <5-10 minutes
  - IV regional anesthesia: <5-10 minutes

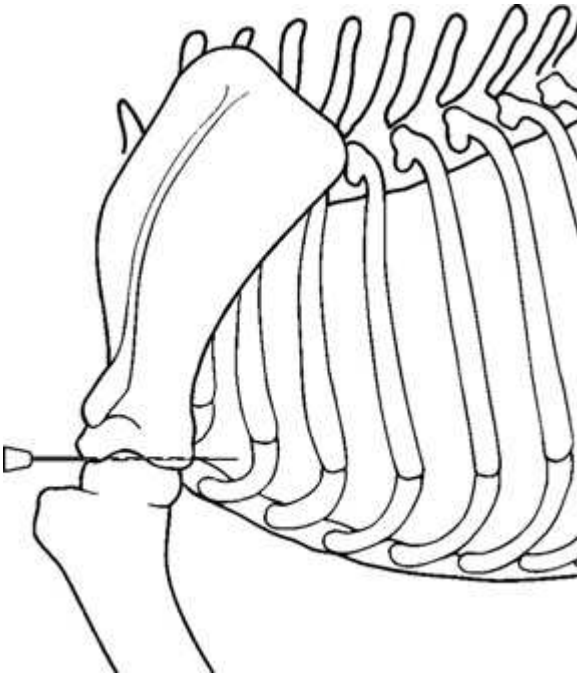
PREPARATION: IMPORTANT CHECKPOINTS

- Ensure that injection site(s) is clipped (if applicable) and aseptically prepared.
- Adhere to strict aseptic technique during all procedures—doing this is mandatory.

- Ensure that drug solutions are free from contamination (especially for epidural and intraarticular techniques).

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Systemic local anesthetic toxicosis is possible with any technique and is usually associated with inadvertent IV injection/excessive drug doses.
- Infiltrative anesthesia:
  - Incisional block: inadvertent IV or intraarterial injection, penetration of body cavities/organs
- Peripheral nerve blocks:
  - Dental nerve block: self-mutilation following sensory loss to tongue and lips (rare)
  - Brachial plexus block: inadvertent IV or intraarterial injection or injection into the thoracic cavity with possible pneumothorax/pulmonary laceration
  - Distal radial, ulnar, median nerve blocks: self-mutilation following sensory loss to distal paws (very rare)
  - Intercostal nerve block: inadvertent intrathoracic injection with possible pneumothorax/pulmonary laceration
- Epidural anesthesia/analgesia: inadequate block, hypotension, urinary retention, transient neurologic deficits (rare)
- Other regional techniques:
  - Intraarticular anesthesia/analgesia: articular cartilage damage
  - Interpleural anesthesia: pneumothorax, pulmonary laceration
  - IV regional anesthesia: ischemic limb damage; systemic local anesthetic toxicosis due to tourniquet failure



LOCAL AND REGIONAL ANESTHESIA Brachial plexus nerve block. Place needle medial to scapulohumeral joint, lateral to thoracic wall, toward costochondral junction, parallel to vertebral column.

(From Fossum TW, et al: Small animal surgery, ed 2, St Louis, 2002, Mosby.)

PROCEDURE

For selected techniques only:

- Peripheral nerve blocks:
  - Dental nerve blocks:
    - Infraorbital: palpate infraorbital foramen rostral and ventral to medial canthus of eye; insert needle into foramen and aspirate. If there is negative pressure (no blood), inject local anesthetic.
    - Mandibular: palpate mandibular foramen intraorally on the medial surface of the mandible, and insert needle percutaneously from the ventromedial aspect of the mandible toward the foramen and aspirate. If there is negative pressure (no blood), inject local anesthetic.
  - Brachial plexus block:
    - From a cranial approach, insert the needle medial to the scapula just ventral to the body of the sixth cervical vertebra; advance until the tip of the needle is just beyond the first rib and aspirate. If there is negative pressure (no blood), inject one-fourth dose of a local anesthetic; withdraw needle partially and aspirate. If

there is negative pressure (no blood), inject another one-fourth dose of anesthetic; repeat until needle is completely withdrawn and all drug has been injected.
    - Distal radial, ulnar, median nerve blocks; three injections required per paw:
        - On dorsal aspect, insert needle just proximal to the first phalanx and aspirate; if negative pressure (no blood), inject local anesthetic.
        - On palmar aspect, insert needle just medial to accessory carpal pad and aspirate; if negative pressure (no blood), inject local anesthetic.
        - Remove needle and insert just lateral and proximal to accessory carpal pad and aspirate; if negative pressure (no blood), inject local anesthetic.
- Epidural anesthesia/analgesia (see p.1260):
    - Place animal in lateral or sternal recumbency, and locate the lumbosacral space as follows: palpate the cranial edges of the ilial wings (this is at the level of the sixth lumbar vertebra), palpate the dorsal process of the seventh lumbar vertebra caudal to this area, and then palpate a large depression corresponding to the lumbosacral space farther caudally.
    - Insert spinal needle directly over the lumbosacral space at an angle perpendicular to the skin, and advance needle slowly through the ligamentum flavum until a loss of resistance and characteristic “pop” is appreciated, indicating that the epidural space has been penetrated.
    - Remove stylet, and ensure that blood or cerebrospinal fluid (CSF) is not evident in needle hub.
    - Inject 1 mL of air, using a glass syringe to confirm lack of resistance, and correct needle placement; inject local anesthetic, opioid, or other analgesic.
- Other regional techniques:
    - Interpleural anesthesia:
        - Insert catheter in the ninth intercostal space on the midlateral aspect of thorax.
        - Aspirate to remove air/blood.
        - Inject local anesthetic (lidocaine should be injected first in conscious animals to minimize discomfort and can be followed by bupivacaine if a long-duration block is desired).

POSTPROCEDURE

- If local/regional anesthesia is being used for supplementing analgesia in conjunction with general anesthesia, injectable and inhalant anesthetic requirements may be markedly reduced.
- Animals must be monitored for adequacy of analgesia and treated accordingly.

ALTERNATIVES AND THEIR RELATIVE MERITS

Pain associated with surgery, trauma, and a variety of medical conditions can usually be managed using systemic analgesics (e.g., opioids, nonsteroidal antiinflammatory drugs [NSAIDs]); however, these agents are not able to block peripheral nociceptive input. The inclusion of a local or regional technique constitutes a multimodal approach to anesthesia and pain management and is simply good medical practice.

AUTHOR: LEIGH A. LAMONT

Liver Biopsy, Laparoscopic

OVERVIEW AND GOALS

- Allows visualization of entire organ in order to obtain biopsy samples from appropriate lobe/lobes
- Easy access to gall bladder for examination/aspirate
- In most cases, pancreas can be examined/biopsied as well.
- Samples superior in size/number in most cases (compared to ultrasound-guided samples)
- Can be performed safely in dogs and cats

INDICATIONS

- Abnormal results of liver function tests (bile acids/ammonia)
- Persistently elevated serum liver enzyme levels
- Abnormal liver size or architecture ultrasonographically
- Ascites of unknown origin
- Elucidation of etiology in cases of suspected triaditis

CONTRAINDICATIONS

- Bleeding disorder
- Hepatic encephalopathy
- Surgical disease (e.g., bile duct obstruction/biliary mucocele)
- Peritonitis (septic/neoplastic)
- Diaphragmatic hernia
- Very small patient (<2 kg)

EQUIPMENT, ANESTHESIA

Instrumentation:

- Telescope: 5 mm (0 degrees)
- Veress needle
- Trocar cannulas: two sufficient for most liver biopsies
- Biopsy forceps: punch and oval
- Palpation probe
- Light source and cable: 130- to 300-watt xenon bulb
- Video camera and monitor
- CO2 insufflator

ANTICIPATED TIME

An experienced laparoscopist can perform the procedure in less than 20-30 minutes in most instances.

PREPARATION: IMPORTANT CHECKPOINTS

- Coagulation profile and buccal mucosal bleeding time
- Blood pressure
- Packed cell volume/total solids (PCV/TS)
- Bladder must be emptied prior to Veress needle insertion
- Sterile surgical prep from the 10th intercostal space to pubis

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Lack of insufflation: Veress embedded in omental fat, poor placement for insufflation based on CO2 flow. Withdraw Veress and replace.
- Laceration of spleen: usually not an emergency. Place patient in slight left lateral recumbency to avoid.
- Bladder impalement: empty bladder prior to procedure.
- Gall bladder leakage post aspiration: attempt aspiration of full contents to avoid.
- Postoperative seroma formation at trocar sites: avoid with double layer closure.

- In rare cases, patients showing respiratory compromise due to abdominal distension require ventilator support.

PROCEDURE

Ventral approach:

- Establish pneumoperitoneum: ventral midline placement of Veress needle into the abdomen, 1-2 cm caudal to the umbilicus.
- Insufflate the abdomen with CO_2 to set pressure maximums and flow rates based on the patient's size.
- Remove Veress needle once sufficient insufflation achieved, place first trocar at the Veress incision site, replace CO_2 flow to the trocar flow port.
- Place telescope through trocar, examine abdominal contents.
- Under telescopic guidance, place a second trocar in a right or left lateral position, depending on liver access/size/distribution of lesion(s).
- Transfer CO_2 line to the second trocar to prevent moisture accumulation on telescope lens.
- With telescope in central port, biopsy/probes in the lateral port, a liver biopsy can be obtained.
- Multiple lobes should be sampled from the edge of a given lobe or from the middle of a lobe of interest. Areas should be examined for excessive bleeding. Should this occur, pressure can be applied with a blunt probe, or gel foam can be inserted at the site.

POSTPROCEDURE

- Remove telescope and biopsy/blunt probes from trocars.
- Discontinue CO_2 flow.
- Open trocar flow ports, and gently place pressure on the abdomen to release gas via the trocars.
- Once abdomen is sufficiently deflated, trocars can be withdrawn from the abdominal wall.
- Each incision is closed in a two-layer fashion of the laparoscopist's choice.
- In most cases, patients can be sent home the same day, provided postoperative parameters (PCV/TS/blood pressure) are within normal and expected range.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Ultrasound-guided liver biopsy: less invasive, quicker procedure time, smaller sample
- Open liver biopsy via laparotomy: benefits are those associated with full abdominal exploratory surgeries but more invasive, longer healing.

SUGGESTED READING

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AUTHOR: MAUREEN CARROLL

Lithotripsy

SYNONYMS

Stone fragmentation, electrohydraulic lithotripsy (EHL), laser lithotripsy (holmium-doped yttrium, aluminum, garnet [Ho : YAG] laser)

OVERVIEW AND GOALS

Removal of urinary tract stones through natural orifices

INDICATIONS

Treatment of bladder and urethral stones in dogs

CONTRAINDICATIONS

Untreated coagulopathy

EQUIPMENT, ANESTHESIA

General anesthesia, flexible ureteroscope (males), rigid cystoscope (females), saline, protective eyewear, Ho : YAG laser or EHL probe, stone basket, 60-mL syringes

ANTICIPATED TIME

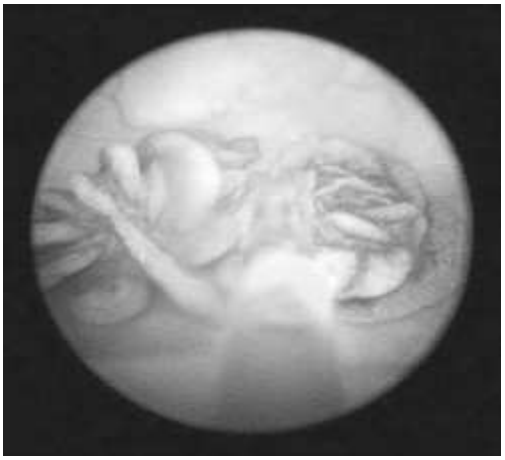
Variable (mean 60 minutes). Depends on stone location (longer in bladder than in urethra), sex of the patient (longer in males than in females), number, size and shape of the stones (longer for smooth and large stones)

PREPARATION: IMPORTANT CHECKPOINTS

- Urine culture and sensitivity 5 days before the procedure and appropriate antibiotic therapy if needed
- Coagulation profile:
    - The following breeds are predisposed to von Willebrand disease: Doberman pinscher, standard poodle, Shetland sheepdog, German shepherd, German shorthaired and wirehaired pointers, Scottish terrier, Chesapeake Bay retrievers. Factor measurement may be indicated.
- Protective eyewear
- Gauze squares on the eyes of the patient

POSSIBLE COMPLICATIONS

- Most complications occur either during or within 24 hours of the procedure.
- Complications related to cystoscope-guided laser lithotripsy occurred in 5 of 28 female dogs and 6 of 45 male dogs (Adams, 2008).
- Common: hematuria, stranguria usually self-limiting within 48 hrs
- Rare: urethral or bladder perforation (due to laser contact with the mucosa or secondary to voiding urohydropulsion [VUH]), urethral obstruction, indwelling urinary catheter for 1-5 days after the procedure, urinary tract infection
- Scope damage: probe activated within the scope
- Precautions:
    - Avoid firing laser against the mucosa or closer than 1 mm, flush abundantly, use rigid cystoscope in female whenever it is possible.
    - VUH the day after the lithotripsy if remaining fragments
    - Selection of candidates depending on the sex, the size/shape/location of the stones



LITHOTRIPSY Endoscopic image demonstrating 2 uroliths in the bladder of a dog. The probe is seen emerging from the bottom of the image and contacting the urolith on the right in preparation for fragmentation.

PROCEDURE

- Performing lithotripsy requires at least 2 people (clinician and assistant).
- Patients are put under general anesthesia. Females are positioned in dorsal recumbency and males in lateral recumbency. The vulva or prepuce is aseptically prepared. The scope is passed through the urethra. Saline is injected through the scope to distend the bladder and localize the stones.
- The probe is passed through the working channel of the scope until it contacts the stone. As soon as the stones are broken (small enough to pass through the urethra), VUH is performed (saline) to remove the fragments from the urinary tract.
- The scope can then be reintroduced to check for remaining fragments and if needed, a new series of fragmentation and urohydropulsion is performed. A stone basket can be used to remove fragments more rapidly. Stone fragments should be sent for culture and mineral analysis.

POSTPROCEDURE

- Analgesia (opioids and nonsteroidal antiinflammatory drugs)
- Radiographs or ultrasound to check for the presence of stones/fragments
- Stone analysis
- 5 days of broad-spectrum antibiotics (amoxicillin or cephalexin)
- If remaining fragments, repeat lithotripsy and/or VUH depending on their size. These fragments could serve as a nidus for future stone formation.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Surgery is the standard of care for urocystoliths in dogs and cats. Cystotomy allows the removal of bladder stones, but the sutures can serve as nidus for new stone formation.
- Obstructive urethral stones may sometimes be retropulsed into the bladder and removed by cystotomy. Lithotripsy is an excellent minimally invasive alternative to urethrotomy.
- Extracorporeal shock wave lithotripsy (ESWL) consists of fragmenting urinary tract stones by delivering external shock waves through a water bath or a specific fluid-filled cushion. It has been very successful in fragmenting nephroliths and ureteroliths in dogs but less successful with cystoliths and urethroliths. Feline nephroliths and ureteroliths are more resistant to fragmentation, and fragments may obstruct small feline ureters.
- A laparoscopic approach to cystolith removal can be used in male cats and small male dogs (<5 kg) when the scope is too large to pass through the urethra.

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AUTHORS: ALICE DEFARGES, MARILYN DUNN

Laryngeal, Pharyngeal, and Oral Examination

SYNONYMS

Laryngoscopy, pharyngoscopy

OVERVIEW AND GOAL

Complete examination of oral cavity, oropharynx, larynx, and part of the nasopharynx

INDICATIONS

- Anorexia (secondary to oral discomfort)
- Oronasal fistula evaluation
- Mandibular/maxillary fracture assessment
- Cervical/oral/facial trauma
- Precise occlusion evaluation
- Ptyalism/hypersalivation
- Gagging
- Halitosis
- Facial deformity
- Voice change
- Dysphagia
- Noisy respiration, especially inspiratory stridor with a radiographically normal trachea
- Respiratory distress, especially inspiratory

CONTRAINDICATIONS

Severe respiratory distress necessitating oxygen supplementation, endotracheal intubation, or emergency tracheostomy

EQUIPMENT, ANESTHESIA

VENOUS ACCESS:

- Hair clippers with a #40 blade
- Surgical skin scrub preparation materials
- IV over-the-needle catheter of appropriate size for the animal (18-24 gauge)
- T-port or PRN to cap catheter
- White cloth tape, 1½ inches (3.5 cm) and 1 inch (2.5 cm), for catheter fixation
- 5 mL heparinized saline

ANESTHETIC AGENTS:

- Premedication:
  - It may be preferable to avoid premedication when evaluating laryngeal function. The use of thiopental without premedication significantly increases arytenoid motion before recovery, which is optimal when compared to other protocols (propofol, ketamine, and diazepam; acepromazine and thiopental; acepromazine and propofol). This is the recommended protocol for evaluating laryngeal function (Tobias et al., 2004).
  - If the lack of premedication when potentially evaluating laryngeal function is unacceptable to the clinician, an alternative is glycopyrrolate (0.01 mg/kg IV, IM, or SQ) and butorphanol (0.1 mg/kg IV, IM, or SQ).
  - If no evaluation of laryngeal function is judged necessary, a standard sedation or premedication protocol is acceptable if the animal is stable. Examples (see also inside back cover of book):
    - Glycopyrrolate (0.01 mg/kg IV, IM, or SQ) + acepromazine (0.05 mg/kg IM or SQ) + butorphanol (0.1 mg/kg IM or SQ); *or*
    - Glycopyrrolate (0.01 mg/kg IV, IM, or SQ) + hydromorphone (0.1 mg/kg IM) ± acepromazine (0.05 mg/kg IM or SQ)
- Induction:
  - For evaluation of laryngeal function, thiopental (20 mg/kg IV, give half the volume as a bolus and then "to effect") or propofol (2 mg/kg with premedication, or 6 mg/kg if no premedication) are preferred over ketamine-diazepam (Gross et al., 2002).
  - If no evaluation of laryngeal function is judged necessary, routine agents are appropriate. Examples in stable animals

include:
    - Thiopental (as above); *or*
    - Propofol (as above); *or*
    - Ketamine (10 mg/kg) + diazepam (0.5 mg/kg) IV
- Stimulation of respiration:
    - The use of doxapram HCl helps differentiate normal dogs from dogs with laryngeal paralysis. In these dogs, administration of doxapram seems to enhance paradoxical arytenoid motion:
        - Doxapram HCl, 5-10 mg/kg IV

POSITIONING:

- To maintain head in the upright position:
    - Conformable roll gauze (e.g., 2-inch [5 cm] Kling)
    - Two poles (of the type used for IV fluid administration, optional)

ORAL EXAMINATION:

- Oral speculum (mouth gag)
- Light source/transilluminator
- Laryngoscope
- Dry gauze sponges:
    - For manipulating the tongue
    - To dry up secretions

LARYNGEAL EXAMINATION:

- Oral speculum
- Light source/transilluminator
- Laryngoscope
- One or two tongue depressors taped end to end for dorsal retraction/elevation of the soft palate

OROPHARYNGEAL AND NASOPHARYNGEAL EXAMINATION:

- As for oral and laryngeal examination (above) + spay hook for cranial retraction of soft palate
- Small mirror used in dentistry, with antifogging agent or immersed in warm (38○C) water/saline
- Small flexible endoscope (see Alternatives section, below)

FINE-NEEDLE ASPIRATION/BIOPSIES:

- A set of 10-mL syringes, 22-gauge needles, and microscope slides for fine-needle aspiration and cytologic examination
- Biopsy kit:
    - A #15 scalpel blade
    - Adson forceps
    - Needle holder
    - Small scissors
    - Suture scissors
    - Appropriate size resorbable suture (surgeon's preference)

ENDOTRACHEAL INTUBATION:

- Appropriate size tube (see p. 1293)
- Conformable 1- or 2-inch tape or gauze for tube fixation
- A 5- to 10-mL empty syringe for cuff inflation
- Anesthesia machine verified with appropriate circuit for the animal (semiopened or semiclosed):
    - Functional
    - Oxygen
    - Inhalant anesthetic agent

ANTICIPATED TIME

About 15-30 minutes

PREPARATION: IMPORTANT CHECKPOINTS

- Use preoxygenation with a mask if possible.
- Always perform this examination on animals that have been fasted, because the airway is not always protected during the exam. There is the possibility of regurgitation of gastric contents and subsequent aspiration pneumonia.
- Always be prepared for orotracheal intubation of animal and possible ventilation with oxygen through an anesthetic circuit.
- In animals in respiratory distress, always be prepared to perform an emergency tracheostomy (see p. 1344).
- In animals with moderate or marked inspiratory stridor or any degree of upper airway distress, owners must pre-emptively hear and understand options to consider (surgical intervention if problem correctable, euthanasia on the table if noncorrectable obstructive disorder) in case severe laryngeal infiltration, a nonresectable mass, or other equally serious problem is identified.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Incomplete examination
- May give a false-positive diagnosis of laryngeal paralysis because animal is too heavily sedated or not enough time is given for animal to come out of light anesthesia. To minimize the occurrence of this situation, prepare doxapram HCl and administer if needed.

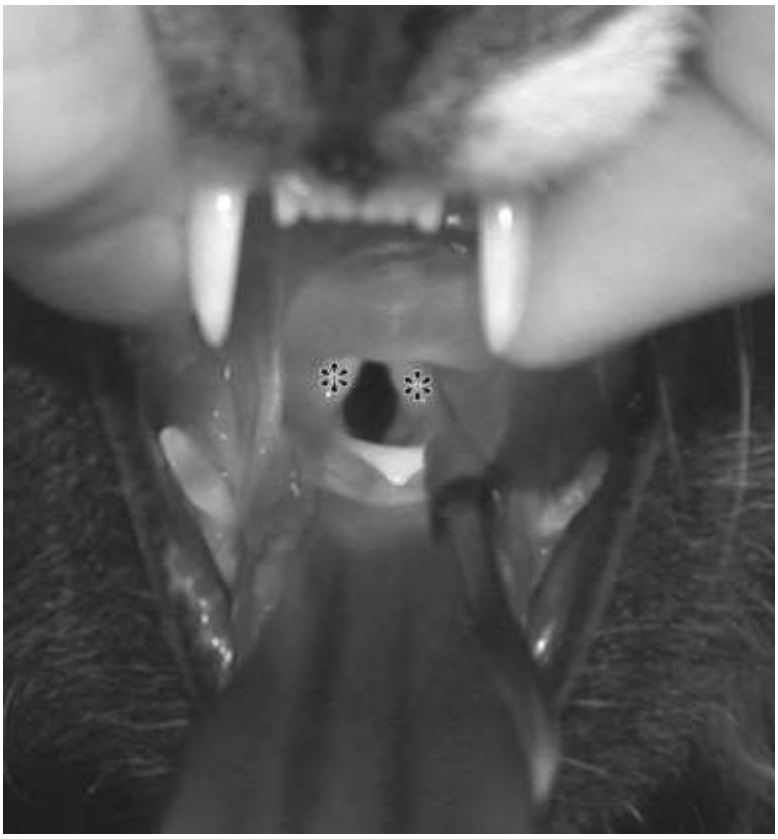
PROCEDURE

When dogs are extremely dyspneic due to laryngeal paralysis, the diagnosis often can be made on the awakened animal: a bright light source (e.g., Finnoff transilluminator) is directed into the oral cavity during the severe dyspnea, and failure of the arytenoid cartilages to abduct is clearly apparent in the conscious animal. Otherwise, proceed as follows:

- Venous access:
  - Prepare site for IV catheter insertion (clip, clean, and prep skin).
  - Insert IV catheter.
  - Close catheter with a T tube or a PRN.
  - Fixation of catheter to skin
  - Flush catheter with heparinized saline.
- Premedication:
  - Administer premedication if judged necessary.
- Preoxygenation:
  - Animal in sternal recumbency
  - If possible, use a mask to preoxygenate animal for 5 minutes.
- Induction of anesthesia:
  - IV administration of predetermined anesthetic agent:
    - Very light anesthetic plane is used for evaluation of laryngeal function:
      - If anesthetic plane is too deep, give time (5-10 minutes) for animal to partially recover from anesthesia, and then continue to evaluate.
    - Deeper anesthetic plane is used for evaluation of oral cavity and pharynx and anatomic evaluation of the larynx.
- Positioning of the head:
  - Assistant holds head upright using a piece of conformable roll gauze (Kling) passed behind the upper canine teeth.
  - Alternatively, two IV poles, one on each side of the table, can be used; the conformable gauze is passed behind the upper canine teeth, and the gauze is attached to each IV pole, thus supporting the head in the upright position.
  - Place oral speculum of appropriate size.
- Oral examination:
  - All structures of the oral cavity should be evaluated:
    - Lips, cheeks, teeth (abscess, fracture, occlusion), gingiva, tongue (under and at the base), hard palate, soft palate (mass, elongation), tonsillar crypts/tonsils.
- Oropharyngeal examination:
  - Soft palate should be palpated for thickness, mobility.
  - Elevate soft palate dorsally with a tongue depressor or two depressors taped end to end in a large dog.
  - Depress base of the tongue ventrally with a laryngoscope. This permits evaluation of the upper esophageal sphincter.
- Laryngeal examination:
  - After the evaluation of the oropharynx, it is appropriate to evaluate the anatomy of the larynx: epiglottis, aryepiglottic folds, arytenoid cartilages (cuneiform and corniculate processes) vocal cords, laryngeal ventricles.
  - Then evaluate the function of the larynx:
    - Normal:
      - Observe active abduction of the arytenoid cartilages synchronized with inspiration.
      - Observe passive adduction of the arytenoid cartilages synchronized with expiration.
    - Abnormal:
      - Observe no movement of cartilages:
        - Is it significant? Animal is usually too deeply anesthetized; wait until motion returns or

administer doxapram HCl (seep. 635).
- Observe paradoxical movement of arytenoid cartilages, indicating laryngeal paralysis:
  - Adduction at inspiration
  - Abduction at expiration

- Nasopharyngeal examination:
  - Palpate the soft palate, then press firmly to detect masses that could be in the nasopharynx (e.g., a nasopharyngeal polyp could deform the soft palate and could be palpated).
  - Use a spay hook to retract the caudal edge of the soft palate cranially, permitting the visualization of part of the nasopharynx.
  - Use a small, dental-type mirror to “look back” into the nasopharynx.
  - Use a small flexible endoscope if available.



LARYNGEAL, PHARYNGEAL, AND ORAL EXAMINATION Typical appearance of glottis of a healthy, anesthetized cat. Tongue is depressed with a laryngoscope, revealing epiglottis ventrally (tip appears as a white triangle in center of image), soft palate dorsally, and arytenoid cartilages laterally *(asterisks)*. Slightly deeper and ventral to arytenoid cartilages, vocal cords are seen (slight obliquity; animal's left vocal cord is seen more clearly here than right one).

POSTPROCEDURE

- Airway protection:
  - When the examination is completed, perform orotracheal intubation, inflate cuff, and secure tube to avoid complications secondary to regurgitation/aspiration pneumonia.
- Administer oxygen via anesthesia circuit.
- Monitor recovery from anesthesia.
- Extubation of animal when reflexes are reestablished, especially the deglutition reflex.

ALTERNATIVES AND THEIR RELATIVE MERITS

In a study comparing three techniques for the diagnosis of laryngeal paralysis, direct per os laryngoscopy combined with the knowledge of the clinical history and physical examination was preferred over echolaryngoscopy and transnasal endoscopy (Radlinsky et al., 2009).

NASOPHARYNGEAL ENDOSCOPY:

- The use of a small flexible endoscope can permit a more precise evaluation of the nasopharynx because it can be retroflexed 180○ over the soft palate and advanced in the nasopharynx, permitting visualization of the nasal choanae.

- Involves a substantial investment (endoscope, monitor, camera, image processor, light source).

TRANSNASAL ENDOSCOPY:

- The use of transnasal endoscopy has been reported in large dogs (over 20 kg) for the evaluation of the nasopharynx and of laryngeal structure and function. General anesthesia is not required, which might be an advantage. Dogs are heavily sedated, and topical anesthesia (2% lidocaine) is used in the left nasal passage.
- This technique does not permit evaluation of the oral cavity and oropharynx, so it is of limited use for a complete evaluation as described here.
- Involves a substantial investment (endoscope, monitor, camera, image processor, light source)

ULTRASOUND:

- Sonographic evaluation of laryngeal paralysis has been evaluated in 40 dogs (30 with laryngeal paralysis and 10 normal). Results have shown a high degree of sensitivity and specificity with this technique.

SUGGESTED READING

Gross ME, et al: A comparison of thiopental, propofol, and diazepam-ketamine anesthesia for evaluation of laryngeal function in dogs premedicated with butorphanol-glycopyrrolate. J Am Anim Hosp Assoc 38:503, 2002.

Monnet E: Laryngeal paralysis and devocalization. In Slatter D, editor: Textbook of small animal surgery, ed 3, Philadelphia, 2003, WB Saunders, pp 837–845.

Radlinsky MG, Mason DE, Hodgson D: Transnasal laryngoscopy for the diagnosis of laryngeal paralysis in dogs. J Am Anim Hosp Assoc 40:211, 2004.

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Rudorf H, Barr FJ, Lane GJ: The role of ultrasound in the assessment of laryngeal paralysis in the dog. Vet Radiol Ultrasound 42(4):338–343, 2001.

Tobias KM, Jackson AM, Harvey RC: Effects of doxapram HCl on laryngeal function of normal dogs and dogs with naturally occurring laryngeal paralysis. Vet Anesth Analg 31(4):258, 2004.

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AUTHOR: BERTRAND LUSSIER

Myelography

Additional Images Available on Website

OVERVIEW AND GOALS

Myelography is the introduction of positive-contrast media into the subarachnoid space. It is used for demonstrating lesions in the spinal cord or lesions extrinsic to the spinal cord that may be causing cord compression. This procedure is used for supplementing or confirming information obtained with plain-film radiography.

INDICATIONS

- Clinical signs of spinal cord disease (± spinal trauma)
- Spinal pain or neurologic deficits without diagnosis on plain films or laboratory tests
- Confirmation of suspected lesion on plain films
- Aid in surgical planning (define exact location of lesion)
- Determine amount of spinal cord swelling
- Exclude compressive lesions of the spinal cord; by process of elimination, make presumptive diagnosis of non-compressive spinal disorder
- Rule out intraspinal lesion
- Disparity between clinical signs and plain radiographs
- Recurrence of clinical signs after decompressive spinal surgery

CONTRAINDICATIONS

- Cerebrospinal fluid (CSF) analysis indicates inflammation or infection: condition aggravated by irritation from contrast medium.
- Increased CSF pressure: possible herniation of cerebellum through foramen magnum
- Known hypersensitivity to contrast medium

EQUIPMENT, ANESTHESIA

- General anesthesia
- Intrathecal contrast material: low osmolar, nonionic, water-soluble iodines, such as iohexol or iopamidol (180-300 mg iodine/mL most commonly used):
    - Full spine dose is 0.45 mL/kg; regional dose is 0.30 mL/kg.
- A 20- to 22-gauge spinal needle with stylet and short bevel, 1½-3½ inches (depending on size of animal)
- Appropriately sized syringe (3-35 mL)
- Flexible extension tubing or T-port (catheter cap with side line and port)
- Hair clippers
- Surgical scrub solution, rubbing alcohol, and gauze/sponge for prep-ping skin
- Sterile surgical gloves

ANTICIPATED TIME

About 45-60 minutes, not including pre-procedural anesthesia time

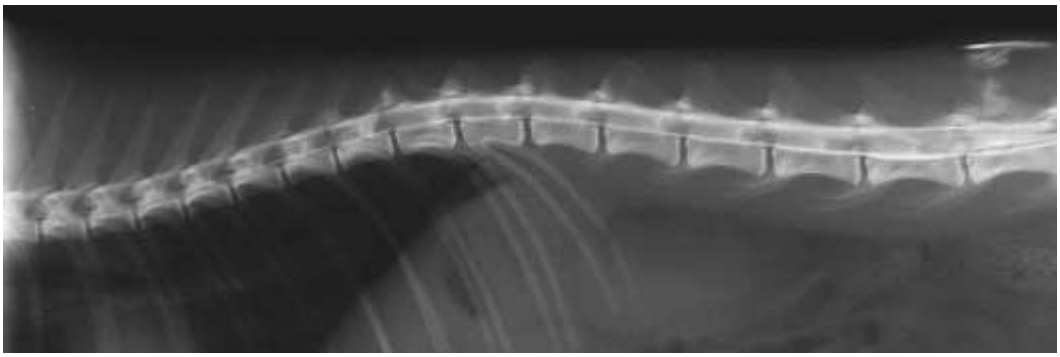
PREPARATION: IMPORTANT CHECKPOINTS

- Perform CSF analysis to ensure no evidence of infection or inflammation.
- Ensure adequate hydration status to decrease risk of neurotoxicity. Administer IV fluids as appropriate.
- Metastasis imaging (three-view thoracic radiographs are also indicated if malignancy is part of the differential diagnosis for the spinal problem).
- Advise owner the hair will be clipped in a large area near the injection site(s).

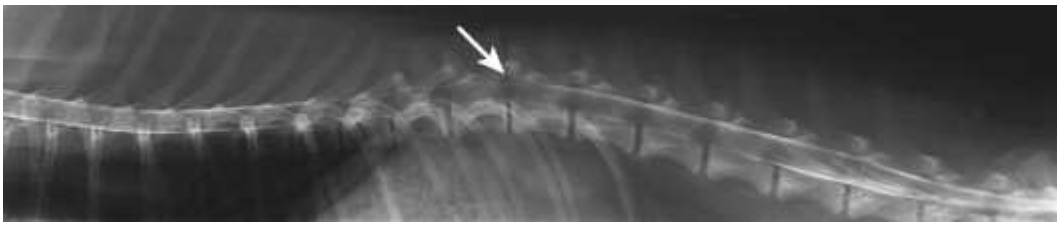
POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- The most common complication of myelography is postprocedure seizures. Recover the animal with head elevated to minimize risk. If directly induced by contrast, seizures are expected to occur during anesthetic recovery. Seizures occurring thereafter are virtually never caused by the contrast injection.

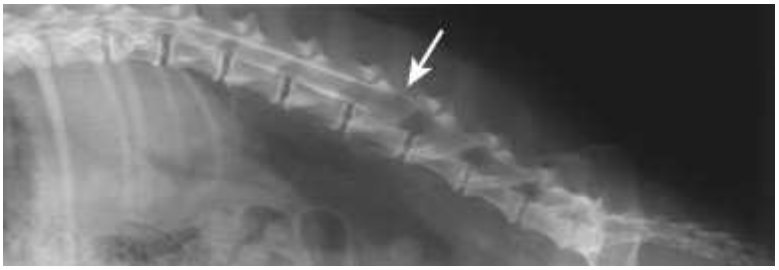
- Bradycardia is sometimes seen in animals during injection of the contrast material.
- Epidural injection may occur with lumbar puncture: wavy pattern is apparent radiographically both dorsally and ventrally.
- Subdural injection:
    - Central canal filling: thin line in center of cord
- Administration of air bubbles
- Use of the incorrect type of contrast agent can be fatal. Ionic contrast agents (e.g., diatrizoate or any other product) should never be used in any amount in myelography; only low-osmolar, nonionic, water-soluble iodines are indicated.
- Lumbar puncture: inability to enter the space is commonly due to a nonmidline location of the needle (needle is inadvertently located parallel and lateral to dorsal midline).
- Extension of the neck for neck-extended views can cause permanent cord injury, especially in animals with neck pain prior to the procedure and animals with severe cervical intervertebral disk disease (IVDD). These views should be preceded by nonextended views (diagnosis may be apparent without extension) or avoided altogether.



MYELOGRAPHY 1 Myelogram of cat, lateral projection. Lumbar and caudal thoracic portion. Normal study. Incidental finding is a small amount of intramuscular and subcutaneous accumulation of contrast material at site of lumbar injection.



MYELOGRAPHY 2 Myelogram of dog, lateral projection. Mild dorsal deviation of ventral subarachnoid contrast column and attenuation of dorsal contrast column, most pronounced at T12-T13 *(arrow)* are seen, identifying lesion as extradural. Mineralization of T11-T12 intervertebral disk is an incidental finding.



MYELOGRAPHY 3 Myelogram of dog. Attenuation of both dorsal and ventral contrast columns over L4 on this lateral projection is consistent with either an intramedullary lesion or a lateralizing extramedullary lesion *(arrow)*.

PROCEDURE

- Obtain survey radiographs of the area of interest (ventrodorsal and lateral views).
- Clip a large area of hair near the injection site (depending on cisternal or lumbar puncture).
- Aseptically prepare the site for injection with surgical scrub solution, isopropyl alcohol, and gauze/sponges.
- Sterile surgical gloves should be worn from this point on, and a sterile technique should be used (nonsterile materials will need to be handled by an assistant).
- Draw correct contrast dose into syringe.
- Attach flexible extension tubing to the syringe, and fill with contrast so no air bubbles are present.
- Cisternal puncture (see p. 1228):
    - Commonly used for evaluating suspected cervical spinal cord lesions

- Animal is placed in lateral recumbency with neck fully flexed at atlanto-occipital joint.
- Insert needle on midline, with bevel directed caudally, at the center of the triangle formed by the external occipital protuberance and the wings of the atlas.
- Advance needle slowly until ligamentum flavum and dorsal dura are punctured. Since the puncturing may not be apparent, a good approach is to advance 1-2 mm at a time, removing the stylet and checking for CSF in the hub of the needle each time before replacing the stylet and advancing further.
- Once the subarachnoid space is entered and CSF flows, obtain a CSF sample for immediate analysis.
- If CSF analysis does not provide a diagnosis, the procedure may be continued.
- Attach tubing to the needle and inject contrast material slowly.
- Once contrast material is injected completely, the needle is removed.
- Elevate head prior to obtaining radiographs to allow contrast material to flow caudally from the atlanto-occipital site of injection.
- Standard radiographic views (lateral, ventrodorsal, 45° obliques) are then obtained.
- Optional views (lateral, neck flexed, neck extended, and traction views). Caution with neck-extended views, which may cause permanent damage to the spinal cord in some animals, particularly those with severe cervical IVDD.

- Lumbar puncture:
  - Commonly used for evaluating suspected thoracolumbar lesions
  - More technically difficult—fluoroscopy beneficial (see p. 1228).
  - Animal in lateral recumbency.
  - Sixth lumbar spinous process is palpated. For anatomic localization of this spinous process, see p. 1260.
  - With bevel directed cranially, introduce needle at 30-60° angle at this site just to the side of the spinous process.
  - Reposition needle until tip enters interarcuate space between L5 and L6. It may be necessary to flex the spine—especially in older animals with degenerative bony changes.
  - The tail or hind limbs may twitch as the needle enters the spinal cord.
  - Advance needle to canal floor.
  - Remove stylet and check for CSF; if no CSF is visualized, withdraw needle slowly until flow is obtained.
  - Compressing the jugular veins may increase CSF pressure, allowing CSF to flow more readily.
  - Once CSF is obtained and no contraindications have been identified on CSF analysis, attach tubing to the needle, and inject contrast material slowly into subarachnoid space.
  - Once contrast material is injected, the needle is removed.
  - Standard radiographic views (lateral, ventrodorsal, 45° obliques) are then obtained.

POSTPROCEDURE

- The animal's head should be elevated so contrast material does not accumulate around the brain.
- The animal should be monitored for seizure activity.
- If seizures are encountered, diazepam (0.5-1 mg/kg IV) can be administered.
- Many clinicians recommend keeping the animal under general anesthesia for 30 minutes to 1 hour after myelography to decrease the incidence of seizures.
- Myelographic effect on CSF: increased cell count (pleocytosis), increased percentage of neutrophils, increased protein, false-positive Pandy score, and high specific gravity. These effects are transient, and the normal state usually returns in 24-48 hours.
- Maintain adequate hydration status: IV fluids ± fluid diuresis.

ALTERNATIVES AND THEIR RELATIVE MERITS

- CT scan:
  - Requires general anesthesia and knowledge of cross-sectional anatomy
  - Provides axial images without superimposition of other structures, more detailed than standard radiography, ability to postprocess
  - Equipment and CT scan examination more costly than myelography and CT often requires intrathecal injection of contrast prior to the scan
- MRI:
  - Requires general anesthesia and knowledge of cross-sectional anatomy
  - Provides axial images without superimposition of other structures; more detailed than standard radiography
  - Sensitive, accurate, noninvasive, and does not involve the use of ionizing radiation
  - Equipment and MRI examination more costly than myelography or CT scan.

AUTHOR: LEEANN PACK

Muscle and Nerve Biopsy

OVERVIEW AND GOAL

Minimally invasive procedure for collection of muscle specimens for histologic, histochemical, immunohistochemical, and ultrastructural analyses. Nerve biopsy should only be performed by persons trained in the procedure.

INDICATIONS

- Chronic muscle atrophy, hypertrophy
- Weakness, hypotonia
- Exercise intolerance
- Nonorthopedic gait abnormalities
- Contractures
- Chronically elevated creatine kinase activity, myoglobinuria
- Myalgia, cramping
- Clinical evidence of muscle or peripheral nerve disease

CONTRAINDICATIONS

- Bleeding disorder
- Poor anesthetic risk

EQUIPMENT, ANESTHESIA

- General anesthesia usually required; muscle biopsies can be taken under heavy sedation and local anesthetic if indicated.
- General surgical pack including self-retaining retractors
- Containers for biopsy specimens:
  - Plain red-top tubes (5-10 mL) for unfixed biopsy specimens
  - Biopsy jars containing fixatives: 10% formalin for routine histopathologic evaluation, 2.5% glutaraldehyde in phosphate buffer or Karnovsky's fixative for electron microscopy
- Tongue depressors or wooden sticks and suture material or pins: for maintaining length of nerve specimens
- Method of refrigeration prior to shipping specimens
- Styrofoam containers for shipping refrigerated specimens to a specialized laboratory

ANTICIPATED TIME

- About 60-90 minutes if the biopsy is combined with electrophysiologic examinations (see online chapter: Electromyography and Nerve Conduction Velocity)
- About 30-45 minutes if nerve and muscle biopsy only

PREPARATION: IMPORTANT CHECKPOINTS

- It is essential that details of fixation and transportation be obtained from the laboratory that processes the tissues prior to taking biopsies.
- Determine if problem is generalized or localized to specific muscle groups: this will help in the selection of which muscle and nerve should be biopsied.
- Knowledge of anatomic localization of specific muscle groups
- It is critical that unfixed biopsy specimens are kept refrigerated and shipped by courier for processing within 24-36 hours. Do not ship biopsy specimens on a Friday.

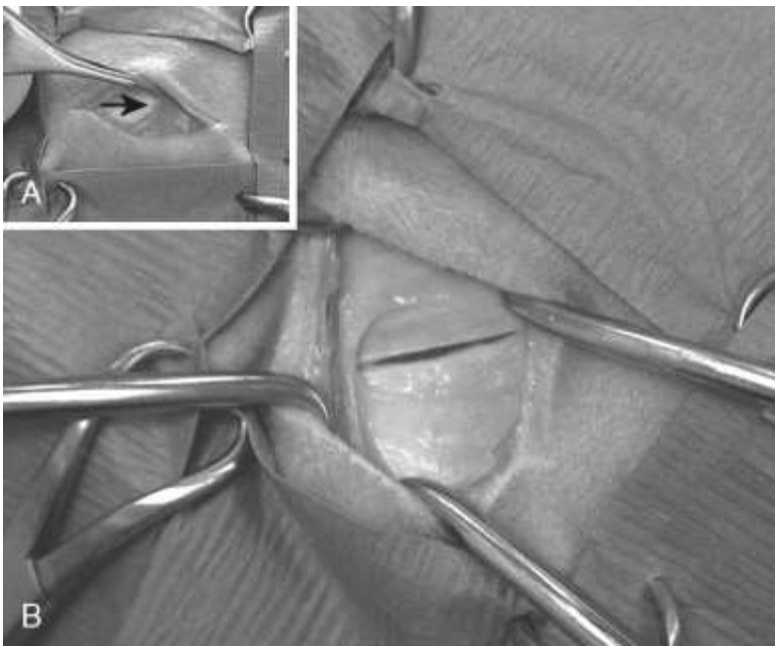
POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Complications (hematoma, swelling) are rare following muscle biopsy.
- Transient neurologic dysfunction (knuckling, proprioceptive deficits) possible on the side of a nerve biopsy. The owner should be warned before the procedure of the expected short-term deficits.
- Artifacts in histologic specimens due to poor fixation or traumatic collection; handle tissue carefully.
- Biopsy of wrong muscle (e.g., frontalis instead of temporalis for masticatory muscle myositis)

PROCEDURE

For biopsy of muscle (biceps femoris) and nerve (common peroneal) through the same incision, an open biopsy procedure is necessary:

- Palpate the location of the common peroneal nerve on the lateral aspect of the distal femur just caudal to the proximal tibia.
- Clip hair, aseptic scrub/prep.
- Incise skin and overlying fascia to expose muscle.
- Establish orientation of the muscle fibers.
- Make parallel incisions along the longitudinal direction of the muscle fibers.
- Collect biopsy specimens 0.5 cm (width) × 0.5 cm (depth) × 1 cm (length).
- Transect the ends of the biopsy, handling carefully to minimize artifact.
- Wrap tissue in a saline-moistened gauze sponge (only moistened, not dripping wet).
- Place in dry, watertight container and keep chilled (not frozen).
- Collect a second smaller piece of muscle from same site, and place freely in 10% buffered formalin.
- Locate the nerve as it passes over the lateral head of the gastrocnemius muscle.
- Isolate the nerve carefully by blunt dissection.
- A 5-0 or 6-0 silk suture is placed through the caudal one-third to one-half of the nerve at the proximal end of the biopsy site, allowing minimal gentle traction.
- A 3-4 cm fascicular biopsy is excised using fine iris scissors.
- Lay nerve specimen on a tongue depressor or stick, and either pin or tie ends with suture to maintain length. Do not stretch.
- Immerse nerve biopsy into either 10% buffered formalin or Karnovsky's fixative.
- The fascial layer is closed with absorbable suture (e.g., polydioxanone).
- Skin closure with monofilament nylon or staples.



MUSCLE AND NERVE BIOPSY Biopsies obtained from temporalis muscle for diagnosis of masticatory myositis. **A**, Frontalis muscle *(arrow)*, first muscle encountered after making skin incision. Muscle should be incised and retracted, allowing visualization of the thick fascia that overlies temporalis muscle. **B**, Fascia has been incised and retracted, allowing access to temporalis muscle.

(For a more complete description of anatomy of the masticatory muscles, refer to Melmed et al, 2004.)

Open muscle biopsy procedures are also recommended if a peripheral nerve biopsy is not collected at the same time. For collection of temporalis muscle, make sure that the frontalis muscle is not collected by mistake.

Percutaneous needle/core biopsy is not recommended for routine muscle biopsy collection in dogs and cats:

- Inadequate sample size
- Difficult to orient tissue
- Artifact

Needle biopsies may be beneficial in research situations where sequential biopsy samples may be required over time; may be guided by ultrasonographic localization of specific lesions.

POSTPROCEDURE

- Treatment of hemorrhage, swelling, or hematoma if these occur (rare)
- External dressings are not normally required.
- Animals should be monitored to prevent interference with the sutures.
- Proprioceptive deficits as already described; usually self-resolving in 3-4 days; long-term deficits are extremely uncommon.

ALTERNATIVES AND THEIR RELATIVE MERITS

- For muscle diseases, there is no alternative to the muscle biopsy for determining the specific diagnosis and therapeutic options.
- MRI studies may help localize focal lesions and allow for guided muscle biopsies.
- Electrophysiologic examinations can provide important information on peripheral nerve diseases, but a peripheral nerve biopsy should still be collected for histologic evaluation.

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Melmed C, Shelton GD, Bergman R, et al: Masticatory muscle myositis: pathogenesis, diagnosis, and treatment. Compend Contin Educ Pract Vet 26:590–605, 2004.

AUTHOR: G. DIANE SHELTON

Magnetic Resonance Imaging Scan

SYNONYMS

MRI, MR

OVERVIEW AND GOALS

- Magnetic resonance imaging (MRI) is a method of cross-sectional imaging that does not involve ionizing radiation. When compared to radiography, MRI allows improved evaluation of areas of complex anatomy by avoiding superimposition of multiple structures. The contrast resolution of MRI is vastly superior to that of radiography and computed tomography (CT).
- Magnetic resonance imaging can be used for assessing any area of the body. In veterinary medicine, common uses include assessment of the brain and spinal column. Musculoskeletal imaging (scapulohumeral joint, stifle etc) is also increasing in popularity in small animal practice.

INDICATIONS

Disease of the central nervous system; best method available for imaging of the brain

CONTRAINDICATIONS

- Inability to tolerate general anesthesia
- Presence of a pacemaker: in a minority of patients, the MRI magnetic field may alter the pacemaker program or cause the pacemaker to oscillate in the patient. In human medicine, MRI suites bear warnings forbidding entry to any person with a pacemaker, so it is unlikely that an MRI technician will allow a veterinary patient with a pacemaker to be scanned.
- Presence of ferrous (iron-containing) metal including implants and intestinal foreign bodies:
    - Movement of the metal when in the magnetic field, causing soft-tissue trauma
- Presence of large metallic implants (nonferrous) in the area of interest:
    - Heating of the metallic implants → tissue damage
    - Imaging artifact severely limits the value of the study.

GENERAL MRI SAFETY CONSIDERATIONS:

- Injury to the patient and/or damage to the MRI magnet can occur if careful attention is not paid to basic MR safety as regards the presence of metallic objects within the MRI suite.
- The MR magnet is the core of the MRI unit, and the magnet is always “on,” 24 hours a day. Therefore, it is never safe to have loose metallic objects in the vicinity of the magnet—that is, anywhere in the same room as the MRI unit (MRI suite).
- Since the chemical composition of metal objects (ferrous or nonferrous) may not be known, all metallic objects should be regarded as potential safety hazards and excluded from the MRI suite.
- All equipment used in the area of the MRI magnet must be constructed of plastic and/or nonferrous metal or must be kept a safe distance from the magnet and secured. Recorded instances where this guideline was not followed have produced injury and death in patients and hospital personnel through blunt trauma caused by large objects which transform into projectiles owing to their strong attraction to the magnet.
- The safe distance from the magnet will depend on the field strength of the magnet, the shielding of the magnet and the amount of ferrous metal in the object. A distance of 36 inches (3 meters) is generally sufficient for a magnet of 1.0 tesla or less field strength.
- Because of the safety hazards associated with MRI imaging, it is best to limit the number of personnel in the MRI suite to the minimum necessary to perform the study and monitor the patient.

EQUIPMENT, ANESTHESIA

General anesthesia is required. MRI studies are prolonged and generally performed using gas anesthesia. Constant rate infusion of intravenous anesthetic agents can be used, but gas anesthesia is preferred because of the duration of the procedure.

- Endotracheal tube, NOT wire reinforced:
    - A laryngoscope can only be used if the patient is intubated in an area isolated from the MRI magnet.
- Gas anesthesia:
    - Anesthesia machine:
        - Unit specified as being MRI safe (nonferrous metals and plastic used in construction)

        - Generic anesthesia unit with long breathing circuit; minimum distance to magnet ~3 feet (1 meter)
- Constant rate infusion:
    - Infusion pump:
        - Unit specified as being MRI safe (nonferrous metals and plastic used in construction)
        - Generic infusion pump with extension tubing; minimum distance to magnet ~3 feet (1 meter)

Monitoring equipment:

- Pulse oximeter:
    - The patient attachment and cables must be specially constructed of nonferrous metal and/or plastic:
        - Fiberoptic technology is employed; an example is the Nonin 7500 FO unit.
- Blood pressure/CO2 measurement:
    - The patient attachment and cables must be specially constructed of nonferrous metal and/or plastic:
        - Surgivet monitors
- Electrocardiogram (ECG):
    - ECG electrodes for MRI use are available:
        - Because of radiofrequency interference, usable ECG tracings cannot be acquired during image acquisition.
- Emergency kit:
    - As with any procedure performed under general anesthesia, the equipment and drugs necessary for emergency cardiopulmonary cerebral resuscitation (CPCR) should be immediately available.
    - Great care should be exercised to ensure that metallic objects are not introduced near the magnet during CPCR. In the case of emergency, the patient will need to be removed from the MRI suite and resuscitative efforts performed at a safe distance from the magnet.

Intravenous contrast agent:

- Paramagnetic agents:
    - Gadolinium diethylenetriamine penta-acetic acid (Gd-DTPA): Magnevist
    - Gadodiamide: Omniscan
        - Nephrogenic systemic fibrosis has been reported as a sequela to the injection of intravenous paramagnetic contrast agents in human patients with renal insufficiency. This syndrome has not been reported in veterinary patients, but care should be taken when administering these agents to patients with renal dysfunction. Gadodiamide has a higher safety ratio than Gd-DTPA.
- Intravenous fluids
- Blankets/heated fluid pads or bags

ANTICIPATED TIME

The time required to perform the study depends on many factors:

- Field strength of the magnet: the higher the field strength of the magnet, the more quickly the study can be performed.
- Configuration/size of the radiofrequency coils
- Size of the area to be scanned
- Number and type of imaging sequences performed: unlike CT, MRI involves multiple separate image acquisitions. Images are obtained in multiple planes and using multiple different imaging parameters; the more acquisitions performed, the longer the study.

APPROXIMATE TIMES (Based on use of a 1.0-tesla magnet):

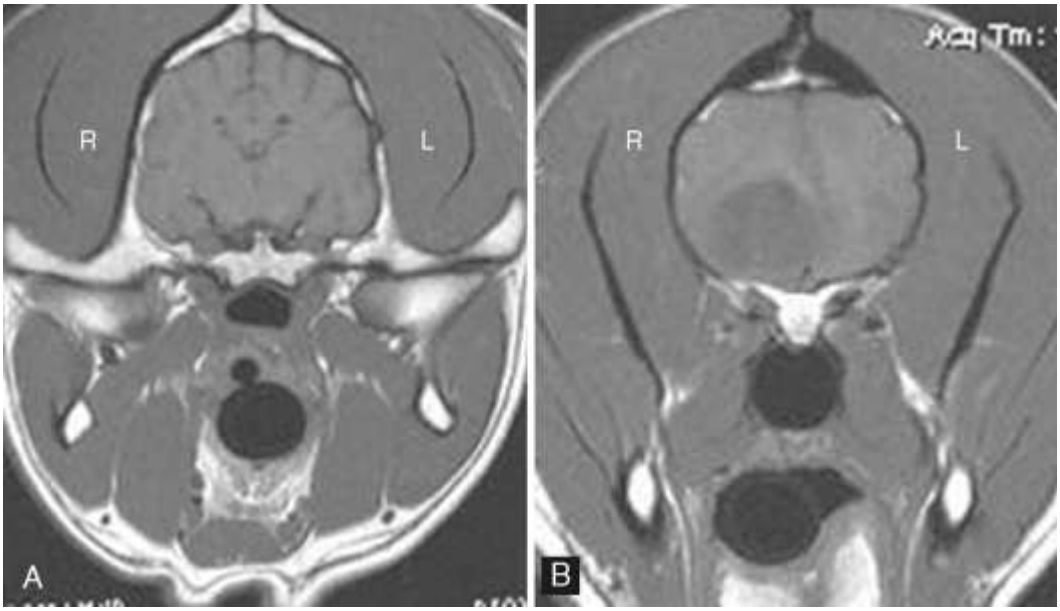
- Brain: 1-1.5 hours
- Spinal column:
    - Cervical: 1-1.5 hours
    - T3-L3: 1.5-2 hours
    - Lumbar: 1-1.5 hours

Because of long scan times, it is important to determine neuroanatomic localization of spinal lesions so that only the affected area of the spinal column is scanned, particularly in large dogs.

PREPARATION: IMPORTANT CHECKPOINTS

- Obtain thorough patient history: pacemaker? nonferrous metallic implants/foreign bodies? ferrous metallic implants/foreign bodies?
- Routine laboratory evaluation: CBC, serum biochemistry panel

- +/− Thoracic radiographs
- +/− Abdominal radiographs or ultrasound
- Many patients undergoing MR imaging are older and may have multiple diseases. Routine laboratory evaluation and thoracic and abdominal screening may be indicated in these patients for two reasons: to rule out the presence of concurrent disease that may affect the patient's ability to tolerate general anesthesia and to identify the presence of any potentially life-shortening disease process unrelated to the primary complaint (e.g., “incidental” splenic mass).
- Make sure all needed equipment is available and functional. This is especially important if the study is to be performed at an outside (e.g. nonveterinary) facility.
- Preparation for general anesthesia:
    - Routine preanesthetic fasting
    - Place IV catheter: when placing the catheter, the anticipated position of the patient within the MRI unit must be considered, and the catheter should be placed to allow easy access to it during the procedure. For example, in patients undergoing MR scan of the head, it is convenient to have the IV catheter placed in the saphenous vein. This is, however, not an absolute requirement, because the forelimb can be extended caudally for ease of access if the catheter is in a cephalic vein.
    - Clipping of hair in areas where monitoring devices are to be applied (dependent on type of monitoring devices used)



MAGNETIC RESONANCE IMAGING SCAN A-B, T1-weighted magnetic resonance images from a normal **(A)** and abnormal **(B)** canine brain. Images are from rostral to midcerebrum. In MRI, the imaging characteristics of tissues are determined by the imaging sequence used. To define the tissue characteristics of a lesion, multiple different imaging sequences are performed, and the appearance of the lesion in these images is compared. The term *intensity* is used for describing the appearance of tissues in MRI.

In the normal patient, there is a subtle difference in intensity between gray matter and white matter of the brain, and intensity of muscle is different from that of brain. This illustrates the level of soft-tissue contrast achieved with MRI.

In the abnormal patient, note the large, round hypointense lesion with a slightly hyperintense rim within the right ventral cerebrum; the lesion causes left deviation of falx cerebri. Differential diagnoses for mass lesions within the brain include neoplasia, granuloma formation, and abscess formation. In this case, the appearance of the lesion in multiple imaging sequences was consistent with a diagnosis of neoplasia with a central necrotic component.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Complications associated with general anesthesia
- Burns induced by placement of cables
    - Objects within the magnet can become hot due to the effect of radiofrequency pulses. Monitoring cables within the magnet should not be coiled and should not be placed on the patient. Wrapping the cables in fabric (towels, blankets, etc.) will provide further protection.
- Injury to the patient and/or damage to the magnet can occur if careful attention is not paid to basic MR safety as regards the presence of metallic objects within range of the magnet. See above.

PROCEDURE

- Anesthetize and intubate the patient.

- Move the patient to the MR area and position within the MR gantry; positioning of the patient depends on the area of interest and the configuration of the radiofrequency coils.
- Connect IV fluids and monitoring devices, place blankets and water bottles.
- Scan.
- +/− Inject intravenous contrast agent:
    - Contrast is routinely used in brain imaging but rarely used for imaging of the spinal column.
    - Gd-DTPA: Magnevist:
        - 0.2 mL/kg IV bolus
    - Gadodiamide: Omniscan:
        - 0.2 mL/kg IV bolus
- Rescan for postcontrast images.
- Briefly review images:
    - Evaluation of the images may suggest additional imaging sequences of the area being examined that may be useful in the particular case (e.g., obtaining T2-weighted images in suspected hemorrhagic lesions).
    - Rarely the images obtained will identify an additional area of concern that should be scanned before the patient is allowed to recover from general anesthesia.

POSTPROCEDURE

No additional considerations beyond routine monitoring of the patient during recovery from general anesthesia

ALTERNATIVES AND THEIR RELATIVE MERITS

CT:

- Advantages:
    - Shorter imaging time (and therefore, shorter time under general anesthesia)
    - Better imaging of bone
- Disadvantages:
    - Far inferior contrast resolution
    - Image acquisition is in only one plane.
    - Reformatted images have much lower spatial resolution than original images or MR images.

If available, MRI is the preferred imaging method for evaluation of the central nervous system.

AUTHOR: PATRICIA L. ROSE

Neurologic Examination

OVERVIEW AND GOAL

To evaluate a patient's neurologic function through clinical physical assessment of mentation, gait, posture, postural reactions, spinal nerve reflexes, and cranial nerve examination. Specifically, the goal in an animal with a nervous system lesion is to establish the anatomic location of that lesion. The anatomic diagnosis will determine the differential diagnosis and the choice of ancillary studies to be recommended.

INDICATIONS

Reasons for an owner to present an animal for a neurologic examination include:

- Seizures, abnormal spontaneous uncontrolled movements, pacing, circling, head pressing, tremors
- Abnormal mentation: depressed to unresponsive, no recognition of owner, loss of trained habits, excreting indoors
- Abnormal gait: lame, paretic, ataxic, paralyzed, collapsing
- Loss of balance, hearing, vision
- Head tilt, unable to close eyelids, unable to prehend food or swallow, protruded third eyelid, pupil asymmetry, eye deviation
- Regurgitation, dyspnea

CONTRAINDICATIONS

- Aggressive patient
- Injured patient where manipulation may exacerbate the nervous system lesion and the examination is limited to the recumbent patient

EQUIPMENT, ANESTHESIA

- Quiet area
- Outdoor area or a room large enough to evaluate the gait
- Nonskid floor surface; indoor-outdoor carpet works well.
- Plexímeter, source of bright light, small forceps

ANTICIPATED TIME

About 10-20 minutes

PREPARATION: IMPORTANT CHECKPOINTS

- Assess for contraindications (as already noted).
- Note: To avoid introducing bias, review existing diagnostic test results (lab tests, radiographs, etc.) *after* performing the neurologic examination.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Do not be biased by a single abnormality.
- Do the same methodical, thorough evaluation on every patient regardless of the complaint or the signs that are evident.

PROCEDURE

There are five main components to the neurologic examination: sensorium, gait, postural reactions, spinal reflexes, and cranial nerves. The order in which the five components are evaluated depends on the animal's behavior and chief complaint.

- Sensorium: owners are best able to evaluate subtle changes in their animal's behavior or sensorium. In increasing severity, sensorium changes are depression, lethargy, obtundation, semicoma (stupor), and coma.
- Gait: diagnosis of gait disorders is based on pattern recognition for specific anatomic sites in the nervous system (and musculoskeletal system). These are best evaluated with the animal moving on grass or a rug where slipping is not a problem.

As a rule, changes are best seen with the animal walking slowly and taking numerous slow turns. There are two qualities of paresis and three qualities of ataxia that are considered in gait analysis:

- Paresis (neurogenic abnormality of muscle tone/strength):
  - Lower motor neuron (LMN) paresis causes a loss of ability to support weight, reflected in rapid short strides with collapsing on the affected limb. The animal walks with a “lame” gait.
  - Upper motor neuron (UMN) paresis interferes with gait generation, delaying the protraction of the affected limb and lengthening the stride. This form of paresis cannot be separated from general proprioceptive (GP) ataxia because of the close association of the caudal projecting upper motor neuron tracts and cranial projecting general proprioceptive tracts in any transverse section of the spinal cord.
- Ataxia (“incoordination”):
  - GP ataxia creates the appearance of the animal not knowing where its limb(s) is/are located in space. This also results in a delay in protraction of the limb, and the animal may show an excessive medial (adduction) or lateral (abduction) excursion of the limb as it is protracted. The stride may also be prolonged. Both UMN and GP deficits can cause the animal to occasionally stand on the dorsal aspect of its paw.
  - Vestibular ataxia is evident when the animal has a head tilt and drifts or stumbles to the side from loss of balance.
  - Cerebellar ataxia is characterized by a delay in protraction and an excessive response, a dysmetric abrupt gait generation that usually is associated with some balance loss.

- Postural reactions: normal postural reactions require that most components of the peripheral and central nervous systems be intact. The most reliable of the postural reactions is the hopping response.
  - Hopping response: each limb is tested by holding the animal so that most of the weight is borne on the limb to be tested, and the animal is moved laterally on that limb:
    - First, straddle the animal so that both you and the animal are facing in the same direction.
    - Palpate the thoracic limbs to determine if any denervation or disuse atrophy is present.
    - Flex and extend the limbs to determine range of motion and muscle tone.
    - Place the paw on its dorsal surface—the paw replacement test—and observe how quickly it is replaced. Note: This is not just a test of conscious proprioception (CP), because disorders of the UMN, LMN, and/or general somatic afferent cutaneous receptors all can result in a delay in this response. A sole CP deficit cannot be determined, and that term should be discarded from the neurologic examination. Be aware that many normal animals may delay in replacing the paw to its supporting position.
    - Brace your own elbow on your ipsilateral knee and support the abdomen so that most of the animal's weight is on its thoracic limbs.
    - With your other arm, pick up the animal's thoracic limb on that side, and push the animal laterally away from that limb. This will force the animal to hop on the opposite thoracic limb.
    - After three or four hops, do not move, but just reverse both arms so that you can pick up the opposite forelimb and hop the animal back on the contralateral thoracic limb.
    - Compare one forelimb with the other only when it is being hopped laterally.
    - Move back to the pelvic limbs, and repeat the muscle palpation, range of motion, and paw replacement.
    - At that time, check the tail and anus for tone and reflex response.
    - Stand beside the animal, and with one arm placed under the sternum, pick the animal up so it is standing on its pelvic limbs.
    - Pick up the closest pelvic limb, and push the animal away so that it hops laterally on the opposite pelvic limb.
    - Repeat this maneuver on the opposite side.
    - Always compare the thoracic limbs with each other and then the pelvic limbs with each other, because the pelvic limbs normally tend to be slower than the thoracic limbs.
    - For very large dogs, it is easier to make the same observations while the dog is “hemiwalked.”
    - For hemiwalking, stand beside the dog and pick up both limbs so they are located at your side; then push the animal gently away.
    - These hopping responses are much more reliable than the paw replacement test.
- Spinal reflexes; for spinal reflex testing, the animal should be placed in lateral recumbency:
  - Manipulate the limbs to assess muscle tone.
  - With the animal relaxed and the stifle slightly flexed, elicit the patellar reflex by tapping on the patellar tendon. If it is not present in one or both limbs, always place the dog in the opposite recumbency, and repeat the patellar reflex before concluding that it is absent. Some old dogs with no neurologic complaints lack the patellar reflex. This is the only reliable tendon reflex, because the other myotactic reflexes (triceps, biceps, extensor carpi radialis, etc.) may not be present in some normal animals.
  - The withdrawal-flexor reflex is routinely tested by gently compressing the base of the claw in each paw with forceps and observing the strength of the limb flexion and the animal's response (e.g., abrupt turning, vocalization) to the noxious stimulus. Note: The sensory modality that is tested is not pain. It is a noxious stimulus that is used, and what is observed is the animal's reaction to this conscious perception (nociception). Pain is the animal's response to a noxious stimulus. It is difficult to determine an animal's response to a minimal noxious stimulus, and there is no practical value to differentiating light and deep pain.
- Cranial nerves: sitting down on the floor with your back against the wall and knees flexed is the best position from which to evaluate small dogs and cats. Place the animal between your thighs and hold its head while testing the function of the cranial nerves. You can perform this cranial nerve exam on larger dogs by straddling them so that you and the dog are both looking

in the same direction. Proper evaluation requires a relaxed, nearly motionless animal. Use a regional approach, starting with the eyes:

- Menace response:
  - The menace response assesses vision and facial nerve function as long as the stimulus of the hand thrust at the animal's face does not touch the face or whiskers, or create excessive air movement.
  - If there is no response, be sure the eyelids are able to close (i.e., there is no facial paralysis).
  - If there is a normal palpebral reflex or spontaneous eyelid closure but still no menace response, then tap the eyelids or face gently to get the animal's attention, and then repeat the menace gesture.
  - Failure to close the eyelids to a menace in an animal > 10 weeks old with normal facial nerve function, or the lack of eyeball or head retraction in a patient with facial paralysis, indicates a lesion in some part of the visual pathway from the eyeball to the occipital lobe.
  - Animals with significant cerebellar disorders that have no menace response are still visual.
  - Assessing the menace response prior to shining a light in the animal's eyes avoids falsely compromising the menace response with the glare of the light.
- Pupil size and pupillary light reflex:
  - With a strong light source, assess the size and symmetry of the pupils from a distance.
  - Bring the light to about 1-2 cm from the eye, and swing it from one eye to the other and back again.
  - Repeat this to be sure that with the light in one eye, the pupils of both eyes are constricting.
  - Deficits in this light reflex implicate a lesion in the eye/optic nerve (optic chiasm or tracts) and/or the general visceral efferent component of the oculomotor nerve.
- Ocular position and movement:
  - Observe the position of the eyeballs for strabismus, and test abduction (abducent, VI) and adduction (oculomotor, III) nerve function by moving the head side to side while observing the eyes.
  - Look for a resting nystagmus. If not present, then look for a positional nystagmus with the head held flexed laterally to either side and then extended dorsally. Occasionally, it is worthwhile to look for this sign with the animal placed in dorsal recumbency.
- Trigeminal nerve (V):
  - Palpate the muscles of mastication (motor V) for denervation atrophy.
  - Recheck the palpebral reflex by stimulating the lateral and medial canthi with blunt forceps (sensory V; motor VII).
  - Place the blunt forceps against the nasal septum on each side to assess ophthalmic V and the nociceptive pathway to the opposite somesthetic cortex.
  - Observe for ear movement and lip symmetry and tone (VII).
  - Open the jaw to assess muscle tone (motor V) and range of motion.
- Glossopharyngeal (IX), vagus (X), and hypoglossal (XII):
  - Observe the tongue for its size and movements (XII).
  - Place one finger in the oropharynx to determine the muscle tone and the animal's response to the presence of the finger—the gag reflex (IX and X).

POSTPROCEDURE

By establishing the anatomic diagnosis (the location of the lesion in the nervous system), the results of the neurologic exam will allow a differential diagnosis to be established and a diagnostic plan to be created.

AUTHOR: ALEXANDER DELAHUNTA

Nebulization, Coupage, and Respiratory Therapeutics

Client Education Sheet Available on Website

SYNONYMS

- Aerosolization and percussion
- Pulmonary (chest) physiotherapy or bronchial drainage/positioning
- Early ambulation
- Vibration/shaking
- Airway suctioning

OVERVIEW AND GOALS

- Nebulizers are used for aerosolizing saline in order to humidify airway secretions or to aerosolize drug solutions to obtain high local concentrations of medication in the respiratory tract while minimizing systemic absorption and toxicosis.
- Coupage or chest wall percussion aids in the removal of secretions from the tracheal bronchial tree.
- Pulmonary (chest) physiotherapy or bronchial drainage/positioning is a therapeutic modality that utilizes gravity-assisted positioning to improve pulmonary hygiene through the mobilization of airway secretions.
- Early ambulation facilitates mobilization and clearance of airway secretions, changes the lung regions being ventilated, and maintains muscular tone and strength.
- Thoracic wall vibration/shaking is a modality used for moving loosened secretions from small airways to larger airways so they can be coughed up or suctioned from the airway.
- Airway suctioning, as the name implies, is the active removal of airway secretions to clear the airway in patients with impaired mucociliary clearance. Reduces the risk of lower-airway contamination from oropharyngeal contamination as well as formation of airway mucus plugs leading to atelectasis.

INDICATIONS

Patients with inhalation injury (e.g., smoke inhalation) or retained secretions (recumbent patients, bacterial or fungal pneumonia, asthma, eosinophilic bronchopneumopathy, mechanically ventilated patients/intubated patients)

CONTRAINDICATIONS

- Percussion and vibration/shaking may not be suitable in patients with significant thoracic wall damage (i.e., fractured ribs or recent thoracotomy).
- Currently, nebulized antibiotics are only recommended in humans for multidrug-resistant gram-negative infections that are susceptible to aminoglycosides or polymyxin E (colistin); gram-positive bacterial infections are relative contraindications.

EQUIPMENT, ANESTHESIA

Three types of nebulizers:

- Jet nebulizers: employ oxygen under high pressure to generate the aerosol. The rate of droplet generation and the droplet size distribution are dependent on the jet flow rate.
- Ultrasonic nebulizers: the aerosol is produced by the vibration of a piezoelectric crystal. Drug output and droplet size are determined by the frequency and vibration amplitude.
- Vibrating mesh nebulizers: use a mesh or plate with multiple openings to generate the aerosol. These are the newest nebulizers, with reported better lung parenchymal penetration.

*Note: most aerosolized drugs listed are extrapolated from experimental and human clinical studies and are considered off-label use for dogs and cats.

Drugs that are specifically formulated or reported to be aerosolized*:

- Antibiotics: aminoglycosides (amikacin, tobramycin/tobramycin solution for inhalation [TSI], and gentamicin), polymyxins (colistin or polymyxin E), and vancomycin
- Airway humidification: sterile 0.9% saline
- Antifungals: amphotericin B
- Bronchodilators: racemic epinephrine, β2-agonist
- Antiinflammatory: corticosteroids
- Mucolytic drugs: *N*-acetylcysteine
- Oxygen free-radical scavengers: heparin/*N*-acetylcysteine combination

ANTICIPATED TIME

- Nebulization time of 15-30 minutes is recommended to allow sufficient time for adequate drug delivery/effect. Longer times are generally not tolerated by the patient or the operator (poor compliance). Nebulization and coupage should be performed every 6-12 hours.
- Chest physiotherapy, ambulation, vibration/shaking, and airway suctioning should be performed every 2-4 hours initially and gradually tapered as secretions improve.

PREPARATION: IMPORTANT CHECKPOINTS

- Ensure equipment used for nebulization and airway suction is maintained sterile. Ideally, sterile gloves or, at minimum, clean gloves should be worn when manipulating the equipment. Nebulization reservoirs should be replaced or cleaned daily and a new suction tip used for each suction.
- In-line suction units for mechanically ventilated patients can reduce the risk of iatrogenic infections.
- Equipment should be cleaned and disinfected between patients. Any replaceable part (e.g., nebulization reservoirs) should be exchanged daily if contaminated and always between patients.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Nebulization and coupage:
  - Bronchoconstriction: most common and serious side effect arising during nebulization. The use of nonaerosolized drug formulations increases the risk of clinically significant bronchoconstriction. Pretreatment or concurrent use of a bronchodilator may reduce the risk of bronchoconstriction.
  - Environmental waste: many nebulizers will continuously aerosolize drug even if the patient is not inhaling, allowing significant drug to be lost to the ambient air.
  - Operator exposure: owing to environmental contamination, operators may inhale some of the aerosolized drug or saline; use of a protective facemask can reduce the risk of exposure.
  - Low deposition of certain drugs: to allow deep penetration to the lower airways, the majority of the droplets produced should be within the range of 1-5 micrometer. Nebulizer type, use of nonaerosolized drug formulations, and highly viscous solutions are causes of poor drug penetration.
- Airway suctioning:
  - Reported complications following suctioning include tracheal irritation and bleeding, abrupt drop in partial pressure of oxygen, vagal stimulation, and bradycardia. Preoxygenating and limiting suction time have been shown to reduce the risk of hypoxemia.

PROCEDURE

- Nebulization and coupage:
  - Manufacturer instructions should be carefully followed to ensure proper use with each individual type and model of nebulizer. In general, sterile 0.9% saline or the specific drug diluted with sterile 0.9% saline to the required volume is instilled in the nebulizer reservoir. The nebulizer is turned on, and the reservoir is placed approximately 2-3 inches (5-8 cm) from the patient's nose for a minimum of 15-30 minutes. Certain nebulizers can be attached to the inspiratory limb of the ventilation circuit, facilitating nebulization in mechanically ventilated patients.
  - Immediately after nebulization, coupage is performed by repeatedly percussing both sides of a patient's chest wall simultaneously, typically while standing above and behind the patient (i.e., facing in the same direction as the patient) and using cupped hands and gentle force. Duration is typically 15-30 seconds, or less if coupage triggers repeated coughing.
- Pulmonary (chest) physiotherapy:
  - In the true sense, this involves 12 basic positions for postural drainage. The simplest and most practical form for clinical practice is to turn patients side to side every 2 hours to aid in mobilization of airway secretions.
- Early ambulation:
  - Involves assisting and encouraging patients to ambulate even for short distances. In the author's experience, this is essential in the successful treatment of pneumonia in recumbent large-breed dogs (e.g., wolfhounds).
- Thoracic wall vibration/shaking:
  - Manual or mechanical vibrations can be used to vibrate the thoracic cage.
- Airway suctioning:
  - The patient should be hyperoxygenated with 100% oxygen for a minimum of 1 minute prior to suctioning. The patient should be positioned with the head raised at a 45○ angle, and the catheter inserted into the trachea/endotracheal tube. Suction should begin while the catheter is gradually withdrawn from the airway. The patient should not be suctioned for more than 15 seconds without reoxygenation. Also, oropharyngeal secretions should be suctioned following tracheal suctioning.

POSTPROCEDURE

Patients should be monitored closely after the application/administration of any of the above therapies, because desaturation and worsening hypoxemia may occur. Decompensation may occur as a result of bronchoconstriction, incomplete mobilization of mucus causing airway obstruction, tracheal irritation or exhaustion.

ALTERNATIVES AND THEIR RELATIVE MERITS

Metered dose inhaler (MDI; see p. 1289): is a more practical alternative for at home delivery of specific medications. Unfortunately, only certain medications are routinely available in MDI form.

SUGGESTED READING

Conway SP: Nebulized antibiotic therapy: the evidence. Chronic Resp Dis 2:35–41, 2005.

Luyt et al: Aerosolized antibiotics to treat ventilator-associated pneumonia. Curr Opin Infect Dis 22:154–158, 2009.

Micak et al: Respiratory management of inhalation injury. Burns 33:2–13, 2007.

AUTHOR: MICHAEL ETHIER

Nasal Infusion of Clotrimazole

OVERVIEW AND GOAL

Intranasal infusion of clotrimazole is a minimally invasive technique for treating confirmed nasal aspergillosis in dogs. Treatment is performed for 1 hour. Resolution of clinical signs is achieved in one half to two thirds of dogs with fungal rhinitis after a single treatment.

INDICATIONS

Dogs with confirmed nasal aspergillosis; confirmation requires either histopathologic confirmation of fungal hyphae in nasal tissues or at least two of the following: positive *Aspergillus fumigatus* serum titer, positive *Aspergillus* culture, radiographic/CT scan findings suggestive of fungal rhinitis (turbinate loss, fungal granulomas; see p. 96).

CONTRAINDICATIONS

- Cribriform plate erosion/damage secondary to fungal rhinitis. If advanced imaging (CT scan or MRI) of the cribriform plate is not available, owners should be warned that cribriform integrity has not been assessed. Topical therapy in animals with known cribriform damage has not been reported.
- Bulky fungal granulomas within the frontal sinus. Massive fungal disease within the frontal sinuses often recurs following topical therapy. It is assumed that the treatment does not adequately penetrate the center of these granulomas. Either rhinoscopic or surgical (sinusotomy) removal of bulky disease, followed by topical clotrimazole, should be considered.

EQUIPMENT, ANESTHESIA

- General anesthesia is required.
- A cuffed endotracheal tube (mandatory)
- Two 12 Fr Foley catheters, one 24 Fr Foley catheter, and two 10 Fr polypropylene or red rubber catheters
- Laparotomy sponges
- Two 60-mL syringes, one 12-mL syringe
- One pack of 3-0 nylon suture
- Suction canister and tubing
- Three hemostats
- One pair operating scissors
- One long-handled needle holder
- Four 30-mL vials of 1% clotrimazole in a polyethylene glycol base

ANTICIPATED TIME

About 2 hours total: 30 minutes for setup and anesthetic induction, 1 hour for treatment, and 30 minutes for recovery

PREPARATION: IMPORTANT CHECKPOINTS

Imaging studies are followed by rhinoscopic evaluation and then clotrimazole infusion during the same anesthetic episode if diagnostic results are highly suggestive of fungal rhinitis.

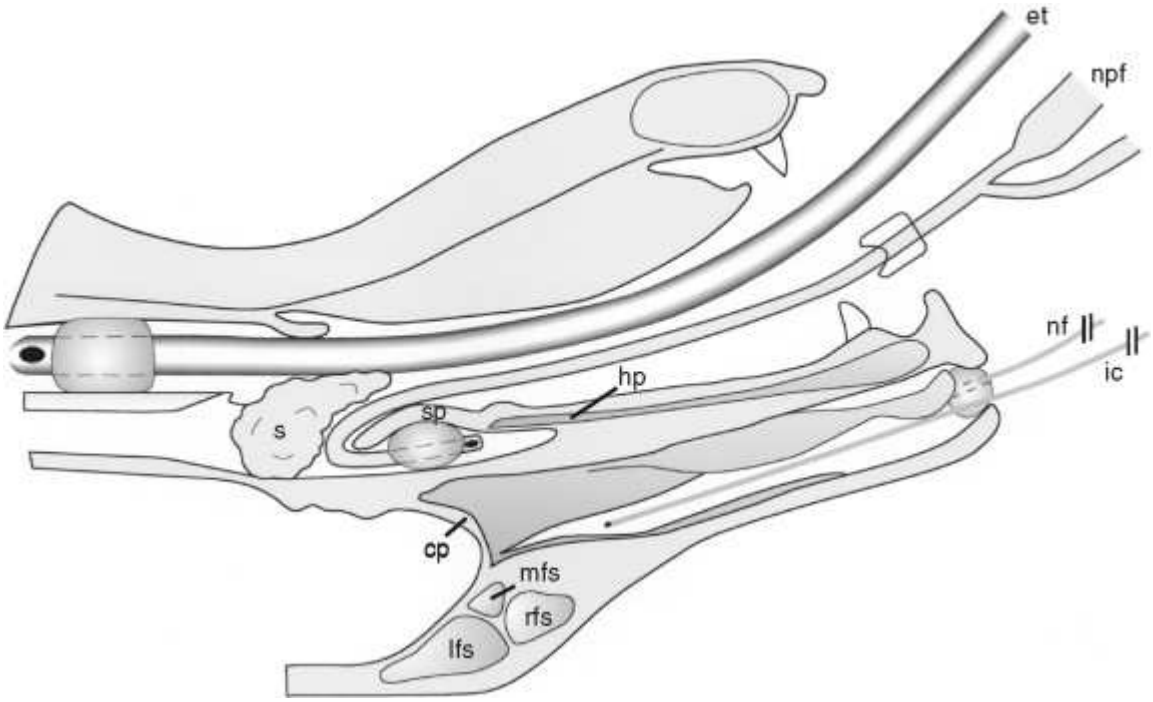
POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

The inflated balloon of the nasopharyngeal Foley catheter must be palpated through the soft palate, just caudal to the hard palate. The balloon is initially held in place with a finger, which is then replaced with laparotomy sponges. Failure to fully inflate the balloon or ensure proper positioning will result in leakage of clotrimazole into the oropharynx.

PROCEDURE

- Place animal into lateral recumbency.
- Pass a 24 Fr Foley catheter orally and then into the nasopharynx with the aid of a long needle holder. Bend the Foley catheter tip 180○ so that the tip flips and comes to be seated dorsal to the soft palate. While palpating through the soft palate, fill the Foley balloon with air. Withdraw the balloon if necessary until it is just caudal to the hard palate. Place laparotomy sponges in the oropharynx to prevent caudal migration of the balloon.
- Pass a 10 Fr polypropylene or red rubber infusion catheter through each nostril and into each dorsal meatus (premeasure to the medial canthus).

- Place a 12 Fr Foley catheter into each nostril to prevent solution from leaking out the nostrils. Place a single nylon suture in each nostril to prevent rostral balloon migration. Fill balloons with air until obstruction occurs.
- Roll animal into dorsal recumbency.
- Fill two 60-mL syringes with the 1% clotrimazole solution (Lotrimin solution [Schering Corp., Kenilworth, New Jersey]). Administer 60 mL per side each hour via the infusion catheters.
- Place hemostats across any Foley if fluid is present within the catheter.
- Position the animal's head during infusion: 15 minutes dorsal, 15 minutes left lateral, 15 minutes right lateral, and again 15 minutes dorsal. The animal's body should remain in dorsal recumbency.



NASAL INFUSION OF CLOTRIMAZOLE Sagittal section of an anesthetized dog in dorsal recumbency. Image shows position of endotracheal tube *(et),* nasopharyngeal Foley catheter *(npf),* pharyngeal sponges *(s),* infusion catheter *(ic),* and rostral nasal Foley catheter *(nf)* in relation to the hard palate *(hp),* soft palate *(sp),* cribriform plate *(cp),* rostral frontal sinus *(rfs),* medial frontal sinus *(mfs),* and lateral frontal sinus *(lfs).*

(Reprinted with permission from Mathews KG, Koblik PD, Richardson EF, et al: Computed tomographic assessment of noninvasive intranasal infusion in dogs with fungal rhinitis, Vet Surg 25:309–319, 1996.)

POSTPROCEDURE

Following treatment, the animal is placed in sternal recumbency. All catheters and sponges are removed and counted. Clotrimazole is allowed to drain out of the nares by tilting the animal's nose downward at the edge of the treatment table. Suction and dry sponges are used for ensuring that the pharynx is dry prior to recovery from anesthesia. Repeat treatment if nasal discharge does not cease by 2 weeks after treatment. Additionally, new evidence suggests that affected dogs should be rhinoscopically reevaluated approximately 1 month post treatment to determine if any fungal plaques persist.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Orally administered antifungal drugs may be used in place of intranasal infusion of clotrimazole or as an adjunct to topical therapy. Itraconazole (5 mg/kg, q 12 h PO with food, for at least 2 months) has been associated with the greatest response rate (60%-70%) and requires intermittent monitoring of liver enzymes. A single 1-hour infusion of clotrimazole is equally effective if the medication is injected via catheters placed in dorsal sinusotomies.
- Enilconazole can also be applied topically via dorsal sinusotomy catheters but requires daily administration of small volumes (5-10 mL per side) for 10-14 days.
- There is new evidence that shows fungal granulomas can be adequately débrided by trained rhinoscopists, without the need for sinusotomy. Endoscopic placement of sinus catheters followed by 1-hour infusion with 1% clotrimazole has a similarly high success rate.
- Instillation of 1% clotrimazole cream into the frontal sinuses following fungal débridement may improve outcome by acting as an antifungal drug depot (increased antifungal contact time), but the number of cases reported at this time is limited.

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AUTHOR: KYLE G. MATHEWS

Nasal Flush

SYNONYM

Nasal lavage

OVERVIEW AND GOALS

- To obtain cells and/or tissue for diagnostic sampling of intranasal inflammation, infection, or neoplasia
- To remove small nasal foreign bodies

INDICATIONS

- Chronic nasal discharge (unilateral or bilateral)
- Intranasal obstruction
- Chronic sneezing
- Nasal foreign body
- Epistaxis with normal coagulation profile and blood pressure (BP)
- Maxillary mass/deformity

CONTRAINDICATIONS

- High-risk anesthetic animals (i.e., severely compromised metabolic, cardiac, or neurologic disease)
- Documented loss of integrity of cribiform plate (relative contraindication)
- Coagulopathy/bleeding disorder

EQUIPMENT, ANESTHESIA

- General anesthesia
- Endotracheal intubation
- Bowl of lukewarm tap water
- Rolls of gauze to pack the pharynx (one to three rolls, depending on size of animal)
- A 60-mL feeding tip syringe; the larger the diameter of the syringe tip, the more forceful the water jet can be generated by pushing on the plunger.
- Sterile saline solution for flush (1-L bag)
- Two bath towels
- Sterile water-soluble lubricant

ANTICIPATED TIME

- Time for general anesthesia
- Actual procedure takes <10 minutes per nostril.

PREPARATION: IMPORTANT CHECKPOINTS

- Thoroughly soak the rolled gauze in tap water, and then wring it out just before using it.
- Fill the 60-mL syringe to capacity with sterile saline solution.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Improper placement or insufflation of the cuffed endotracheal tube, thus allowing water to enter the trachea of the anesthetized animal.
- Unevenly distributed or insufficient gauze, allowing the diagnosis (cells and tissue) to be flushed back into the esophagus.
- Forgetting to remove the gauze from the pharynx once the flush procedure is finished.
- Excessive force of flushing in patients with uncertain or compromised cribiform plate structure
- Using loose 4 × 4 gauze sponges—some may be forgotten after the procedure is finished and occlude the larynx or trachea.
- In case of severe nasal destruction, epistaxis may develop.

NASAL FLUSH Large-bore syringe is inserted into nostril of anesthetized patient to perform nasal flush procedure. End of gauze roll can be seen protruding from mouth.

PROCEDURE

- General anesthesia induction and maintenance; endotracheal intubation:
  - Verification of appropriate endotracheal tube cuff inflation
- Sternal recumbency, head and neck extended
- Unwind gauze and soak in water, and then retrieve and wring out excess water.
- Place damp gauze dorsal to and on both sides of the endotracheal tube as far caudally as possible, past the caudal edge of the soft palate.
- Gently insert lubricated end of syringe into the ventral meatus of the nose as far as it will go. This is most easily achieved by pushing the philtrum of the nose dorsally while aiming the tip of the syringe toward the septum. Slide into the nasal passage without using force.
- Place towel over the head and nose of the dog to avoid a spray of back flush onto the operator.
- While holding the syringe firmly in place, briskly empty the 60 mL of saline into the nasal passage using moderate pressure on the plunger.
- A powerful stream of fluid is required to dislodge foreign bodies or pieces of abnormal tissue.
- Repeat several times for each nostril; other towel may be used to control spillage if saline flows from mouth.
- When finished, gently pull gauze from the pharynx, and examine carefully for foreign bodies or tissue clumps.

POSTPROCEDURE

- Remove the gauze from the caudal pharynx.
- Once the gauze is removed, examine the animal's mouth and pharynx for any material that was flushed out of the nose but not trapped into the gauze.
- Observe the animal for sneezing and bleeding after termination of general anesthesia.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Rhinoscopy, nasal radiography series, CT scans, or MRIs normally precede nasal flush.
- Nasal radiography series, CT scans, and MRIs provide specific information on intranasal structure that is not obtained with nasal flush.

AUTHOR: HANS GELENS

Oxygen Supplementation

SYNONYM

Oxygen therapy

OVERVIEW AND GOALS

Supplemental oxygen is easily administered, readily available, and if used correctly, safe. There are very few contraindications to oxygen supplementation. Oxygen therapy is often used in emergency and critical care medicine because hypoxic cellular metabolism is less efficient and may lead to organ dysfunction and death. The critical care supplier must understand the physiology of oxygen delivery and recognize cases that will benefit from oxygen therapy. A worthwhile rule of thumb is if there is uncertainty about whether to supplement oxygen, supplementation should be initiated pending clarification.

INDICATIONS

- Clinical situations in which oxygen therapy may be of benefit include respiratory distress, sepsis, pyometra, severe bite wounds, hyperthermia, pleural space disease, congestive heart failure, anemia, all forms of shock, pulmonary contusions, pulmonary hypertension, seizures, and head trauma.
- Clinical signs caused by hypoxemia include an anxious expression, extended head and neck, open-mouth breathing, abducted elbows, tachypnea, tachycardia, cyanosis, cardiac arrhythmias, and syncope.
- The hallmark clinical sign of diminished arterial oxygen content is cyanosis. For cyanosis to be detected, there must be >5 g/dL of unoxygenated hemoglobin in the peripheral capillaries (corresponds to SpO2 75%-80%); therefore, cyanosis indicates severe hypoxemia, and anemic animals may have critical hypoxemia without cyanosis.

CONTRAINDICATIONS

Causing distress to an already compromised animal is a contraindication. Several methods of oxygen delivery are available. Selection of the optimal technique depends on the animal's respiratory status, desired inspired O2 content, anticipated duration of therapy, equipment available and its size, and conformation and temperament of the animal.

EQUIPMENT, ANESTHESIA

See description for placement of devices.

ANTICIPATED TIME

Less than 10 minutes for any of the procedures

PREPARATION: IMPORTANT CHECKPOINTS

Pretreat animal with an anxiolytic that is not hypotensive and does not decrease respiratory effort. Most of these cases are in respiratory distress, so the less anxiety the better. Low-dose benzodiazepines or morphine, buprenorphine, or fentanyl are feasible choices.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

Excessive oxygen supplementation: Administration of 100% oxygen for 12 hours or 80%-90% for 18 hours can lead to alterations in pulmonary function and signs of oxygen toxicosis. Oxygen toxicosis is often difficult to recognize because the clinical signs can be similar to those seen with hypoxemia. However, oxygen toxicosis is relatively uncommon, takes at least 12 hours to occur, is preventable, and is reversible in the early stages if oxygen is discontinued. Supplementation with 50% oxygen appears safe in the dog.

PROCEDURE

Emergency oxygen supply: holding an oxygen-delivery tube so a high flow occurs directly into the animal's mouth is an option that can be used in an emergency situation until more optimal oxygen-delivery methods are instituted.

MASK: The mask is perhaps the easiest and least invasive technique for oxygen supplementation. Purpose-made veterinary masks are preferable (better fit). These masks come in an assortment of sizes that range from pediatric size to large dog size and are designed to fit over the muzzle. It is often awkward to administer oxygen via mask to brachycephalic dogs and some cats. The mask can be connected via tubing to a 100% oxygen source, and if used for long periods of time, the oxygen should be humidified. With a well-fitted mask, flow rates of 8-12 L/min achieve a fraction of inspired oxygen (Fio2) of 0.4 to 0.5 (room air 0.2). The advantages of a mask are related to ease and speed of administration, and no specialized equipment is required. In addition, during oxygen administration, the animal can be closely monitored. Disadvantages of this technique include lack of tolerance by some animals and the requirement of constant manual application of the mask unless the animal is moribund or otherwise immobile.

INTRANASAL CANNULA: There are various types of tubes available for nasal catheterization, including feeding tubes and urinary catheters. Some clinics use flexible feeding tubes or Foley catheters with multiple fenestrations to avoid mucosal jet lesions. The largest tube size possible should be passed. These tubes are placed in the conscious animal, but local anesthesia is recommended. Topical 2% lidocaine is used. The toxic lidocaine dose is 4 mg/kg in the cat, and one-fourth to half this dose is usually sufficient therapeutically.

- The tube is premeasured to the medial canthus of the eye, and the level of the external nares is marked on the tube to indicate the maximal distance of insertion.
- The animal's head is tilted with the muzzle pointing upwards. A few drops of lidocaine are applied to the external nares to desensitize the nasal mucosa.
- The tube is advanced until the tip is at the level of the medial canthus of the eye (until mark on tube is at nares). Insertion is usually easier if the nostril is pushed dorsally and the tube is directed medially.
- Once placed, the tube can be secured as close to the nostril as possible with suture or methacrylate glue (superglue).
- The tube should also be attached on the muzzle, below the eye and on the neck.
- These animals should also be fitted with an Elizabethan collar to prevent self-directed removal of the tube.

The advantages of this technique include ease of application, no special equipment required, versatility in animals that are different sizes, and lack of interference with animal monitoring. Disadvantages include lack of animal tolerance, variable flow rates required to provide oxygen, nasal mucosal irritation, and gastric distention at high flow rates (rare). Recommended flow rates to achieve a specific Fio2 are listed in the table.

TRANSTRACHEAL: Oxygen may be administered transtracheally via a nasal catheter, which is advanced through the nasopharynx to the proximal trachea or through a catheter placed percutaneously through the cervical trachea. A long, flexible IV (jugular-type) catheter can be placed percutaneously into the trachea through the cricothyroid membrane or between tracheal rings. These catheters can be over-the-needle types or through-the-needle types. The entry area should be infiltrated with a local anesthetic prior to catheter introduction. In an emergency situation (e.g., cat with critical laryngeal spasm), a hypodermic needle or an over-the-needle catheter attached to a fluid extension set can be used for administering oxygen intratracheally. Oxygen lines used with this technique should be humidified. The disadvantages of this technique include difficulty with tube placement and poor animal tolerance when it awakens or is more alert.

Reproduced with permission from Drobatz KJ, Hackner S, Powell S: Oxygen supplementation. In Bonagura JD, editor: Kirk's current veterinary therapy XII: small animal practice, Philadelphia, 1995, Saunders, pp 175–179.

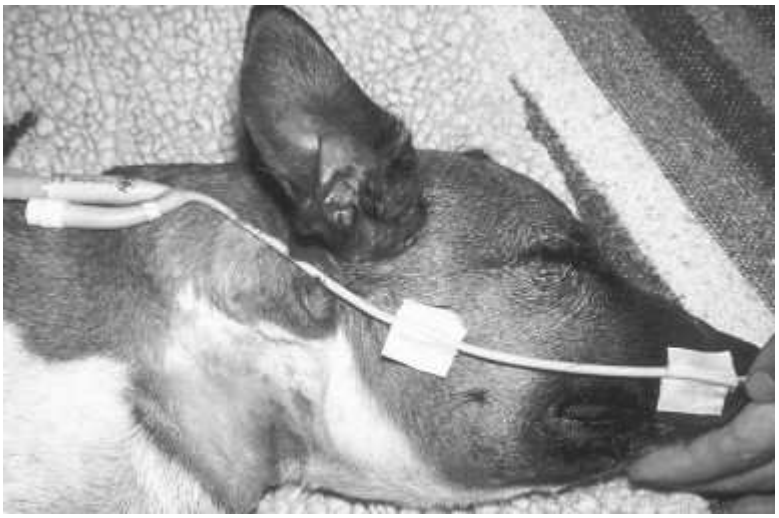
Intranasal flow rates of >3l per minute often are not tolerated by animals; these rates may cause the animal to close its oropharynx in response to rapid air/O2 flow. If a hissing sound is heard because oxygen is mostly or entirely refluxing from the nostrils, common sense dictates that the tube and apparatus be checked; if no defects are found, the clinician should try a lower flow rate.

Approximate Oxygen Flow Rates for Supplementation Administration Via Nasal Catheter

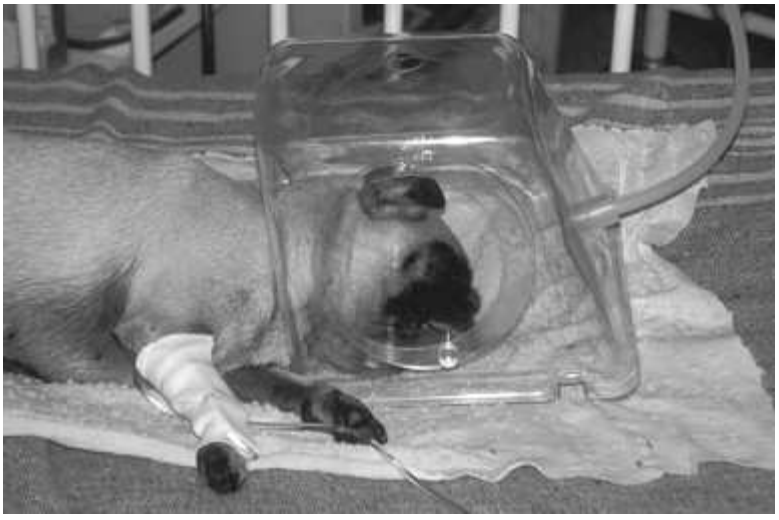
OXYGEN FLOW RATES (L/MIN) REQUIRED TO DELIVER AN Fio2 OF:			
	30%-50%	**30%-75%**	**75%-100%**
Weight (kg)			
0-10	0.5-1	1-2	3-5
10-20	1-2	3-5	>5
20-40	3-5	>5	?

OXYGEN CAGE: Oxygen-cage equipment usually involves a chamber that can be flooded with oxygen to provide an oxygen-enriched environment. The advantage of this equipment is a controlled environment. The disadvantages include poor access to animal, difficulty in monitoring the animal, and inadvertent uncontrolled environmental conditions (especially overheating). Alternative oxygen-enriched environments include oxygen tents or a cage with a “fitted door” into which O2 is pumped. These systems are inefficient and generally have no way to remove or scavenge CO2. This works well for cats that present in acute congestive heart failure or status asthmaticus, because the clinician can supplement oxygen for a period of time without the stress of nasal oxygen. Human neonatal incubators have also been used for supplementing oxygen in small animals, and kits to modify normal clinic cages into oxygen cages are available. Covering some of the carrier holes with cellophane and providing a humidified oxygen source can

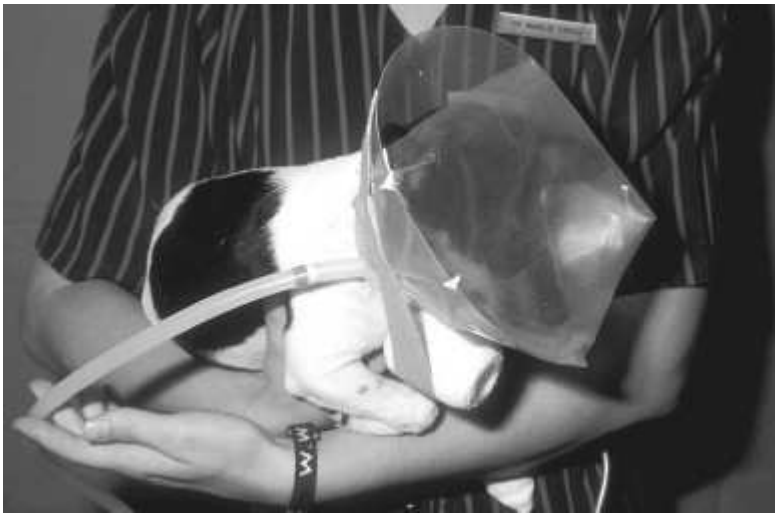
convert pet carriers into emergency oxygen cages. Elevated temperatures and carbon dioxide levels may be a problem with this technique, however.



OXYGEN SUPPLEMENTATION Animal receiving oxygen supplementation via an intranasal Foley catheter.



OXYGEN SUPPLEMENTATION Animal receiving oxygen supplementation via a tent.



OXYGEN SUPPLEMENTATION Animal receiving oxygen supplementation via an Elizabethan collar partly covered with cellophane, creating an oxygen canopy. Note the oxygen tube entering through the caudal edge of the collar.

MISCELLANEOUS: With an Elizabethan collar, cellophane, and a humidified oxygen line, it is possible to easily create an oxygen

canopy.

- The animal is fitted with an Elizabethan collar (E-collar), and the lower 50%-75% of the collar diameter is covered with cellophane.
- The oxygen line is run inside the E-collar and provides oxygen into the cellophane-covered area.
- In this way, the animal's head is essentially within an oxygen tent.
- In areas with high ambient temperatures, this device is poorly tolerated.
- The advantages of this technique include ease of application and no special equipment requirements.
- The major disadvantage is animal intolerance.

Note: Oxygen can also be administered in acute situations via a transparent plastic bag placed over the animal's head.

POSTPROCEDURE

- Most animals requiring oxygen supplementation will be hospitalized in an intensive care unit and observed closely because of the nature of the underlying disease. In addition, it is important to closely monitor the typical vital parameters, including temperature, pulse, and respiratory rate. Specific evaluation for animals on oxygen supplementation includes thoracic auscultation, observation of respiratory effort, evaluation of mucous membrane color, capillary refill time, blood gas analysis, and/or pulse oximetry.
- Knowing when and how to discontinue oxygen therapy can present the clinician with a dilemma. Generally it is worthwhile to slowly wean animals off oxygen supplementation. The rate of tapering should be based on the animal's condition and response but is generally done over a 24-48 hour period. It is also important to remember that oxygen is often an adjunctive therapy, and treatment directed toward the underlying disease process is paramount.

AUTHOR: DAVID MILLER

Otoscopy (Video)

OVERVIEW AND GOALS

- Minimally invasive examination technique for the external ear canal, tympanic membrane, and middle ear
- Allows excellent visualization, sampling, and documentation during ear flushing, myringotomy (deliberate perforation of the tympanum), removal of feline ear polyps, and biopsy procedures

INDICATIONS

- When clinical signs of ear disease are present: otic discomfort, pruritus, discharge, swelling or erythema, head-shaking, Horner's syndrome, vestibular signs, deafness
- Ear flushing using video otoscopy is indicated in unresponsive or recurrent otitis or if otitis media or a mass in the ear canal is suspected.

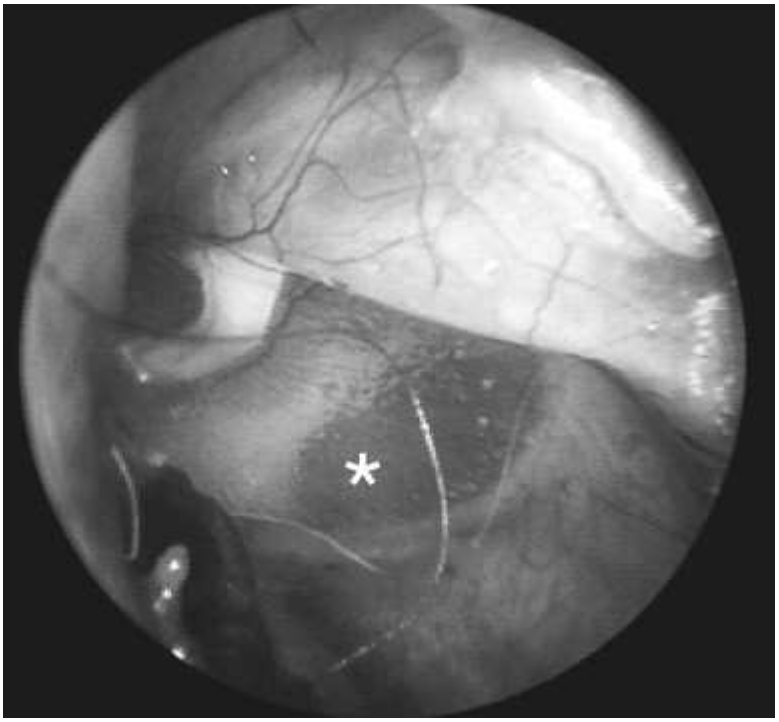
CONTRAINDICATIONS

- Very painful ears (in conscious animal)
- Severely stenotic ear canals

EQUIPMENT, ANESTHESIA

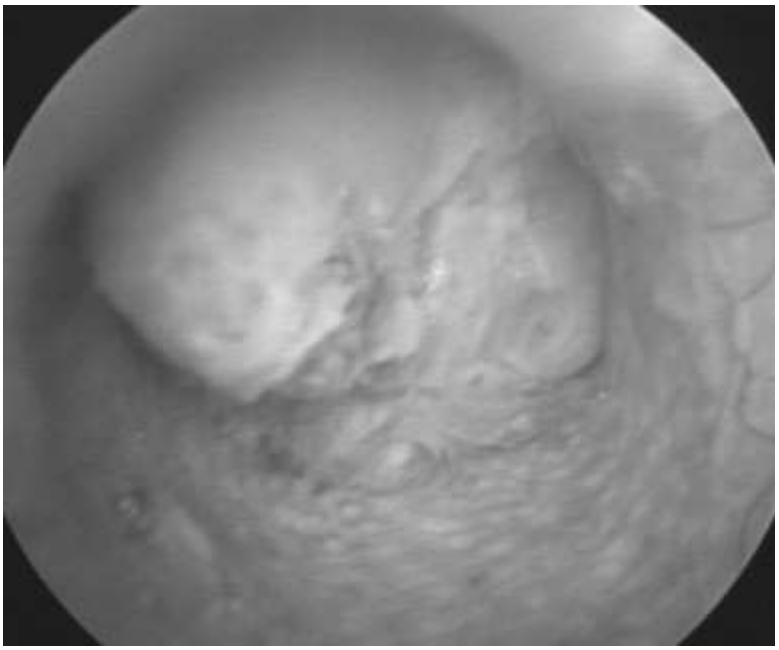
The main piece of equipment for the procedure is a video otoscope.

- Ear examination:
  - The examination can be performed in a conscious animal if the ear is not too painful.
  - Manual restraint by an experienced handler is required.
  - A small amount of isopropyl alcohol is needed for cleaning the otoscope tip; a commercial antifog solution improves visualization.
- Ear flushing:
  - Ear flushing, myringotomy, and biopsy procedures require general anesthesia and endotracheal intubation to prevent lower respiratory tract contamination.
  - Analgesia is essential and should be part of the anesthetic protocol.
  - Ceruminolytic agent (dogs only)
  - Bulb syringe
  - Sterile physiologic saline solution, approximately 1 L in bowl (may be warmed to body temperature)
  - A 5 Fr, 22-inch (56 cm) polypropylene urinary catheter, red rubber feeding tube or Tomcat catheter, tip dulled by heating briefly over a flame
  - Two 30-mL syringes
  - Three-way stopcock valve
  - Culturette tubes
  - Video otoscope: compatible biopsy and grasping instruments and ear curettes are available.
  - Optional: suction unit and flushing and suction apparatus



OTOSCOPY (VIDEO) Otoscopic view of a normal ear canal and tympanum. The asterisk indicates the optimal site for myringotomy.

(Courtesy Dr. Louis N. Gotthelf.)



OTOSCOPY (VIDEO) Otoscopic view of an external ear canal partially obstructed by a large polyp in a dog.

(Courtesy Dr. Michel Chenier.)

ANTICIPATED TIME

- Ear examination: <5 minutes in conscious animal
- Ear flushing: 10-30 minutes per ear, 30-60 minutes for anesthesia

PREPARATION: IMPORTANT CHECKPOINTS

Ear examination:

- Avoid having topical medication or cleaning solution instilled in the ears for 12 hours prior to procedure.
- Use adequate restraint to prevent harm to pet and handler.
- Sedation and analgesia are recommended in painful ears.

Ear flushing:

- Revision of the ear anatomy of cat and dog, localization of the myringotomy site
- Collect cytologic analysis and culture samples before instilling fluids or cleaning solutions in the ear.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

Ear examination:

- Discomfort, trauma to ear canal

Ear flushing:

- Vestibular signs, deafness, Horner's syndrome, facial nerve injury, pain, tympanic membrane rupture:
  - Usually temporary but may persist
  - More common in cats; therefore, the use of strong ceruminolytic agents should be avoided in this species
- Flushing very inflamed ears may increase discomfort and induce a rapid return of debris to the ear canal.
- Should not be attempted in extremely stenotic ear

PROCEDURE

Ear examination:

- Use a disinfected otoscope head for each animal (follow manufacturer's recommendation for disinfection).
- Wipe otoscope tip with isopropyl alcohol.
- Pull pinna gently away from skull.
- Slowly introduce otoscope into ear canal, using video image for guidance.
- If thorough examination is not possible because of swelling of the ear canal, the procedure may be attempted after 1-2 weeks of topical therapy, cleaning, ± oral corticosteroids (no topical medication on day of recheck).

Ear flushing:

- Many techniques have been described.
- General anesthesia
- Inflate endotracheal tube cuff.
- Sternal recumbency, head may be tilted to each side slightly as needed.
- Tilt head down (neck ventroflexion) so solutions exit from the nose if the tympanic membrane is ruptured.
- Collect cytologic analysis and culture samples.
- For tenacious or waxy debris, instill ceruminolytic agent, massage, and remove using saline and bulb syringe (dogs only) or a 30-mL syringe.
- Introduce catheter through otoscope so tip is visible, and attach one 30-mL saline-filled syringe and one empty 30-mL syringe on a three-way stopcock valve.
- Assistant flushes saline solution, using small pulses, and aspirates using the three-way stopcock valve.
- Direct catheter tip as needed to dislodge debris.
- Removal of debris reveals area of tympanic membrane at end of ear canal.
- If tympanic membrane is ruptured, the catheter can be advanced a short distance ventrally into the middle ear cavity.
- If tympanic membrane is intact but abnormal or if otitis media is suspected, myringotomy may be performed by introducing a fine instrument (open-ended Tomcat catheter cut to create a beveled edge, or a small culture swab) through the otoscope and directing it through the caudoventral portion of the pars tensa.
- May collect samples for cultures and cytologic analysis from middle ear
- Gently flush middle ear with saline solution at body temperature.
- Suction excess saline solution from the ear canal, and instill topical medication if appropriate.

POSTPROCEDURE

- Oral ± topical corticosteroids reduce the inflammation induced by otoscopy and flushing.
- Ear medications should be started immediately after flushing; start cleaning ear the following day.
- Analgesic protocol

ALTERNATIVES AND THEIR RELATIVE MERITS

Handheld otoscopes are adequate for cursory examination of the ear canal but much less useful for ear-flushing procedures. Advantages of handheld otoscope:

- Less expensive
- Convenient and portable
- Less prone to condensation
- Smaller plastic tip may be better tolerated.

Advantages of video otoscope:

- Greatly improved optics and magnification
- Increase client's compliance to treatments by allowing them to view the ear lesions when used in the examination room
- Allows documentation
- Vastly superior for ear flush procedures, because the ear canal can be visualized very well through saline solution during the flush procedure, allowing for a very thorough cleaning with minimal trauma
- Allows for much more precise and thus safe placement of instruments for biopsy, myringotomy, foreign-body removal, and polyp removal

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AUTHORS: KINGA GORTEL, MICHEL CHÉNIER

Orthopedic Examination

OVERVIEW AND GOAL

To identify and localize an orthopedic disorder by performing a thorough and reproducible examination of the axial and appendicular skeleton, joints, and musculature

INDICATIONS

Any animal with abnormal musculoskeletal function due to injury, joint, muscle, or bone-related disease

CONTRAINDICATIONS

In trauma cases, life-threatening problems should be addressed and animal stabilization ensured before performing a detailed orthopedic evaluation.

EQUIPMENT, ANESTHESIA

- Specialized equipment is usually not required.
- Goniometer to measure joint angles is optional.
- Sedation/general anesthesia is rarely necessary.

ANTICIPATED TIME

About 20-30 minutes

PREPARATION: IMPORTANT CHECKPOINTS

Detailed history tailored to the individual case, including:

- Signalment:
  - Breed-specific orthopedic disorders
- Owner assessment of problem
- Duration of problem
- Speed of onset
- Relationship to trauma, exercise, or time of day
- Course of problem
- Influence of rest or medications
- Associated or independent systemic disease
- Previous orthopedic problems and associated treatments and outcomes
- “Family” history
- Diet and exercise regimen
- Observation in the examination room noting how the animal sits, stands, and moves around
- Observation of different gaits in an open area

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Do not overinterpret breed-specific disorders.
- Beware of misinterpretation of neurologic disorders for orthopedic problems and vice versa:
  - Postural reactions such as proprioceptive testing and tactile placement responses, together with spinal cord reflexes, can help differentiate between orthopedic and neurologic disorders.
- Perform neurologic examination after orthopedic examination (see p. 1311).

PROCEDURE

- Strive to palpate entire musculoskeletal system.
- Palpate all joints for swelling, thickening, crepitus, pain, and instability.

- Palpate all muscles for swelling, atrophy, pain, and asymmetry.
- Palpate bones for irregularity, pain, and instability.
- Palpate entire spine (including flexion, extension, and lateral deviation of the head and neck; tail head flexion and flexion and extension of the lumbosacral joint) for pain and sensitivity.
- Place all joints through a full range of motion.
- Know normal range of motion for all joints.
- When appropriate, use opposite limb as "normal" for comparison, best achieved in a standing position.
- Specific orthopedic tests include an Ortolani maneuver for hip joint laxity and a cranial drawer/sign test or a tibial thrust test for stifle joint instability.
- Ortolani maneuver:
    - The femur is forced dorsally and perpendicular to the spine in an attempt to subluxate the hip joint.
    - Slow abduction of the limb allows the femoral head to return to the acetabulum.
    - An audible or palpable "clunk" is a positive sign, suggesting hip laxity.
- Cranial drawer/sign test (see p. 261):
    - The examiner places a finger and thumb of one hand on the patella and lateral fabella proximal to the joint; the finger and thumb of the other hand are placed on the fibular head and tibial crest distal to the joint.
    - Cranial translation of the tibia can be applied to the joint in stifle flexion and extension. A torn cranial cruciate ligament will produce cranial subluxation (cranial movement) of the tibia relative to the femur.
- Tibial thrust test (see p. 261):
    - Evaluates the same instability as a cranial drawer test (i.e., tests mainly for cranial cruciate ligament integrity)
    - Dorsiflexion of the hock while the stifle is in slight flexion
    - Positive result consists of a tibial thrust motion (cranial movement of the tibial plateau relative to the rest of the stifle), appreciated by placement of an index finger on the tibial crest.
    - Animal cooperation will determine whether the examination requires sedation or even general anesthesia.
- Perform a rectal examination in cases of pelvic trauma.

POSTPROCEDURE

- Inform owner that some animals may be sore or painful after an orthopedic examination.
- Use nonsteroidal antiinflammatory drugs (NSAIDs) if the animal shows evidence of discomfort or pain (e.g., lameness) after manipulation.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Plain radiographs:
    - May require sedation
    - Minimum of two views of the localized region
    - Normal opposite limb can be useful as a control for comparison
    - In trauma patients, thoracic radiographs should precede orthopedic radiographs as part of a minimum database.
    - Initial radiographic assessment of spinal injuries should ideally be performed without sedation.
    - Radiographic information and clinical/physical examination are complementary; one cannot entirely replace the other, because some animals with radiographically severe lesions are clinically mildly affected and vice versa.
    - Specific radiographic studies may be indicated (e.g., PennHIP, dorsal acetabular rim [DAR] view of pelvis, hyperflexed or hyperextended view of joint).
- Arthrocentesis (see p. 1199):
    - Where joint swelling is palpated, arthrocentesis may be indicated for cytologic evaluation of synovial fluid.
- CT scan (see p. 1233) and MRI (see p.1200) techniques can be extremely useful in specific cases:
    - Rule in or rule out diagnosis that is unclear from examination and routine testing
    - CT scan is usually preferred for bone analysis, and MRI is usually preferred for soft-tissue analysis, including ligament and articular cartilage damage.
    - Requires general anesthesia
    - Cost or availability may be prohibitive.
- Bone scan and nuclear scintigraphy:
    - Helpful to localize an occult orthopedic lameness
    - Highly sensitive yet nonspecific
    - Requires sedation and hospitalization of "hot" animal, and cost or availability may be prohibitive.
- Diagnostic ultrasound:
    - Limited uses in identifying orthopedic disorders
    - In skilled hands, can identify biceps, triceps, infraspinatus, and Achilles and iliopsoas tendon lesions
- Arthroscopy (see p. 1200):
    - Allows minimally invasive visualization and diagnosis ± surgical repair of a joint disorder
    - Requires general anesthesia, and cost or availability may be prohibitive.

AUTHOR: NICHOLAS J. TROUT

Ophthalmic Examination

OVERVIEW AND GOAL

Basic examination of the structure and function of the eyes and adnexa (surrounding structures) to establish an ophthalmic diagnosis, prognosis, and treatment plan and evaluate the need for additional diagnostic testing or referral

INDICATIONS

- An abnormal appearance to the eye(s) or adnexa
- Ocular discomfort or trauma
- Vision impairment/loss
- Systemic disease that may have ocular manifestations

CONTRAINDICATIONS

A very aggressive patient, particularly with a fragile eye, that will not tolerate eye examination may not be examinable awake.

EQUIPMENT, ANESTHESIA

- Exam table in a quiet room that can be darkened
- Bright focal light source (Finnoff transilluminator or otoscope without a cone)
- Schirmer tear test (STT) strips (optional)
- Fluorescein dye–impregnated strips
- Sterile saline/irrigating solution
- Topical anesthetic (e.g., proparacaine)
- Tonometer (Schiøtz, TonoPen)
- 1% tropicamide (optional)
- Condensing/fundic or magnifying lens (lens strength of 20-28 D is best for general use)
- Direct ophthalmoscope (optional)
- Muzzle for aggressive dogs
- Sedation and/or anesthesia are generally not necessary and may in fact hinder a good examination, owing to globe position, reduced alertness, and anesthetic drug effects.

ANTICIPATED TIME

About 10-20 minutes

PREPARATION: IMPORTANT CHECKPOINTS

- Adequate restraint will greatly aid examination and is generally best performed by an assistant, not the owner. Muzzle dogs if necessary.
- Examine the animal at eye level (on exam table); large dogs may be examined on the floor, sitting up, and if cooperative, backed into a corner.
- Cats especially can become enophthalmic during examination; occasional repositioning is often necessary to stimulate the cat and reduce enophthalmos.

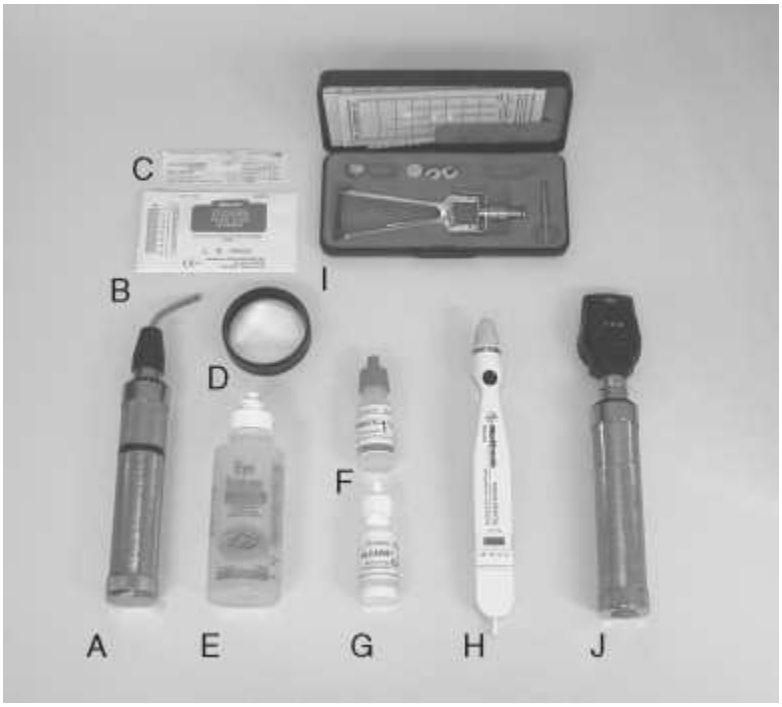
POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Fragile eyes (ruptured eyes, descemetoceles) should be handled extremely gently if at all. Note: Do not palpate, retropulse, or measure intraocular pressure in these eyes.
- Perform STT before any solutions are applied (solutions alter fluid content of tears), assess fluorescein staining before tonometry (tonometry may give false appearance of corneal lesions), assess pupillary motion before pharmacologic mydriasis (mydriatic drugs block miotic response).

PROCEDURE

- Grossly assess functional vision as the animal walks to the exam room: does the animal show signs of adequate vision, such as confidently maneuvering and successfully avoiding objects? Or does it walk slowly and cautiously with head down, using its whiskers and other senses to navigate? Is it easily frightened by obstacles? Does vision appear to be worse on one side than the other?
- Looking at the face head-on in normal room light, assess the overall appearance and symmetry of the head and orbits; resting pupil size; and globe size, position, and motility. Note any ocular discharge or tear staining:
    - Evaluate the eyelid shape and conformation before manipulating the head and eyes.
    - Palpate the muscles of mastication, and assess the degree of globe retropulsion through the closed lids. Palpate both eyes simultaneously to best assess symmetry.
    - Retropulsing each eye individually also elevates the nictitans, which can then be evaluated for presence, shape, coloration, and abnormalities.
- Assess the cranial nerves bilaterally (see):
    - Menace response (II afferent, VII efferent): covering one eye, perform a menacing gesture to the open eye to elicit a blink, without stimulating the vibrissae (whiskers) or face. Hold your hand flat and vertical with its lateral aspect toward the animal's eye to allow testing of different areas of the visual field while minimizing air motion:
        - Note that diffuse cerebellar disease may cause absence of the menace response without loss of vision.
        - Note that very young puppies and kittens normally do not menace.
    - Palpebral reflex (sensory V afferent, VII efferent): lightly touch the lateral and medial canthi to stimulate blinking. Observe for completeness of blinking:
        - Note that facial paralysis disables blinking, in which case globe retraction and nictitans elevation (± III, IV, VI efferent) or head withdrawal may be seen instead.
    - Dazzle reflex (II afferent, VII efferent): rapidly apply a very bright focal light to one eye. This should cause the eye to blink (subcortical pathway). An intact dazzle does not alone signify vision so much as some degree of retinal and optic nerve function.
    - Pupillary light reflex (PLR; II afferent, III efferent): apply a bright light to one eye, and observe ipsilateral (direct PLR) and contralateral (indirect or consensual PLR) pupillary constriction. Also note degree of pupillary constriction.
- Test vision by tossing cotton balls or gauze into the visual field:
    - Functional vision can also be tested utilizing an obstacle course in an enclosed area. The best obstacles are relatively large, safe to bump into, and free of odor. Vary the course during the test. Do not provide excessive nonvisual guidance (sound, food). Repeat in dim light if indicated.
- If significant mucoid ocular discharge is present, measure tear production:
    - Gently wipe away very large clumps of discharge without touching the lid margins or ocular surface.
    - Keeping the proximal end of the STT strip in the package, fold at the notch. Place the folded tip between the lower lid and globe. Close lids if necessary; keep strip in for 60 seconds, and immediately replace if blinked out.
    - Low is <10 mm/min, borderline is 10-15 mm/min, normal is >15 mm/min wetting in dogs and cats (even lower for many normal cats).
- If corneal ulceration is suspected, apply fluorescein. Place a drop of sterile saline on a fluorescein strip, and lightly touch the strip to the bulbar conjunctiva. Allow the lids to blink. Flush excess fluorescein with saline to prevent false-positive results. Examine in a darkened room, ideally with cobalt light/Wood's lamp:
    - In 1-5 minutes, fluorescein may appear at the nostril(s) or mouth, indicating nasolacrimal patency (positive Jones test). Note that a negative Jones test does not necessarily indicate nasolacrimal duct obstruction.
- Retroilluminate the eyes to identify opacities in the visual axis:
    - Hold the transilluminator above your ear and shine it into the animal's eyes. Adjust your position (usually to below the level of the animal) until you see the fundic reflection, and then scan from side to side to visualize opacities in the clear ocular media, which will appear silhouetted.
- Carefully examine the surface and anterior segments of the eyes in dim light with the transilluminator. Note the lid margins, nasolacrimal puncta, bulbar and palpebral conjunctiva, cornea and anterior chamber, iris surface, pupil, and anterior lens:
    - Holding the light from the side will aid greatly in accentuating the three-dimensionality of anterior chamber structures.
- Examine the fundus, noting the optic nerve, retinal vessels, tapetum, and nontapetum:
    - A drop of 1% tropicamide may be given for mydriasis if there is no suspicion of glaucoma. Wait 20-30 minutes after applying; the effects will last for 2-4 hours.
    - Indirect ophthalmoscopy: the preferred method, as it provides a wider view that is easier to interpret, allows three-dimensional visualization, and is safer for the examiner:
        - Using a fundic lens and transilluminator, position yourself as for performing retroillumination (as described above) an arm's length away from the animal. The assistant should hold the lids open. If using an aspheric lens, hold the lens' flatter side (white rim) toward the animal. Place the lens 1-2 inches from the animal's eye, and then move it toward you slightly until the fundic view appears (inverted and backwards) to fill the lens. Examine the whole fundus, adjusting as if the “fulcrum” of the line of sight is at the animal's lens (e.g., move laterally for a more medial view).
    - Direct ophthalmoscopy: provides a highly magnified view of very small areas of the fundus:
        - To allow the widest area to be examined, use your right eye to examine the animal's right eye, and use your left eye to examine the animal's left eye.
        - With the largest white circle setting and the diopter dial set on 0, focus on the fundus by viewing the eye from 2-6 inches (5-15 cm) from the animal. View as many areas as possible, adjusting the focus if needed by changing diopter settings. These lenses allow for focusing at different depths (for a fixed distance from the

animal) and also can adjust for any correction required by your eyes. The view through the direct ophthalmoscope is a direct image (not reversed).
    - If the light causes blepharospasm or resistance on the part of the animal, dim the light, apply the polarizing filter, or use a smaller circle size.
    - The slit beam (thin rectangle) setting may help in detecting three-dimensionality and depth in anterior segment or fundic lesions.
    - The crosshairs in the fixation aperture may be used for measuring very small retinal lesions. Size comparison may also be made to the size of the optic nerve head (optic disc).
    - The red-free (green) filter allows for differentiation between fundic blood, which appears black, and melanin, which appears brown.
    - An optional cobalt filter may be used for detecting fluorescein-positive corneal lesions.
- If the eye is red or cloudy, the pupil is abnormal, or there is vision loss, perform tonometry. Note that "digital tonometry" (mere globe palpation with the fingers) is inadequate to measure intraocular pressure. Apply a drop of topical anesthetic (may not be necessary with TonoVet). Avoid pressure on the ventral neck.
    - Schiøtz: assemble the tonometer and clean the footplate. Test the tonometer by placing it on the included test block (gives a scale reading of 0). Position the animal with iris plane parallel to floor (dorsal recumbency or sitting up with nose pointed to the ceiling). Holding the tonometer by the handles and keeping it vertical, gently rest the footplate on the central cornea (not the third eyelid or sclera) until a single reading is produced. Repeat two to three times, and use included chart to get actual intraocular pressure (IOP). If IOP is >25 mm Hg, repeat with next additional weight. Record IOP in mm Hg (not as scale readings). Clean tonometer after use.
    - Tono-Pen: Properly fit a clean tip cover, turn on, and calibrate if necessary. Gently touch the instrument tip to the cornea, keeping it perpendicular to the eye; it does not need to be horizontal. Repeat several times until a long beep is heard. A bar over the "5%" at the bottom indicates a statistically significant reading (mean given in mm Hg).
    - TonoVet: Properly insert a new probe tip. Turn on and ensure that proper species calibration is on. Holding the instrument horizontal with the tip 4-8 mm from the cornea, repeatedly press the button to take readings until a long beep is heard. A nonblinking "d" before the reading indicates a statistically significant, dog/cat-calibrated reading.
    - Normal IOP in dogs and cats is 15-25 mm Hg.



OPHTHALMIC EXAMINATION Equipment and materials that may be used during an ophthalmic examination. **A**, Finnoff transilluminator. **B**, STT strips. **C**, Fluorescein dye–impregnated strip. **D**, Lens. **E**, Sterile eye irrigating solution. **F**, 1% tropicamide solution. **G**, 0.5% proparacaine solution. **H**, Tonometer—Tono-Pen. **I**, Tonometer—Schiøtz. **J**, Direct ophthalmoscope.

POSTPROCEDURE

Flush corneas of excess fluorescein if necessary. Protect eyes from light if mydriatics were used.

AUTHOR: JANE CHO

Prostatic Sampling Techniques

SYNONYMS

- Prostatic fine-needle aspiration (FNA)
- “Tru-cut”: automated needle biopsy
- Prostatic massage
- Traumatic catheter biopsy

OVERVIEW AND GOAL

Nonsurgical techniques for obtaining prostate tissue samples for culture and cytologic and histopathologic examination in practices with ultrasound capabilities

INDICATIONS

- Pyuria
- Hematuria
- Penile/urethral discharge
- Prostate enlargement
- Prostatic mineralization
- Asymmetric/irregular/nodular prostate

CONTRAINDICATIONS

- Inadequate restraint
- Bleeding disorder
- Prostate abscess (for automated needle biopsy and large-needle FNA)
- Acute prostatitis

EQUIPMENT, ANESTHESIA

FNA:

- 18-gauge needle
- 12-mL syringe
- Usually does not require sedation
- Ultrasound machine

Automated needle biopsy:

- Automated biopsy needle (14-20 gauge)
- General anesthesia
- Ultrasound machine

Prostatic massage:

- Urinary catheter that is long enough to reach the urinary bladder
- Two 5-mL syringes
- Two 5-mL aliquots of sterile saline
- Two sterile sample containers capable of holding at least 5 mL of fluid
- Manual restraint to general anesthesia, depending on the demeanor of the patient

Traumatic catheterization:

- Urinary catheter that is long enough to reach the prostatic urethra
- 12-mL syringe
- Sedation pending patient

- Ultrasound or x-ray machine are helpful.

ANTICIPATED TIME

- Abdominal ultrasound time will take between 10 and 40 minutes depending on operator expertise.
- FNA takes about 5 minutes.
- Automated needle biopsy with anesthesia, prostatic massage, or traumatic catheterization will take about 20-30 min.

PREPARATION: IMPORTANT CHECKPOINTS

- The patient can be in lateral or dorsal recumbency.
- These procedures usually require the attending veterinarian and one to two assistants.
- Needle aspiration can be performed on a fully awake animal, provided the animal is adequately restrained.
- Automated needle biopsies require heavy sedation with analgesia or general anesthesia.
- For prostatic massage and traumatic catheterization, both digital rectal palpation and urethral catheterization are necessary. If the patient resists these procedures, sedation is advised.
- A soft red rubber (Sovereign type) feeding tube is less traumatic than a polypropylene catheter.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- FNA and automated needle biopsy procedures require the placement of a needle or biopsy instrument directly into the prostate. Adjacent large vessels such as the distal abdominal aorta and caudal vena cava can be lacerated with patient movement or a biopsy miss.
- These procedures should not be performed on animals with inadequate coagulation systems.
- If acute bacterial prostatitis is present, the prostatic massage could result in release of bacteria into the bloodstream, and septicemia.
- Traumatic catheterization and automated needle biopsy may lacerate the urethra.
- If an abscess or cyst is present, rupture is possible secondary to all of these procedures.

PROCEDURE

Fine-needle aspiration, guided:

- The animal should undergo a full abdominal ultrasound evaluation, and an appropriate area for aspiration should be identified.
- The skin is clipped of hair and aseptically prepared with surgical scrub.
- The needle with a syringe attached is then advanced through the skin into the prostate under ultrasound guidance.
- The prostate gland is aspirated, and the sample is handled for evaluation (as already described)

Fine-needle aspiration, nonguided:

- If the prostate is sufficiently enlarged that it can be palpated externally (abdominally) and stabilized by caudal abdominal palpation, then the procedure can be performed nonguided (without the use of ultrasound).
- The external surface of the skin over the prostate is clipped of hair and aseptically prepared with surgical scrub.
- The needle is affixed to the syringe, the needle tip is placed through the prepared skin, and the tip is advanced into the prostate gland.
- Material is aspirated into the needle by drawing on the syringe plunger to create negative pressure in the syringe.
- Negative pressure is released before withdrawing the needle.
- The needle and syringe are then withdrawn quickly, the syringe is detached from the needle and filled with air, and then the syringe is reattached to the needle; the contents are vigorously expelled onto a microscope slide to make fresh smears for cytologic analysis.
- A portion of the material can be placed in appropriate media for culture and sensitivity (C&S) instead of being smeared, or else the procedure can be repeated to obtain more material for this purpose.

Automated needle biopsy:

- Automated needle biopsies are attained either guided or nonguided as described above for needle aspiration. As this is a more invasive and painful procedure, general anesthesia is recommended.
- Care must be taken not to transect the urethra with this full-thickness biopsy procedure. With this in mind, the biopsy should be taken in an orientation parallel to the urethra, not perpendicular to the urethra.
- A portion of the biopsy is taken for culture. The biopsy is then rolled on a slide for cytologic analysis. The sample is then placed in formalin and processed for histopathologic examination.

Prostatic massage:

- The tip of the penis is extended from the prepuce and cleaned with a mild disinfectant.
- A urinary catheter is placed into the bladder, and the urine is completely removed.
- Sterile saline (5 mL) is instilled into the bladder. This fluid is then aspirated back and placed in a sterile tube labeled *tube #1*.
- The veterinarian then places an index finger in the rectum and palpates both the prostate and the catheter. The catheter is retracted until the tip can be felt caudal to the prostate. The prostate is then massaged for 1 minute.
- The palpating finger is retracted until it is caudal to the holes in the catheter. Pressure is applied to the catheter rectally so that fluid injected into the catheter will not leak out of the penis but will move forward into the bladder.
- Another 5 mL of sterile saline is then injected into the catheter. The fluid flows across the prostatic urethra into the bladder.
- The catheter is then pushed into the bladder, and the fluid is aspirated into a syringe and placed into a sterile tube labeled *tube #2*. Both tubes are presented for fluid analysis and culture.
- Sample #1 will have only bladder material, whereas sample #2 will have both prostate and bladder material. Comparing the two samples allows the clinician to localize the disease process to the prostate and/or the urinary bladder.

Traumatic catheterization:

- Prepare the penis and empty the bladder as above.
- The urinary catheter is placed into the prostatic urethra. Correct catheter placement can be verified by digital rectal examination, by radiograph, or by ultrasound.
- A 12-mL syringe is attached to the end of the catheter, and negative pressure is applied so that prostate tissue is aspirated into the holes of the catheter.
- While maintaining negative pressure on the syringe, remove the catheter from the urethra. This will tear tissue from the prostate that is aspirated into the catheter. This prostatic tissue can be evaluated by cytologic analysis, and sometimes a large enough piece is obtained for histopathologic evaluation.

POSTPROCEDURE

- These are outpatient procedures, and the client may be sent home the same day provided that its clinical condition allows.
- The patient should be sent home on an antibiotic for 5 days or longer if the culture comes back positive.
- The client should be counseled that there may be hematuria transiently postprocedure.

ALTERNATIVES AND THEIR RELATIVE MERITS

A technique for performing a needle aspiration biopsy of the prostate per rectum using a guarded needle has been described. This technique has the problem of injecting bacteria directly into the prostate, as the colon cannot be sterilized. The advent or ultrasound-guided techniques has made this procedure obsolete.

AUTHORS: DONALD KRAWIEC, LENORE MOHAMMADIAN

Prostatic Massage

SYNONYMS

Expressed prostatic fluid sampling by urethral catheter, prostatic wash or washing, traumatic catheter biopsy

OVERVIEW AND GOALS

Nonsurgical technique for obtaining prostate tissue samples for practices without ultrasound capabilities. This technique can also be performed when needle aspiration of the prostate has provided inconclusive or inadequate results.

INDICATIONS

- Pyuria
- Hematuria
- Penile/urethral discharge
- Prostate enlargement
- Asymmetric, irregular, or nodular prostate

CONTRAINDICATIONS

- Inadequate restraint
- Bleeding disorder
- Acute prostatitis
- Prostatic or rectal pain (contraindication to performing the procedure awake)

EQUIPMENT, ANESTHESIA

- Urinary catheter of sufficient length to reach the urinary bladder. A soft, red rubber (Sovereign-type) feeding tube is preferable because it is less traumatic than a polypropylene catheter.
- Two 5-mL syringes
- Two 5-mL aliquots of sterile saline solution
- Two sterile sample containers capable of holding at least 5 mL of fluid
- Routine surgical scrub soap and gauze squares for disinfecting the distal penis
- Manual restraint to general anesthesia, depending on the demeanor of the animal

ANTICIPATED TIME

Approximately 20-30 minutes

PREPARATION: IMPORTANT CHECKPOINTS

- The patient can be standing or in lateral recumbency.
- The procedure usually requires three people: the veterinarian and two assistants.
- The procedure requires both digital rectal palpation and urethral catheterization. If the animal resists these procedures, sedation or anesthesia is advised.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- This procedure requires digital massage of the prostate. If acute bacterial prostatitis is present, the prostatic massage could result in release of bacteria into the bloodstream, and septicemia.
- If an abscess or cyst is present, rupture is possible secondary to this procedure.
- The urinary bladder must be completely empty before starting the procedure, or the prostate sample will be diluted by the excess urine.
- Premeasuring the catheter makes it possible to place the catheter into the urinary bladder without causing catheter-induced bladder trauma or allowing it to loop back on itself to form a knot.
- Bladder infections will make the prostate wash difficult to interpret. Animals with bacterial cystitis should be treated with an

appropriate antibiotic before undergoing a prostatic wash.

PROCEDURE

- While one assistant restrains the animal, the other assistant retracts the prepuce to expose the penis and cleans the distal penis with a mild surgical disinfectant.
- The veterinarian passes a urinary catheter into the urethra until the tip is in the bladder and completely removes the urine.
- The veterinarian instills 5 mL of sterile saline via the catheter into the bladder.
- This fluid is then aspirated back with a syringe and placed in a sterile tube labeled *tube #1*.
- The veterinarian then places an index finger in the animal's rectum and palpates both the prostate and the catheter.
- The catheter is retracted until the tip can be felt to be distal (caudal) to the prostate.
- The prostate is then gently massaged for 1 minute.
- The palpating finger is retracted until it is distal/caudal to the holes in the catheter, and gentle pressure is applied to the catheter rectally so that fluid injected into the catheter will not leak out of the penis but will move cranially into the bladder.
- A total of 5 mL of sterile saline is then injected into the catheter so the fluid flows across the prostatic urethra into the bladder.
- The catheter is then advanced into the bladder, and the fluid is aspirated into a syringe and placed into a sterile tube labeled *tube #2*.
- Both tubes are presented for fluid analysis and culture.

If the above procedure yields either inadequate sample size or equivocal results, a traumatic catheter biopsy can be performed. General anesthesia or sedation with systemic analgesia is indicated.

- The urinary catheter in placed into the urethra as already described. The tip of the catheter should be in the prostatic urethra. Correct catheter placement can be verified by digital rectal examination or by radiograph.
- A 12-mL syringe is attached to the catheter, and negative pressure is applied so that prostatic tissue is aspirated into the holes of the catheter.
- While maintaining negative pressure on the syringe, the catheter is withdrawn from the urethra. Doing so will tear tissue from the prostate that is then aspirated into the catheter. This prostatic tissue can be used for cytologic evaluation, and sometimes a sufficiently large piece is obtained to allow histopathologic examination.

POSTPROCEDURE

- The animal should be discharged with an antibiotic for 5 days to reduce the risk of inducing a bladder infection.
- Sample #1 will have only bladder material, whereas sample #2 will have both prostate and bladder material. Comparing the two samples allows the clinician to localize the disease process to the prostate and/or the urinary bladder.

ALTERNATIVES AND THEIR RELATIVE MERITS

Prostatic washings are done infrequently since the advent of ultrasound-guided prostate biopsy procedures; however, washings do provide a representative prostate tissue sample.

AUTHOR: DONALD R. KRAWIEC

Porcupine Quill Removal

OVERVIEW AND GOAL

To safely remove all porcupine quills embedded in the tissues of a patient (almost always dogs). Although most patients are brought to veterinary attention within 24 hours of exposure to quills, extensive migration can occur in just 1-2 days; therefore, immediate removal is appropriate.

INDICATIONS

- Any witnessed or unwitnessed encounter with a porcupine
- Suspected prior porcupine encounter, presenting with signs of quill migration (ocular, thoracic, abdominal, or other site of discomfort, possibly with draining tract). In regions where porcupines are part of the natural fauna, a history of prior porcupine quill trauma should always be investigated when evaluating a patient weeks or months later for vague, nonspecific signs.

CONTRAINDICATIONS

None

EQUIPMENT, ANESTHESIA

General anesthesia is almost always required both for accessing remote (oral) quills and for pain control during the procedure. Quills routinely penetrate the mouth and pharynx; therefore, complete oral exam under general anesthesia is required even if quills initially appear to be confined to the muzzle.

ANTICIPATED TIME

30 minutes to 3 hours or more, depending on number of quills and depth of penetration

PREPARATION: IMPORTANT CHECKPOINTS

- Prior to beginning the procedure, advise owners that even with diligent removal of all visible quills, some may have penetrated beyond the point where they can be seen and can cause health problems in the future.
- Prior to induction, the clinician should be sure to inspect the surface of the face/body on which the dog will be lying once anesthetized to avoid having quills inadvertently driven more deeply into tissue during anesthesia.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Failing to remove all quills:
  - Remaining quills can migrate to deeper tissues and body cavities, including lungs and heart.
  - The number and location of quills at initial presentation do not appear to be associated with the risk of quill retention and infection.
  - Time from quill injury to the development of complications can range from days to months.
- Quill breakage during extraction. Requires dissection to remove the retained fragment.

PROCEDURE

- It is important to perform a full oral exam on the patient, as quills can be embedded in the oropharyngeal region and hard palate (see p. 1295).
- Quills are extracted one at a time with hemostats or needle drivers, beginning on the exterior (skin) and working into the mouth and pharynx.
- Removal is safest when grasping the quill as close to the skin as possible and pulling straight out. Doing so minimizes the likelihood of breaking the quill. If the quill should break, careful dissection to retrieve the remainder of the quill should be performed while attempting to minimize soft-tissue trauma.
- Placing quills in a bowl with gauze and water facilitates the removal process and minimizes risks of injury to those removing the quills.
- Quill removal in locations other than skin depend on the location:
  - Thoracoscopy or thoracotomy is needed to remove quills from the thoracic cavity.
  - An ophthalmologist should be consulted if there are quills embedded in the ocular or periorbital areas.
  - Ultrasonography can be useful in identifying migrating quills in the eye, joint space, thorax and abdomen. A quill appears as two distinct hyperechoic lines.

- Additional diagnostic tests such as thoracic radiographs, echocardiography, MRI, and complete blood work may be indicated on a case-by-case basis, generally if a chronically retained quill is suspected to be causing persistent problems.

POSTPROCEDURE

- Many dogs do not learn from their previous encounters with porcupines. Therefore, it is important to educate owners to avoid repeat events.
- After quill removal, antibiotic administration may be indicated (e.g., amoxicillin-clavulanate, 13.75 mg/kg PO q 12 h):
  - Porcupine quills themselves possess antibiotic properties, and infections after quill removal are not common. However, if significant trauma of the skin or subcutaneous tissues has occurred secondary to dissection, or if the quill has migrated to an atypical location, broad-spectrum antibiotics may be warranted.
  - A longer course of antibiotics is indicated in certain situations, such as migration to the pleural space or central nervous system.
- Analgesia: opiates (e.g., buprenorphine, 0.01-0.02 mg/kg IV or IM) and/or nonsteroidal antiinflammatories (e.g., meloxicam, 0.1 mg/kg PO q 24 h)

ALTERNATIVES AND THEIR RELATIVE MERITS

There are no humane alternatives to removing the quills.

SUGGESTED READING

Grahn BH, Szentimrey D, Pharr JW, et al: Ocular and orbital porcupine quills in the dog: a review and case series. Can Vet J 36:488–493, 1995.

Johnson MD, Magnusson KD, Shmon CL, et al: Porcupine quill injuries in dogs: a retrospective of 296 cases (1998-2002). Can Vet J 47:677–682, 2006.

McCarthy TC: Porcupine quill retrieval with thorascopy. Vet Med 99:15–16, 2004.

AUTHOR: CASS ROGERS

Physical Rehabilitation

SYNONYMS

Physical therapy, physiotherapy Note: In some U.S. states, the *term physical therapy* (and possibly physiotherapy) is a protected term reserved only for human physical therapists. Therefore, claiming to practice such therapy without being a licensed physical therapist is potentially misleading and illegal. The term *physical rehabilitation* is safe and recommended for veterinary medicine.

OVERVIEW AND GOALS

Using modalities, manual therapies, and therapeutic exercises to increase function by strengthening an animal's muscles, accelerating the healing of damaged tissues, increasing flexibility and ranges of motion, and decreasing pain. These therapies are becoming more common in veterinary medicine.

INDICATIONS

- Postoperative orthopedic/joint surgery (e.g., fractures, cranial cruciate ligament tears, total hip replacements, femoral head and neck ostectomy)
- Postoperative laminectomy/hemilaminectomy or other spinal surgery
- Acute neurologic diseases (fibrocartilaginous embolism/stroke, trauma, intervertebral disk disease [IVDD])
- Osteoarthritis/spondylosis
- Vestibular disease and other balance/proprioceptive problems
- Postoperative amputation
- Soft-tissue injuries (e.g., sprains and strains, tendon repairs, muscle tears)
- Obesity/conditioning

CONTRAINDICATIONS

- Unstable and/or infected fractures and joints
- Therapeutic ultrasound is contraindicated over metal implants, tumors, growth plates, eyes, heart, and pregnant uteruses.
- Neuromuscular electrical stimulation may be contraindicated in animals with seizure disorders.
- Heat is contraindicated over acutely inflamed tissues.
- Swimming and underwater treadmill exercise are contraindicated in animals with diarrhea.

EQUIPMENT, ANESTHESIA

Physical rehabilitation can be successfully performed with a minimal amount of equipment. The practitioner's hands are the greatest asset. The following are, however, recommended for optimal results, depending on the case:

- Manual restraint at times
- Goniometer to measure angles of joints
- Gulick II tape measure (to measure limb circumference/muscle mass)
- Heat packs
- Cold/ice packs
- Inflatable exercise/yoga balls and/or rolls
- Therapeutic ultrasound unit (with ultrasound gel)
- Neuromuscular electrical stimulation (NMES) unit
- Treadmills (underwater or land)
- Swimming area (pools for larger animals, tubs for smaller animals)
- Canine life vests
- Various slings and carts
- Cavaletti rails (horizontal bars or poles at varying heights for the animal to walk over; a ladder lying flat works well)
- Stairs
- Balance boards (“wobble” and “rocker” boards)
- Elastic resistance bands
- Leg weights
- Extracorporeal shockwave therapy unit (usually requires sedation)
- Low-level (“cold”) lasers
- Various splints and orthotics

ANTICIPATED TIME

- About 20-90 minutes
- Usually performed several times a week
- Note: Most postop orthopedic cases require an average of 1 month of rehabilitation, neurologic cases average 2-3 months, and osteoarthritis cases may continue indefinitely (or may benefit from intermittent rehabilitation such as 1-2 month stints several times a year).

PREPARATION: IMPORTANT CHECKPOINTS

- Be sure that any surgical repair is stable.
- Watch for any swelling or signs of infected tissues, which could contraindicate treatment.
- Be sure that the animal's condition is not deteriorating with rehabilitation.
- Exercise animals on an empty stomach (subjectively, doing so may decrease risk of gastric dilation/volvulus).
- Take joint range-of-motion measurements (goniometry) in flexion and extension using a goniometer:
    - Normal values are published for some breeds.
    - The measurements should be rechecked every 2-4 weeks to monitor progress.
- Measure thigh or forearm circumference as a rough measure of muscle mass.
    - The measurement of this circumference is done with a tape measure, preferably the Gulick ll to decrease margin of error.
    - This measurement also should be monitored every few weeks for progress.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Do not institute hydrotherapy (e.g., swimming, underwater treadmill) until skin incisions have successfully sealed (at least 5 days).
- It is easy to overwork the animal, especially in the initial treatments. Be sure the animal can easily handle the work regimen in the beginning. As a general rule, exercise can be increased about 20% per week if the animal is improving.
- Do not stress the tissues too much (remember time frames for tissue healing):
    - For example, bone healing (fracture, surgical osteotomy) takes 8-12 weeks to be complete under ideal conditions. A classic pitfall would be applying too much force too early or allowing the dog to apply too much via inappropriate exercise. Signs of pain and palpable instability could be warning signs. Consultation with the surgeon on the stability of the repair is recommended.
- In the immediate postoperative period, therapeutic exercise may be contraindicated. These animals may still benefit from cryotherapy and gentle passive range-of-motion exercises three to four times daily.

PROCEDURE

- Thermal treatments (cryotherapy, heat therapy) are applied to the affected area and should not create discomfort.
- If acute inflammation is present (e.g., first few days after surgery, flare-up of chronic conditions), initiate cryotherapy with an ice pack or cold pack first. Apply for 10-15 minutes over the site of the inflammation. Cryotherapy aims to decrease edema, inflammation, and pain.
- For chronic situations, heat therapy is indicated. This is accomplished by massage, warm packs for superficial areas, or therapeutic ultrasound for deeper tissues (2-5 cm under the skin). Heat will increase blood flow to the tissues, increasing flexibility and decreasing the chance of injury with exercise. It can also reduce pain.
- After the warm-up period, stretching can be instituted if the procedure does not contribute to tissue injury. Tissue injury is avoided through precautions, including heeding the normal time frame of bone healing if relevant (as already described) and using an appropriately limited degree of force during healing, such as avoiding excessive force (animal vocalizes or resists).
- If the animal is vocalizing, then the practitioner may be going too far. Of course, some animals will squirm or vocalize without even being touched, so individual personalities are taken into consideration.
- The individual joints are brought to a comfortable end range in flexion and then extension for 10-15 seconds each. This is repeated 6-15 times.
- Passive range-of-motion (PROM) exercises are also instituted at this point. The entire limb is cycled through its ranges of motion, being sure to incorporate all desired joints. This will increase flexibility and minimize adhesions and contractures.
- NMES can be used for artificially eliciting a muscle contraction:
    - Electrical current is delivered by pads through the skin to the motor end plate, thereby causing the muscle belly to contract.
    - NMES is primarily used for strengthening muscles and increasing endurance as well as to attenuate atrophy.
    - This modality is most helpful in animals that are paralyzed and paretic.
- After successfully undergoing such treatments, the animal (depending on the individual case) may now be ready for therapeutic exercises. These are designed to increase strength, balance, and proprioception as well as encourage weight bearing on affected limbs as indicated. Therapeutic exercise is also helpful in improving active range-of-motion (AROM) in joints, flexibility, and overall function. Therapeutic exercises include the following:
    - Assisted standing exercises, using slings or exercise balls and rolls, are used in the early stages, especially for patients that are paralyzed or paretic.
    - These exercises are designed to encourage the patient to bear as much of his/her own weight as possible.

- The patient is supported in a standing position with the assistance of either slings or yoga balls under the trunk.
- The patient can be rocked side to side or front to back. If the patient begins to collapse, he/she is then lifted back up to the original position, and the exercise begins anew.
- Weight-shifting exercises are designed to shift the patient's weight onto the affected limb(s) to encourage weight bearing. This is achieved with balls and rolls, balance boards, wheelbarrowing and dancing exercises, or simply discouraging use of the contralateral limb in a normal standing position.
- Sit-to-stand exercises are used for increasing ranges of motion and strength in the hind limbs. The dog is commanded to sit squarely on its rear end and then to stand up. Small treats can be used.
    - Note: To get the dog to flex the hind limb squarely, the affected limb can be positioned against a wall to prevent “cheating.”
- Stair climbing is used for improving strength, coordination, and flexibility.
- Underwater treadmills are valuable tools that can be used in most cases:
    - Water height can be adjusted to different levels to change the animal's buoyancy and thereby the amount of weight the limbs are bearing.
    - Changing water heights also changes the active ranges of motion for all the joints of the limbs, depending on which ones are breaking the plane of the water.
    - Most units will also allow variations in speed, time, and incline.
    - Resistance jets can be installed.
    - Life vests and slings for assistance should be used as needed.
- Land treadmills can also be used.
- Cavaletti rails are used for increasing AROM, strength, balance, and coordination:
    - These are typically created with traffic cones with holes drilled through at different heights.
    - PVC pipes can then be inserted at the desired heights to create an obstacle course for the dog to negotiate.
    - The dog must lift its limbs to walk over these rails, thus encouraging active range of motion.
    - The cones and poles can be arranged to also force the dog to weave in and out of the cones, further strengthening the patient's balance and coordination skills.
- Elastic resistance bands and leg weights can be used to further challenge the dog with many activities. Be careful where these are placed—do not put undue stress or torque on susceptible tissues; usually reserved for advanced cases, when a patient has progressed from simpler exercises:
    - Can be used for a postoperative patient with cranial cruciate ligament repair toward the end of its treatments or a patient with osteoarthritis that has successfully progressed to a point that it needs to be further challenged
- Balance boards are used for increasing proprioceptive awareness and balance as well as strength:
    - These are typically flat wooden boards with a fulcrum underneath, on which the dog stands and tries to balance itself.
    - Indications in some animals with vestibular disease, ataxia of various causes, amputees.

PHYSICAL REHABILITATION Dog on underwater treadmill. Treadmill speed and depth of water can be adjusted to optimize level of activity.

POSTPROCEDURE

- Stretching after exercise is usually indicated.
- Cryotherapy (10-15 minutes) is also frequently indicated after the treatment to reduce muscle spasms, pain, and swelling.
- Any progression of lameness or signs of pain must be noted. If observed, reduce the next treatment by about 50%. Note: Be

careful to differentiate orthopedic pain from muscle soreness. Muscle soreness is expected after the first few treatments.
    - Palpate the muscle bellies and move the joints to identify the source of pain.
- Antiinflammatory medications can be used as needed:
    - Carprofen: 2.2 mg/kg PO q 24 h to q 12 h
    - Deracoxib: 1-2 mg/kg PO q 24 h
    - Firocoxib: 5 mg/kg PO q 24 h

ALTERNATIVES AND THEIR RELATIVE MERITS

- Acupuncture (see p. 1195) may also be helpful with pain control and neurologic diseases.
- Chiropractic therapy may be helpful in some cases.

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AUTHOR: TIMOTHY V. HATT

Phlebotomy

SYNONYM

Venipuncture

OVERVIEW AND GOAL

To obtain blood with minimal stress to the patient for diagnostic or monitoring purposes, treatment of certain blood disorders, transfusion, or to administer medications

INDICATIONS

- Diagnostic testing
- Blood transfusion
- Polycythemia
- Hemochromatosis

CONTRAINDICATIONS

- Infection or injury at the sampling site
- Jugular venipuncture in animals with coagulopathy

EQUIPMENT, ANESTHESIA

- Alcohol
- Clippers (+/−)
- Needle and syringe/Vacutainer collection system:
  - Method used depends on vessel size, blood volume required, operator's preference.
- Tourniquet (+/−)
- Sample tubes
- Gauze and tape/bandage wrap (+/−)
- Sedation is dependent on the disposition and the health of the animal.

ANTICIPATED TIME

1-5 minutes

PREPARATION: IMPORTANT CHECKPOINTS

- Ensure that the proper criteria have been meet prior to diagnostic testing (e.g., animal fasted) and the required sampling containers are on hand.
- Using jugular veins spares the cephalic veins for IV catheterization and allows for a larger volume to be collected faster.
- Experienced restrainers reduce the stress to the patient and improve the chance for successful venipuncture.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Hematoma
- An insufficient amount of sample can produce an incorrect blood-to-anticoagulant ratio and result in erroneous values:
  - Use 0.5-mL pediatric containers for neonates/exotics (e.g., BD Microtainer tubes)
- Blood collection for coagulation profiles should be drawn with minimal trauma (first attempt) to prevent tissue thromboplastin from entering the sample.
- Improper handling of the specimen can alter results.

PROCEDURE

- Positioning of the patient depends on the ability to restrain the patient and operator preference.

- Apply isopropyl alcohol to the area. In animals with dense hair coats, it may be necessary to clip the area if the vein is neither visible or palpable.
- Jugular vein:
  - Occlude the vein by inserting pressure with your thumb at the thoracic inlet. Using the same hand, palpate the vein with your index finger.
- Cephalic or saphenous vein:
  - Hold the leg and apply slight traction to help stabilize the skin and vein while the restrainer uses one hand to create a tourniquet effect at the elbow. Placing your thumb alongside the vein may prevent it from moving.
- Insert the needle through the skin with bevel up:
  - If using a syringe, apply gentle negative pressure. If you do not have blood in the hub of the needle, draw back your needle (do not come out of the skin) and advance towards where you can palpate the vein. After obtaining the sample, release the pressure on the vein before withdrawing the needle.
  - If using a Vacutainer collection system, push in the Vacutainer tube with your thumb after you have penetrated the skin. Carefully watch for blood while you are advancing, and stop when blood enters the tube. If you get a flashback of blood and then it stops, you may have gone through the vein. Slowly back your needle out until blood flows. When changing Vacutainer tubes (needle still in the vein), be sure to firmly stabilize the plastic Vacutainer holder. Often the act of changing the tubes will push the needle ahead. If no blood flows after changing tubes, slowly back the needle out 1-2 mm until you see blood flow. If this is unsuccessful, withdraw (not out of the skin) and redirect the needle. After obtaining the sample, remove the tube and release the pressure on the vein before withdrawing the needle from the skin.
  - In veins that roll laterally and are difficult to penetrate, an assertive forward movement will aid in successful venipuncture.
  - If blood flow stops during aspiration, rotate the needle slightly in the vein.
  - Excessive negative pressure can cause the vein to collapse and hemolysis to occur.
- After the desired amount of blood has been drawn and the needle is removed, the restrainer applies digital pressure until hemostasis occurs.
- Marginal ear vein prick:
  - Puncture marginal ear vein with a needle or lance. Some apply a thin film of petroleum jelly or other hydrophobic substance to the surface being pricked, which can help the blood bead rather than run. Collect blood onto test strip or capillary tube. Apply pressure to puncture site afterwards to aid hemostasis.

POSTPROCEDURE

Patients with coagulopathy require that pressure be applied to the vein for at least 5 minutes after venipuncture.

ALTERNATIVES AND THEIR RELATIVE MERITS

Central venous catheter: technically challenging, expensive, facilitates multiple blood draws for monitoring in clinic patients

AUTHOR: ELAINE REVELER

Peritoneal Dialysis

OVERVIEW AND GOAL

Exchange of dialyzable solutes and fluid between the peritoneal capillary vessels and the dialysate solution. Exchange occurs across the semipermeable peritoneal membrane as a result of diffusion, ultrafiltration, and convection.

INDICATIONS

- Acute renal failure unresponsive to conventional medical management
- Hyperkalemia or hypercalcemia (severe)
- Intoxication from dialyzable toxin or drugs (e.g., ethylene glycol <24 hours post ingestion, barbiturates, ethanol)
- Hypothermia or hyperthermia
- Resistant metabolic acidosis (severe)

CONTRAINDICATIONS

- Peritoneal fibrosis (impaired semipermeable membrane)
- Pleuroperitoneal leak (predisposed to pleural effusion)
- Recent thoracic or abdominal surgery (including percutaneous endoscopic gastrostomy [PEG] tubes)
- Inguinal or abdominal hernia
- Severe hypercatabolic states (e.g., burn patients)

EQUIPMENT, ANESTHESIA

- General anesthesia (stable patient) or sedation and regional anesthesia (critical patient)
- Clippers
- Surgical scrub
- A #15 scalpel blade
- Local anesthetic (e.g., 2% lidocaine at 1-2 mg/kg)
- Small surgical pack
- Suture material
- Sterile surgical drapes
- Adhesive dressing (e.g., OpSite)
- Closed “Y” connection system or a three-way stopcock with one attachment to dialysate line and the other to sterile collection system
- Dialysate solution (see below)
- Peritoneal dialysis (PD) catheter (see below)

ANTICIPATED TIME

About 30-45 minutes of anesthesia for placement

PREPARATION: IMPORTANT CHECKPOINTS

- Catheterize and drain the urinary bladder prior to PD catheter placement to reduce the risk of iatrogenic puncture.
- Ensure patient is rehydrated prior to anesthesia, and carefully monitor and correct hypotension to minimize further renal compromise.
- Peritoneal dialysis catheters:
  - Regardless of method of placement or catheter type, all catheter types should be tunneled subcutaneously to decrease the risk of dialysate leak and the incidence of peritonitis.
  - Percutaneous placement options include silicone tube catheter with trocar or guidewire-inserted silicon tube (e.g., MILA chest tube) for use in emergency situations or for short-term use, as omental obstruction is a common occurrence.
  - Mini-surgical approach options include fenestrated modified silicone catheters with or without Dacron cuffs such as Tenckhoff catheters, fluted T catheters, Blake surgical drains, or Jackson Pratt surgical suction drains. Dacron cuffs facilitate fibrous attachments, decreasing the risk of dialysate leakage and incidence of peritonitis.
- Dialysate solution:
  - Commercial dialysate prepared as 1.25%, 2.5%, or 4.5% glucose solutions or alternatively, a homemade solution using lactated Ringer's solution (LRS), 0.9% NaCl, or 0.45% NaCl with dextrose added can be used.
  - Homemade solutions are more cost effective, but strict aseptic technique (mask and sterile gloves) must be followed

during preparation to reduce the risk of contamination. Use only single-use or new vials for adding medications or electrolytes to the dialysate. Wipe all injection ports with alcohol prior to injection.
    - Add the following to the solution:
        - Dextrose to act as an osmotic agent; concentration is dependent on patient's hydration status. A 4.5% solution (85 mL of 50% dextrose/L) should be used in fluid overloaded patients, whereas a minimum 1.25% solution (30 mL of 50% dextrose/L) must be used in normovolemic patients to approximate a normal patient's osmolality.
        - Unfractionated heparin (250 to 1000 U/L) for the first few days to reduce the risk of catheter obstruction by fibrin clots
        - Electrolytes should be added based on regular serum electrolyte monitoring.
    - Prophylactic antibiotics are not routinely added. In the event of suspect peritonitis, empirical therapy using cefazolin can be added to the dialysate solution while awaiting confirmation from cytologic analysis and bacterial culture and sensitivity. A one-time loading dose of 1000 mg/L of dialysate followed by a maintenance dose of 250 mg/L of dialysate is recommended.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Hypoalbuminemia
- Dialysate retention (obstruction by omentum or fibrin, improper placement, kinking of catheter)
- Peritonitis (septic)
- Subcutaneous leakage/limb edema
- Electrolyte imbalances (hypochloremia, hypokalemia, hyponatremia, hypomagnesemia, hypocalcemia, hyperkalemia, hyperglycemia)
- Overhydration and pleural effusion
- Hemorrhage
- Dialysis dysequilibrium

PROCEDURE

- General anesthesia for mini-laparotomy approach in stable patients or sedation and regional anesthesia in critical patients or percutaneous technique
- With the animal in dorsal recumbency, clip the abdomen from the xiphoid to the pubis.
- Aseptically prep and drape the area.
- Administer a prophylactic dose of a first-generation cephalosporin (e.g., cefazolin) 30 minutes prior to PD catheter insertion.
- *Mini-surgical approach for catheter placement* (author's preference):
    - At the level of the umbilicus make a small 2-3 cm paramedian skin and subcutaneous incision.
    - Place a small stay suture in the rectus sheath to facilitate manipulation of the body wall.
    - Tent the abdominal wall, and make a small stab incision into the peritoneum.
    - Grasp the PD catheter using a curved hemostat, and advance the catheter into the abdomen towards the pelvic inlet. Release the catheter and remove the hemostat.
    - Secure the Dacron cuffs (if present) within the rectus muscle (inner cuff) and within the subcutaneous tissues (outer cuff), using a pursestring suture.
    - Tunnel the distal end of the catheter through the subcutaneous tissues, and exit the skin 2-5 cm away from the abdominal insertion site. If no Dacron cuffs are present, begin tunneling under the external sheath of the rectus abdominis muscle prior to tunneling subcutaneously.
    - Before closure, connect the PD catheter to the dialysate solution in a sterile manner, and infuse a small volume of dialysate (2-5 mL/kg) into the abdomen to verify proper placement. The dialysate should be readily retrieved via the collection system if no occlusion is present. If unable to retrieve the solution, redirect the PD catheter.
    - Close the entry site through the external sheath of the rectus abdominis muscle over the PD catheter with a simple interrupted pattern using an absorbable monofilament.
    - Close the skin incision with a simple interrupted pattern using nonabsorbable monofilament.
    - Secure the catheter to the exit site using a purse string and fingertrap suture.
    - Apply a sterile gauze and adhesive dressing (e.g., Opsite) over the catheter exit site.
- *Percutaneous catheter placement:*
    - Make a paramedian incision at the level of the umbilicus small enough to form a tight seal around the chosen catheter.
    - Tunnel the trocar subcutaneously for several centimeters before penetrating the abdominal muscles and into the abdomen.
    - Advance the PD catheter off the trocar, directing it caudally into the pelvic inlet until completely in the abdomen.
    - Secure the catheter to the skin with a pursestring suture or with fixation provided in the PD kit (if available).
    - Apply a sterile adhesive dressing over the catheter exit site.
- Dialysate exchange:
    - *Inflow:* initial infusion volumes should be small (10-20 mL/kg) to reduce the risk of leakage. After the first 24 hours, increase the volume to 30-40 mL/kg if tolerated. Dialysate solutions should be warmed to body temperature and infused over 10 minutes either by gravity flow or IV infusion pump. Monitor for signs of nausea, discomfort, or

respiratory compromise, and reduce infusion volumes as needed.
    - *Dwell time:* initial dwell times should be short (30-40 minutes) until the patient improves and uremia stabilizes, and then extend to 4-6 hours.
    - *Outflow:* dialysate removal can be done by gravity over 15 minutes, by placing the collection system below the patient. Alternatively, a negative suction drain can be installed to actively remove the effusate. Effusate volume should equal infused volume when using a 1.25% dextrose solution and exceed infusion volume when using a 2.5% or 4.5% dextrose solution to correct overhydration.
- The entire exchange process is repeated every 1-2 hours until the patient improves clinically and the uremia stabilizes, and then every 4-6 hours.

POSTPROCEDURE

Patient care:

- Analgesia and excellent nursing care should be provided to minimize stress and discomfort.
- Adequate nutritional support (parenteral, enteral or combination of both) is essential to reduce the risk if hypoalbuminemia and peritonitis.
- Careful monitoring of hydration status (frequent body weights, packed cell volume/total solids [PCV/TP], central venous pressure [CVP], dialysate inflow/outflow volume) is essential.
- Assessment of PCV/TP, electrolytes, venous blood gas, blood glucose, blood urea nitrogen (BUN), creatinine, and serum albumin should be performed every 8-12 hours initially and then once daily after stabilization. Adjustments in dialysate and IV fluid composition may be required pending serum chemistry values.

Catheter care:

- Strict aseptic technique (washing hands, wearing sterile gloves) during handling and delivery of dialysate is essential to minimize risk of peritonitis. All line connections should be covered with either chlorhexidine or povidoneiodine soaked sponges/gauzes.
- The PD catheter insertion site should be examined daily for any signs of discharge, swelling, redness, or discomfort to indicate possible infection.
- The dialysate should be monitored daily for signs of cloudiness suggesting peritonitis. If a cloudy dialysate develops, cytologic analysis, Gram stain, and culture and sensitivity on the dialysate should be performed.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Pleural dialysis is technically less demanding than other alternatives, but it is the least effective, with greater complication risks.
- Intermittent hemodialysis (IHD; see p. 1286) is a reliable alternative for the treatment of uremia, but it is limited to specialized centers equipped and trained to offer this service.
- Continuous renal replacement therapy (CRRT) similar in efficacy to IHD, but CRRT is proposed to result in less complications. Specialized equipment, training, and higher cost limit its widespread availability.

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AUTHOR: MICHAEL ETHIER

Pericardiocentesis

SYNONYMS

Pericardial drainage, pericardial tap

OVERVIEW AND GOAL

A catheter is used for removing a volume of pericardial effusion for diagnostic and/or therapeutic purposes.

INDICATIONS

- Pericardial effusion causing cardiac tamponade
- Pericardial effusion of unknown etiology

CONTRAINDICATIONS

Small volume of pericardial effusion (difficult to safely enter the pericardial space)

EQUIPMENT, ANESTHESIA

- Local anesthesia (2% lidocaine)
- Manual restraint; sedation needed only rarely.
- Hair clippers
- Surgical scrub solution, rubbing alcohol, and gauze/sponge for prepping skin
- 0.5-12 mL 2% lidocaine for local anesthesia; volume based on body weight 1-70 kg. Note: Discomfort of lidocaine infusion can be reduced by adding 0.05-0.2 mL 8.4% sodium bicarbonate and warming to body temperature (armpit method).
- Sterile surgical gloves
- A #11 scalpel blade
- A 14-gauge over-the-needle catheter (e.g., equine IV catheter)
- A 6-mL syringe
- Two 35- or 60-mL syringes
- Kidney bowl for effusion
- Lavender- and red-top tubes for sample
- Tissue glue

ANTICIPATED TIME

About 15-40 minutes

PREPARATION: IMPORTANT CHECKPOINTS

- Ultrasound guidance: not usually used during the procedure. Immediately prior to the procedure, however, ultrasound-based localization of an area with maximal pericardial effusion and minimal lung is extremely useful.
- Electrocardiogram (ECG) may be used during the procedure; appearance of premature ventricular complexes (PVCs) suggests catheter/stylet is touching heart and should not be advanced farther. However, such contact with the heart is generally palpable (heartbeat hitting catheter tip), and PVCs may occur independently of the catheter in animals with pericardial effusion.
- Clinicians should tell clients that the procedure is often palliative, and effusion can recur, with the likelihood and speed of recurrence depending on the underlying cause. Rapid re-effusion or even hemodynamic collapse postcentesis is possible with atrial tear and with malignancies such as hemangiosarcomas.

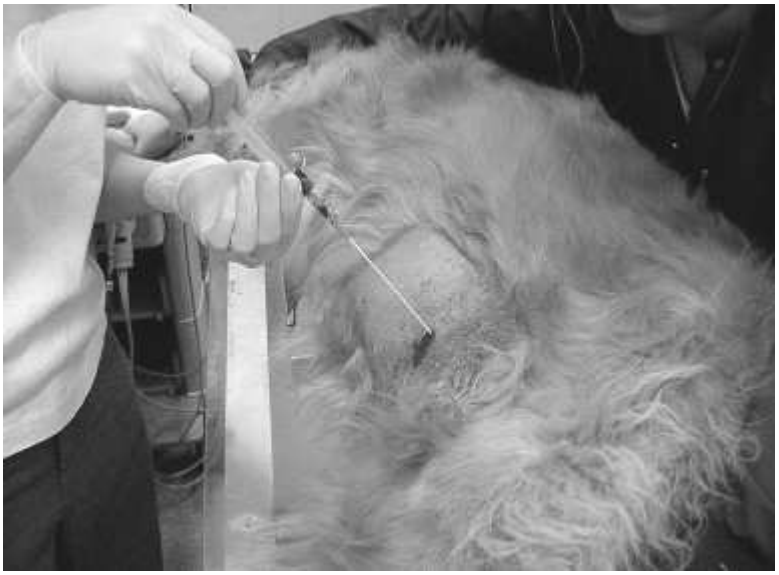
POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Inability to obtain pericardial fluid. Ultrasound guidance is useful before reattempting.
- Effusion that clots in the syringe, either due to excessive advancement (catheter tip is in the heart) or to a rapidly bleeding pericardial effusion. Differentiation: disconnect syringe from catheter/stylet. If catheter is intracardiac, flow should be pulsatile

± vigorous.
- Coronary artery laceration; unlikely with right-sided approach

PROCEDURE

- The animal is restrained in left lateral recumbency for the whole procedure. The approach will be via the right side of the thorax to minimize the risk of catheter-induced coronary artery laceration.
- Ultrasound is used for confirming that pericardial effusion is present in sufficient volume to allow safe centesis (width of effusion on echocardiogram > 1 cm). In the absence of ultrasound guidance, the site of entry is at the level of the costochondral junction, right fifth intercostal space.
- The area is widely clipped of hair and aseptically prepared. The wide clipping of hair should allow the procedure to be done without a sterile drape.
- The designated site of centesis is again confirmed with ultrasound.
- Lidocaine is infused subcutaneously, intramuscularly (intercostal muscle), and subpleurally. Doing so requires that the needle be repeatedly withdrawn until almost out of the skin and then redirected and reinserted until a region at least 2 cm square and spanning the entire thickness of the chest wall has been infiltrated.
- The clinician puts on sterile gloves and makes a 3-mm skin incision in the center of the site using the scalpel blade.
- The catheter, which covers a metal stylet, is attached to the 6-mL syringe, and the tip of the catheter-stylet combination is inserted into the skin incision.
- The clinician advances the syringe-catheter-stylet combination (which is grasped in the palm as a handle to advance the catheter and stylet) while drawing back on the syringe plunger to create negative pressure. The orientation is perpendicular to the chest wall and is neither cranially nor caudally directed.
- When a flashback of effusion is seen to enter the syringe, the syringe-styletcatheter apparatus is advanced only 2-3 mm farther into the chest.
- With continuing negative pressure on the syringe (effusion flowing into syringe), the syringe and stylet are kept in the same position, while the catheter is advanced several centimeters farther. In this way, the catheter is seated well within the pericardial space.
- Using a large-volume syringe (35 or 60 mL), the effusion is withdrawn. Ideally, an assistant helps by emptying one syringe while the clinician is filling the other with pericardial effusion; thus, two syringes can aseptically be traded back and forth until the pericardium is empty.
- When the effusion has partially or completely been removed, the catheter is withdrawn, and the skin incision is closed with tissue glue.



PERICARDIOCENTESIS Pericardiocentesis in a dog with severe cardiac tamponade and hemorrhagic pericardial effusion. Left lateral recumbency; head is beyond the lower right corner of the image. The syringe-catheter-stylet combination has been advanced to the point of entering the pericardium, and effusion is seen in the hub of the stylet and the syringe. Next, the catheter will be advanced off the stylet.

POSTPROCEDURE

- Ascites caused by cardiac tamponade should resolve spontaneously over the 12- to 36-hour period following pericardiocentesis.
- A recheck echocardiogram immediately post centesis and another echocardiogram 12-24 hours later are recommended

(assess remaining volume, and note in record). Rapid reaccumulation of effusion suggests malignancy, atrial rupture from stretch, or coagulopathy.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Pericardiectomy: long-term palliation
- Diuretic: contraindicated in acute treatment (does not mobilize effusion but does deplete circulating blood volume, worsening cardiac filling); advocated by some for chronic treatment to delay of recurrence of idiopathic or malignant effusions

AUTHOR: ETIENNE CÔTÉ

Parenteral Nutrition

SYNONYMS

PN, partial parenteral nutrition (PPN), total parenteral nutrition (TPN)

OVERVIEW AND GOALS

- Parenteral nutrition (PN) is nutrition delivered by the IV route.
- It can be life saving in animals that cannot tolerate enteral feeding.
- Used when no other feeding option exists, and the need for nourishment is a critical factor in clinical outcome.

INDICATIONS

Animals in need of nutritional support when:

- Enteral nutrition is contraindicated (e.g., gastrointestinal [GI] dysfunction or risk of pulmonary aspiration).
- Sufficient nutrition cannot be provided by the enteral route alone (e.g., severe malabsorptive disease).

CONTRAINDICATIONS

- Animals that can be fed safely and effectively by the enteral route
- Animals that are at risk with catheter placement:
  - Central venous catheters in animals at high risk of thromboembolic disease (e.g., protein-losing nephropathy or enteropathy, hyperadrenocorticism, disseminated intravascular coagulopathy)
  - Jugular catheters in animals with increased cerebral pressure (e.g., head trauma)
- Animals experiencing fluid overload (e.g., animals with heart failure, oliguria, or severe hypoproteinemia)

EQUIPMENT, ANESTHESIA

- Venous access:
  - A dedicated catheter is required for delivery of the nutrient solution to avoid septic complications and drug-nutrient interactions.
  - Treat catheter placement as a surgical procedure (surgical prep, draping, and the use of sterile gloves) (see p. 12935/19/2011).
  - Place a central venous catheter to deliver TPN, because the nutrient solution is hyperosmolar. Solutions that are more dilute can be prepared, but the resulting large volume that must be infused can become a limiting factor.
  - Catheters made of nonthrombogenic materials (polyurethane or silicone) are preferred, particularly for peripheral infusion.
  - Multilumen central or peripherally placed central catheters (PICC lines) can be used if one of the ports is dedicated for PN.
- Nutrient admixture:
  - Amino acid solutions (3%-10%) are used for providing protein. These solutions come with and without added electrolytes.
  - Nonprotein calories can be provided by a combination of lipid emulsions (10% or 20%) and dextrose (10%-50%) or dextrose alone.
  - Electrolytes can be added to the nutrient solution as needed or provided separately in the animal's crystalloid fluid therapy. The latter allows greater flexibility. Alternatively, a combination amino acid and electrolyte solution can be used.
  - Special parenteral vitamin and mineral preparations are available. However, because most companion animals receive PN for relatively short periods of time (<2 weeks), only certain vitamins and minerals are commonly added to the nutrient admixture (B complex, ± potassium phosphate, magnesium sulfate, and trace elements [zinc, copper, manganese, and chromium]).
- Monitoring and nursing care:
  - PN is best delivered continuously (although this is not absolutely necessary), so 24-hour nursing care is desirable both for administration and for catheter vigilance/catheter care.
  - Many of the complications of PN can be life threatening, so careful monitoring of the animal is mandated. This includes frequent checking of serum glucose and electrolyte concentrations; hence, the ability to do some in-house serum chemistry analyses is necessary.

PREPARATION: IMPORTANT CHECKPOINTS

- Venous access:
  - Reserve a dedicated venous catheter (or port of a multilumen catheter) for PN. Insert the catheter under aseptic conditions, and do not use for any other purpose.
- Nutrient admixture:
  - Prepare PN solutions under aseptic conditions. In addition, solutions must be compounded in a specific sequence and carefully mixed.
  - Use the services of a home infusion service or a human hospital pharmacy to compound PN solutions when the veterinary practice lacks the facilities and expertise.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

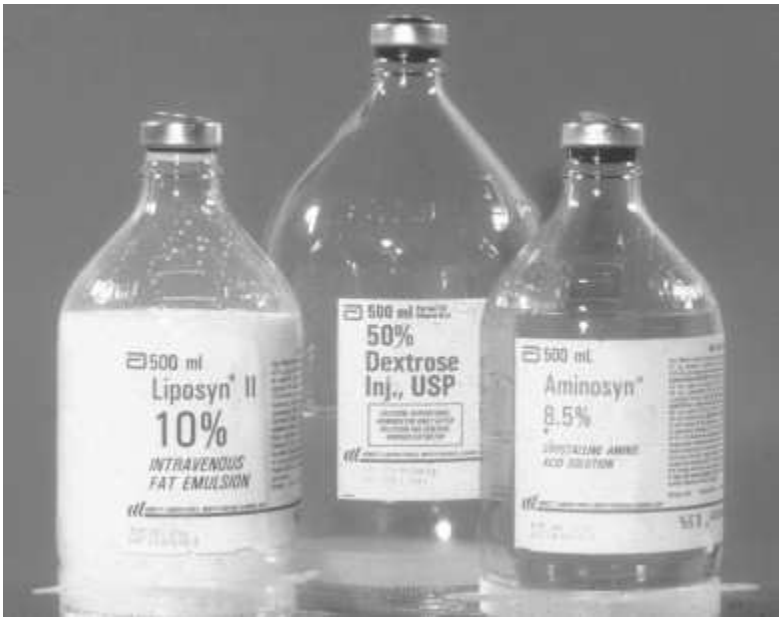
- Common metabolic complications:
  - When addressing electrolyte abnormalities, delivering supplements in the IV fluids rather than in the PN solution allows greater flexibility. Later, when the amount of supplementation for maintenance is established, it can be included in the PN formulation.
  - Hyperglycemia: if present, reduce the percentage of nonprotein calories from dextrose, or give regular insulin.
  - Hypokalemia: if present, supplement IV fluids with potassium chloride. Monitor for hypomagnesemia (see online chapter: Refeeding Syndrome).
  - Hypophosphatemia: if present, supplement IV fluids with potassium phosphate, or add potassium phosphate to PN formulation.
  - Hypomagnesemia: if present, supplement IV fluids with magnesium sulfate or add magnesium sulfate to PN formulations.
  - Hyperlipidemia: if present, reduce or omit the lipid emulsion.
- Catheter complications:
  - Loss of venous access secondary to catheter malposition or thrombosis: if occurs, replace catheter.
  - Thrombophlebitis: if occurs, replace catheter. Select peripheral catheters that are long and made of nonthrombogenic materials.
  - Infection: if occurs, remove catheter and culture the tip. Replace with a new catheter in a new location.

PROCEDURE

PN PRESCRIPTION FORMULATION:

- Choose between central or peripheral venous administration.
  - Central venous administration is preferred because smaller volumes of PN solution are required, and thrombophlebitis is less likely to occur.
  - Peripheral venous administration is possible when central venous access is not available, but the animal must be fluid tolerant because required lower tonicity means larger volume of infusate.
  - Note: For peripheral venous infusion, long catheters made of nonthrombogenic materials reduce the likelihood of thrombophlebitis.
- Calculating the caloric goal:
  - Calculate the resting energy requirement (RER) using the animal's current body weight (or the animal's estimated ideal weight if overweight).
  - Formula: RER = 70 + 30 × (body weight in kilograms) for animals weighing 2-30 kg; use 70 × (body weight in kilograms)$^{0.75}$ for animals that weigh outside this range.
  - Start with a caloric goal of RER, and adjust based on animal response.
- Decide what percentage of calories will be delivered as protein depending on the animal's level of protein tolerance or deficiency.
  - Dogs: provide 15%-25% of goal calories as protein.
  - Cats: provide 25%-30% of goal calories as protein.
  - Amino acid solutions: provide 4 kcal/g.
  - To calculate the volume of amino acid solution required:
    - Divide the protein calories by 4 kcal/g = grams of amino acids required.
    - Divide the grams of amino acids required by the grams of amino acids per milliliter in the solution = volume of amino acid solution.
  - Note: For peripheral infusion, use =6% amino acid solutions because of high osmolarity.
- Decide what percentage of nonprotein calories will be delivered as dextrose with the remainder to be delivered as lipid:
  - 100% of the nonprotein calories can be delivered as dextrose, but hyperglycemia is a common sequela; 50% dextrose provides 1.7 kcal/mL.
  - Alternatively, lipid emulsions can be used for delivering 50%-70% of the nonprotein calories; 20% lipid emulsions provide 2 kcal/mL.
  - Note: For peripheral venous infusion, a high percentage of nonprotein calories from lipid is preferred because the lipid emulsions are isoosmolar. They are also more calorically dense than dextrose solutions that can be safely infused peripherally (=20% dextrose).

- Add 0.2 mL/100 mL total infusate of vitamin B complex.
- Decide whether electrolytes and minerals will be added.
    - Supplementation may not be necessary if amino acid solutions containing additional electrolytes are used.
    - Caution: Supplementation is contraindicated in animals with kidney disease/renal failure.
    - Potassium phosphate: 8 mEq/1000 kcal
    - Magnesium sulfate: 0.8 mEq/100 kcal
    - Zinc: 1 mg/kcal
- Calculate the hourly infusion rate by dividing the total volume by 24.



PARENTERAL NUTRITION Lipid, dextrose, and amino acid solutions.

Sample PN Worksheet for a 17.5 kg (39 lb) Dog: Centrally Administered PN Calculation

CANINE HIGH-PROTEIN REGIMEN

Weight: 17.5 kg	Resting energy requirement (RER) = 600 kcal/day
Day 1 goal	50% RER = 0.5(600) = 300 kcal
Day 2 goal	100% RER = 600 kcal
% Protein calories	25%
Nonprotein calories	50% from lipid, 50% from dextrose

- **Solutions:**
- 8.5% Amino acids (without electrolytes)
- 50% Dextrose
- 20% Lipid emulsion
- MTE-4 trace element solution containing 0.8 mg zinc/mL
- Potassium phosphate (3 mM/mL)
- Injectable B complex

- **Day 1 Calculations:**
- ***Amino Acids***
- (0.25 × 300 kcal) = 75 kcal from protein
- There are 4 kcal/g protein; therefore, the animal needs 18.75 grams of protein: (75 kcal ÷ 4 kcal/g = 18.75 g).
- 8.5% amino acid solution = 0.085 g protein/mL; therefore, the animal needs 220 mL 8.5% amino acid solution: (220 mL = 18.75 g ÷ 0.085 g/mL).

- ***Nonprotein Calories***
- (0.75 × 300 kcal) = 225 kcal
- 50% dextrose to provide 50% nonprotein calories = 112.5 kcal. 50% dextrose solution = 1.7 kcal/mL; therefore, the animal needs 66 mL 50% dextrose solution: (66 mL = 112.5 kcal ÷ 1.7 kcal/mL).
- 20% lipid emulsion to provide 50% nonprotein calories = 112.5 kcal. 20% lipid emulsion = 2 kcal/mL; therefore, the animal needs 56 mL 20% lipid emulsion: (56 mL = 112.5 kcal ÷ 2 kcal/mL).

- ***Trace Elements***
- Dosed at 1 mg zinc/kcal delivered
- MTE-4 contains 0.8 mg zinc/mL; therefore, the animal needs 0.37 mL: (0.37 mL = 300 kcal ÷ [0.8 mg/mL × 1000]).

- ***Potassium Phosphate***
- Dosed at 8 mM/1000 kcal delivered; therefore, the animal needs 2.4 mM potassium phosphate: (2.4 mM = [8 mM × 300 kcal] ÷ 1000 kcal).
- Potassium phosphate solution = 3 mM/mL; therefore, the animal needs 0.8 mL potassium phosphate: (0.8 mL = 2.4 mM ÷ 3 mM/mL).

- ***Vitamin B Complex***
- Dosed at approximately 2 mL/L infused
- Total infusate for day 1 = 343 mL; therefore, 1 mL B complex should be sufficient.

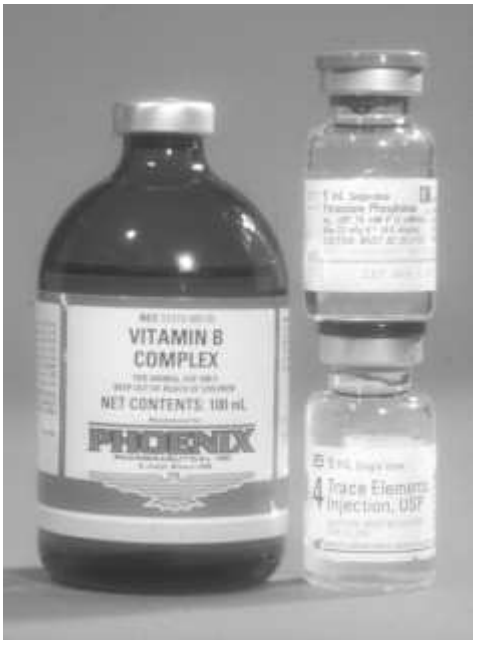
- ***Infusion Rate***
- 343 mL ÷ 24 h = 14 mL/h

- ***Day 2 Calculations:***
- Same calculations as those for day 1, but substitute 600 kcal for 300 kcal.

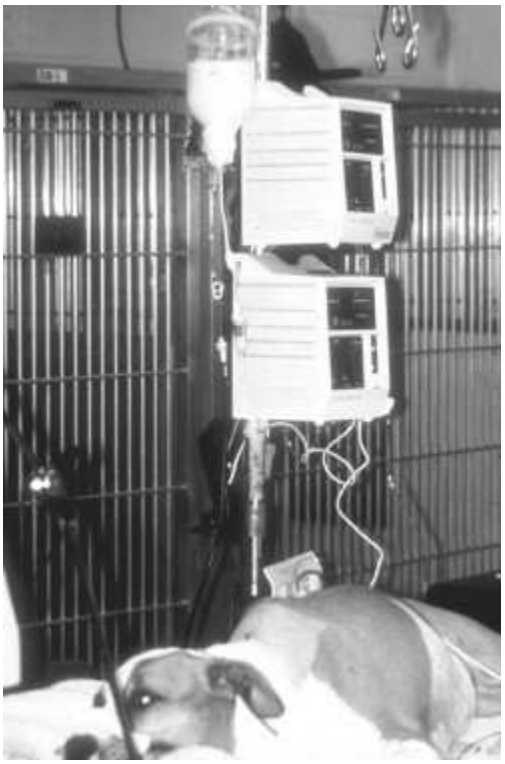
CANINE HIGH-PROTEIN REGIMEN

POSTPROCEDURE

- Delivery:
  - Deliver the solution at a constant rate using an infusion pump if possible.
  - Administer 50% of the goal infusion, and monitor for metabolic complications the first day, advancing to the goal rate the next day if no problems occur that cannot be addressed.
  - Do not discontinue PN abruptly, especially in animals that are not eating. If an animal cannot be weaned, monitor for hypoglycemia.
- Catheter care:
  - Examine the catheter site at least daily for signs of phlebitis or infection, changing the dressing as needed.
  - Change the drip set at least every other day.
  - Never use the catheter for any purpose other than the delivery of PN (no blood sampling, administering medications, fluid therapy, or measuring central venous pressure).
- Monitoring:
  - In addition to the routine monitoring appropriate for any animal on IV fluid therapy, animals receiving PN should be monitored for metabolic complications.
  - Animals should have blood glucose monitored at least every 12 hours and serum electrolytes at least once daily depending on circumstances and whether any PN supplementation is required.
  - When a packed cell volume (PCV) is performed, the serum should be examined for evidence of lipemia.
  - A complete serum chemistry profile and CBC should be performed as indicated but at least once weekly.



PARENTERAL NUTRITION Vitamin, electrolyte, and mineral solutions.



PARENTERAL NUTRITION Animal receiving PN.

ALTERNATIVES AND THEIR RELATIVE MERITS

Enteral nutrition:

- In general, nutrient delivery by the enteral route is safer and less costly than PN.
- Enteral nutrition has trophic effects on the GI tract and supports both the structure and function of the mucosa and the barrier function of the gut.
- Preferred over PN whenever feasible.

SUGGESTED READING

Chan DL: Parenteral nutritional support. In Ettinger SJ, Feldman EC, editors: Textbook of veterinary internal medicine, ed 7, St Louis, 2010, Elsevier, pp 701–707.

Chan DL, Freeman LM, Labato MA, et al: Retrospective evaluation of partial parenteral nutrition in dogs and cats. J Vet Intern Med 16(4):440–445, 2002.

Pyle SC, Marks SL, Kass PH: Evaluation of complications and prognostic factors associated with administration of total parenteral nutrition in cats: 75 cases (1994-2001). J Am Vet Med Assoc 225(2):242–250, 2004.

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Pacemaker: Transthoracic Cardiac Pacing

SYNONYM

Temporary cardiac pacing

OVERVIEW AND GOALS

Noninvasive, rapidly implemented temporary cardiac pacing system used for support of heart rate and blood pressure (BP) in animals that are under anesthesia and that have medically refractory bradyarrhythmias. Typical applications are stabilization for permanent pacemaker implantation and emergency treatment of life-threatening bradyarrhythmias.

INDICATIONS

- Support of heart rate and BP during general anesthesia for dogs with medically refractory bradyarrhythmias undergoing permanent pacemaker implantation or another surgery unrelated to pacemaker implantation
- Emergency treatment of hemodynamically unstable, medically refractory, complete atrioventricular block until more definitive therapy can be instituted
- Bradyasystolic arrests (e.g., digoxin overdose)

EQUIPMENT, ANESTHESIA

- General anesthesia and tracheal intubation required
- Continuous electrocardiogram (ECG) and transthoracic pacing system required, including disposable adhesive transthoracic patch electrodes. Newer versions of transthoracic patch electrodes are available that allow not only noninvasive cardiac pacing but can be used for defibrillation, synchronized cardioversion and ECG monitoring.
- A No. 10 clipper blade (to shave the hair from the left and right precordia (area of the thorax overlying the heart)
- Occasionally, a neuromuscular blocker (and hence mechanical ventilation) may be desirable to limit jerking of skeletal muscles during surgical procedure.

ANTICIPATED TIME

Pacing system can be attached and pacing implemented in just a few minutes, especially in urgent situations.

PREPARATION: IMPORTANT CHECKPOINTS

- Have pacing system prepared (patch electrodes on chest and ECG monitoring ongoing) at induction of general anesthesia in dogs undergoing permanent pacemaker implantation or other dogs at risk for bradyarrhythmic complications with general anesthesia. This is a precaution in the event of bradyasystole during induction.
- Ensure clear ECG tracing to allow accurate sensing of dog's intrinsic heartbeat before starting transthoracic pacing.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Most common complications are skeletal muscle twitching and pain associated with pacing stimulus.
- Pain or distress experienced in awake dogs requires rapid induction of general anesthesia for continued use of the temporary pacemaker. Analgesia (opiate or nonsteroidal antiinflammatory drug [NSAID]) is also recommended.
- Skeletal muscle twitching, more pronounced in smaller dogs, may require neuromuscular blockade to lessen the jerking of forelimbs and chest during surgical procedure.
- Most common error is suboptimal placement of patch electrodes, causing inconsistent pacing. Ensure placement directly over the palpable cardiac impulse beats. Readjustment of patch electrodes may be necessary.
- Obese dogs or dogs with pleural space disease may require higher than expected pacing threshold.

PROCEDURE

The procedure is typically performed in dogs undergoing anesthesia for permanent pacemaker implantation. ECG and pacing patch electrodes are in place prior to induction. The pacing system is usually turned on shortly after induction of anesthesia.

- ECG leads are connected to the dog, and a good-quality ECG tracing is obtained.
- Patch electrodes are placed directly over cardiac impulse on left and right hemithorax. The fur on the chest is shaved, and a small dollop of ECG paste is placed on the surface of the patch electrode facing the skin. Dogs ideally should be placed in lateral recumbency.
- Ensure accurate ECG sensing of dog's intrinsic cardiac rhythm by adjusting ECG gain and lead selection. A sensing marker will appear on the animal's QRS complex, signaling accurate sensing.
- After setting the pacing rate (range 40-170 beats per minute), the pacing current (range 0-200 mA) is gradually increased until ventricular capture is confirmed on the ECG monitor and by palpation of a corresponding arterial pulse. Ventricular capture is recognized by a wide QRS complex and T wave following a pacing spike on the ECG. The pacing current is maintained just above the capture threshold.
- Pacing rate and current usually range between 60 and 80 beats per minute and from 50-110 mA, respectively.

POSTPROCEDURE

Pacing patch electrodes are removed from skin. Adhesive remover can be used.

ALTERNATIVES AND THEIR RELATIVE MERITS

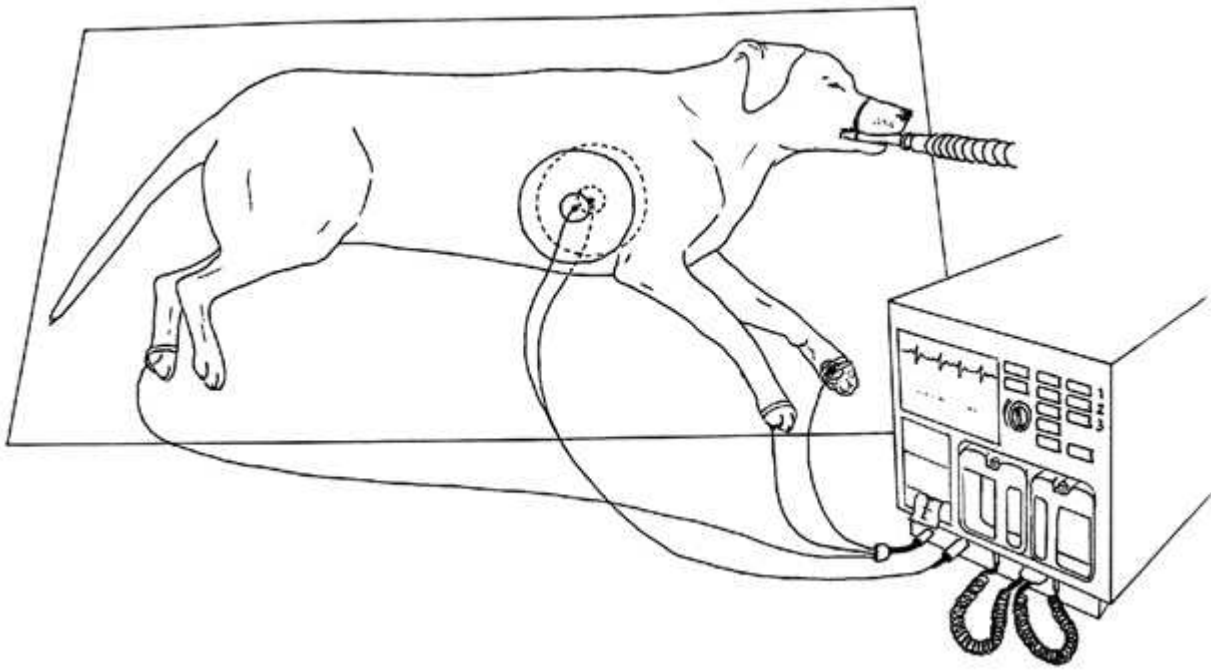
Transvenous pacing:

- Specialized transthoracic pacing system not required (very expensive)
- No skeletal muscle twitching or pain associated with pacing stimulus
- Procedure is more invasive, and implementation requires more time and expertise.
- Can be associated with infection, bleeding, lead wire displacement, lead wire-induced arrhythmia, cardiac perforation, and thromboembolism.

Transesophageal pacing:

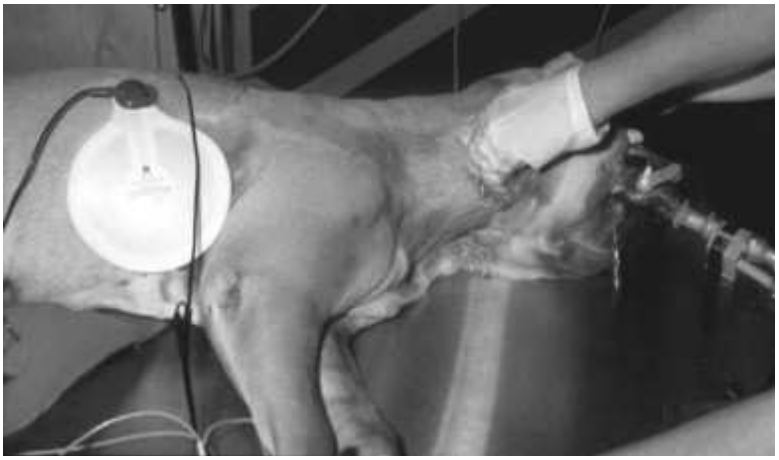
- Same merits as with transvenous pacing in terms of no pain or twitching associated with pacing stimulus and less expensive pacing system
- Less invasive and less expertise needed as compared to transvenous pacing
- However, based on limited clinical experience in dogs, only the atria can be paced. No ventricular pacing is possible.

AUTHOR: TERESA DEFRANCESCO



PACEMAKER: TRANSTHORACIC CARDIAC PACING Illustration of anesthetized, laterally recumbent dog with properly placed electrode patches and connection to pacing system.

(Courtesy DeFrancesco TC, et al: Noninvasive transthoracic temporary cardiac pacing in dogs. J Vet Intern Med 17:663–667, 2003.)



PACEMAKER: TRANSTHORACIC CARDIAC PACING Animal undergoing transthoracic pacing while the neck is aseptically prepared for permanent transvenous pacemaker implantation.

Rhinoscopy

OVERVIEW AND GOALS

Minimally invasive, endoscopic approach to the nasal cavity for visual evaluation and swab, flush, and biopsy procedures

INDICATIONS

- Chronic nasal discharge
- Intranasal obstruction
- Chronic sneezing
- Nasal foreign body
- Epistaxis with normal coagulation profile and blood pressure (BP)
- Maxillary mass/deformity

CONTRAINDICATIONS

Coagulopathy/bleeding disorder

EQUIPMENT, ANESTHESIA

General anesthesia and endotracheal intubation with optimal endotracheal tube cuff seal are required. The following equipment is recommended:

- Mouth gag (speculum)
- Sterile, water-soluble lubricant
- Sterile saline solution for flush
- Gauze squares for packing off pharynx
- Flexible, fiberoptic endoscope (small; 3-mm diameter maximum for patients <20 lb [9 kg])
- Vacuum source for endoscopic suction
- Microbial culture swab
- Biopsy forceps (intraendoscopic or separate, such as Jackson mare 2, 4, or 6 Fr endometrial biopsy forceps)
- Biopsy jar with 10% buffered formalin
- Phenylephrine (e.g., Neo-Synephrine drops) for postoperative epistaxis

ANTICIPATED TIME

- Usually 60-90 minutes anesthesia time (about 30-60 minutes endoscopy time)
- Up to 3-4 hours possible with complex foreign bodies

PREPARATION: IMPORTANT CHECKPOINTS

- Warn owners that epistaxis is common, sometimes for 1-3 days after the procedure.
- Check that current coagulation profile (prothrombin [PT], activated partial thromboplastin time [APTT], platelets) and BP are normal.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Biopsy sample not representative of entire process (very common with small through-the-endoscope pinch forceps, especially if dull)
- Inability to see beyond first few millimeters of nasal passages (common, especially in cats and small dogs; an endoscope that is too big can be a contributing factor).
- Hemorrhage after biopsy (rarely before biopsy, although blood from scraping mucosa with scope can obscure view).
- Inability to see choanae during retroflexed view of nasopharynx (common in large dogs)
- Anesthetic complications

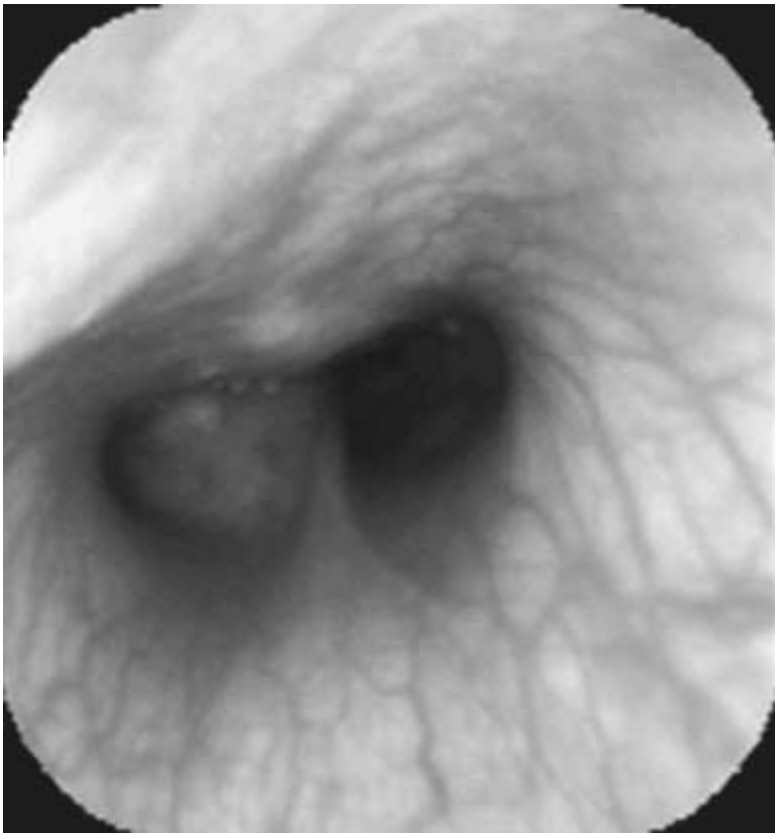
PROCEDURE

TECHNIQUE, INITIAL:

- General anesthesia
- Endotracheal intubation; check good seal on cuff (but not excessive inflation pressure)
- Ventral recumbency
- Animal facing endoscopist; head at edge of table elevated on folded towels
- Fill caudal pharynx with gauze (one to two 3 × 3 [8 × 8 cm] squares for cats, several for dogs; count number to ensure complete retrieval after procedure).
- Swab with sterile culture swab for microbial culture (usually aerobic bacterial).
- Measure length from tip of nostril to medial canthus of eye:
    - This is the maximal length of insertion of the endoscope.
    - Going farther than this measurement can perforate cribriform plate if diseased and enter the brain.

TECHNIQUE, MAIN:

- Advance endoscope into one nostril.
- Easiest route is medial and very dorsal.
    - Push dorsal edge of nostril caudally and dorsally with thumb.
    - Enter just alongside nasal septum for easiest access.
- Begin saline infusion through endoscope for better visualization.
- Catch outpouring of saline in waste bucket or on towels on floor.
- Examine dorsal, middle, and ventral nasal meatus systematically.
- If lesion noted, biopsy after completing visualization (otherwise, blood obscures field).
- Repeat process for contralateral nostril.
- When finished with both nostrils, prop mouth open with speculum.
- Enter oral cavity with endoscope.
- Curve endoscope tip to about 160° so that it reaches behind edge of soft palate.
- Examine choanae.
- Pull body of endoscope gently forward (cranially) to better observe choanae.
- Biopsy lesions if applicable.
- Withdraw endoscope.



RHINOSCOPY Endoscopic view, retroflexed behind the soft palate to show the choanae. Dog's right is on left side of the image. A fleshy mass is present in the right choana.

TECHNIQUE, COMPLETION:

- Suction caudal pharynx as necessary.
- Remove gauze sponges in caudal pharynx. Count number to confirm all removed.
- Instill phenylephrine (few drops in each nostril) if voluminous epistaxis.
- Anesthetic recovery:
    - Neck elevated/nose down to reduce inhalation of blood
    - Extubation as late as safely possible to avoid inhalation of blood.

POSTPROCEDURE

- Epistaxis common; treatment options:
    - Instill 2-5 drops of phenylephrine in bleeding nostril (best time is prior to complete anesthetic recovery—deeper instillation).
    - Tranquilization (butorphanol IV and/or low-dose acepromazine IM)
    - Very rarely, large-volume arterial epistaxis requires carotid ligation (bilateral carotid ligation can safely be done without risking hypoperfusion).
    - Phenylephrine nasal drops may be tried at home.
- Sneezing is common (often decreases to the same intensity as sneezing prior to procedure—if any—within 48 hours after the procedure).

ALTERNATIVES AND THEIR RELATIVE MERITS

- Nasal swab:
    - No anesthesia
    - Possibly acceptable for culture and sensitivity (C&S) of nasal discharge but commonly contaminated with normal flora
    - Poor cytologic yield because animal is awake
- Nasal flush (see online chapter: Nasal Flush):
    - Minimal tissue disruption means less epistaxis but also fewer cells for diagnosis.
    - Can flush out foreign material/foreign body
- Blind nasal biopsy:
    - Quick
    - Location nonspecific
    - May provide good yield if large sample (e.g., with Jackson forceps) and if oriented based on imaging results (radiographs, CT scan, MRI)
- Open-mouth transpalatal biopsy:
    - Caudal nasal biopsy possible without rhinotomy
    - Nasopharyngeal biopsy possible
    - Palatine artery must be avoided.
- Rhinotomy:
    - Most likely to give definitive diagnosis of nasal disease
    - Most invasive: incision through maxillary bones, disruption of large amounts of nasal mucosa
    - Often delayed until lesser invasive means have failed
- CT scan or MRI (see pp. 1233 and 1302):
    - Imaging techniques: no therapeutic value by themselves
    - More specific localization of lesion (CT scan usually preferred because of bone)

AUTHOR: ETIENNE CÔTÉ

Rectal Scraping

SYNONYMS

Rectal scrape, rectal cytologic analysis

OVERVIEW AND GOAL

The goal of rectal scraping is to obtain samples of mucosal tissue for cytologic examination.

INDICATIONS

Animals with signs of disease of the rectum or distal colon, such as hematochezia and tenesmus, especially when rectal mucosa has a diffusely thickened or cobblestone feel per rectal palpation. Most commonly indicated for the diagnosis of rectal histoplasmosis, protothecosis, pythiosis, or neoplasia.

CONTRAINDICATIONS

Suspicion of rectal perforation or deep ulceration

EQUIPMENT, ANESTHESIA

- Often performed without anesthesia or sedation. Sedation may be required for animals with pain on rectal palpation or for animals with an uncooperative temperament.
- Wooden tongue depressor (alternatively, cotton tipped applicator or blunt-tipped metal spatula like those for pharmacy use)
- Exam glove
- Lubricant
- Microscope slides

ANTICIPATED TIME

5-10 minutes

PREPARATION: IMPORTANT CHECKPOINTS

The rectum should be empty of formed fecal matter. Allowing the animal to defecate shortly before the procedure or manual evacuation of the rectum is sufficient (i.e., bowel cleansing or enemas are not required).

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Rectal perforation is possible with vigorous scraping or overzealous insertion of the instrument.
- Splintered or sharp edges of the tongue depressor should be smoothed or covered with a gloved finger.

PROCEDURE

- The rectum should be emptied before the procedure.
- Depending on the size of the patient, the tongue depressor may be left intact or broken lengthwise to a smaller width.
- The depressor is held in a gloved hand to the length of an outstretched index finger. If the depressor has been broken, the finger should cover the roughened edge.
- Lubricant is applied to the finger but not to the tongue depressor.
- The finger and depressor are inserted approximately 2 inches (5 cm) into the rectum.
- The finger is used to apply gentle but firm pressure to the tongue depressor while making two to three sweeping motions covering 20%-50% of the circumference of the rectum.
- The gloved finger and tongue depressor are removed.
- The edge of the tongue depressor is scraped against a microscope slide.
- Gentle smears are made from the material gathered during the scraping. Try to minimize the amount of lubricant which contaminates the slide.

- Slides are processed for cytologic examination in a routine fashion.
- For animals with extremely friable rectal tissue or for very small animals, a cotton-tipped applicator can be used in place of the tongue depressor.

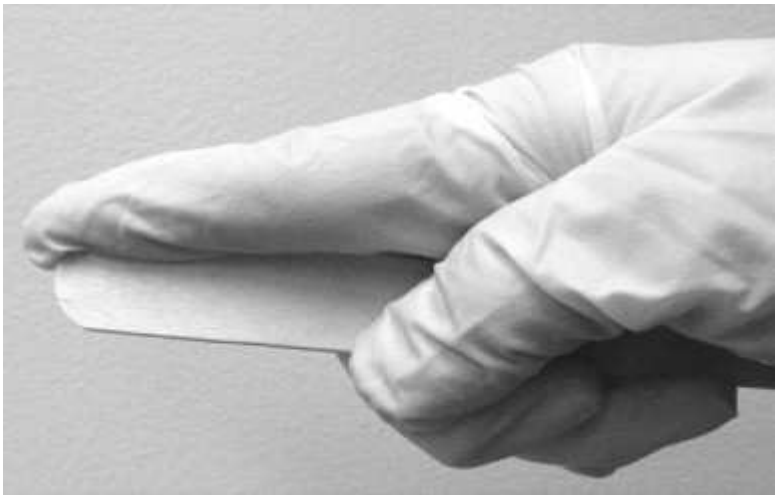
POSTPROCEDURE

Special care is not required afterwards but the animal should be monitored for worsened pain or evidence of new systemic illness which might indicate rectal perforation.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Noninvasive fecal flotation or examination of direct fecal smear may detect intestinal parasites responsible for large-bowel signs.
- Tissue biopsy provides larger samples with intact architecture but requires general anesthesia and bowel cleansing.
- Serologic tests, with varying sensitivity and specificity, are available for both histoplasmosis and pythiosis.

AUTHOR: LEAH COHN



RECTAL SCRAPING One side of a tongue depressor is covered with a gloved finger prior to insertion of both the lubricated finger and the depressor approximately 2 inches (5 cm) into the rectum. Once in the rectum, gentle pressure is used to move the depressor in an arcing motion to obtain tissue for cytologic examination.

Rectal Palpation

SYNONYMS

Digital palpation, rectal exam, transrectal palpation

OVERVIEW AND GOALS

Tactile assessment of the urethra, caudal aspect of the trigone of the urinary bladder, bony pelvic canal, aortic trifurcation, pelvic diaphragm, anal sacs, rectal mucosa, and either the prostate gland (males) or vagina (females)

INDICATIONS

Part of any complete routine physical exam in adult dogs; generally not feasible in puppies or cats

CONTRAINDICATIONS

- Animals weighing <5 kg
- Relative contraindication: anal/rectal pain. Requires that the rectal exam be performed under sedation or general anesthesia.

EQUIPMENT, ANESTHESIA

- Sedation or anesthesia only if required for patient comfort
- Latex or other clean, nonsterile exam glove
- Lubricant (e.g., K-Y Jelly or Vaseline)
- Cotton wool or other absorbent material to receive contents expressed from anal sacs
- Microscope slide with drop of saline

ANTICIPATED TIME

About 30-60 seconds

PREPARATION: IMPORTANT CHECKPOINTS

Review elements of animal's history (dysuria, hematuria, tenesmus, hind limb lameness, etc.), remainder of physical exam, and any diagnostic findings (e.g., hypercalcemia) that could be pertinent to rectal examination findings.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Rectal perforation: extremely uncommon when gentle technique is used.
- Anal sac rupture: also uncommon; however, impacted, infected/abscessed sacs may be more fragile. If anal sacs are large and/or painful, and gentle pressure is unrewarding or distressing to the patient, anesthesia is recommended, and anal sac cannulation may then be performed.
- Perianal fistulae may make it difficult to assess the exact location of the anal opening; time and caution are warranted to avoid exacerbating a fistula through blunt probing.
- Rectal peristalsis may be confused with perineal hernia or rectal stricture. If uncertainty exists, the rectal exam can be prolonged by 1-2 minutes; a wave of peristalsis will pass, but a stricture will not.

PROCEDURE

- Animal is restrained in a standing position by technician holding the head and neck.
- The right-handed examiner puts a glove on his or her right hand; the right index finger is lubricated.
- The examiner stands behind the animal and lifts its tail with the left hand to expose the anus.
- The right index finger is placed on the anus, and then after a few seconds of accommodation by the animal, the finger is gently introduced through the external anal sphincter.
- The tail may be released; most dogs will hold the tail elevated during the rectal exam.
- The left hand, no longer holding the tail, reaches under to the animal's caudal abdomen and cups the ventrocaudal abdomen.

- In addition to this cupping motion, the examiner draws the hand caudally toward his or her body to elevate the viscera of the caudal abdomen toward the right index (palpating) finger. With sufficient upward pressure, and without discomfort to the animal, it is possible to palpate the prostate of even giant-breed dogs this way.
- The palpation reaches to the maximal depth allowed by the examiner's finger and the animal's comfort; the examiner can also turn the finger circumferentially to assess both left and right walls of the pelvic canal and the roof of the pelvic canal.
- Once the exam is completed, the examiner withdraws the index finger, ensuring to first palpate the integrity of the pelvic diaphragm (assess for perineal hernia) and, if necessary, to express the anal sacs located at the 4 and 8 o'clock positions if the anus is pictured as a clockface.
- Finally, the feces coating the glove are examined grossly for blood or other abnormalities and smeared on a microscope slide for cytologic examination.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Fecal flotation and fecal occult blood test: identifies microscopic abnormalities (parasites, blood) but is of little use regarding structural malformations of the rectum and perirectal area.
- Abdominal ultrasound: excellent visualization of many organs of caudal abdomen and cranial pelvic canal; however, the bony pelvis and colon severely narrow the acoustic window and compromise ultrasound assessment of urethra, distal colon, and much of the pelvic canal, which is the area that a rectal examination accesses best.

AUTHOR: ETIENNE CÔTÉ

Slings, Casts, and Other Forms of Immobilization

Client Education Sheet Available on Website

SYNONYM

External coaptation

OVERVIEW AND GOAL

To provide appropriate temporary support and allow healing of musculoskeletal injuries, either alone or as augmentation of surgical repairs

INDICATIONS

- Robert Jones bandage: temporary immobilization of unstable fractures; control of edema and swelling. Appropriate for open fractures following wound dressing.
- Splints: temporary immobilization of fractures or peripheral joint luxations; also used following surgery for joint injuries, arthrodeses, or tendon injuries
- Casts: immobilization of distal limb fractures when mechanically stable; also appropriate following surgical repair—similar to splints
- Slings: partial immobilization of all joints of the limb and prevention of weight bearing. Ehmer sling is used primarily following reduction of hip luxation to prevent recurrence.

CONTRAINDICATIONS

Excessive duration of immobilization may lead to muscle and joint contracture and permanent loss of mobility. Use with caution, especially in pediatric animals.

EQUIPMENT, ANESTHESIA

Sedation may be required for appropriate placement of splints and bandages if animal is in pain or uncooperative. General anesthesia is required for reduction of fractures or joint luxations prior to immobilization. Materials required (amounts and material widths depend on animal size):

- Appropriate wound dressing, if needed
- A 0.5- or 1-inch (1.25 2.5-cm) wide roll of tape
- Rolls of cast padding, 2-6 inches (5-15 cm) width
- Rolls of conforming gauze, 2-6 inches (5-15 cm) width
- Rolls of self-adherent stretch tape

Additional materials:

- Roll of cotton, 12-inch (30-cm) width (for Robert Jones bandage)
- Fiberglass resin or plaster-impregnated casting tape, 2-4 inches (5-10 cm) in width for casts
- Stretch stockinette (for casts, optional)
- Rigid Mason metasplint, lateral plastic limb splint, fiberglass or thermoplastic splint (for splints)

ANTICIPATED TIME

About 10-30 minutes for application of most casts, splints, and slings

PREPARATION: IMPORTANT CHECKPOINTS

Wounds should be treated and an appropriate dressing applied before splinting or bandaging.

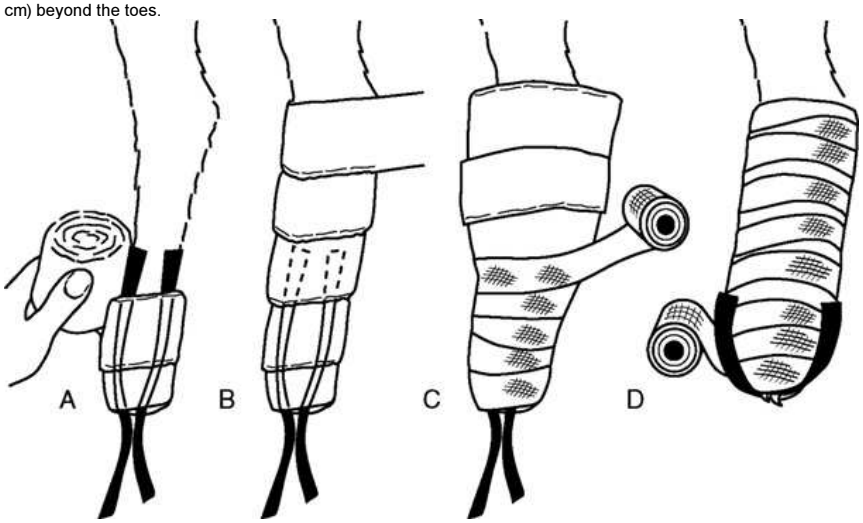
POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Toes of the third and fourth digits should be left visible whenever possible to allow monitoring for coolness, swelling, cyanosis, or discharge, any of which warrants removal of the splint, cast, or bandage for closer evaluation of the soft tissues.
- All bandages, splints, slings, and casts should be checked frequently for limb swelling or discoloration, skin abrasions, loosening or slippage, moisture, or odor.
- Severe ischemia can result from poor application or management.

PROCEDURE

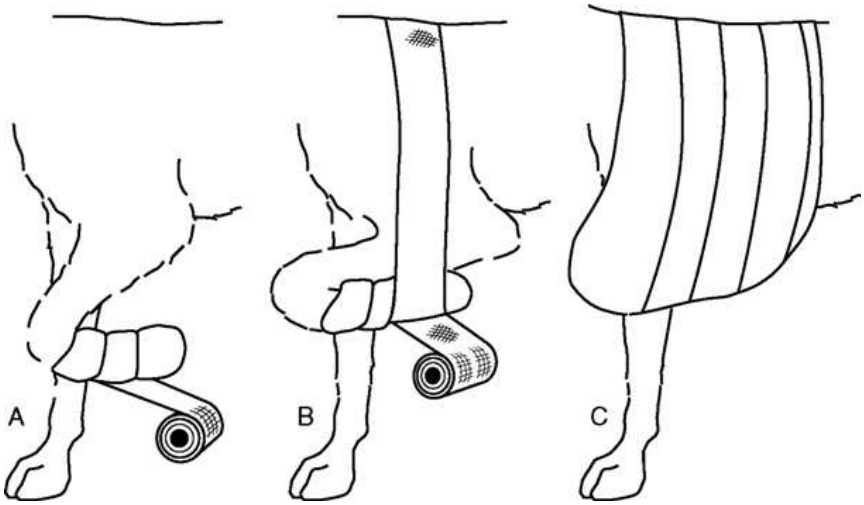
ROBERT JONES BANDAGE:

- Divide bulky roll cotton lengthwise and in thickness; reroll to create several smaller, narrower rolls.
- Apply adhesive tape stirrups directly to the skin of the medial and lateral or cranial and caudal surfaces of the distal limb, extending from the carpus or tarsus distally 4-6 inches (10-15 cm) beyond the toes.



SLINGS, CASTS, AND OTHER FORMS OF IMMOBILIZATION Robert Jones bandage. **A**, Adhesive tape stirrups (shown in black) are applied to skin on opposite sides of distal limb. Wound dressing is applied as needed. Roll cotton (or for small patients, cast padding) is wrapped evenly around foot. **B**, Cotton is continued proximally well above site of injury, with

overlap of about 50% at each turn, to create the full length of the bandage. **C**, Conforming gauze is applied in same manner from distal to proximal but pulled tight at each turn. Cotton should be evenly compressed. **D**, Tape stirrups are reflected proximally and stuck to bandage. An outer tertiary layer of conforming elastic tape is applied over the cotton. Finished bandage should be firm with even compression over entire surface. Toes must be visible for monitoring.



SLINGS, CASTS, AND OTHER FORMS OF IMMOBILIZATION Velpeau sling. **A**, Conforming gauze bandage material is wrapped loosely around the paw, with direction of wrapping causing the gauze to pass from medial to lateral on the dorsal surface of the paw, as shown. **B**, With carpus, elbow, and shoulder all flexed, gauze is brought from paw over lateral aspect of limb and shoulder, over chest and back, and caudal to the opposite axilla. It then continues across the ventral chest, back to the starting point. **C**, Several more layers of gauze are applied in a similar manner, and a few layers are brought around (cranial to) the flexed carpus to prevent extension of the elbow. Such extension could force the distal limb out of the bandage. Wide elastic tape is used for covering the gauze in a pattern similar to that used for the gauze application which completes application of the splint.

- Apply cotton, winding it around the leg from distal to proximal as far as possible into the axillary or inguinal space.
- Each turn of the cotton should overlap the last layer by 50%.
- Wrap the cotton as evenly as possible.
- Apply conforming gauze around the cotton as tightly as possible, working from distal to proximal.
- Cotton should be evenly compressed until the bandage is firm to the touch.
- Pull the tape stirrups proximally, and apply them onto the bandage. Their purpose is to prevent the bandage from slipping off the limb.
- Cover with a tertiary layer of conforming tape.
- Goal of this bandage is even compression and firm support over the entire limb.
- Properly applied, the finished bandage should make a thumping sound like a ripe melon when it is percussed.
- Tips of toes must be visible for monitoring. Owing to the high compression, this bandage can cause severe ischemic injury if applied poorly.

SPLINTS:

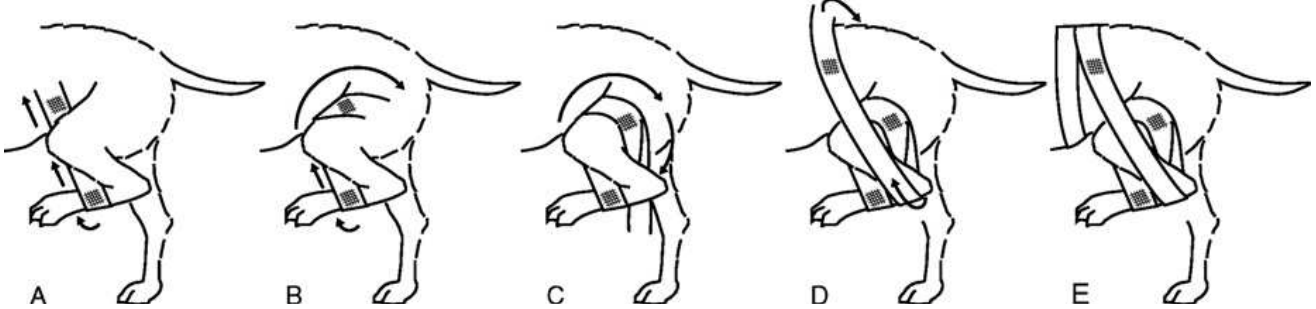
- Apply tape stirrups as for the Robert Jones bandage.
- Apply cast padding, starting distally and winding around the limb as far proximally as needed.
- Apply a layer of conforming gauze from distal to proximal area.
- Place rigid splint material, usually on the caudal or lateral side of the limb.
- Repeat another one to two layers of conforming gauze.
- Cover with an outer layer of conforming tape.

CASTS:

- Apply adhesive tape stirrups.
- Roll stockinette over the limb, allowing extra length proximally and distally. Stockinette is optional but does give the cast a more finished appearance.
- Apply a light layer of cast padding over stockinette.
- Apply roll gauze with light and even compression.
- Apply casting tape over the gauze in distal-to-proximal direction, overlapping by 50% and avoiding digital pressure and wrinkles during application. Layer as needed for appropriate strength.
- Support the limb at multiple points while hardening to avoid dents or incorrect alignment.
- Roll stockinette ends over the cast ends.
- Apply the stirrups to the cast. Their purpose is to prevent the cast from slipping off the limb.
- Cover with an outer tertiary layer of elastic conforming tape.

SLINGS:

- *Velpeau sling (forelimb):*
  - Lightly pad the foot and carpus with cast padding to prevent excessive flexion.
  - Wrap conforming gauze around the foot from medial to lateral.
  - Hold the limb adducted against the body wall with the carpus, elbow, and shoulder in flexion.
  - Roll the conforming roll gauze around the limb and thorax, passing caudally to the opposite forelimb to prevent slipping.



SLINGS, CASTS, AND OTHER FORMS OF IMMOBILIZATION Ehmer sling. **A**, Adhesive tape is passed around the lightly padded metatarsal region, coming up the lateral side of the metatarsus. **B**, Tape is twisted 180○, and stifle and tarsus are held in flexion. Adhesive side of tape is applied to medial side of stifle, continuing up and over thigh as

proximal into inguinal space as possible. **C**, Tape is again twisted 180○ to keep adhesive side against skin and is applied to medial side of hock, then around to starting point on lateral side of metatarsals. Tape is continued for another 1-2 layers over same pattern for greater support. **D**, To support hip reduction, tape may be continued over the back, with the hip in slight abduction. **E**, Tape is passed once around the body and stuck to itself as a belly band.

- Continue on the same pattern for two to three layers, incorporating the entire carpus and foot.
- Apply a light tertiary layer of conforming tape over the gauze in the same pattern.
- The easiest way to perform these steps is with the patient awake and standing.
- To avoid joint contracture, the sling should not be used for more than 2 weeks.

- *Ehmer sling (hind limb)*:
  - Lightly pad the metatarsal region with cast padding.
  - Hold the stifle and tarsus in flexion.
  - Pass adhesive tape around the padded metatarsal region, coming up the lateral side of the metatarsus.
  - Twist tape 180○ to keep the adhesive side against the skin, and pass medially to the stifle.
  - Pass the tape over the lateral thigh as far proximally into the inguinal region as possible.
  - Again twist the tape to keep the adhesive against the skin, and pass distally medial to the hock.
  - Continue tape back up to the starting point at the lateral side of the metatarsal region.
  - Repeat the pattern two to three times to layer the tape.
  - If maintaining hip reduction, following the last pattern, pass the tape over the lateral side of the flexed leg over the back and around the abdomen as a belly band; stick the tape to itself on the abdominal wall, taking care to exclude the prepuce in males. Note: Adhesive tape must be stuck directly to haired skin to avoid slippage.
  - To avoid joint contracture, the sling should not be used for more than 2 weeks.
  - The limb must be monitored frequently for swelling or skin abrasion.

POSTPROCEDURE

- Check toes and distal limb at least q 12 h for any signs of ischemic injury.
- Monitor contact points of bandage materials, especially around bony prominences and joints.

SUGGESTED READING

Bandage techniques. In Bojrab MJ, Ellison GW, Slocum B, editors: Current techniques in small animal surgery. Baltimore, 1998, Williams & Wilkins, pp 1295–1318.

Simpson AM, Beale BS, Radlinsky MA: Bandaging in dogs and cats: external coaptation. Compend Contin Educ Pract Vet 23(2):157–164, 2001.

AUTHOR: PETER MOAK

Transtracheal Wash

SYNONYM

Tracheal lavage, tracheal wash, tracheal wash via endotracheal tube

OVERVIEW AND GOAL

Minimally invasive method of obtaining specimens from the trachea for cytologic examination and culture; done frequently

INDICATIONS

- Chronic cough
- Suspicion of tracheal infection or inflammation
- Alveolar and bronchial radiographic lung patterns

CONTRAINDICATIONS

Compromise of unstable animal with respiratory disease via stress, sedation, anesthesia, or restraint

EQUIPMENT, ANESTHESIA

- May only need restraint in depressed animal, or use minimal sedation/anesthesia to avoid suppressing the cough reflex and to minimally depress respiration.
- Administration of supplemental oxygen is possible through a catheter placed in trachea via oral cavity or endotracheal tube. Ensure that the patient cannot bite/sever the catheter or tube.
- Both the transtracheal wash and the tracheal wash via endotracheal tube require:
    - Sterile saline 0.5-2 mL/kg (often separated into two syringes to allow repetition)
    - Additional sterile syringe (empty) for aspiration:
        - Should be larger than infusion syringe for better aspiration
    - Sterile tube designated for aerobic and fungal cultures
    - Microscope slides (for fresh smears/cytologic analysis)
    - Sterile tube designated for aliquot of sample for cytologic examination:
        - EDTA (purple top) tube for aliquot of sample for cytologic analysis may improve cell preservation or cell counts. Fill tube completely to avoid crenation artifact of cells.

TRANSTRACHEAL WASH

- Clipper for hair
- Sterile scrub supplies and isopropyl alcohol
- Sterile paper/cloth drape if desired
- 2% lidocaine for local subcutaneous injection (0.5-1 mL)
- A sterile #11 scalpel blade for small nick in skin (<1 mm)
- A sterile 18- to 22-gauge through-the-needle (introducer) jugular catheter of appropriate length
- Roll cast padding and Vetrap-type releasing elastic bandaging for cervical wrap

TRACHEAL WASH WITH USE OF STERILE ENDOTRACHEAL TUBE

- Topical 2% lidocaine solution applied by spray or swab as needed to laryngeal and pharyngeal regions (notably in cats)
- Sterile endotracheal tube
- Sterile red rubber catheter, 5 Fr, preferably long enough to reach fourth through sixth intercostal space (ICS)

ANTICIPATED TIME

About 15-20 minutes

PREPARATION: IMPORTANT CHECKPOINTS

- Recent thoracic radiographs
- Supplemental oxygen available
- Advise owner of risks of techniques, including possible nondiagnostic findings.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

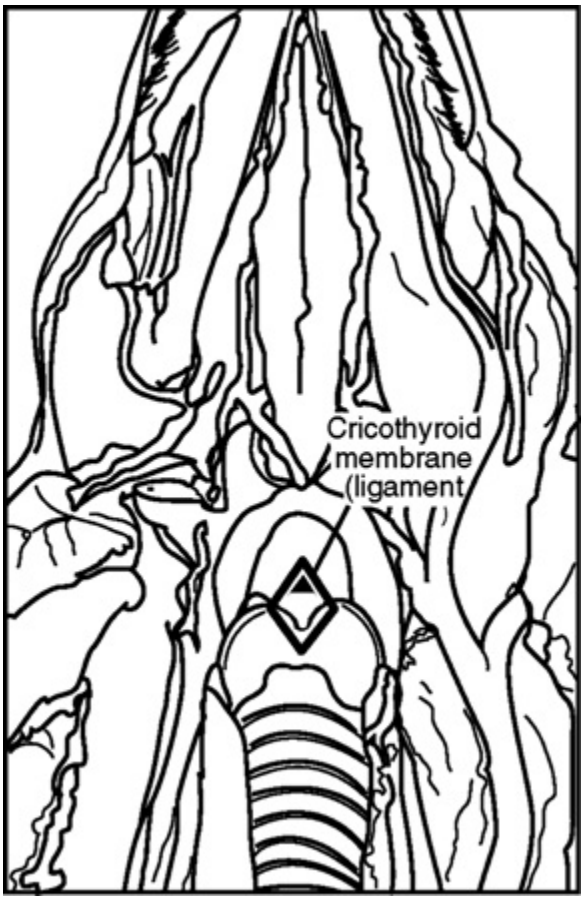
- Contamination of specimens via oral cavity if using endotracheal tube technique
- Subcutaneous emphysema or pneumomediastinum with transtracheal approach
- Being too hesitant (inadequate) in volume of saline instilled
- Withdrawal of catheter against the insertion needle can cut catheter off in the tracheal lumen.
- Cyanosis/hypoxemia in animals with borderline hypoxemia prior to procedure

PROCEDURE

Decide between techniques based on value of sample purity versus patient risk factors; transtracheal approach lessens contamination but slightly increases risk of complications.

TRANSTRACHEAL WASH:

- Patient in sitting or sternal position, ideally at the front end of a table to have the site of entry into the trachea at operator's eye level
- Head and neck elevated to horizontal or further vertical (45○ toward ceiling); if one side of the lungs is of greater interest, then have this be the dependent (down) side, using lateral recumbency.
- Palpate the small cricothyroid membrane at the caudal aspect of the ventral larynx.
- Clip and prepare the area using sterile technique.
- Infiltrate 0.5-1 mL lidocaine in SQ tissue overlying the cricothyroid membrane.
- Make a small (<1 mm) incision with the #11 scalpel blade.
- Prepare jugular catheter.
- Insert jugular catheter needle at oblique angle caudodorsally through the small incision in the skin, then through the cricothyroid membrane.
- When the needle is in the tracheal lumen, a slight cough upon entry is common. Take care to avoid lacerating the dorsal wall of the trachea with the needle tip.
- Slide the catheter down into the tracheal lumen in a caudal direction; remove the stylet partially.
- Back out the insertion needle so it is outside the trachea and skin, hold catheter steady (catheter position stays unchanged), and apply the needle guard.
- Remove stylet and flush initial volume. It is important to aspirate immediately after flushing and to not aspirate against negative pressure (catheter tip lodged against respiratory mucosa; release negative pressure and reposition). May switch to larger syringe to aspirate as much fluid sample as possible; if no specimen is obtained, the second volume is flushed and aspirated again. Saline that passes down the trachea is expectorated or coughed back toward the catheter; mucus and turbidity are seen in the fluid. Often, only 1-2 mL will be retrieved out of every 10 mL infused.
- Withdraw catheter.
- Gently wrap neck over insertion site with cast padding, roll gauze, and Vetrap to reduce risk of SQ emphysema. Keep the neck wrap in place preferably 12 hours, ensuring that it is not too tight.



TRANSTRACHEAL WASH Anatomic diagram of ventral neck of dog; dissected specimen (cranial is toward top of image). Diamond-shaped outline identifies the cricothyroid membrane, through which a catheter is introduced for performing transtracheal wash.

TRACHEAL WASH VIA ENDOTRACHEAL TUBE:

- Sedate or anesthetize animal, and place oral speculum to hold mouth open.
- Pass sterile endotracheal tube to an appropriate level while trying to avoid gross contamination of its lumen and sides; use topical lidocaine on larynx if needed.
- Pass sterile red rubber catheter through the endotracheal tube to level of thoracic inlet or bronchial bifurcation; lavage with same technique as already described.
- Can follow flush procedure with covered endoscopic cytology brush if desired.

POSTPROCEDURE

- Provide supplemental oxygen if needed (see p. 1318).
- Divide specimen into aliquots for cytologic analysis and cultures and fresh slides for cytologic analysis; can request routine staining and Gram stain.
- If respiratory distress occurs, tilt the animal's body (head down, allowing fluid to flow cranially), perform coupage, consider reintubation and oxygen supplementation/positive-pressure ventilation.
- Radiographs to assess for pneumomediastinum if needed

ALTERNATIVES AND THEIR RELATIVE MERITS

Tracheobronchoscopy:

- Visualization of airways to bronchi
- Provides reduced contamination and superior estimate of cell numbers from lavage specimen
- Catheter lavage and brush cytologic analysis can both be performed.
- Requires additional equipment, expertise, and longer procedural time
- Tracheobronchoscopy is more accurate than tracheal wash if both options are available.

AUTHOR: MARK E. HITT

Transfusion Therapy

SYNONYM

Blood transfusion, component therapy

OVERVIEW AND GOALS

Safely collect and administer blood products

INDICATIONS

FRESH WHOLE BLOOD:

- Improve oxygen delivery:
  - Hemolysis
  - Blood loss
  - Nonregenerative anemia
- Provide clotting factors:
  - Anticoagulant rodenticide toxicity
  - Liver disease
  - von Willebrand disease (VWD)
  - Disseminated intravascular coagulation (DIC)
  - Hemophilia A
  - Other factor deficiencies
- Support oncotic pressure:
  - Protein-losing disease (enteropathy, nephropathy, massive skin wounds or burns, serosal inflammation)
- Fresh whole blood is not recommended for treatment of thrombocytopenia unless significant active hemorrhage and anemia exist.

STORED WHOLE BLOOD: Same as for fresh whole blood except for VWD, liver disease, hemophilia A, and DIC: After 6 hours of storage, platelets, factors V and VIII, and von Willebrand factor all decrease.

PACKED RED BLOOD CELLS (PRBCs):

- Improve oxygen delivery:
  - When oncotic support and clotting factors are not required
  - When volume overload is a concern (cardiac disease, renal failure, chronic anemia)

FRESH FROZEN PLASMA:

- Provide clotting factors (same as fresh whole blood)
- Support oncotic pressure (same as fresh whole blood)
- Pancreatitis (controversial) or colostrum replacement
- Must be separated and frozen within 6 hours of collection

FROZEN PLASMA (plasma frozen more than 6 hours after collection or fresh frozen plasma stored more than 1 year):

- Anticoagulant rodenticide toxicity and hemophilia B (factors II, VII, IX, and X preserved)
- Support oncotic pressure
- Pancreatitis (controversial) or colostrum replacement

OTHERS: Platelet-rich plasma and platelet concentrate are rarely used in private practice (labor intensive, 2 to 3 day storage times, special storage conditions).

CONTRAINDICATIONS

- Animals with normal to increased packed cell volume (PCV)
- Administer cautiously in patients with volume overload, heart disease, or renal failure.

- Incompatible recipients:
  - Cross-match dogs that have received a transfusion more than 4 days previously, even if using the same previously cross-matched compatible donor.
  - Cats: all require blood typing and/or cross-matching prior to transfusion (cross matching will detect Mik incompatibilities in cats while AB blood typing will not).
- First-time transfusions to dogs are usually safe without prior blood typing and/or cross-matching, although compatibility testing is still recommended to decrease future incompatibilities.

EQUIPMENT, ANESTHESIA

BLOOD COLLECTION: Hair clippers and material for sterile prep

Dogs:

- Donor dogs should be healthy adults, weigh >30 kg, and have a normal physical exam and negative heart-worm and rickettsial serologies.
- Butorphanol, 0.1-0.2 mg/kg for IV use
- Sterile 450-mL collection bag with tubing, needle, and anticoagulant (commercially available)
- Digital gram scale
- Hemostat forceps
- Scissors
- Hemoclips and stripper sealer (optional)

Cats:

- Donor cats should be healthy adults, weigh >4 kg, have a normal physical exam and normal blood smear, and be negative for feline leukemia and feline immunodeficiency virus serologies.
- Ketamine HCl, 1-2 mg/kg for IV use
- Two 35-mL syringes (a 60-mL syringe may collapse the vein).
- Anticoagulant (citrate-phosphate-dextrose-adenine-1 or adenine-citrate-dextrose)
- A 19-gauge butterfly needle
- Note: Heparin (300 units per 50 mL blood collected) can be used as an anticoagulant in an emergency.
  - Dilute heparin in 3 mL of saline to facilitate mixing.
  - Heparin contains no preservatives: administer blood within 24 hours.
  - Heparin activates platelets: avoid in thrombocytopenic animals.

BLOOD ADMINISTRATION:

- IV or intraosseous (IO) catheter
- Transfusion set with filter (dogs)
- A 170-µm syringe filter and an IV extension set (cats)

ANTICIPATED TIME

- Whole blood collection: 20-40 minutes
- Administration: minutes to maximum of 4 hours, depending on animal's condition

PREPARATION: IMPORTANT CHECKPOINTS

- Check PCV of recipient and donor prior to transfusion.
- Save hematocrit tube containing recipient plasma for future comparison if hemolytic reactions occur.
- Aseptic technique is essential.
- See Cross-Match and Blood Typing, .

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

TRANSFUSION REACTIONS (see p. 1111):

- Monitor temperature, heart rate, and respiratory rate every 10 minutes for 30 minutes, then every 60 minutes until transfusion completed.
- Uncommon (3%) and rarely fatal (<1%) if cross-matched
- Stop transfusion.

- Evaluate signs: if mild without evidence of hemolysis or bacterial contamination, restart transfusion at a slower rate and monitor closely.
- Risk of reactions is reduced by:
    - Using donor dogs negative for DEA 1.1 and preferably negative for DEA-1.2 and DEA 7
    - Cross-matching all donors with recipients
    - Using proper collection, administration, and storage techniques
    - Not adding anything other than 0.9% saline to blood products

Hemolytic transfusion reaction; may be acute or delayed:

- Acute:
    - Can see signs within 20 minutes
    - Restlessness, fever, tachycardia, vomiting, hemoglobinuria, hemoglobinemia
    - Very rarely: renal failure, collapse, shock, and death
    - Stop transfusion.
    - Look for hemolysis: check plasma color of a spun hematocrit tube (compare to pretransfusion plasma color).
    - Check blood pressure (BP) and urine output.
    - Administer fluids (address shock, prevent DIC).
    - Corticosteroids and antihistamines will not prevent acute hemolytic reactions.
- Delayed:
    - Can occur 3-14 days after transfusion
    - Decreases transfusion efficacy but usually produces no clinical signs

Anaphylactic reactions:

- Usually mild
- Fever, urticaria, erythema, pruritus
- Stop transfusion.
- Administer antihistamines (e.g., diphenhydramine, 1-2 mg/kg IM) and glucocorticoids (e.g., dexamethasone SP 0.1-0.2 mg/kg IV).
- Can usually restart transfusion at a slower rate

Volume overload:

- Cough, dyspnea, jugular distention
- Stop transfusion.
- Administer furosemide (e.g., 2 mg/kg IV) ± oxygen supplementation.

Bacterial contamination: examine blood for discoloration, and submit blood for culture and Gram stain if animal is febrile.

OTHER CONCERNS:

- Dogs that receive a first-time crossmatched compatible transfusion can develop antibodies against the donor blood in 1-2 weeks, and any subsequent transfusion (even if using the same donor) should be cross-matched.
- Microembolism
- Hypothermia
- Acidosis
- Citrate toxicity

PROCEDURE

BLOOD COLLECTION FOR BANKING:

Blood donor dogs:

- Administer butorphanol, 0.2 mg/kg IV.
- Place in lateral recumbency on an elevated surface.
- Clip ventral neck (center over jugular furrow).
- Perform sterile scrub.
- Place collection bag on the scale at a level below the animal (blood collects via gravity).
- Zero the scale (collection bag + anticoagulant ≈ 85 g).
- Note: If less than 450 mL of blood is to be collected, anticoagulant must be expressed from the collection bag to maintain the 1 : 7 anticoagulant-to-blood ratio (e.g., to collect 225 mL blood, discard half the anticoagulant [32 g]).
- Clamp tubing with hemostat (near needle).

- Hold off jugular vein for visualization.
- Remove needle cap and insert needle (16-17 gauge) into jugular vein.
- Remove hemostat; collection begins.
- During collection, gently rock the bag intermittently to mix blood with the anticoagulant.
- Rotate/adjust needle delicately if flow stops.
- Continue collection until scale reads 450 g (± 45 g).
- Release jugular vein pressure.
- Reclamp tubing near needle.
- Remove needle from jugular vein.
- Recap needle.
- Strip blood from tubing into bag to mix with anticoagulant.
- Allow tubing to refill.
- Tie/hemoclip tubing at 6- to 10-cm intervals for storage and cross-match.
- Remove hemostat.
- If collection technique is questionable, blood should be used within 24 hours.

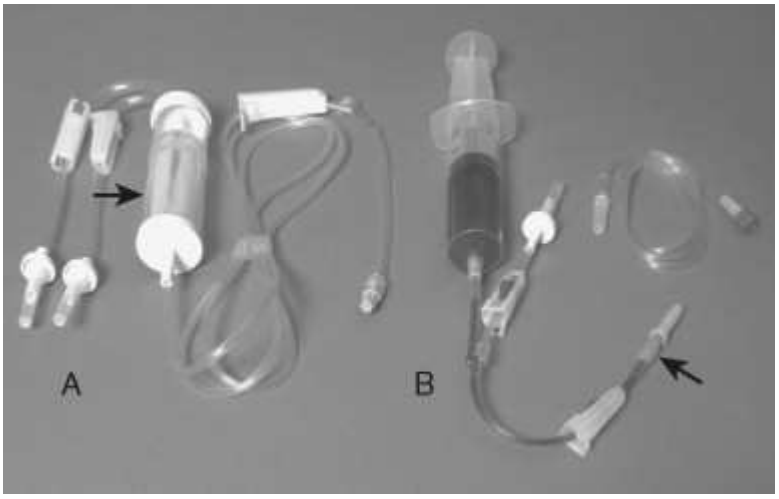
Blood donor cats:

- Sedate (1-2 mg/kg ketamine IV; may add diazepam, 0.1 mg/kg IV if necessary).
- Clip ventral neck (center over jugular furrow).
- Perform sterile scrub.
- Use a separate needle to put 4 mL ACD or CPDA-1 into each sterile 35-mL syringe.
- Connect one 35-mL syringe to a butterfly needle.
- Hold off jugular vein to visualize.
- Remove needle guard.
- Insert butterfly needle into jugular vein.
- Gently aspirate 27 mL of blood while slowly rocking the syringe to mix anticoagulant and blood.
- Disconnect syringe from butterfly catheter.
- Cap syringe with a sterile needle.
- Attach second anticoagulant-filled syringe, and gently aspirate 27 mL of blood as already described.
- Release jugular pressure.
- Remove needle from jugular vein.
- Note: A similar technique can be used in dogs (60-mL syringe with 7 mL ACD or CPDA-1) if collection bags are unavailable; refrigerate and use within 24 hours.

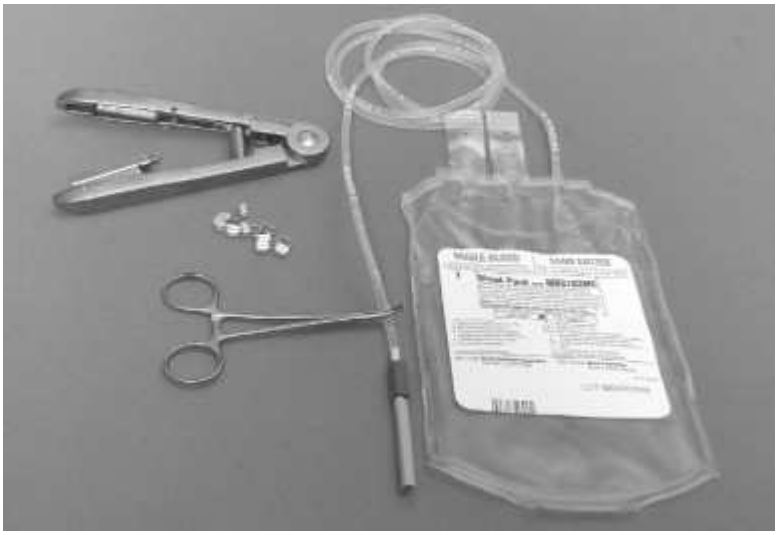
ADMINISTRATION:

- For all blood products:
  - Always use a filter.
  - Start slowly (0.5 mL/kg/h) for 15-20 minutes.
  - Monitor for reactions.
  - Increase rate if no reactions occur.
  - Complete transfusion by 4 hours (decreases bacterial contamination).
  - Normal rate is 5-10 mL/kg/h.
  - Can increase to 20 mL/kg/h in unstable hypovolemic animals
  - Can administer as rapidly as possible in a severe crisis
  - For heart disease, renal failure, or potential volume overload, administer at 1-4 mL/kg/h, and monitor for volume overload (as already described).
  - Can divide dosage into smaller aliquots and refrigerate up to 24 hours (allows slower administration with minimal risk of bacterial contamination)
- From a syringe:
  - Attach syringe filter to syringe.
  - Attach IV extension set to filter.
  - Prime system with blood product.
  - Connect extension set to IV catheter.
  - Use syringe pump or intermittent administration (i.e., healthy cats: 5 mL over 5 minutes then wait 6-12 minutes and repeat).
- From a collection bag:
  - Use blood administration set with filter (see manufacturer instructions).
  - Prime administration set with blood product.
  - Attach to IV catheter.
  - Set drip rate.
  - Some infusion pumps can be used; check manufacturer specifications.
- Dosages:
  - Whole blood: 10-20 mL/kg:

        - Generally: 2 mL/kg increases PCV ≈ 1%
    - PRBCs: 5-10 mL/kg:
        - Generally: 1 mL/kg increases PCV 1%.
        - Can dilute with 50-125 mL of 0.9% saline to decrease viscosity
    - Alternatively: PRBCs or whole blood (milliliters) dose = BW (kilograms) × 90 × (PCV desired — PCV recipient)/PCV of donor blood; substitute 90 with 60 for cats.
- Warming whole blood or PRBCs is not essential; indications to warm:
    - Multiple transfusions
    - Hypothermic animals
    - Neonates
    - Warm by room air or water bath.
    - Do not exceed 37○C (hemolysis).
- Fresh frozen/frozen plasma, 10-20 mL/kg:
    - Plastic is fragile when frozen; handle frozen units delicately.
    - Thaw in 37○C water bath in a waterproof plastic bag.
    - Give within 4 hours for clotting factors.
    - Can store 24 hours in refrigerator after thawing if clotting factors not required
    - Repeat dosage if coagulopathy persists.



TRANSFUSION THERAPY AND COLLECTION TECHNIQUES FOR BLOOD BANKING Two blood transfusion systems; arrows indicate filters. **A**, A transfusion set with filter chamber typically used for larger volumes (medium- and large-breed dogs). **B**, A 170-µm syringe filter and IV extension set typically used for cats and toy breed dogs.



TRANSFUSION THERAPY AND COLLECTION TECHNIQUES FOR BLOOD BANKING Materials for blood collection. A blood collection bag, tubing, and needle *(right)* are shown, with a hemostatic clamp placed on the tubing to prevent leakage of the anticoagulant. Hemoclips and a stripper-sealer *(left)* are also shown.

POSTPROCEDURE

- Blood donors: administer fluids if hypovolemic (tachycardia, pale mucous membranes, prolonged capillary refill time) or if the fluid equivalent of more than 2% of the body weight in kilograms is collected.
- Patients/recipients: check PCV 2 hours after the transfusion is complete, and check coagulation profile after administering plasma for coagulopathies.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Polymerized hemoglobin (Oxyglobin):
  - Improves oxygen delivery
  - Provides colloidal support but no other plasma benefits
  - Dogs: 10-30 mL/kg at a maximum of 10 mL/kg/h
  - Cats: 5-10 mL/kg at a maximum of 5 mL/kg/h
  - Monitor closely for signs of volume overload, especially in cats.
- Synthetic colloids:
  - Hypoalbuminemia requires large volumes of whole blood or plasma to correct.
  - Synthetic colloids should be considered instead to support colloidal pressure (bolus 5-20 mL/kg then 10-20 mL/kg/day; use lower doses for cats).
  - Human albumin: role is controversial; use with caution, as fatal reactions reported. Further studies are required before recommendations can be made (suggested guidelines if used: dogs, 2-7 mL/kg of 25% or 10-35 mL/kg of 5% over 4-6 hours).

AUTHOR: SØREN R. BOYSEN

Transcervical Insemination

SYNONYM

TCI

OVERVIEW AND GOAL

- Transcervical insemination (TCI) involves the endoscopic visualization of the cervix and its catheterization. Semen is then injected through the catheter and into the uterine lumen.
- The two primary methods of intrauterine insemination are catheterization of the cervix by TCI or injection of semen into the uterine lumen by laparotomy.
- TCI requires specific equipment and careful breeding management.

INDICATIONS

- Intrauterine insemination is required when using frozen-thawed semen.
- Female subfertility
- Cases where the semen is reduced in viability or dose (<150 million progressively motile, morphologically normal sperm)
- TCI can be used to rule out vaginal or cervical abnormalities through visualization of these areas and catheterization of the cervix.

CONTRAINDICATIONS

If the bitch is not in late estrus, the vaginal wall is more sensitive, and the procedure will be uncomfortable and more likely to require sedation.

EQUIPMENT, ANESTHESIA

- Endoscope:
  - Extended-length rigid cystourethroscope with a working length of 29 cm and 22 Fr diameter; ideal for dogs 25-75 lbs (12-35 kg). It should have a 30○ viewing angle with a sheath and a bridge. Use with urinary catheters 6-8 Fr diameter.
  - Cold light source and cable
- Camera and video tower system
- Adjustable-height exam table with nonslip surface
- Anesthesia or sedation is not usually required; a bitch in estrus will tolerate the procedure very well. Smaller breeds are more likely to require sedation.

ANTICIPATED TIME

10-40 minutes

PREPARATION: IMPORTANT CHECKPOINTS

Breeding management (see online chapter: Breeding Management) and insemination timing:

- The ideal timing for TCI is days 5 to 7 after the luteinizing hormone (LH) surge (LH surge = day 0). This is based on both oocyte viability and the degree of cervical relaxation required for catheterization. Secondary oocytes are only present after day 4-5, and by day 8, the oocytes become senescent. Prior to day 4, the cervix will be difficult to catheterize.
- The LH surge can be timed either directly by testing LH or indirectly by monitoring serum progesterone and looking for the rise above 1.5-3 ng/mL.
- When timing the insemination, it is also important to consider the longevity of the semen based on its handling and state (fresh versus cooled shipped versus frozen).
- Typical breeding management with any type of semen would include 2 inseminations between days 4 and 7:
  - The frequency of insemination using TCI is limited only by the ability to catheterize the cervix. Once daily inseminations, though not usually necessary, are possible from day 4-7 or as long as the cervix can be catheterized.

Semen preparation and evaluation:

- The minimum intrauterine dose of semen is 75 million.
- Since the space in the uterine lumen is limited, the volume of semen used is reduced. The maximum volume should be less than 3 mL. The size of the bitch and the capacity of the uterus will determine the ideal insemination volume.
- If using freshly collected semen, every effort should be made to fractionate the collection to separate the sperm-rich portion. The volume of the sperm-rich fraction is usually less than 3-5 mL. If TCI is scheduled to occur within a short time, the unextended sperm-rich fraction can be used. If additional volume is needed, the prostatic fluid can be used to follow the semen into the uterus and “flush” the catheter.
- If using cooled shipped semen or semen extended to a volume greater than 5 mL, the semen should be centrifuged at 900g for frac12; min/mL. The supernatant should be drawn off until the ideal volume is achieved, and the remaining pellet is resuspended.
- Frozen semen should not be thawed until the cervix is successfully catheterized. Thaw instructions and procedures should be followed. It is recommended to prepare for thawing in advance to ensure that insemination occurs with a few minutes of catheterization of the cervix.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Occasionally, it will not be possible to catheterize the cervix. This is affected by factors such as the stage of the estrous cycle, size of the female, and parity. The natural angle of the cervical canal is craniodorsal. Adjusting the angle of the endoscope can straighten the vagina and cervix. It may also be necessary to use a catheter with a narrower diameter.
- Inadequate insufflation can result in poor visualization of the external cervical os.
- Excessive discharge, especially in early estrus, can hinder visualization.

PROCEDURE

- To limit the time the animal is restrained on the table, equipment and semen should be prepared in advance.
- The dog is restrained in a standing position on a table. Restraint should include a person or device to limit forward movement, side-to-side movement, and prevent sitting or lying. The table is adjusted to a comfortable height for the operator/inseminator.
- The rigid endoscope is placed at the vulvar lips and advanced, noting important anatomical landmarks:
    - The caudal vagina of the bitch has a steep incline as it extends over the pubic bone (see p. 1360).
    - The scope should be held against the dorsal surface of the caudal vagina to avoid the sensitive clitoris and urethra.
    - In the cranial vagina, the vaginal folds become longitudinal, and the prominent dorsal vaginal fold or pseudocervix can be visualized.
    - The cervix is located on the dorsal vaginal wall at the cranial extent of the dorsal vaginal fold. It typically angles in caudal ventral direction. The tissue of the cervix will appear more fibrous and sharply creased than the surrounding vaginal tissue.
    - The vaginal fornix extends cranial to the cervix and is a blind pocket.
    - Location within the vagina can also be determined by transabdominal palpation.
- It is often necessary to insufflate the vagina to improve visualization as the scope is advanced:
    - The vulvar lips may need to be held shut to prevent air from escaping.
- Once the cervix is visualized, the catheter is advanced, and the external os of the cervix is probed. A twisting motion may help the catheter penetrate the cervix.
- The catheter should be visualized as it is advanced through the cervix. It should be placed as far as it will go into the uterine lumen, as long as no pressure is felt.
- Once the catheter is in place, the semen is injected. If backflow is observed through the cervix, the catheter should be repositioned and the injection of semen continued. The catheter should be flushed with an appropriate amount of air, extender, as prostatic fluid to ensure all has entered the uterine lumen.
- The catheter is withdrawn, and then the rigid endoscope is retracted.

POSTPROCEDURE

It has been recommended to elevate the hind quarters for 10 minutes to facilitate movement of the semen from the uterus into the uterine tubes.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Surgical insemination involves the direct injection of semen through the uterine wall into the lumen. This method is precise but invasive and should only be performed once per estrous cycle.
- The Norwegian intrauterine insemination catheters are rigid catheters 20-50 cm long with a tip diameter of 0.5-1 mm. These catheters are advanced into the cervix blindly relying only on transabdominal palpation for correct placement. This procedure requires a significant level of operator experience and risks traumatizing the vagina and cervix, but it does eliminate the need for expensive equipment.

AUTHOR: BRONYWN CRANE

Tracheostomy

OVERVIEW AND GOALS

The creation of a temporary hole through which a tube or a permanent stoma in the trachea can be placed. Tracheostomy facilitates airflow into the trachea distal to the nose, mouth, nasopharynx, and larynx.

INDICATIONS

Temporary tube tracheostomy:

- Emergency procedure to establish airflow in situations of acute upper respiratory distress or upper respiratory obstruction that does not allow stabilization with supplemental oxygen or oral intubation; occurs with trauma, neoplasia, laryngeal edema/collapse, certain foreign bodies
- Elective procedure to provide alternative airflow for surgical procedures of the oropharynx
- Long-term ventilatory support

Permanent tracheostomy:

- Salvage or palliative procedure
- Upper respiratory obstructions causing respiratory distress that cannot be treated otherwise; occurs in neoplasia, hemorrhage, laryngeal collapse

CONTRAINDICATIONS

Respiratory distress due to intrathoracic disease

EQUIPMENT, ANESTHESIA

- Anesthesia:
  - General anesthesia if elective procedure
  - Local anesthesia if too unstable for general anesthesia ± analgesia/sedative
  - If the animal is unconscious due to upper airway obstruction, tracheostomy is generally indicated in the absence of general or local anesthesia. Anesthesia is then administered/titrated if necessary after the tracheostomy has been performed but prior to the return of consciousness.
- Aseptic surgical preparation if elective procedure (and if time allows in cases of emergency tracheostomy):
  - Hair clippers
  - Surgical scrub solution, alcohol, gauze sponges
- Instruments:
  - Sterile gloves
  - A #11 sterile scalpel blade
  - Scalpel handle
  - 2-0 to 4-0 polydioxanone/polypropylene suture on a taper needle
  - Needle holders
  - Brown-Adson forceps
  - Kelly hemostat forceps
- Tracheostomy tubes:
  - Diameter: tubes should be no larger than half the size of the trachea. Intratracheal length: tube should extend six to seven tracheal rings. Composition: tubes should be made of autoclavable, nonreactive material (silver, silicone, nylon).
  - Single-lumen tubes must be removed and replaced for cleaning.
  - Double-lumen tubes have a removable inner cannula for cleaning, which is more convenient and is comfortable for the animal, but they may be too large for smaller animals, and mucus can still accumulate distal to the inner cannula.
  - Cuffed tubes are used for ventilator support. High-volume, high-compliance cuffs that are able to inflate with low pressures and less blood flow compromise are indicated.
  - The Shiley tracheostomy tube is the most common, and the company offers many varieties for treating veterinary patients.

ANTICIPATED TIME

- Temporary: 10 minutes
- Permanent: 30 minutes

PREPARATION: IMPORTANT CHECKPOINTS

- Have all supplies at hand before beginning procedure.
- Label stay sutures to aid in replacement of tube.
- Inform owner of potential complications of procedure and long-term prognosis of condition.

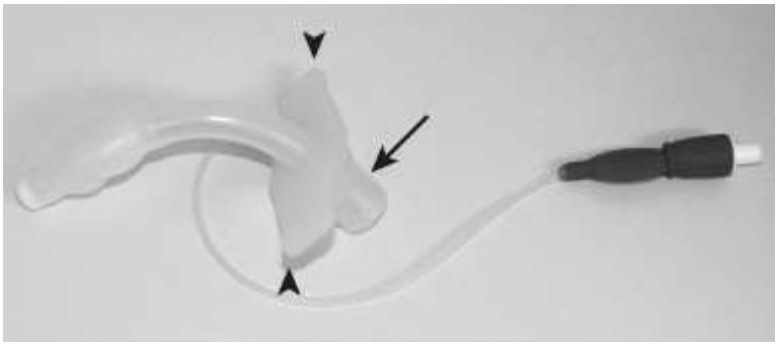
POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Tracheostomy emergencies: obstruction, extubation, and cuff leakage
- Tube "cleaning" cannot involve pushing secretions and debris back into the trachea. Proper suctioning and, if double-lumen tube, removal of the inner cannula are essential.
- Infection
- Hemorrhage
- Subcutaneous emphysema, pneumomediastinum, pneumothorax
- Tracheal malacia
- Tube tracheostomy:
    - Gagging, vomiting, and coughing, especially during suctioning
    - Tube obstruction
    - Tube dislodgement
    - Tracheal irritation causing tracheocutaneous or tracheoesophageal fistulas
    - Vascular erosions
    - Stricture or stenosis from pressure necrosis and mucosal erosions
- Permanent tracheostomy:
    - Stomal occlusion by mucus, skin folds, stenosis
    - Mucus accumulation
    - Coughing and gagging from tracheal irritation

PROCEDURE

TEMPORARY TRACHEOSTOMY:

- Place animal in dorsal recumbency, and clip hair from ventral and lateral neck.
- Surgically prep the skin if time permits (all elective procedures and as much as possible with emergency cases).
- Make a ventral, cervical midline skin incision extending caudally from the distal aspect of the larynx. A typical length for the incision is 2-3 cm in a medium-sized dog.
- Expose the trachea by bluntly dissecting on the midline between the paired sternohyoid muscles and retracting the muscles and skin laterally.
- Either a horizontal (transverse) or a vertical (midline) incision can be made into the trachea.
- Prior to incising the tracheal cartilages/rings, stay sutures should be placed, encircling cartilages proximally and distally (horizontal tracheostomy) or laterally (vertical tracheostomy) to the proposed tracheal incision.
- A horizontal tracheostomy can be made by incising through the annular ligament between the third and fourth tracheal cartilages, with the incision not extending more than half the circumference of the trachea.
- A vertical tracheostomy can be made by incising through the ventral midline of the third through the fifth tracheal cartilages.
- Insert a tracheostomy tube by placing tension on the sutures to temporarily enlarge the tracheal opening and using a hemostat to manipulate the tube through the incision.
- Alternatively, a tracheal flap tracheostomy can be performed by making a U-shaped incision into the cartilage based at the second tracheal ring and extending distally two to three rings. The cartilage flap is raised, and the endotracheal or tracheostomy tube is inserted. This technique is best for long-term intubation or ventilation, because it decreases pressure on the tissue and granulation tissue formation.
- Secure the tube by suturing it to the skin or tying it with gauze around the neck.
- If necessary, skin cranial and caudal to the tube can be sutured together.
- Leave stay sutures in place while tracheostomy tube is present to aid in tube replacement should it become dislodged or obstructed.



TRACHEOSTOMY A single-lumen, cuffed tracheostomy tube. Curved and cuffed portions are inside the patient. External plate *(arrowheads)* is sutured to the skin of the ventral neck or tied around the neck with umbilical tape. Proximal extremity of tube *(arrow)* either is left open or attached to a ventilator.

PERMANENT TRACHEOSTOMY:

- Place animal in dorsal recumbency, and clip hair of the ventral and lateral neck.
- Surgically prep the skin.
- Make a ventral cervical midline skin incision extending caudally from the distal aspect of the larynx. A typical length for the incision is 6-8 cm in a medium-sized dog.
- Expose the trachea by bluntly dissecting between the paired sternohyoid muscles and retracting laterally.
- Identify the third through sixth tracheal cartilages/rings.
- Create a tunnel dorsal to the trachea in this region through gentle blunt dissection and, using this tunnel, place several horizontal mattress sutures with 2-0 or 3-0 polydioxanone/polypropylene through the tunnel and sternohyoid muscles to deviate the trachea ventrally and decrease tension.
- Make an incision through the ventral aspect of the third to sixth tracheal cartilages to the mucosal level, and remove a rectangular segment with a length of three to four cartilages and a width one-third of the tracheal circumference. The size of the segment removed should be approximately 50% larger than the size of the desired stoma.
- Using thumb forceps and the blunt edge of the scalpel blade, dissect free the edges of the incised cartilage from the underlying mucosa.
- Resect a rectangular segment of skin from the edges adjacent to the tracheostomy site similar to the size and shape of the tracheostoma. Excise excess skin or fat if present.
- Using interrupted intradermal sutures of 3-0 polydioxanone/polypropylene, suture the skin around the tracheostoma to the peritracheal tissues laterally and the annular ligaments proximally and distally. These sutures will promote skin adhesion to the trachea and decrease seroma formation and suture tension.
- Make an I- or H-shaped incision into the tracheal mucosa.
- Fold the mucosa over the cartilage edges, and suture it to the skin edges using simple interrupted sutures at the corners and a simple continuous pattern of 4-0 polypropylene for the remainder of the area.

POSTPROCEDURE

TEMPORARY TRACHEOSTOMY TUBE CARE:

- Proper care is necessary to prevent airway infection and occlusion.
- Inner cannulas are removed and cleaned or replaced at least every 24 hours or as needed. The inner cannula is soaked in 2% chlorhexidine solution and rinsed before replacement.
- Aseptic technique and sterile equipment should always be used when clearing the airways.
- Preoxygenation is performed for 2-5 minutes prior to suctioning to minimize hypoxemia.
- A sterile suction catheter no larger than half the size of the tracheostomy tube, with a blunt end and side suction holes, should be used. The catheter should be inserted without vacuum until obstruction is encountered, and then intermittent suction is performed while rotating the catheter as it is removed. The catheter should not remain in the airway for more than 15 seconds.
- Frequency of suctioning is determined by the amount of secretions produced by the animal and may range from every 15 minutes to 6-8 hours.
- Humidification or instillation of 0.1 mL/kg (minimum 1 mL, maximum 5 mL) sterile saline every 1-2 hours as well as coupage to aid in clearing secretions

CUFFED TUBES:

- Cuffs are inflated for airway sealing to prevent air leakage during ventilatory support.
- A stethoscope is placed over the trachea adjacent to the cuff to auscultate leaks.
- Air is removed in 0.25-mL increments until a small leak is detected at maximal airway pressure, which is considered minimal

occluding volume.
- Cuff deflation is not recommended unless there is evidence of difficulty achieving positive-pressure ventilation or airway pressure.

PERMANENT TRACHEOSTOMY CARE:

- Frequent cleaning of the opening (often every few hours for an indefinite period of time) is necessary to remove mucus, hair, and foreign material.
- Application of ointment, such as petroleum jelly, decreases mucosal drying and aids in removal of debris.
- Monthly clipping of the hair around the stoma to prevent matting.
- No swimming; avoidance of environments that may allow aspiration of particulate debris.

TEMPORARY TRACHEOSTOMY TUBE REMOVAL:

- The tube should be removed as soon as upper airway airflow has been reestablished. The original tube is removed and replaced with a smaller tube, the cuff is kept deflated, and respirations are observed for 10 minutes for appropriate ventilation through and around the smaller tube. If respiratory effort is satisfactory, the tube is then occluded, and the animal is observed for appropriate ventilation via oral-nasal respirations. If the animal continues to breathe comfortably, the tube is removed.
- The surgical site should be allowed to heal by second intention.
- For flap tracheostomy, the site should be débrided of granulation tissue and the flap sutured back into its original area, using interrupted sutures of absorbable suture to align the cartilages.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Oral/endotracheal intubation (seep. 1292): always attempted first in patients with acute-onset severe upper airway obstruction. Advantages over tracheostomy are speed of mobilization of the airway, technical simplicity, and minimal invasiveness. When such intubation is not possible (e.g., upper airway obstruction cannot be relieved, and patient is suffocating), tracheostomy is the procedure of choice.
- Oxygen supplementation (seep. 1318): sufficient as initial management in patients with mild upper airway obstruction but often inadequate as sole therapy in cases of moderate or severe obstruction.

AUTHORS: SARAH ALLEN, ANN MARIE MANNING

Tracheal Stent Placement

SYNONYM

Self-expanding tracheal stent placement, endo-/intraluminal tracheal stent placement

OVERVIEW AND GOAL

- Tracheal stent placement is most often utilized for the management of tracheal collapse in dogs. Tracheal stents may also be utilized for the management of tracheal neoplasia or other causes of tracheal obstruction. The following information will describe the technique for tracheal stent placement for the management of tracheal collapse.
- Conservative management of tracheal collapse is centered on medical management including cough suppressants, corticosteroids, and management of concurrent problems including but not limited to pneumonia, bronchitis, obesity, and heart disease.
- When conservative management cannot adequately control the clinical signs, medications are poorly tolerated, or quality of life is compromised, palliative interventions including surgery for prosthetic ring placement or image-guided tracheal stent placement must be considered. It is critical for the client to accept that these interventions are palliative and will not cure the problem. Instead, the goal of these procedures is a significant improvement in clinical signs and less reliance on medical therapies.
- Tracheal stent placement offers a rapid, minimally invasive, image-guided technique for the management of tracheal collapse.

INDICATIONS

- Tracheal collapse no longer amenable to conservative therapy as described above, involving extrathoracic and/or intrathoracic segments of the trachea
- Emergency management of dogs presented in crisis due to tracheal collapse that cannot be extubated due to recurrent airway obstruction
- Palliation of airway obstruction due to tracheal neoplasia

CONTRAINDICATIONS

- Dogs with tracheal collapse and concurrent laryngeal obstruction and/or dysfunction
- Dogs with severe mainstem bronchial collapse and only mild signs of tracheal collapse

EQUIPMENT, ANESTHESIA

- Fluoroscopic guidance is most often utilized for tracheal stent placement. Digital radiography systems have been employed but lack the “real-time” image acquisition that allows for optimal stent placement. Bronchoscopic guidance has been described.
- General anesthesia is required for tracheal stent placement. Most often, a premedication that includes an opioid for its antitussive effects is utilized. Propofol induction and inhalant anesthetic in oxygen are appropriate in most patients undergoing tracheal stent placement.
- Endotracheal tubes with a radiopaque marker extending to the tip of the tube
- Bronchoscope adapter allows for maintenance of the anesthetic circuit during tracheal stent deployment.
- Inventory of various lengths and diameters of self-expanding metallic stents. Most commonly utilized brands include the Vet-Stent Trachea (Infiniti Medical LLC, Malibu, Calif.) and the Wallstent or Ultraflex (Boston Scientific, Natick, Mass.). A complete inventory allows the veterinarian to transition smoothly from diagnosis to treatment during a single anesthetic event.
- Shortening charts for the brand of stent utilized. These charts provide information about stent length when the stent does not open to its nominal diameter.
- Standardized marking device (marker catheter) placed at the level of the trachea during imaging to allow for accurate measurements of the tracheal dimensions such that the effects of magnification can be minimized. The marker catheter has radiopaque markings that are spaced 1 cm apart.
- Two 0.035-in standard-stiffness, hydrophilic angled guide wires (HGW)
- Basin with 0.9% NaCl (500 mL)
- Software package for making measurements from fluoroscopic images or calculator for manual measurements

ANTICIPATED TIME

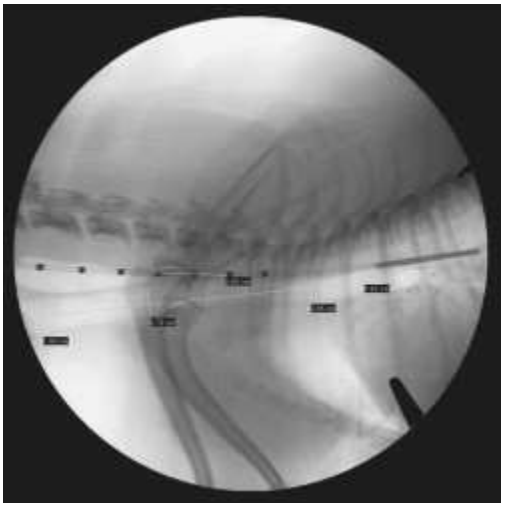
30 minutes

PREPARATION: IMPORTANT CHECKPOINTS

- Perform fluoroscopy on the patient with tracheal collapse prior to anesthesia induction to determine the length of the airway obstruction relative to anatomic landmarks. Note the presence of concurrent mainstem bronchial collapse.
- Perform a laryngeal exam at anesthetic induction. If structure or function is abnormal, these problems will require management.
- Perform tracheobronchoscopy to assess the severity of tracheal and mainstem bronchial collapse. Contrast with fluoroscopic assessment to definitively determine the location and severity of the tracheal collapse.
- Position the patient in lateral recumbency such that the airway is in a straight line from nose to carina.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Acute complications of tracheal stent placement are very rare when the technique is performed appropriately.
- Without a marker catheter or similar measurement standardization device placed at the level of the trachea, magnification could significantly (and adversely) affect measurements.
- Undersizing of the tracheal stent may occur if the trachea is not appropriately distended with positive pressure (20 cm H2O) during measurement. Undersizing results in stent migration.
- Foreshortening is a property of many woven self-expanding metallic stents. When constrained on the delivery system, the stent will appear longer than its nominal (relaxed) diameter. As the stent is deployed, it will shorten towards its nominal length. Conversely, if the stent does not fully expand within the trachea (as expected owing to oversizing), it will be longer than the nominal length. Failure to recognize the properties of the stent can result in choosing a stent longer or shorter than is needed.
- Tracheal stents may be accidentally deployed into the carina, endotracheal tube, or larynx if inappropriately sized for the length of the tracheal collapse.



TRACHEAL STENT PLACEMENT Measurements of the trachea are taken at the cervical, thoracic inlet, and intrathoracic trachea. Magnification is accounted for through calibration against the marker catheter.

PROCEDURE

- Position the endotracheal tube to terminate just beyond the larynx.
- Advance a saline moistened HGW down the esophagus.
- Advance a lubricated 5 Fr marker catheter over the HGW.
- Anesthetist is asked to hold a positive pressure breath at 20 cm H2O in the anesthetic circuit while a radiograph is acquired. This maneuver is critical to determine the maximal tracheal diameter. Measurements of the tracheal diameter are then performed in the cervical and intrathoracic trachea.
- The stent diameter should be chosen to exceed the maximal tracheal diameter (usually a cervical measurement) by 10%-20%. As an example, if the cervical trachea measures 10 mm and the thoracic trachea measures 8 mm, then a 12-mm stent is chosen (10%-20% larger than the maximal tracheal diameter).
- The length of the stent is chosen based on the known extent of the collapse as viewed fluoroscopically during spontaneous breathing. An actual measurement of this distance is also acquired (using anatomic landmarks) from the image taken during the positive pressure breath as described above. Example: if the trachea collapses from the thoracic inlet to just in front of the carina, this distance should be measured on the image acquired during the positive pressure breath. As a general rule, the collapsed area should be spanned by 1 cm on either side. If the entire trachea is to be spanned with the stent, the stent should extend from 1 cm caudal to the cricoid cartilage to 1 cm cranial to the carina.
- Consult shortening charts to determine the expected length of the chosen stent when it is deployed, recognizing that it will not open completely (because a diameter was chosen that was 10%-20% larger than the actual tracheal diameter).
- Advance a sterile, wet HGW down through the working channel of the bronchoscope adapter to the level of the carina.
- Flush the hub (cannula) and Y-piece (sheath) of the stent delivery system with sterile saline to facilitate smooth passage over the guide wire and deployment. Advance the stent over the guide wire and into position.

- In order to deploy the stent such that its position does not change, it is critical to smoothly move the hub and the Y piece (sheath) towards each other in equal increments. This maneuver should be practiced prior to attempting it in clinical patients. If the stent is only partially (50%-70%) deployed and the positioning is not optimal, the reverse motion may be performed to recon-strain the stent within the delivery system. The stent is then repositioned and redeployed. Note that the endotracheal tube may have to be withdrawn over the delivery system into the larynx during deployment to avoid deployment of the stent into the endotracheal tube.
- Withdraw the delivery system and guide wire under fluoroscopic guidance. The endotracheal tube may be very gently advanced into the lumen of the stent under fluoroscopic guidance to maintain a patent airway if needed.
- Acquire lateral and VD images to determine expanded stent dimensions.
- Remove marker catheter and guide wire from esophagus.

POSTPROCEDURE

- Hospitalize for one night after the procedure.
- Medical management is ongoing and will include a cough suppressant (hydrocodone, 0.22 mg/kg PO q 6-12 h), prednisone (0.2-0.5 mg/kg PO q 12 h × 14 days then gradual weaning to lowest possible dose), and an antibiotic effective against *Mycoplasma* spp.
- A dry cough is expected for approximately 1 month.
- If mainstem bronchus (MSB) collapse is present, coughing related to MSB collapse will persist. Persistent coughing should be treated aggressively. Persistent coughing may apply considerable forces to the stent and these forces may be involved in stent fracture.
- Complications that may be encountered in the weeks to years after stent placement include bacterial tracheitis, stent fracture, and granulation tissue formation within the stent.
- Recheck exam including radiography is usually performed 3-4 weeks after placement and then every 6 months thereafter.

ALTERNATIVES AND THEIR RELATIVE MERITS

Placement of extraluminal prosthetic rings is the most commonly utilized surgical technique for the management of tracheal collapse. This technique is most often utilized in dogs with extrathoracic tracheal collapse and collapse at the thoracic inlet. Extraluminal prosthetic ring placement is technically challenging and associated with significant surgical morbidity.

SUGGESTED READING

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AUTHOR: MATTHEW W. BEAL

Thoracoscopy

SYNONYM

Thoroscopy, video-assisted minimally invasive thoracic surgery

OVERVIEW AND GOAL

- A procedure for endoscopic exploration, biopsy and surgical procedures of the thorax (pericardial window, vascular ring surgery, patient ductus arteriosus ligation, thoracic duct ligation, lung lobectomy)
- Thoracoscopy is performed almost exclusively on dogs; size limitations limit visualization and safe manipulation in patients < 7 kg.
- Goals depend on the specific indication.
- Most commonly used for creating a pericardial window, allowing pericardial biopsy and alleviating recurrent cardiac tamponade; and for performing pleural biopsies (idiopathic pleural effusion)

INDICATIONS

- Recurrent pericardial effusion: common
- Idiopathic pleural effusion: occasional
- Idiopathic pneumothorax: rarely done, may be done as adjunctive step for surgical planning for thoracotomy
- Vascular ring anomaly: rarely done
- Patent ductus arteriosus: rarely done
- Idiopathic chylothorax: rarely done
- Primary pulmonary disease: rarely done
- Biopsy of mediastinal, pulmonary masses: rarely done

CONTRAINDICATIONS

- Clotting hemothorax
- Uncorrected bleeding tendencies (coagulopathies, thrombocytopenia, platelet function disorders)
- Small patients < 7 kg (approximately)

EQUIPMENT, ANESTHESIA

Equipment needs:

- Mechanical respirator (desirable but not absolutely required)
- Rigid endoscopic telescope (0○, 5-mm diameter scope)
- Endoscopic camera
- Xenon light source
- Video display
- Endoscopic trocars (5-mm diameter, one needs to be a minimum of 15 cm long)
- 12 Fr soft suction tubing (to use as chest tube)
- Endoscopic instruments. For basic pericardial window or pleural biopsy: 360○ rotatable Metzenbaum scissors, Babcock atraumatic grasping forceps, cup biopsy instrument
- Bipolar cautery (administered via the endoscopic instruments)
- Basic surgical supplies (towels, drapes, towel clamps, bowl, sterile saline, suction tubing)
- Basic surgical instruments (#12 blade, Brown-Adson forceps, needle holders)
- Suture (3-0 absorbable monofilament suture, 2-0 nonabsorbable monofilament suture)

Anesthesia:

- Premedication with opioid (e.g., hydromorphone, 0.1-0.2 mg/kg IM or IV) and benzodiazepine (e.g., midazolam, 0.2-0.4 mg/kg IV or IM); anticholinergic agents administered only as needed.
- Anesthetic induction with either propofol (e.g., 3-6 mg/kg slow IV to effect) or etomidate
- Anesthetic maintenance with oxygen/isoflurane inhalation
- Anesthetic monitoring including pulse oximetry, capnography, blood pressure and ECG monitoring

ANTICIPATED TIME

30 minutes or more, depending on procedure, experience of endoscopic team

PREPARATION: IMPORTANT CHECKPOINTS

- The entire ventral and lateral thorax and abdomen should be clipped and aseptically prepared to facilitate quick conversion to an open thoracotomy or laparotomy in an emergency setting.
- Be sure all video equipment is working properly prior to anesthetizing the patient.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Main complication is hemothorax.
- Inadvertent puncture of intraabdominal or intrathoracic structures
- Insufficient procedural analgesia will result in “bucking” of the ventilator (voluntary breaths, not coordinated with mechanical ventilation). This results in rapid oxygen desaturation.
- The rigid endoscopic telescope should be prewarmed in very warm saline for >5 minutes to avoid fogging of the lens.

PROCEDURE

Anesthetic induction and maintenance; dorsal recumbency; aseptic preparation of the whole ventral and lateral thorax; mechanical ventilation. The following describes the procedures using typical (nonselective two-lung ventilation) intubation:

- A Duke's trocar is used for inducing pneumothorax and to allow the threading of a 12 Fr suction tube into the left approximately 10th intercostal space (ICS) just dorsal to the mid-left thorax. After placing a three-way stopcock, additional room air is introduced into the thorax (≈10-20 mL/kg) to create a space in which to work, but being mindful of excess (e.g., overinsufflation causing inadequate oxygen saturation/hypoxemia).

Pericardial window:

- The long (=15 cm) trocar is introduced through an approximately 8-mm stab incision through the skin and subcutaneous tissues approximately 5 cm caudal and to the left of the xiphoid process. The trocar is introduced at a downward angle (i.e., craniodorsally) and then positioned parallel to the abdominal body wall and aimed toward the left shoulder joint. The trocar is removed and the endoscope placed through the trocar when the sensation of crossing the diaphragm is felt or at any point to monitor progress. The trocar is almost fully inserted when traversing the diaphragm of large dogs.
- Two additional instrument ports are placed on the left hemithorax in a triangulated orientation: approximately at the eighth ICS 5-10 cm below (dorsal to) the costochondral junction, and the seventh ICS 2-5 cm below the costochondral junction. Exact location depends on chest conformation and heart size. Prior to introduction of the trocars, the selected intercostal locations are palpated and visualized internally with the endoscope to decide if they are suitable, considering heart and lesion location. If so, an 8-cm stab wound is made into the skin to allow placement of a 5-mm endoscopic trocar with a closed valve.
- With ports created and instruments in place, the heart is visualized, and the forceps (in the cranial port) and scissors (in the caudal port) are visualized within the thorax. The pericardium is grasped. This may be difficult in patients with pericardial effusion at the time of the procedure or in patients with a very thick pericardial sac. The pericardial sac must be grasped—not just the fatty layer adjacent to it—to allow for adequate manipulation. One clue is the apex beat of the heart that can be felt on the forceps when the pericardium, but not pericardial fat, is contacted.
- When the pericardium is grasped, a small incision should be made into it, close to the tips of the forceps and with the pericardium tented up and away from the underlying heart. Care should be taken to not inadvertently clip any pulmonary tissue. Upon successful entry of the pericardium, fluid will be released in patients with pericardial effusion. The pericardium can then be repositioned with one jaw of the forceps within the pericardial sac for better control. The goal with a pericardial window is to make an opening approximately 4-5 cm in diameter for a large-breed dog. This will result from a small incision in a normal elastic pericardium, or a larger amount of tissue removed in multiple pieces when the pericardium is diseased and more rigid. The pericardial window should be made on the sternal surface of the heart to avoid the phrenic nerves coursing craniocaudally along the dorsal third of the pericardium.
- After the pericardial window is completed, the pericardium is tented to attempt a brief look inside the pericardial sac for mass lesions at the heart base. Tumors may be visualized in this position occasionally, but care should be taken to not induce arrhythmias or cause tumor bleeding. Tumor biopsy may be considered.
- Limited exploration of the thorax is made, looking for pulmonary metastatic lesions.
- The instrument ports are removed, using internal visualization of the sites for hemorrhage suggesting transection of an intercostal artery. Once adequate hemostasis is confirmed, the camera and transabdominal port are removed.
- The incisions are closed with a single cruciate suture in the subcutis (3-0 absorbable) and a single staple or cruciate suture in the skin. The chest tube is anchored with a modified Chinese-finger-trap suture (2-0 nonabsorbable suture). The air and any fluid are evacuated from the thorax. For local analgesia, bupivacaine (0.2 mL/kg) is diluted 1 : 1 with saline and placed into

the thorax through the chest tube, with the patient in left lateral recumbency. The chest tube is additionally secured with a light chest wrap.
- The patient is weaned off mechanical ventilation and recovered routinely.
- Postoperatively, hydromorphone is administered for a minimum of two doses as dictated by patient recovery.

For patients with idiopathic pleural effusion, the transabdominal approach is not used in order to avoid possible neoplastic contamination of the abdominal cavity:

- Induce pneumothorax as previously described.
- A short, 5-cm diameter endoscopic trocar is introduced in the approximately ninth intercostal space just dorsal to the costochondral junction. The camera is introduced and facilitates preliminary exploration of the thorax.
- A second trocar is introduced approximately in the fourth to fifth intercostal space just dorsal to the costochondral junction. Care is taken to introduce the trocar just through the chest wall, and then remove the sharp inner cannula to further introduce only the blunt outer cannula. The camera is positioned carefully across the mediastinum to the right hemithorax.
- A biopsy instrument is manipulated over (ventral to) the heart and toward the field of vision of the endoscope, using the transillumination of the skin as a guide to facilitate biopsy selection of the pleura. In patients with a normal-appearing parietal pleura, attempts are made to select biopsy samples from the diaphragmatic pleural reflection, which may be a place where occult mesothelioma cells may be easier to find.
- If the disease process appears lateralized, the procedure may be repeated on the other side of the thorax (from the right side to biopsy the left hemithorax).

Patients requiring more sophisticated surgical techniques and/or better surgical exposure to the heart base will require single-lung anesthesia using either a bronchial blocking tube (placed with bronchoscopic guidance into the surgical side) or selective intubation (using special endotracheal tubes and bronchoscopic guidance of the contralateral side).

POSTPROCEDURE

- Repeat chest tube aspirations to collect residual effusions/air and to monitor for bleeding complications.
- Oxygen supplementation until awake and ventilating fully
- Repeat opioid administration as needed for pain control.
- Nonsteroidal antiinflammatory drug (NSAID) generally started the first postoperative day after patient starts eating (unless contraindicated) and continued for 2-3 days (e.g., carprofen, 1 mg/kg PO q 12 h).
- Chest tube is removed 6-12 hours post procedure unless there are large amounts of ongoing fluid or air drainage.
- Monitor packed cell volume/total solids (PCV/TS) in patients with hemorrhagic pleural fluid.
- Patients generally discharged on postoperative day 1

ALTERNATIVES AND THEIR RELATIVE MERITS

For recurrent pericardial effusion:

- Repeat pericardiocentesis:
  - Advantage: technically easier, relatively inexpensive initially
  - Disadvantage: recurrent cardiac tamponade may be dangerous, frequent, unpredictable and cumulatively expensive.
- Thoracotomy:
  - Advantage: complete thoracic exploration, easier hemorrhage control, and facilitates full subtotal pericardectomy in patients with restrictive pericardial disease. Less specialized equipment required.
  - Disadvantage: patient morbidity, longer recovery time, higher cost. This is a particularly significant disadvantage in patients with malignant causes of disease.

AUTHOR: NANCY J. LASTE

Thoracocentesis

SYNONYM

Chest tap, pleural tap, thoracentesis (human medicine)

OVERVIEW AND GOALS

Rapid and technically easy procedure that is both therapeutic (removing air or fluid from the pleural space) and diagnostic (confirming the presence of air or fluid and obtaining samples of fluid for further analysis)

INDICATIONS

- Animals with respiratory distress (increased respiratory rate and effort) and dull lung sounds on auscultation
- Animals that present after trauma (hit by car, bite wounds, falling from height) and those that have undergone positive-pressure ventilation have increased risk for pneumothorax and may require thoracocentesis
- May also be used in the evaluation of smaller volume pleural effusions that are not causing significant clinical signs (diagnostic only; generally more challenging and greater risk of iatrogenic lung laceration)

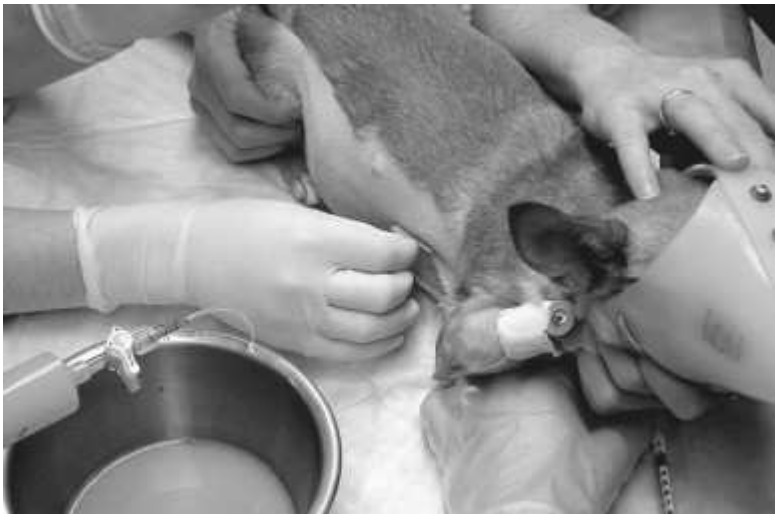
CONTRAINDICATIONS

Severe coagulopathy; fractious behavior

EQUIPMENT, ANESTHESIA

- Clippers
- Antiseptic scrub (e.g., chlorhexidine)
- Sterile gloves
- Large syringe (10-60 ml, depending on size of animal)
- Three-way stopcock
- Sterile extension tubing and a sterile needle, catheter, or butterfly catheter:
  - Large dogs: 1frac12;-inch (4-cm) needle or longer catheter, 18-22 gauge
  - Medium dogs, large cats: 1-inch (2.5-cm) needle or catheter, 20-22 gauge
  - Cats, small dogs: frac34;- to ⅞-inch (2- to 3.5-cm) butterfly needle, 22-23 gauge; 25-gauge needle can be used for diagnostic centesis.
- Bowl (for fluid)
- Red- and purple-top tubes for fluid sample submission
- Sedation may be needed depending on animal's disposition and stability.

THORACOCENTESIS Materials used for thoracocentesis for a cat or small dog. **A**, Sterile gloves. **B**, Butterfly-type catheter. **C**, Three-way stopcock. **D**, Large syringe. **E**, Bowl.



THORACOCENTESIS Thoracocentesis for removal of septic pleural effusion from a Chihuahua. A butterfly catheter with three-way stopcock and a 60-mL syringe are in use. The entry site is at the right seventh or eighth intercostal space, approximately at the level of the costochondral junction. An open muzzle is placed loosely for protection of staff without compromising the animal's respirations.

ANTICIPATED TIME

Procedure is relatively fast (<5 minutes) although can be prolonged (45-60 minutes) if a large amount of fluid or air (i.e., several liters) must be removed or if effusion is viscous, contains fibrin clumps or blood clots, or is compartmentalized.

PREPARATION: IMPORTANT CHECKPOINTS

- If the patient is in severe respiratory distress and has dull lung sounds on auscultation, thoracocentesis should be performed prior to thoracic radiographs.
- In cases where respiratory signs are less severe, thoracic radiographs can be used for confirming the presence of fluid or air in the pleural space prior to thoracocentesis.
- Discuss possible complications with owners.
- Rule out coagulopathy as likely cause of respiratory signs first (from history, physical examination, ± coagulation screening).
- Prepare equipment and supplies.
- Be able to keep animal relatively still, either with restraint or sedation, to minimize risk of iatrogenic pneumothorax or hemothorax.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Iatrogenic pneumothorax
- Intrathoracic hemorrhage
- Reexpansion pulmonary edema in situations of chronic pleural space disease
- Acute death from stress of restraint in animals with severe respiratory com promise

PROCEDURE

- Position animal, preferably in sternal recumbency or standing, but lateral recumbency is also acceptable for pneumothorax.
- Have assistant available to restrain animal or give sedation as needed:
    - Consider brief, quiet rest in oxygen cage if patient is anxious and extremely dyspneic (any restraint or sedation appears hazardous).
    - With mild or no dyspnea, butorphanol, 0.05-0.1 mg/kg IV may be used for light sedation; protocols for heavy sedation or anesthesia (e.g., propofol) will likely require intubation.
- Clip and aseptically prepare appropriate rib space:
    - If expecting fluid or if unsure (fluid versus air), clip at the seventh or eighth intercostal space (ICS), about at the level of the costochondral junction.
    - If expecting air, clip at the eighth or ninth ICS space, approximately one-third of the way down the chest.
- Wear sterile gloves for the insertion of the appropriate-size needle or butterfly catheter.
- Attach needle to syringe.
- Insert needle slowly, bevel side up, just cranial to the rib to avoid intercostal blood vessels. When through skin (beveled edge of needle is no longer visible), begin aspirating with a few tenths of 1 mL of negative pressure for a cat or small dog to 1-2 mL

of negative pressure for larger patients, respectively.

- Observe hub of needle for signs of fluid ("flashback"):
  - If a small amount of frank blood is aspirated or if lungs can be felt rubbing against needle, needle should be moved to a different location.
  - If large amount of blood is obtained, place 1-2 mL in a red-top tube to see if it clots.
  - Blood from hemothorax should not clot, whereas blood from the heart or a blood vessel should clot normally if the animal does not have significant coagulopathy.
- For any other fluid, aspiration should continue until no more fluid can be removed.
- Directing the needle ventrally, rolling the animal slightly to the side on which thoracocentesis is being performed, and reaspirating from a more ventral location can facilitate removal of as much fluid as possible.
- Ultrasound guidance can be beneficial in finding small fluid pockets for diagnostic thoracocentesis.
- Fluid is submitted for fluid analysis and cytologic examination and is saved for future bacterial culture and sensitivity (C&S) (aerobic, anaerobic) if cytologic examination suggests septic exudate.
- Aspiration of air will turn the tubing a slightly foggy white color as the warm air from the thoracic cavity encounters the room temperature tubing:
  - Aspirate until negative pressure is reached.
  - If negative pressure is never obtained, a tension pneumothorax may be present, and chest tubes with continuous suction are needed (see p. 1230).

POSTPROCEDURE

Monitor for returning signs of respiratory distress: could represent return of underlying pleural disease or iatrogenic pneumothorax or hemothorax.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Chest tube placement: continuous removal of fluid and air but is more invasive and is associated with a greater risk of iatrogenic complications.
- Diuretics: slow mobilization of modified transudates (e.g., heart failure) compared to thoracocentesis and ineffective with other causes (e.g., exudates, hemorrhage).

AUTHOR: LORI S. WADDELL

Urethrogram

SYNONYM

Retrograde urethrogram

OVERVIEW AND GOALS

- The urethra cannot be seen on survey radiographs; therefore, a positive-contrast examination is necessary for radiographic evaluation.
- Ultrasound can be used for seeing small portions of the urethra in the male; however, adequate diagnostic imaging of the entire urethra requires radiographic assessment with the injection of water-soluble organic iodide contrast material.
- A simple urethrogram is quick and easy to perform.
- A vaginocystourethrogram is usually performed in the female because of the difficulty of catheterizing the female urethra.

INDICATIONS

- Clinical signs:
  - Dysuria, stranguria
  - Difficulty catheterizing, urethral obstruction
  - Trauma to pelvis or os penis
  - Hematuria in a voided or catheterized urine sample but normal urine on cystocentesis
  - Hemorrhagic preputial discharge with a normal penile/preputial physical exam
- Differential diagnosis:
  - Urethral calculi (especially important with radiolucent calculi)
  - Urethral tear/rupture
  - Urethral stricture
  - Iatrogenic urethral trauma
  - Urethral neoplasia
  - Urethral fistula
  - Other urethral mucosal abnormalities
  - Penile or extrapelvic urethral disease
  - Congenital anomalies
  - Postoperative evaluation of urethra to assess patency and completeness of healing (prostatic disease with communication with urethra)
  - Evaluation of perineal or caudal abdominal masses

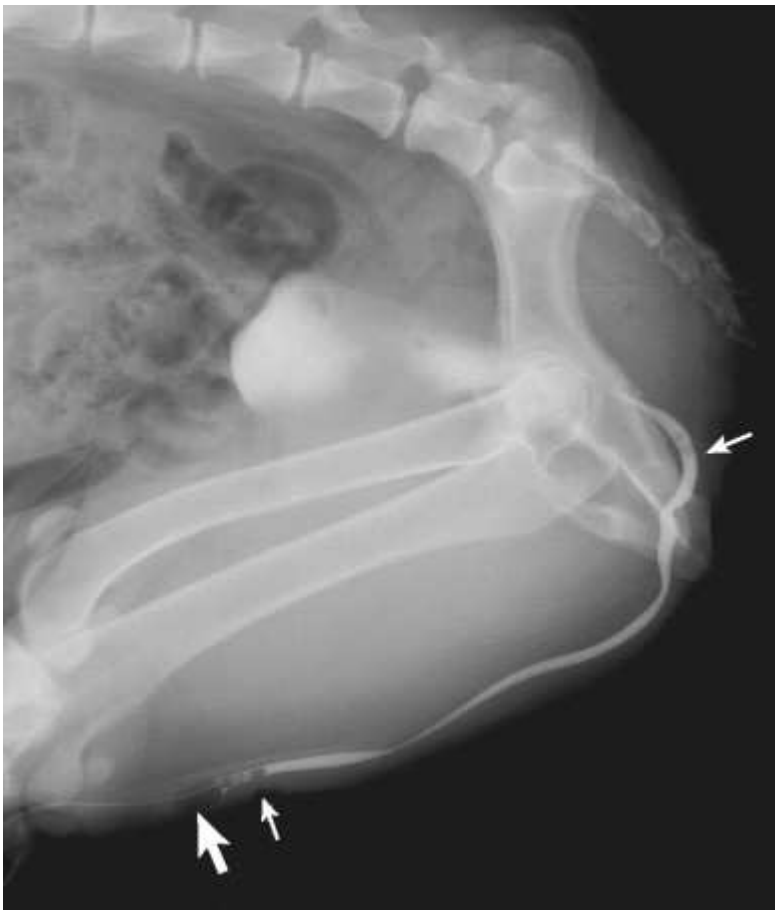
EQUIPMENT, ANESTHESIA

- Heavy sedation is often all that is needed to perform the study in male dogs. General anesthesia can be used if necessary. The male cat should be under general anesthesia for the study.
- Mild surgical scrub solution and gauze/sponges for disinfecting the penis prior to catheterization
- Urinary catheter (preferably with inflatable bulb), such as a Foley catheter
- Iodinated contrast medium (sodium iothalamate, sodium diatrizoate) or low-osmolar, nonionic, water-soluble iodines such as iohexol or iopamidol (180-300 mg iodine/mL most common) can be used.
- Sterile lubricating jelly
- Sterile syringe for contrast (e.g., 12 mL)
- Sterile syringe for inflating the catheter bulb.
- Sterile catheter adapter (Christmas-tree type)
- Sterile three-way stopcock
- Sterile saline
- Sterile gloves
- Enema bag/set
- Open-ended Tomcat catheter (e.g., 3.5 Fr) used for male cats

ANTICIPATED TIME

Approximately 20 to 30 minutes

PREPARATION: IMPORTANT CHECKPOINTS



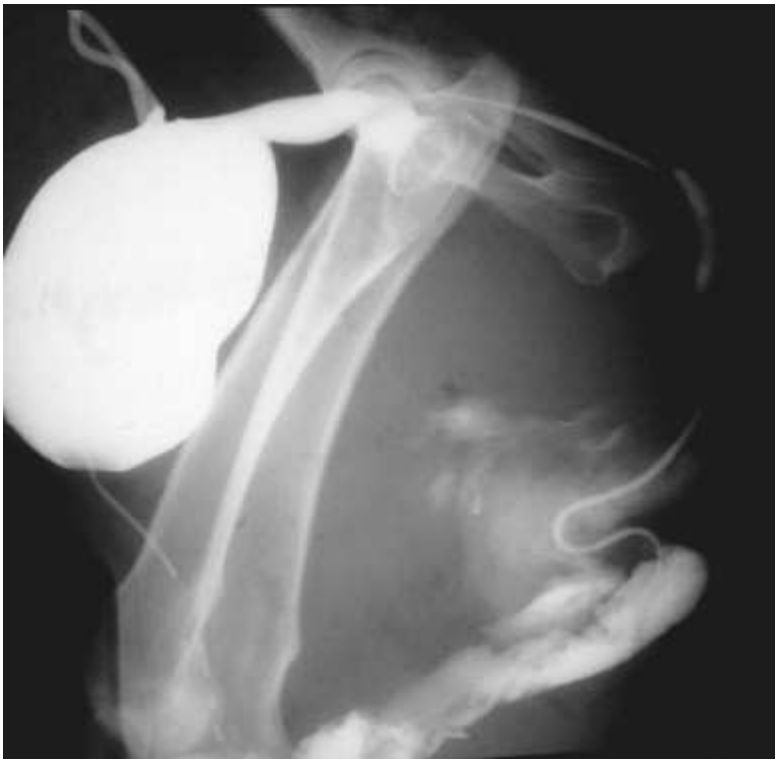
URETHROGRAM Normal male urethrogram (lateral view, cranial to left). Small air bubbles are seen in the pelvic urethra and distal urethra *(small arrow)*, and the inflated bulb of the Foley catheter is also seen *(large arrow)*.

- An enema is given approximately 2 hours prior to the study to ensure the removal of fecal material from the colon. Fecal material may compromise visualization of the urethra.
- Dilute organic iodinated contrast media to 50% solution with sterile saline.
- Sterile gloves should be worn from this point forward in the preparation.
- Draw 12 mL of diluted contrast material into the 12-mL syringe.
- Remove Foley catheter from packaging in a sterile manner, and remove guide wire.
- Attach catheter adapter (Christmas tree) to the open port (lumen) of the Foley catheter.
- Attach three-way stopcock to catheter adapter.
- Load syringe with air for inflating cuff later by drawing appropriate amount of air into the syringe (based on recommendation of Foley bulb size).
- Test integrity of the bulb.
    - Attach syringe containing air to side port (going to bulb, not the catheter lumen).
    - Infuse air into the bulb, filling it to the recommended level to ensure bulb is intact, and hold for a few seconds (test inflation).
    - Once it is clear the bulb will hold air, withdraw the air from the bulb back into the syringe.
- Attach syringe filled with contrast material onto the three-way stopcock, and fill the Foley catheter with contrast material. If this step is bypassed, air bubbles will be injected, resulting in a suboptimal study.
- Close the stopcock to the contrast material.
- In male cats, a sterile Tomcat catheter is used. Diluted contrast material is drawn into the syringe, and the syringe is attached directly to the catheter.

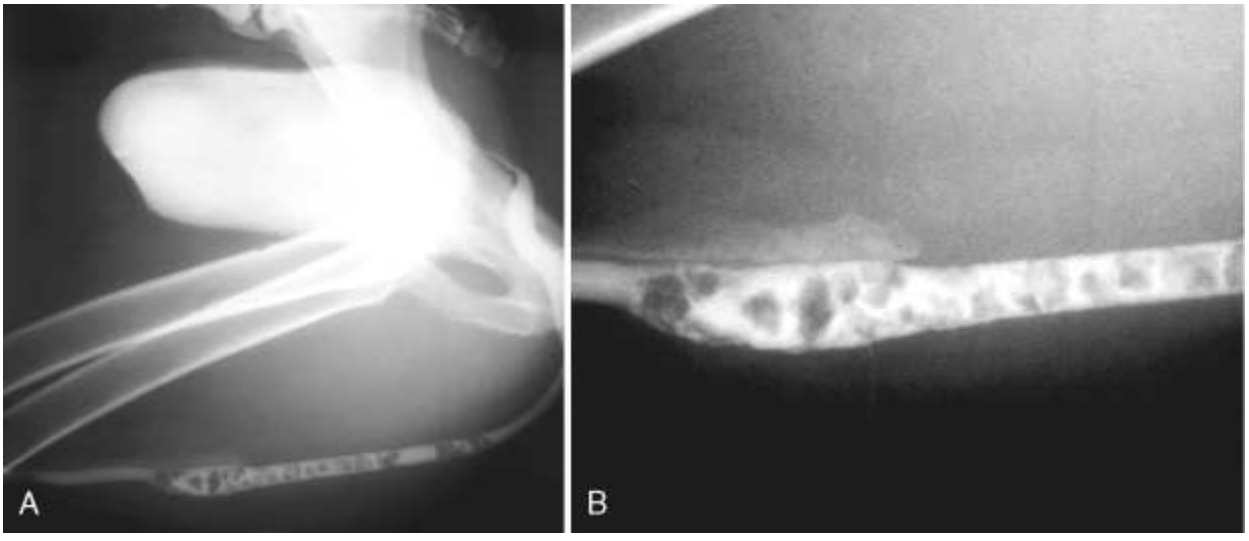
POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Trauma due to overdistention of the cuff.
- Rupture of the urethra; forceful injection when the urethra is obstructed can lead to urethral rupture.
- Mild transient submucosal hemorrhage secondary to balloon (try not to leave urethral catheter in place longer than 15 minutes [urethral trauma caused by local ischemia and mechanical trauma]).

- Urinary bladder-associated complications (hemorrhagic cystitis, catheter kinking or knotting in the bladder lumen, pulmonary air embolism, bladder rupture secondary to overdistention of the bladder) are extremely rare because the catheter remains in distal urethra.
- Bacterial contamination
- False results: catheter in too far (past lesion site), too little contrast, air bubbles
- Contrast media reactions (absorbed systemically though mucosa)
- Anaphylactic reactions: very rare



URETHROGRAM Male dog with urethral rupture (lateral view, cranial to left). Contrast material has leaked widely throughout the soft tissues of the prepuce as a result of the ruptured urethra (bottom right of image).



URETHROGRAM A, Male dog with urethroliths (lateral view, cranial to upper left). **B**, Zoomed view, showing multiple urethroliths.

PROCEDURE

- Preliminary caudal abdominal radiographs (lateral and oblique ventrodorsal) are made to set radiographic technique and ensure adequate preparation of the animal.
- The kilovoltage peak should be set between 65 and 75 to maximize contrast due to the photoelectric effect (K-edge of iodine).
- The animal should be placed in left lateral recumbency (to reduce the risk of air embolism going to the lungs).

- An assistant should then extrude the penis from the prepuce.
- The penis should be prepped with a mild surgical scrub solution.
- Sterile lubricating jelly is placed onto the tip of the Foley catheter.
- Insert Foley catheter into the distal urethra until the bulb can no longer be seen, but no further; the procedure is conducted with the catheter inserted into the urethra a very short distance to avoid passing beyond the site of the lesion.
- Inject air into bulb to inflate bulb, and then close the stopcock to maintain inflation. A suitable volume of air should meet little resistance and yet should provide enough of a seal to prevent backflow of contrast out the urethra during injection.
- Tug very lightly on the catheter to ensure the bulb seal is tight, and adjust bulb inflation (increase or decrease) accordingly.
- With the animal's hind limbs pulled forward to allow an unobstructed radiographic projection of the urethra, inject 12 mL of contrast material rapidly into the urethral catheter. Note: The contrast material should flow smoothly and with no resistance; if resistance is met, stop the injection and make the radiographic exposure.
- Make radiographic exposure just before the end of injection.
- Close the stopcock to the syringe that contained the contrast material, and remove syringe.
- Refill syringe with diluted contrast material in preparation for second injection, and reattach syringe to stopcock; open stopcock to allow contrast flow.
- Place animal in an oblique ventrodorsal position, and inject 12 mL of contrast rapidly. Note: Here again, the contrast material should flow smoothly and with no resistance; if resistance is met, stop the injection, and make the radiographic exposure.
- Make radiographic exposure just before the end of injection.
- For male cats, the animal preparation and survey radiographs are the same as the dog. The penis is extruded and prepped, a lubricated Tomcat catheter is placed just inside the distal urethra, and contrast material is injected.

POSTPROCEDURE

- Once the study is complete, the air should be removed from the Foley bulb before the catheter is withdrawn from the penis.
- If general anesthesia was used: routine anesthetic recovery.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Plain abdominal radiographs: inexpensive means to survey the urethra for radiopaque urethral calculi. Otherwise, contrast medium is needed to visualize the urethra and most of its associated lesions.
- Abdominal ultrasound: can be used for assessing a portion of the urethra; however, ultrasound should only be used in certain instances (e.g., proximal urethral disorders).

AUTHOR: LEEANN PACK

Urethral Obstruction (Feline): Medical Management

OVERVIEW AND GOALS

Complete urethral obstruction is a potentially life-threatening event, culminating in death from uremia within 2-5 days if untreated. Although most causes for urethral obstruction are intraluminal (e.g., urethral plugs, urethroliths, foreign material), mural (e.g., tumors, urethral strictures) and extramural causes (e.g., pelvic fractures, iatrogenic urethral ligation) result in identical clinical consequences.

INDICATIONS

- Matrix-crystalline urethral plugs (common)
- Urethroliths (common)
- Blood clots
- Intraurethral foreign bodies (i.e., buckshot)

EQUIPMENT, ANESTHESIA

- The type and degree of sedation/anesthesia vary depending on patient status and veterinarian's preference.
- Cardiovascular stabilization:
  - Heating pad
  - IV catheter
  - Lukewarm IV replacement fluids
  - Sodium bicarbonate
  - Insulin and glucose to manage hyperkalemia
  - Calcium gluconate to manage hyperkalemia; see p. 556.
- Decompressive cystocentesis:
  - Sterile 1½-inch, 22-gauge needle
  - IV extension tubing
  - Three-way stopcock
  - Several syringes (size: 3-20 mL)
- Retrograde urethral flushing:
  - Sterile isotonic nonirritating solutions (e.g., normal saline, lactated Ringer's solution)
  - Sterile open-ended catheter (e.g., Minnesota olive tip catheter)
  - IV extension tubing
  - Large syringe (12-35 mL)
  - Moistened gauze sponges
- Indwelling urinary catheter placement:
  - Nonabsorbable suture and needle holders
  - Soft, flexible, inert sterile urinary catheter
  - Elizabethan collar

ANTICIPATED TIME

About 20 minutes to 1 hour

PREPARATION: IMPORTANT CHECKPOINTS

- Ensure cardiovascular stabilization prior to general anesthesia or urethral flushing.
- Prevalence of potentially life-threatening abnormalities in cats with urethral obstruction:
  - Hypothermia (<100°F [37.8°C]) = 39%
  - Acidemia (pH <7.2) = 16%
  - Bradycardia (<149 bpm) = 12%
  - Hyperkalemia (>8 mEq/L) = 12%
  - Hypocalcemia (<0.8 mmol/L) = 6%-12%
- Inform owners of the possibility of urinary bladder rupture and guarded short-term prognosis with and without therapy.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Cats with urethral obstruction and cardiovascular collapse rarely show overt signs referable to the urinary system at the time of presentation. Therefore, assessment of urinary bladder size (i.e., palpation or medical imaging) is essential to avoid overlooking urethral obstruction as the primary cause for cardiovascular or respiratory distress.
- Survey radiography is essential to verify, localize, and search for the underlying cause of obstruction; radiographs should be performed early in the diagnostic process prior to initiation of therapy. Nonobstructed dysuric cats usually have small urinary bladders.
- Unsuccessful transurethral insertion of urinary catheters is an unreliable and sometimes unsafe (i.e., urethral tear, rupture, and subsequent stricture) method of confirming and localizing urethral obstruction.
- Caustic, strongly acidic flushing solutions are contraindicated.

PROCEDURE

- Sedate or anesthetize the patient.
- To fragment urethral plugs, gently massage the distal urethra and cautiously compress the urinary bladder with the goal of promoting expulsion of plugs. This is easy to perform but not commonly effective.
- Decompressive cystocentesis:
    - Attach a 1½-inch, 22-gauge needle, IV extension tubing, and a three-way stopcock. Then use a large-volume syringe (20-35 mL) to remove urine from bladder inserting the needle at the center of the bladder with the needle directed obliquely (caudodorsally).
    - By using the IV extension tubing and three-way stopcock between the needle and syringe, the urinary bladder will not have to be repunctured to empty a syringe full of urine.
    - Excessive digital pressure should not be applied to the bladder wall while the needle is in the lumen, to prevent urine from being forced around the needle into the peritoneal cavity.
    - Attempting complete evacuation of the bladder lumen is undesirable, because the sharp point of the needle may then damage the bladder wall; the authors recommend that 5-15 mL of urine remain in the bladder.
    - Properly performed cystocentesis should not contribute to bladder rupture. Any excessive manipulation of a devitalized, overdistended bladder wall may promote rupture.
    - Advantages of decompressive cystocentesis:
        - Obtaining urine sample for analysis and culture
        - Temporarily halting the adverse effects of obstruction
        - Reducing intraluminal bladder pressure to facilitate retropulsion
        - Reducing pain associated with bladder overdistention
    - Disadvantages of decompressive cystocentesis:
        - Potential extravasation of urine into peritoneal cavity
        - Bladder wall trauma
- Flushing plug contents out the external urethral orifice:
    - Attach open-ended catheter, IV extension tubing, and large (35-mL) fluid-filled syringe in that order. Displace air in the tubing by filling tubing and catheter with fluid from the syringe prior to insertion in the urethra.
    - Insert tip of catheter into distal urethral opening.
    - Flush a large quantity of sterile isotonic solution into the urethral lumen, allowing it to reflux out the external urethral orifice.
    - Subsequent application of steady but gentle digital pressure to the bladder wall may result in expulsion of a urethral plug.
- Retrograde urethral flushing (to propel intraluminal contents into urinary bladder):
    - Attach open-ended catheter, IV extension tubing, and fluid-filled syringe (3-20 mL) in that order. Displace air in the tubing by filling tubing and catheter with fluid from the syringe prior to insertion in the urethra.
    - Insert tip of catheter into distal urethral opening.
    - With a moistened gauze sponge, occlude the distal urethra around the catheter.
    - Pull the penile urethra caudally to extend it parallel to the vertebral column.
    - Flush fluid vigorously by emptying syringe.
    - Repeat urethral flushing if needed while also remembering to repeat decompressive cystocentesis if bladder lumen becomes distended with flushing solution.
    - The greatest pressure to retrograde hydropropulse is achieved with the smallest syringe.

URETHRAL OBSTRUCTION (FELINE): MEDICAL MANAGEMENT Assembled catheter, IV extension tubing, and syringe to facilitate removing obstruction in the urethra of cats.

POSTPROCEDURE

In some cases, radiographs are indicated to verify return of uroliths into urinary bladder.

INDWELLING TRANSURETHRAL CATHETERS

- Not always indicated
- When indicated, 3 Fr or 5 Fr flexible feeding tubes composed of material that minimizes foreign body inflammatory response are preferred.
- To minimize urethral trauma, avoid open-end catheters with sharp stylets.
- Indications:
    - Inadequate/poor urine stream following urethral flushing:
        - Urethral spasm/swelling (~1-3 days)
        - Excessive urinary precipitates (~1-2 days)
    - Assist correction of postrenal azotemia (~1-2 days).
    - Promote recovery of detrusor contractility (~1-5 days).
    - Promote repair of urothelial urethral tear (~3-10 days).
- Care and management:
    - Place as atraumatically and cleanly as possible.
    - Maintain a closed collection system.
    - Remove indwelling catheters as soon as possible.
    - If urine is initially sterile, avoid antimicrobial therapy until catheter is removed.
    - If urine is initially infected, treat the infection (see p. 276).
    - Treat potentially life-threatening infections.
    - Do not give the cat corticosteroids.
- Pain medication (buprenorphine, butorphanol, etc.) is indicated for a short duration (1-4 days). Nonsteroidal antiinflammatory drugs (NSAIDs) are contraindicated in cats with compromised renal function or dehydration.
- Prevent negative fluid balance associated with postobstructive diuresis by giving parenteral fluids.
- Not recommended: routine use of urethral smooth-muscle relaxants (e.g., phenoxybenzamine, prazosin), urethral antispasmodics (e.g., propantheline, oxybutynin), and parasympathomimetics (e.g., bethanechol) following urethral manipulation. The efficacy of these agents has not been established by properly controlled clinical trials.

URETHRAL OBSTRUCTION (FELINE): MEDICAL MANAGEMENT Perineum of an anesthetized cat undergoing medical management of urethral obstruction. Cat is in dorsal recumbency; cranial is to right of photo. Occluding the distal urethra around the catheter and pulling the urethra caudally and dorsally to displace urethral kinking will facilitate retrograde flushing of plugs and stones into the urinary bladder.

ALTERNATIVES AND THEIR RELATIVE MERITS

Urethrostomy may be indicated if obstruction cannot be corrected. Contrast urethrography is indicated to localize the site(s) of obstruction and to select the location of surgery.

AUTHORS: JODY P. LULICH, CARL A. OSBORNE

Urethral Obstruction (Canine): Medical Management

OVERVIEW AND GOALS

Complete urethral obstruction is a potentially life-threatening event, culminating in death from uremia within 2-5 days if untreated. Although most causes for urethral obstruction are intraluminal (e.g., urethroliths, foreign material, urethral plugs), mural (e.g., tumors, urethral strictures) and extramural causes (e.g., pelvic fractures, iatrogenic urethral ligation) and functional disorders (e.g., detrusorsphincter dyssynergia) result in identical clinical consequences.

INDICATIONS

- Urethroliths (common)
- Urethral/prostatic neoplasia
- Blood clots
- Intraurethral foreign bodies
- Matrix-crystalline urethral plugs (uncommon)

EQUIPMENT, ANESTHESIA

The type and degree of sedation/anesthesia varies depending on patient status and veterinarian's preference.

- Cardiovascular stabilization:
  - Heating pad
  - IV catheter
  - Warm IV replacement fluids
  - Sodium bicarbonate
- Decompressive cystocentesis:
  - A sterile 1½-inch, 22-gauge needle
  - IV extension tubing
  - Three-way stopcock
  - Large syringe (20-60 mL)
- Retrograde urethral flushing:
  - Sterile isotonic nonirritating solutions (e.g., normal saline, lactated Ringer's solution)
  - Long, flexible large-bore sterile catheter (e.g., 8 Fr, 22-inch red rubber feeding tubes)
  - Large sterile syringe (12-60 mL)
  - Moistened gauze sponges
- Indwelling catheter placement:
  - Nonabsorbable suture and needle holders
  - Soft, flexible, inert sterile urinary catheter

ANTICIPATED TIME

About 20 minutes to 1 hour

PREPARATION: IMPORTANT CHECKPOINTS

- Inform owners of the possibility of urinary bladder rupture and guarded short-term prognosis with and without therapy.
- Inform owners that in many cases, surgery or lithotripsy will be needed to correct intraluminal causes for obstruction; urethral stenting may be needed to manage mural and extramural neoplasia

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Survey radiography is essential to verify, localize, and search for the underlying cause of obstruction. Therefore, radiographs should be obtained early in the diagnostic process prior to initiation of therapy.
- Unsuccessful transurethral insertion and passage of urinary catheters is an unreliable and sometimes unsafe (i.e., urethral tear, rupture, and subsequent stricture) method of confirming and localizing urethral obstruction.

PROCEDURE

- Sedate or anesthetize animal.
- Decompressive cystocentesis:
  - Attach a 1.5-inch, 22-gauge needle, IV extension tubing, and three-way stopcock; then use a large-volume syringe (20-60 mL) to remove urine from bladder, entering at the center of the bladder with the needle directed obliquely (caudodorsally).
  - By using the IV extension tubing and three-way stopcock between the needle and syringe, the urinary bladder will not have to be repunctured to empty a syringe full of urine.
  - Excessive digital pressure should not be applied to the bladder wall while the needle is in the lumen, to prevent urine from being forced around the needle into the peritoneal cavity.
  - Attempting complete evacuation of the bladder lumen is undesirable because the sharp point of the needle may then damage the bladder wall. We recommend that 10-15 mL of urine remain in the bladder.
  - Cystocentesis should not contribute to bladder rupture. Excessive manipulation of a devitalized, overdistended bladder is usually the cause of bladder rupture.
  - Advantages:
    - Obtaining a pretreatment urine sample for analysis and culture
    - Temporarily halting the adverse metabolic consequences of obstruction
    - Reducing intraluminal bladder pressure to facilitate retropulsion
    - Reducing pain associated with bladder overdistention
  - Disadvantages:
    - Potential extravasation of urine into peritoneal cavity
    - Bladder wall trauma
- Retrograde urethral flushing:
  - Lubricate around the urethroliths:
    - Fill one 12-mL syringe with 5 mL of saline and another 12-mL syringe with 5 mL of sterile water-soluble lubricant.
    - Attach these two syringes with a three-way stopcock.
    - Mix the contents of both syringes by emptying one syringe into the other several times.
    - After inserting a urethral catheter, inject 3-8 mL of mixture to lubricate around uroliths.
    - This step is not always necessary.
  - Insert a lubricated large-bore flexible catheter into the distal urethra. The tip of the catheter should remain distal to urethroliths.
  - Occlude pelvic urethra proximal to urethroliths: insert a gloved index finger into the rectum, and occlude the urethral lumen by compressing the urethra against the floor of the bony pelvis.
  - Occlude distal urethra: with a moistened gauze sponge, occlude the distal urethra by compressing the distal tip of penis around the catheter.
  - Forcefully flush fluid through catheter:
    - Fill a large syringe (20-60 mL) with sterile isotonic solution (e.g., saline, lactated Ringer's solution, etc.). The normal bladder holds approximately 7-11 mL/kg of the patient's weight.
    - With the syringe attached to the catheter, turn it upside down, and place the top of the plunger against the tabletop.
    - Hold the syringe by the barrel, and forcefully push it down over the plunger with the goal of rapidly and forcefully emptying the syringe and subsequently dilating the urethral lumen with saline.
  - Relieve occlusion of pelvic urethra: once the urethra becomes dilated, digital pressure applied to the pelvic urethra (but not the penile urethra) should be rapidly released.
  - Continue flushing:
    - Continue flushing fluid through the catheter and urethral lumen to propel urethroliths into the urinary bladder. Use caution not to over-distend the bladder lumen with saline.
    - If the technique is repeated, accumulation of saline in the bladder lumen necessitates repeating decompressive cystocentesis.
  - To perform this technique in female dogs, insert the index finger into the vagina, and apply digital pressure and occlude the distal urethra over the catheter at the urethral papilla. Inserting the index finger in the rectum and applying digital pressure over the catheter in the pelvic urethra can also achieve distal urethral occlusion.

POSTPROCEDURE

- Medical imaging:
  - Radiography provides an appropriate method of assessing whether all radiopaque uroliths have been flushed into the bladder lumen.
  - Transurethral catheterization is not a reliable method of verifying that all uroliths have been flushed out of the urethra.
- Pain medication (i.e., butorphanol, hydromorphone, etc.) is indicated for a short duration (1-2 days). Nonsteroidal antiinflammatory drugs (NSAIDs) are contraindicated in animals with compromised renal function or dehydration.
- Prevent negative fluid balance associated with postobstructive diuresis by administering parenteral fluids.

ALTERNATIVES AND THEIR RELATIVE MERITS

To minimize surgical disfigurement of the urethra (e.g., urethrotomy, urethrostomy), consider lithotripsy to shatter obstructing urethroliths if retrograde urohydropropulsion is not successful.

AUTHORS: JODY P. LULICH, CARL A. OSBORNE

Upper Gastrointestinal Radiographic Contrast Series

SYNONYMS

Barium series, UGI

OVERVIEW AND GOALS

- To identify abnormalities of the stomach and/or small intestinal tract. Morphologic and/or functional abnormalities may be identified.
- The upper gastrointestinal (UGI) radiographic contrast series is most commonly performed using barium, which gives the best mucosal detail and therefore the best evaluation of morphology. The study may be performed with an iodinated contrast agent; these do not give good mucosal detail and are most useful for evaluating gastrointestinal (GI) integrity and patency.

INDICATIONS

- Severe or protracted vomiting
- Hematemesis or melena
- Abdominal pain
- Abnormalities of survey radiographs requiring further investigation
- Determine location of GI structures (i.e., herniation)

CONTRAINDICATIONS

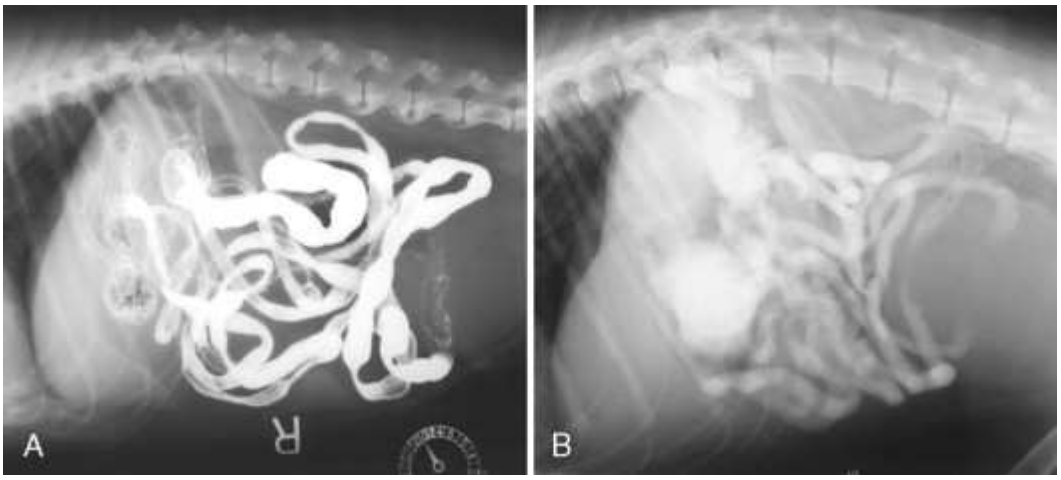
- Survey radiographic evidence of perforation:
  - If perforation is suspected, the study may be performed with an iodinated contrast agent; however, because of their relatively poor opacity, iodinated contrast agents may fail to demonstrate GI leakage.
- Survey radiographic evidence of obstruction:
  - Not an absolute contraindication, but the study is not needed for diagnosis.
- Projectile vomiting:
  - Not an absolute contraindication, but the risks involved in performing the study may outweigh the potential benefits.

EQUIPMENT, ANESTHESIA

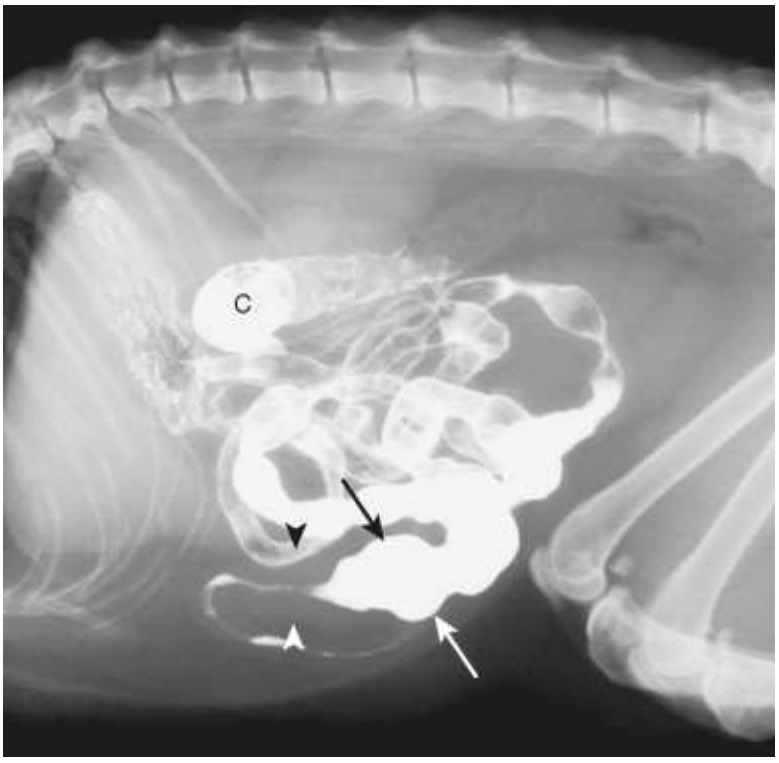
- Contrast agent:
  - Liquid barium (30% weight/volume):
    - 10 mL/kg PO
    - In very obese patients, it may be preferable to dose for desired/lean body weight, not actual weight.
  - Ionic iodinated contrast agent:
    - Gastrografin/Renografin: 2-7 mL/kg PO; total dose not to exceed 50 mL
    - Gastrografin is a contrast agent that was marketed for oral use only; this product is no longer available. Renografin is a contrast agent used for IV injection and may be given orally instead of Gastrografin.
  - Nonionic iodinated contrast agent:
    - Iohexol (Omnipaque):
      - 10 mL/kg PO of diluted iohexol (240-875 mg I/mL, diluted 1:1 to 1:3 with tap water)
      - The greater the iodine concentration of the iohexol, the better the mucosal detail.
      - Administration of undiluted iohexol causes vomiting.
- Syringes for contrast administration
- Orogastric tube of the appropriate size
- X-ray unit
- Protective clothing (lead aprons, gloves, thyroid shields) for personnel
- Paper towels or similar material for cleanup of barium on animal and x-ray table
- Drugs for restraint (used only if absolutely necessary). The following agents have been shown to have the least effect on motility and should be used if a motility disorder is suspected. The effect on gastrointestinal motility of other newer sedative drugs has not been proven, so these agents cannot be recommended:
  - Dogs: acepromazine, 0.055-0.1 mg/kg IV; avoid if animal is elderly or systemically ill.
  - Cats: midazolam, 0.44 mg/kg; ketamine, 13.2 mg/kg:
    - These drugs are given in separate syringes IM approximately 20 minutes prior to the procedure. If a motility abnormality is not of concern (i.e., determining if obstruction is present), the following combination is recommended for cats; this will give better and more consistent restraint than the midazolam/ketamine combination. The following drugs are also given IM approximately 20 minutes prior to the procedure and

should be avoided if animal is elderly or systemically ill:

- Acepromazine, 0.22 mg/kg
- Ketamine, 13.2 mg/kg



UPPER GASTROINTESTINAL RADIOGRAPHIC CONTRAST SERIES A, Right lateral radiograph obtained 30 minutes after administration of liquid barium. Note high opacity of contrast agent and good mucosal detail. **B**, Right lateral radiograph obtained 30 minutes after administration of iohexol. Contrast agent is much less opaque, and mucosal surface is poorly defined.



UPPER GASTROINTESTINAL RADIOGRAPHIC CONTRAST SERIES Right lateral radiograph obtained 2 hours after administration of liquid barium. Distended segment of small intestine *(arrows)* suddenly narrows at an area of intramural thickening *(arrowheads)* caused by a circumferential soft-tissue mass in this cat. Barium is present in cecum (C), indicating bowel is patent.

ANTICIPATED TIME

- About 6 hours to complete the study (barium); actual time spent performing the study is approximately 1.5 hours.
- About 2-3 hours to complete the study (iodinated contrast agents); actual time spent performing the study is approximately 1 hour.
- ± Additional film at 24 hours post contrast administration

PREPARATION: IMPORTANT CHECKPOINTS

Empty GI tract (see Common Errors, below):

- Fasting to empty the stomach
- Remove excess fluid from stomach via tube if present
- Enema: only if colon is very full

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

Complications:

- Vomiting and aspiration of barium: if the animal has projectile vomiting and/or radiographic evidence of severe gastric fluid retention, the risks involved in performing the UGI radiographic contrast series may outweigh the potential benefits.
- Aspiration of iodinated contrast agents: ionic iodinated contrast agents can cause severe (and fatal) pulmonary edema if aspirated. These agents should be administered only via orogastric intubation.

Common errors:

- Administration of too low a volume of barium:
  - This is the most common technical error in this study (occurs more often than administration of the proper volume of barium)
  - Accurate evaluation of gastric emptying time is not possible, and full distension of the intestinal segments is not achieved if the volume of barium is too low. This can lead to serious misinterpretation of the study.
- Failure to empty the stomach of food prior to administration of barium:
  - The presence of food in the stomach makes accurate assessment of gastric emptying time impossible.
- Administration of barium prior to abdominal ultrasound or endoscopy may interfere with visualization; however, sequence of testing may make this unavoidable.

PROCEDURE

- Obtain survey (plain) right lateral and ventrodorsal radiographs of the abdomen.
- Administer contrast:
  - Barium dosage: 10 mL/kg PO. If too low a volume of barium is used, artifactual delayed gastric emptying can occur and distension of the intestinal segments will not be achieved. Administration via orogastric tube is preferred, but barium may be administered per os; *or*
  - Iodinated contrast agent: Gastrografin/Renografin, 2-7 mL/kg PO, with total dose not to exceed 50 mL; *or* iohexol, 10 mL/kg PO of diluted iohexol (240-875 mg I/mL diluted 1:1 to 1:3). Administration via orogastric tube is necessary with the use of ionic iodinated agents (to avoid aspiration); administration via orogastric tube is preferred with the use of nonionic iodinated contrast agents.
  - Obtain films:
    - Film sequence and views for barium. This sequence is a routine timetable. The timing of films can be altered as the study progresses, based on what is found in the study:
      - Immediate: right and left lateral, ventrodorsal and dorsoventral
        - The dorsoventral view provides better evaluation of the body and pyloric region of the stomach and it is important to obtain this view in the immediate film series. However, it can be difficult to position the patient for a dorsoventral view, and ventrodorsal views are preferred for the remainder of the film series.
      - 30 minutes: right lateral and ventrodorsal
      - 60 minutes: right lateral and ventrodorsal
      - 90 minutes: right lateral and ventrodorsal
      - 3 hours: right lateral and ventrodorsal
      - 5 hours: right lateral and ventrodorsal
      - ± 24 hours: right lateral and ventrodorsal
    - Film sequence and views for iodinated contrast agents. This sequence is a routine timetable. The timing of films can be altered as the study progresses, based on what is found in the study:
      - Immediate: right and left lateral, ventrodorsal and dorsoventral:
        - The dorsoventral view provides better evaluation of the body and pyloric region of the stomach, and it is important to obtain this view in the immediate film series. However, it can be difficult to position the patient for a dorsoventral view, and ventrodorsal views are preferred for the remainder of the film series.
      - 15 minutes: right lateral and ventrodorsal
      - 30 minutes: right lateral and ventrodorsal
      - 60 minutes: right lateral and ventrodorsal
      - 2 hours: right lateral and ventrodorsal
- By definition, the UGI radiographic contrast series is considered to be complete when contrast has both emptied from the

stomach and has entered the large intestine.
- Films may be taken beyond this point if an abnormality has been noted during the examination. For example, in an animal with retention of barium in the stomach, the UGI radiographic contrast series should be continued until the stomach empties or an abnormality to account for the barium retention is noted.
- If an abnormality (i.e., obstruction) is identified, the study is considered to be complete even if barium is still present in the stomach and/or has not entered the large intestine.

POSTPROCEDURE

- There are no postprocedure considerations for a routine UGI radiographic contrast series other than informing the client that stools may have a paler color for several defecations after the procedure.
- The findings of the UGI radiographic contrast series may lead to an additional diagnostic test such as exploratory laparotomy or endoscopy.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Endoscopy:
  - Endoscopy allows visualization of the mucosal surface of the stomach and duodenum and allows tissue biopsies to be performed.
  - However, endoscopy does not evaluate the entire small-intestinal tract and requires the use of general anesthesia.
- Abdominal ultrasonography:
  - Ultrasonography is rapid and noninvasive and does not involve ionizing radiation.
  - However, ultrasonographic evaluation of the GI tract can be severely limited by gas in the tract. Interpretation of ultrasound images of the GI tract requires an experienced sonographer, and many GI disease processes do not cause significant changes in the ultrasonographic appearance of the intestine.
- Exploratory laparotomy:
  - Allows assessment of the entire length of the GI tract and full-thickness gastric and intestinal biopsies. However, general anesthesia, invasiveness, and recovery/incision healing time make laparotomy a second-order diagnostic modality after lesser invasive evaluations such as plain radiography, UGI radiographic contrast series, ultrasonography, and/or endoscopy.

SUGGESTED READING

O'Brien T: Esophagus. In O&#65533;Brien T, editor: Radiographic diagnosis of abdominal disorders in the dog and cat: radiographic interpretation, clinical signs, pathophysiology. Davis, Calif, 1981, Covell Park Vet Company, p 141.

AUTHOR: PATRICIA L. ROSE

Vomiting, Induction of

SYNONYM

Emesis, induction of

OVERVIEW AND GOAL

Deliberate induction of vomiting for elimination of ingested noxious materials

INDICATIONS

Confirmed or suspected ingestion of toxic substance

CONTRAINDICATIONS

- Ingestion of alkaline toxic substances: risk of reflux esophagitis
- Ingestion of oily substances: risk of aspiration pneumonia
- Ingestion of sharp or pointed foreign bodies: risk of gastrointestinal (GI) tract perforation
- Ingestions having occurred too long in the past to be effectively offset by vomiting (time is dependent on substance ingested)
- Sedated, mentally depressed, or comatose animal: risk of aspiration pneumonia

EQUIPMENT, ANESTHESIA

- No anesthesia; the procedure is performed awake.
- 3% hydrogen peroxide (Note: Not 30% hydrogen peroxide used for hair bleaching)
- Sterile or nonsterile syringe
- Gastric gavage tube and oral speculum/mouth gag (rarely necessary)
- Alternative for dogs or cats: syrup of ipecac
- Alternative for cats: xylazine, 0.44 mg/kg IV, IM, or SQ single dose

ANTICIPATED TIME

About 5 minutes

PREPARATION: IMPORTANT CHECKPOINTS

- Identification of the ingested substance is essential. Note: Vomiting should not be induced unless a known substance was ingested or exam findings are indicative of such an ingestion (e.g., antifreeze on muzzle, lead pellets in stomach on radiograph).
- If the animal has not eaten recently, canned food corresponding to approximately half a meal can be fed prior to induction of emesis to avoid nonproductive vomiting/dry heaving. If no appetite, simply proceed with emesis.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Aspiration pneumonia: monitor for dyspnea, coughing, fever, and lethargy postemesis. If present, proceed to thoracic radiographs.
- Gastric irritation: common and usually benign
- Esophagitis: usually benign and self-resolving if secondary to vomiting induction alone; may be more serious (e.g., esophageal perforation or stricture) if caused by ingestion of corrosive substance or lacerating foreign body

PROCEDURE

- Calculate appropriate dose of emetic (choose one):
  - Hydrogen peroxide 3%: 0.25-0.5 mL/kg PO once
  - Syrup of ipecac: 2-6 mL total dose PO once
  - Xylazine: 0.44 mg/kg IV, IM, or SQ once (cats only)

- Note: 1 teaspoon = 5 mL; 1 tablespoon = 15 mL; 1 fluid ounce = 28 mL
- Administer once. For orals (hydrogen peroxide or ipecac), it is best to administer via cheek pouch:
    - With animal in sitting position, elevate animal's chin (mouth closed) so neck is extended.
    - Insert tip of syringe into canthus of lips on one side (corner of mouth), with mouth still closed.
    - Infuse peroxide or ipecac over several seconds, watching for swallowing motions.
    - If not swallowed (e.g., if entirely spit up), may redose once immediately.
    - If a syringe is not available, alternatives include plastic human dosing cups, turkey basters (large volumes of peroxide for big dogs), or teaspoons/tablespoons.
- Vomiting should occur within 5-10 minutes; if not, repeat.
- The patient must not have his/her head raised and should not be wearing a muzzle when vomiting is expected; either of these factors would greatly increase the risk of aspiration pneumonia.

POSTPROCEDURE

- Oral emetics: may administer a total of three doses
- Persistent vomiting usually subsides in 15-30 minutes; otherwise, an anti-emetic may be given (very uncommon).
- Treatment for ulcerative gastritis (e.g., H2 blocker) may be instituted prophylactically.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Table salt for emesis: not recommended; risk of critical hypernatremia if emesis does not occur.
- Activated charcoal:
    - Reduces bioavailability of many overdosed drugs and toxic substances
    - Often coadministered 30 minutes after induction of emesis or instead of induction of emesis if vomiting is contraindicated
    - Minimal or no efficacy with corrosive alkalis, mineral acids, or petroleum distillates
- Gastric lavage:
    - Best approach if animal is unconscious (emesis contraindicated)
    - No proven benefit over induction of emesis in terms of efficacy of purging gastric ingesta

AUTHOR: ETIENNE CÔTÉ

Ventilation, Positive Pressure

SYNONYMS

Artificial ventilation, assisted ventilation, mechanical ventilation

OVERVIEW AND GOALS

- Positive-pressure ventilation (PPV) requires intensive 24-hour monitoring and nursing care but can be lifesaving.
- Owner communication and highly trained staff are essential.
- Manual PPV requires a person to manually deliver breaths continually to the animal.
- Mechanical PPV involves a machine that takes the place of the person to deliver breaths.
- Manual PPV is only practical for short-term use (up to several hours), whereas mechanical PPV is required for long-term cases (>6-12 hours).
- The objective of PPV is to maintain normal arterial oxygen (Pao2) and carbon dioxide pressure (PaCO2) until an underlying disease can be identified and treated.
- Therapeutic goal:
  - Pao2 is >60 mm Hg (minimum; >80 mm Hg preferred).
  - PacO2 is <50 mm Hg.
  - End-tidal CO2 is <50 mm Hg.
  - Arterial oxygen saturation (SaO2) is >90% (minimum; >96% preferred)
  - Measure Pao2 and PacO2 with arterial blood gases (ABGs); measure end-tidal CO2 with capnometry (inserted between endotracheal tube and breathing device) and oxygen saturation (SaO2) with pulse oximetry (attached to the tongue).
- Prognosis varies with underlying disease:
  - A reasonable goal is to discharge 25%-40% of mechanically ventilated cases.
  - Animals with ventilatory failure and normal lung function (i.e., opioid or barbiturate overdose, certain toxins, tick paralysis, botulism) have the best prognosis.

INDICATIONS

Early intervention has the greatest chance of success.

- Ventilatory failure: PacO2 is >50 mm Hg and pH is <7.3.
  - Some can be managed with short-term PPV (e.g., reversible opioid overdose).
- Respiratory failure: Pao2 is <50 mm Hg, or SaO2 is <88% despite supplemental oxygen.
  - Often requires >12 hours of PPV
- Animals with sustained extreme respiratory distress: increased work of breathing
  - Often requires >12 hours of PPV

CONTRAINDICATIONS

- Irreversible underlying disease
- Lack of trained personnel
- If >6-12 hours of PPV is anticipated, initiating manual PPV is questionable if mechanical PPV is not available.
- There should be a trained technician with the animal and a veterinarian on the premises around the clock.

EQUIPMENT, ANESTHESIA

- Intubation:
  - Animals can be ventilated via inflated endotracheal (seep. 1292) or tracheostomy (seep. 1344) tubes.
  - Low-pressure, high-volume cuffs are preferred.
  - Endotracheal intubation is more common owing to familiarity, ease of procedure, and minimal risk of tissue damage.
  - If PPV exceeds 24 hours or when heavy sedation is not desired, a tracheostomy may be preferred (allows some dogs to eat and drink).
- Sedation (IV, as needed; more common with endotracheal intubation); options include:
  - Pentobarbital: 2 mg/kg boluses to effect (up to 12 mg/kg) q 4-6 h or as needed to maintain sedation
  - Fentanyl: 5 mcg/kg boluses to effect up to 50 mcg/kg, then 5-7 mcg/kg/h constant-rate infusion (CRI) (can add diazepam)
  - Propofol: 2-8 mg/kg bolus to effect, then 0.1-0.3 mg/kg/min CRI
  - Close cardiovascular monitoring is required in animals under heavy sedation.

- Minimum recommended monitoring:
  - Vital signs
  - Level of consciousness
  - ABGs or pulse oximetry and end-tidal CO2
  - Arterial blood pressure (BP)
  - Continuous ECG
  - Volume of fluids in and out (urinary catheter)
  - Hematocrit, total solids, glucose, and urine specific gravity
  - Ventilator setting should be recorded every hour

MANUAL:

- Ambu bag and attached oxygen:
  - Inexpensive
  - Readily available
  - Pediatric-size bag most common (typically 450-950 mL volume)
  - Can be used without supplemental oxygen (not ideal)
  - Excellent for short-term use (i.e., during cardiopulmonary resuscitation [CPR])
  - Can add positive end-expiratory valves, which create positive end-expiratory pressure (PEEP) to recruit collapsed alveoli and improve oxygen exchange (typically in 0-10 cm or 0-20 cm H2O sizes)
  - Some Ambu bags have a removable safety valve that will open when a specific airway pressure is exceeded (typically 40 cm H2O).
  - Difficult to determine tidal volume and airway pressures delivered (vary with size and degree of manual pressure applied to the bag)
- Anesthesia machine with manual ventilation:
  - Readily available
  - Estimate tidal volume delivered with the size of the reservoir bag
  - Can monitor airway pressure with attached pressure gauge
  - Can apply adjustable PEEP valves (typically range from 0-40 cm H2O)

MECHANICAL:

- Anesthesia ventilators:
  - Limited choice of ventilator modes
  - Typically deliver only 100% inspired oxygen concentrations (Fio2)
  - Increased risk of oxygen toxicosis if ventilating > 12 hours
- Mechanical ventilators:
  - Allow greatest control over type of breath delivered (pressure, volume, flow rate, Fio2, respiratory rate, sensitivity to trigger a breath, and PEEP)
  - Supply humidified oxygen
  - Can be used for long-term care (days to weeks)
  - Relatively expensive

ANTICIPATED TIME

- It can take several minutes to set up mechanical ventilators.
- Initiate manual PPV (takes seconds to initiate) while mechanical ventilators are being set up.
- The overall duration of ventilation time varies with the underlying disease and animal's response.

PREPARATION: IMPORTANT CHECKPOINTS

- Ensure oxygen source, monitoring equipment, and suction devices are available.
- Nutritional support should be available for long-term cases.
- Pleural-space disease (pneumothorax, pleural effusion) should be identified and treated prior to ventilation.
- Perform thoracocentesis (see p. 1338) in suspected cases; untreated pleural space disease is associated with higher incidence of ventilatory complications.
- Check that valves on Ambu bag are functioning properly (not sticking) between uses.
- Check anesthetic machine and anesthesia ventilator, and check that mechanical ventilator tubing is correctly connected, valves are functioning, humidifiers are full, and there are no leaks in the system.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Barotrauma: avoid exceeding 30 cm of H2O airway pressure.
- Cardiovascular effects: PPV increases intrathoracic pressures, which may impede venous return to the heart and can

subsequently decrease cardiac output; at a minimum, monitor heart rate and BP closely.
- Oxygen toxicosis: significant risk after 12 hours if Fio2 remains above 60%.
- Ventilator-associated pneumonia: monitor for deterioration of respiratory function or unexplained fever.
  - Confirm diagnosis with radiographs and endotracheal wash.
- Pneumothorax: more common with high airway pressures (>30 cm H2O):
  - Can cause acute deterioration in ventilatory parameters
  - Auscultation usually reveals dull breath sounds in upper parts of thorax (i.e., dorsally when animal is in sternal recumbency).
  - The absence of a “glide sign” with thoracic focused assessment of sonography for trauma (TFAST) is strongly suggestive of pneumothorax.
  - Perform thoracocentesis in suspected cases.
  - Tension pneumothorax is associated with a severe decrease in cardiac output and hypotension; check for tension pneumothorax in ventilated animals that suddenly develop shock.
- Oral and ocular ulcers: usually avoided with good nursing care:
  - Lubricate eyes with sterile eye lubricant, and cleanse mouth with 0.1% chlorhexidine solution–soaked gauze sponges every 4 hours.

PROCEDURE

Note: Step-by-step guidelines to initiate PPV are beyond the scope of this text, and clinicians should consult more extensive reviews to become familiar with different ventilator modes and their indications. The following are suggested guidelines for starting PPV. Most cases do better in sternal recumbency.

- Ambu bag:
  - Bag size (in milliliters) should be at least 15 × BW (kilograms) to be able to deliver adequate tidal volumes.
  - Set oxygen flow rates at 10-15 L/min (delivers 50%-90% oxygen levels).
  - Attach adjustable PEEP valve to exhaust limb if PEEP desired (requires compatible attachment site). Adjust PEEP by turning valve to the desired level (start with 5 cm H2O).
  - If an oxygen reservoir bag is used, higher (90%-100%) inspired oxygen levels can be achieved.
  - Animals can breathe spontaneously while connected to Ambu bags, although airway resistance is higher.
- Anesthetic machine with manual ventilation:
  - Insert adjustable PEEP valve in the expiratory limb of tubing (bidirectional valves eliminate the risk of occlusion associated with backward insertion of unidirectional valves) if PEEP is desired.

SUGGESTED INITIAL PPV SETTING GUIDELINES (see figure):

- Inspired oxygen concentration (Fio2):
  - Start with 100% Fio2.
  - For long-term (many hours) use, decrease to the lowest Fio2 that maintains desired Pao2/SaO2 to reduce the risk of oxygen toxicosis.
- Respiratory rate (RR):
  - 8-20 breaths per minute (bpm)
  - Increase the RR to decrease the PacO2 if >50 mm Hg.
  - New RR = RR × PacO2/desired PacO2
  - RR often >20 breaths/minute if underlying pulmonary disease is present.
- Oxygen flow rates:
  - Start with 0.5-1 L/kg/min.
  - Often need to increase if underlying pulmonary disease is present.
- Tidal volume:
  - Amount of air delivered with each breath
  - Normal values: 10-15 mL/kg
  - Values of 4-6 mL/kg are associated with fewer lung injuries in people.
  - Volumes in excess of 20 mL/kg are likely to cause lung injury (barotrauma and volutrauma).
  - May need to increase tidal volume if PacO2 does not respond to increased RR
  - General rule: use lowest volume possible to achieve oxygen and carbon dioxide goals.
- Airway pressure:
  - If pressure gauge available
  - Normal airway pressures reach 15-20 cm H2O.
  - Values that are >30 cm H2O are to be avoided (likely to result in lung injury).
- Inspiratory time:
  - Inspiratory time is normally between 1.5 and 2.5 seconds.
- Inspiratory to expiratory (I:E) ratio:
  - Start with values of 1:2-1:4.
  - Try to stay >1:2 to prevent the next breath being delivered before exhalation is complete.
  - Increasing RR or tidal volume will decrease I:E ratio.

- Increasing oxygen flow rates will increase I:E ratio.
- Changing one parameter may require a change in another to maintain desired I:E ratio.

- PEEP:
  - Healthy lungs do not require PEEP.
  - Adding PEEP to diseased lungs often improves oxygenation, prevents further alveolar collapse, and reduces ventilator-induced lung injury.
  - A common starting value is 3 cm H2O.
  - If 3 cm H2O does not achieve desired results (based on Pao2/SaO2), increase the PEEP by 2-4 cm H2O until desired values are achieved.
  - Exceeding 15 cm H2O of PEEP increases the risk of lung injury and may decrease cardiac output.

VENTILATION, POSITIVE PRESSURE Potential ventilator settings for a 40- to 60-kg animal. Volume control ventilation (VCV) with synchronized intermittent mandatory ventilation (SIMV) is shown. The inspired oxygen content is 21% (room air). The peak inspiratory pressure (PIP) is high (34 cm H2O), and efforts should be made to decrease this value by decreasing tidal volume, increasing peak flow rate, or decreasing positive end-expiratory pressure (PEEP).

VENTILATION, POSITIVE PRESSURE Ventilator in use.

POSTPROCEDURE

- Supplemental oxygen is often required after weaning from ventilation (seep. 1318).

- Oxygen supplementation should be set up prior to extubation (nasal oxygen is frequently used).

ALTERNATIVES AND THEIR RELATIVE MERITS

Liquid ventilation using perfluorocarbons shows promise in managing some forms of respiratory failure in people but is cost prohibitive to most veterinary practices and clients.

SUGGESTED READING

Campbell VL, King LG: Pulmonary function, ventilator management, and outcome of dogs with thoracic trauma and pulmonary contusions: 10 cases (1994-1998). J Am Vet Med Assoc 217(10):1505–1509, 2000.

Drellich S: Principles of mechanical ventilation. Vet Clin North Am Small Anim Pract 32(5):1087–1100, 2002.

Mueller ER: Suggested strategies for ventilatory management of veterinary patients with acute respiratory distress. J Vet Emerg Crit Care 11(3):191–198, 2001

AUTHOR: SØREN R. BOYSEN

Vaginoscopy

OVERVIEW AND GOAL

Visual inspection of the surface of the vaginal mucosa. This can be accomplished through a plastic or metal speculum, or is most rewarding with a fiberoptic endoscope.

INDICATIONS

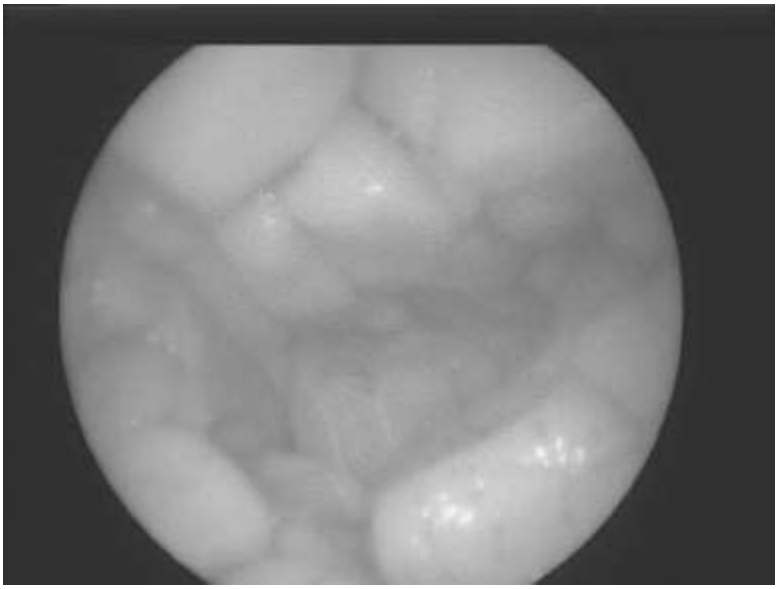
- Examining the physical changes associated with hormonal events of the canine reproductive cycle
- Evaluating abnormal conditions of the caudal reproductive tract (vestibule, vagina, and caudal cervix). Common disorders of the caudal reproductive tract include vaginal septa, vestibulovaginal stenosis (strictures), paramesonephric septal remnants, tumors, foreign bodies, lymphoid inflammation or hyperplasia, and ectopic ureters.
- To facilitate catheterization of the cervix for intrauterine artificial insemination

EQUIPMENT, ANESTHESIA

Bitches in estrus tolerate vaginal procedures well; bitches in early proestrus or anestrus may need sedation or even general anesthesia, depending on the medical reasons to perform the vaginoscopy.

Equipment:

- Endoscope or speculum: if using a rigid endoscope, its size should be compatible with the size of the bitch.
- Sterile water-soluble lubricant
- Light source if not integral part of endoscope/speculum
- Swabs
- Microscope slides



VAGINOSCOPY Endoscopic view of the canine vagina in midestrus.

ANTICIPATED TIME

5-20 minutes

PREPARATION: IMPORTANT CHECKPOINTS

- Be sure to apply lubricant copiously to the endoscope before introducing it.
- Position: if in estrus, most bitches will remain standing while vaginoscopy is being performed, especially if transcervical insemination is to be performed. In anestrous or spayed dogs, care should be taken to not traumatize the vaginal walls,

especially if a rigid endoscope is being used.
- Anesthetized dogs may be positioned in lateral, ventral, or dorsal recumbency; the latter prevents inadvertent fecal contamination of the perineovulvar area.

PROCEDURE

- Once the perineum is cleansed and excessive hair clipped, the vulvar labia are separated, and the instrument is introduced at a craniodorsal angle to avoid the clitoral fossa until the vestibule and vagina are visualized.
- Areas to be inspected: urethral opening, vestibulovaginal junction, vagina, vaginal dorsal median fold that leads to the narrow cranial vagina, vaginal fornix and paracervical area, and cervical caudal os (ostium uteri externum)
- Physical changes due to circulating hormones cause dramatic changes in the appearance of the vaginal mucosa, especially during proestrus and estrus:
    - Under the influence of estrogens produced by ovarian follicles, the vaginal epithelium undergoes hyperplasia and metaplasia during proestrus. The vaginal mucosa becomes edematous, swollen, and appears smooth, round, and plump.
    - As the bitch advances into late proestrus and estrus, declining concentrations of serum estrogens result in a wrinkling and shrinking of the vaginal mucosal folds, progressing to a markedly angulated and crenulated outline during mid to late estrus.

POSTPROCEDURE

Submission of samples, microscopic review of smears

ALTERNATIVES AND THEIR RELATIVE MERITS

- Digital vaginal palpation (see p. 1292): conveys the changes in texture of the vaginal mucosa but does not demonstrate lesions
- Serum progesterone assay: often used in conjunction with vaginoscopy; the appearance of the mucosa (and cornification of cells; see p. 1202) indicate when to begin measuring serum progesterone.

AUTHOR: CARLOS PINTO

Vaginal Palpation in the Bitch

SYNONYM

Digital vaginal examination

OVERVIEW AND GOALS

Minimally invasive digital examination of the vagina to evaluate the vaginal anatomy. Possible lesions in bitches include:

- Vaginal strictures
- Vaginal tumors
- Trauma during breeding
- Congenital anatomic anomalies

INDICATIONS

- Vaginal discharge
- Poor breeding experience
- Urinary incontinence (urine pooling)
- Dystocia

CONTRAINDICATIONS

There are relatively few contraindications to this procedure.

- If infection of the reproductive tract is a consideration:
  - Vaginal culture should be taken first.
  - Culture is followed by vaginal cytologic analysis before a digital examination is performed.

EQUIPMENT, ANESTHESIA

- Minimal restraint usually required
- Antiseptic cleanser
- Sterile exam glove
- Sterile water-soluble lubricant

ANTICIPATED TIME

With a cooperative bitch, the procedure should take less than 5 minutes, from gentle cleansing of the vulvar lips to finishing the exam.

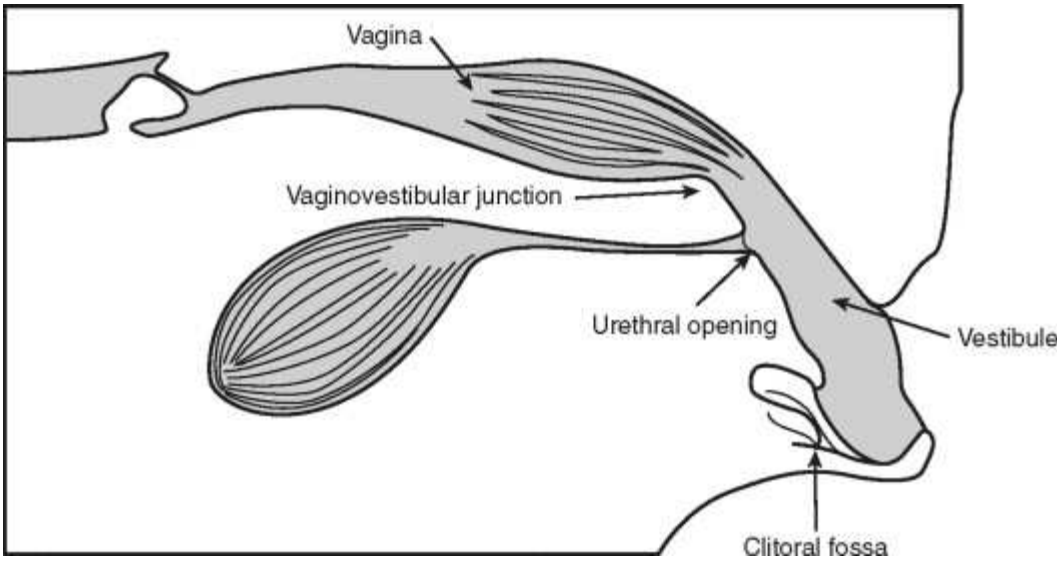
POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Urethral opening lies on the ventral surface of the vestibule and should be avoided:
  - This is not difficult if the finger is passed up to the vestibulovaginal junction perpendicularly to the ground in the standing bitch.
- Vestibulovaginal junction is one barrier to the entrance of the uterus and should not be mistaken for the cervix or a stricture:
  - The canine vagina is very long (up to 12 inches [29 cm] in giant-breed dogs), and thus the cervix is unlikely to be palpated on digital examination of the vagina.
  - The junction acts a barrier to pathogens and will be narrower than the vestibule or vagina. If the examiner proceeds slowly, he or she should be able to pass the finger beyond the junction in most bitches (depending on the size of the bitch and the size of the finger).

PROCEDURE

- Animal should be restrained in standing position.

- Vulvar lips should be gently wiped with a mild antibacterial cleanser.
- Examiner should wear sterile gloves.
- After coating the gloved index finger with the sterile lubricant, the finger is passed into the vulva and turned directly upward (90° angle to the floor in the standing animal). The upward direction is important so the urethral opening is avoided.
- When the finger cannot go any farther dorsally, it is turned directly cranially (parallel to the floor) and advanced over the ischium and into the vaginal vault:
    - As the finger passes over the ischium into the vagina, there may be a slight tightening at the vestibulovaginal junction. Depending on the size of the bitch and the size of the hand, most fingers should pass through this junction.
    - If the finger is well lubricated and it does not pass this point, a vaginal stricture should be considered.



VAGINAL PALPATION Anatomic relationship of vestibule and vagina in the bitch. Dorsal is toward top of image, cranial to left.

ALTERNATIVES AND THEIR RELATIVE MERITS

- Speculum examination (vaginoscopy; see p. 1361) may be performed for the visualization of the vaginal walls and vault:
    - Inflamed walls in vaginitis cases
    - Urine on the floor of the vagina in urine-pooling disorders
    - Evidence of trauma in difficult breeding
    - Evaluation of vaginal folds and mucosa for timing of estrus
- Vaginoscopy with an endoscope to visualize vagina and potentially the cervix

AUTHOR: CAROL A. MCCLURE

Vagal Maneuver

SYNONYMS

- Carotid sinus massage
- Ocular pressure
- Valsalva maneuver

OVERVIEW AND GOALS

A physical manipulation that temporarily increases parasympathetic tone, mainly for diagnostic—and occasionally therapeutic—cardiac rhythm effects

INDICATIONS

Tachycardia in which the rate is so rapid that it is unclear on the electrocardiogram (ECG) whether the rhythm is ventricular or supraventricular (e.g., heart rate is >260 bpm)

CONTRAINDICATIONS

- Ocular disease (for ocular pressure)
- Disorders of the ventral neck (for carotid sinus massage)
- Bradycardia, including the bradycardia-tachycardia syndrome (sick sinus syndrome)

EQUIPMENT, ANESTHESIA

No anesthetic requirement; procedure is performed when the animal is awake. Procedure requires ECG machine with printer to assess and record initial cardiac rhythm and to record effect of vagal maneuver.

ANTICIPATED TIME

<1 minute

PREPARATION: IMPORTANT CHECKPOINTS

A printed ECG tracing of the rhythm prior to the vagal maneuver is necessary.

POSSIBLE COMPLICATIONS AND COMMON ERRORS TO AVOID

- Inadequate vagal response. Subjectively, carotid sinus massage appears to be more effective than ocular pressure in some patients and vice versa in others, but some supraventricular tachycardias (and essentially all cases of ventricular tachycardia) are resistant to both.
- Concerns regarding vagal maneuver. Related harm due to carotid artery atherosclerosis is based on human cardiology but is not expected to be relevant to small animal medicine.

PROCEDURE

- Patient may be standing or recumbent.
- ECG leads are connected, and a good ECG signal should be seen.
- The prevagal-maneuver ECG is traced/printed; about 20-30 seconds of tracing should be recorded.
- The *vagal* maneuver is applied, with the ECG printing continuously. The ECG paper should be marked at the time of onset of the vagal maneuver. Usually, only one maneuver is performed. The ECG should be allowed to continue to run (printing) throughout the duration of the vagal maneuver and for at least 15 seconds after its termination.

VAGAL MANEUVER Placement of fingers for performing carotid sinus massage in a dog.

OCULAR PRESSURE:

- The patient's eyelids are closed, and using the thumb and middle finger of the same hand, both globes are depressed caudally into the orbit.
- A small, smooth massaging motion may be applied to the eyes along with the direct pressure.
- The degree of pressure should be sufficient that the eyes are substantially retracted caudally without, however, provoking any sign of discomfort or resentment. The exact extent of retraction will vary depending on orbit shape and size.
- Pressure is maintained until a substantial decrease in heart rate is noted and the rhythm can be identified or until the maneuver has been applied for 15 seconds.

CAROTID SINUS MASSAGE:

- The target area is the base of the internal carotid artery, which is not palpable as such but is located dorsocranially to the larynx, medial to the angle of the mandible.
    - For localization: the larynx is palpated using the thumb and forefinger. The thumb and forefinger are moved dorsally and cranially from the larynx until resting in the natural depression medial to the angle of the mandible and ventral to the occipital bone.
- Gentle, pincer-like pressure is applied in this area with the thumb and forefinger.
- Pressure is maintained, and a small, smooth, circular massaging motion may be performed.
- The pressure exerted is often sufficient to elicit a gag reflex but should not be so great as to cause discomfort or resentment.
- Pressure is maintained until a substantial decrease in heart rate is noted and the rhythm can be identified or until the maneuver has been applied for 15 seconds.

POSTPROCEDURE

- A vagal maneuver can routinely be terminated abruptly.
- Failure to slow tachycardia with a vagal maneuver should prompt a search for the tachycardia's possible causes, including anxiety/stress of hospitalization, respiratory compromise, structural cardiac disease, and systemic illness.

ALTERNATIVES AND THEIR RELATIVE MERITS

Pharmacologic slowing of tachycardias, such as with injectable propranolol, verapamil, or adenosine, should only be considered

once the aforementioned possible inciting factors have been ruled out or addressed.

AUTHOR: ETIENNE CÔTÉ

Procedures and Techniques

EDITORS

Etienne Côté, DVM, DACVIM (Cardiology, Small Animal Internal Medicine)

Azotemia: Blood Urea Nitrogen/Creatinine Mismatch

From Willard M, Tvedten H: Small animal clinical diagnosis by laboratory methods, ed 4, St Louis, 2004, Saunders.

BUN, Blood urea nitrogen; *GI,* gastrointestinal; *PU/PD,* polyuria and polydipsia.

Increased BUN Plus Normal Serum Creatinine

- ***Increased BUN***
  - Early prerenal azotemia (decreased urine flow rate)
  - High-protein diet
  - GI hemorrhage
  - Tetracycline or corticosteroid administration
  - Fever
  - Loop diuretic administration (e.g., furosemide)
  - Severe tissue trauma(?)
- ***Decreased Creatinine***
  - Decreased muscle mass (severe cachexia needed to cause significant changes)

Increased Serum Creatinine Plus Normal to Low BUN

- ***Decreased BUN***
  - Hepatic insufficiency
  - PU/PD
  - Low-protein diet
- ***Increased Creatinine***
  - Myositis/muscle trauma (unlikely)
  - Cooked meat diet (mild, transient changes)
  - Ketonemia (falsely increased)

Azotemia

Modified from Slatter D: Textbook of small animal surgery, St Louis, 2003, Elsevier.

*Urine specific gravity may be in the normal range in cases of acute anuric renal failure.

Differentiation and Anticipated Metabolic Changes

Parameter	Prerenal	Primary Renal	Postrenal
Creatinine	Increased	Increased	Increased
Blood urea nitrogen (BUN)	Increased	Increased	Increased
Urine specific gravity	Increased	Decreased*	Increased
Urine sediment	Normal	Often abnormal	Often abnormal
Urine production	Decreased	Variable	Decreased
Hematocrit	Increased	Variable	Increased
Serum potassium	Normal or low	Variable	Increased
Serum phosphorus	Normal	Variable	Increased
Metabolic acidosis	Mild	Mild to severe	Mild to severe
Common causes	Dehydration, hypovolemia, heart failure	Nephrotoxins, infectious disease, glomerulonephritis	Urethral obstruction, ruptured bladder

Azoospermia

From Feldman E, Nelson R: Canine and feline endocrinology and reproduction, ed 3, St Louis, 2004, Saunders.

*Decreased libido often associated with these disorders.

Potential Causes for Azoospermia

- **May Be Transient**
- Drugs, hormones*
- Environmental insult
- Systemic illness (current or previous)
- Testicular trauma, hyperthermia
- Infectious orchitis, prostatitis
- Retrograde ejaculation
- Hypothyroidism*
- Hypopituitarism*
- Hyperadrenocorticism*
- Estrogen-secreting Sertoli cell tumor*

- **Usually Permanent**
- Idiopathic testicular degeneration
- Lymphocytic orchitis
- *Brucella canis*
- Duct obstruction
- Bilateral testicular neoplasia
- Congenital defect

Arrhythmias: Ventricular Versus Supraventricular

Modified from Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

Comparison of Ectopic Beats of Supraventricular or Ventricular Origin

Feature	Supraventricular	Ventricular
Wide, bizarre QRS complexes	Rare (concurrent aberrancy)	Common
QRS complex shape	Same as sinus QRS complex	Different from sinus QRS complex
P wave for every QRS complex	Yes; often of different shape (consistent PR interval)	No; P waves occur regularly throughout tracing but independently of QRS complexes (often buried inside QRS complexes or T waves)
T wave	Same as sinus T wave	Different from sinus T wave
Postextrasystolic pause	Usually noncompensatory	Usually compensatory
QRS complex fusion beats as hallmark	No	Yes
Positive response to vagal maneuver	Possible	Virtually never

Arrhythmias: ECG Characteristics

From Kittleson M, Kienle RD: Diagnosis and treatment of arrhythmias (dysrhythmias). In Small animal cardiovascular medicine, St. Louis, 1998, Mosby, p 454.

Electrocardiogram Characteristics

Rhythm	P Wave Rate (bpm)	P Wave Rhythm	P Wave Configuration	QRS Complex Rate	QRS Complex Rhythm	QRS Configuration	P-QRS Relationship
Sinus	Normal	Regular	Normal	Same as P wave	Regular	Normal	1:1
Sinus bradycardia	<Normal	Regular	Normal	Same as P wave	Regular	Normal	1:1
Sinus tachycardia	>Normal	Regular	Normal	Same as P wave	Regular	Normal	1:1
Sinus arrhythmia	Normal	Irregular	Normal or wandering	Same as P wave	Irregular	Normal	1:1
Supraventricular tachycardia	>Normal	Regular	Positive, negative, absent, or buried	Same as P wave	Regular	Normal	1:1
Atrial flutter	>300	Regular	Positive (F waves; sawtooth baseline)	Same or less than P wave rate	Regular or irregular	Normal	Generally more P waves than QRS complexes
Atrial fibrillation	>500	Irregular	None to baseline undulation (F waves)	Less than P wave rate (100-280)	Irregular	Normal	No P waves; more undulations than QRS complexes
Accelerated idioventricular rhythm	Normal	Regular	Normal (often buried in QRS complex)	70-150	Fairly regular; may be irregular	Wide	Dissociated; more QRS complexes than P waves
Ventricular flutter	Not discernable	Not discernable	Not discernible	>350	Regular	Sine wave	Dissociated; more QRS waves than P waves
Ventricular fibrillation	Not discernable	Not discernable	Not discernible	>400	Grossly irregular	No QRS complexes	Dissociated; no QRS complexes
Second-degree AV block	Normal	Regular	Normal	<P wave rate	Irregular	Normal or wide	More P waves than QRS complexes
Third-degree AV block	Normal	Regular	Normal	20-60 (dog), 50-130 (cat)	Regular	Normal or wide	Dissociated; more P waves than QRS complexes; irregular P-R interval

Arrhythmias, Ventricular: Triggers

Causes of or Predisposing Factors for Ventricular Arrhythmias (Premature Ventricular Complexes, Ventricular Tachycardia)

- Hypokalemia
- Hypoxemia (e.g., from pulmonary edema, other causes)
- Anemia
- Structural heart disease (valvular heart disease, cardiomyopathy, congenital heart disease, others)
- Blunt chest trauma (e.g., hit by car)
- Gastric dilatation and volvulus
- Abdominal mass (splenic, hepatic, others)
- Sepsis
- Acidosis
- Systemic inflammatory response syndrome (SIRS)
- Intoxications (digitalis, pseudoephedrine, many other pharmaceuticals; oleander, yew, many other plants)
- Excess catecholamines
- Myocarditis (diagnosis of exclusion)

Antidotes and Reversal Agents in Small Animal Poisoning

CNS, Central nervous system; *GI,* gastrointestinal; *OP,* organophosphate.

Reversal Agent/Antidote	Toxicant/Main Indications	Comment(s)
N-acetylcysteine (Mucomyst)	Acetaminophen/paracetamol overdose	Can be used PO; injectable (Acetadote) available; in addition, can also use SAMe
Flumazenil (Romazicon)	Benzodiazepines (diazepam, alprazolam, lorazepam, clonazepam) overdose	Can help reverse severe CNS depression/coma; short half life; repeat in 1-3 hours if needed.
Pamidronate (Aredia)	Cholecalciferol; calcipotriene; calcitriol	Treats hypercalcemia and hyperphosphatemia; can cause transient azotemia
Cyproheptadine (Periactin)	Serotonin syndrome caused by serotonergic substances	Can be tried per rectum in animals that cannot receive oral medications; can repeat once or twice in 6-8 hours
Methocarbamol (Robaxin)	For tremor control in permethrin toxicosis in cats; can also be tried in cats/dogs for tremors resulting from other pyrethrins/pyrethroids	Not an anticonvulsant; works well in permethrin, metaldehyde, tremorgens, and strychnine toxicosis; injectable preferred for acute treatment; orally may be helpful for mild cases
Atipamezole (Antisedan)	To treat α2-adrenergic agonist effects of amitraz, xylazine, clonidine, and brimonidine overdose	Atipamezole and yohimbine have α2-adrenergic antagonist properties; atipamezole more specific/preferred.
Fomepizole (4-methyl pyrazole; Antizol-Vet)	Ethylene glycol (antifreeze) toxicosis in dogs; some benefit if used within 3 hours of exposure in cats	Good safety margin; does not contribute to acidosis and CNS depression as ethanol does.
Calcium disodium EDTA (Calcium Disodium Versenate)	Lead, zinc, cadmium	Injectable; can cause GI signs and nephrotoxicity; do not use if metal still present in GI tract.
BAL (British antilewisite; Dimercaprol)	Lead, arsenic, mercury	Injection can be irritating and painful; difficult to obtain; helps remove lead from CNS
Atropine sulfate	For treating muscarinic signs in OPs and carbamate toxicosis; certain muscarinic mushrooms	Avoid atropinization (hyperthermia, tachycardia, mydriasis)
2-PAM (Pralidoxime)	For treating nicotinic signs in OP toxicosis in dogs, cats	Not useful for most carbamate toxicoses; most beneficial within 24 hours of exposure but may be useful beyond this time; discontinue after 3 doses if no benefit
D-penicillamine (Cuprimine)	Zinc, cadmium; lead, copper, mercury	Used PO; can cause GI signs; do not use when metal is still present in the GI tract.
Digoxin immune Fab (Digibind)	Digitalis; cardiac glycosides	Expensive but rapid acting and efficacious; can be used in Bufo toad toxicosis
Deferoxamine (Desferal)	Iron chelator; useful in iron toxicosis	Urine color may turn wine color after chelation with iron.

Reversal Agent/Antidote	Toxicant/Main Indications	Comment(s)
Succimer (2-3-dimercaptosuccinic acid; Chemet)	Lead poisoning in dogs; cats, birds	Used PO; anecdotal reports of renal failure in cats; monitor renal values when using in cats; can be used when ingested lead is still present in the GI tract.
Yohimbine (Yobine)	To treat α2-adrenergic agonist effects of amitraz, xylazine, clonidine, and brimonidine overdose	Shorter half-life and less specific than atipamezole; use yohimbine as a second choice if atipamezole is not available.
S-adenosyl-L-methionine (SAMe; Denosyl)	General hepatoprotective agent	Used as an aid in hepatic damage from various causes (mushroom, xylitol, cycad, acetaminophen, etc.)
Naloxone (Narcan)	Opioids/opiates	Can help reverse respiratory/CNS depression; short half life; repeat in 1-3 hours if needed.
Vitamin K1 (phytonadione)	Anticoagulants (warfarin, brodifacoum, bromadiolone)	Parenteral use can cause allergic reaction; use PO for 2-4 weeks or more as needed; works better with fatty food and in divided doses.
Pyridoxine (vitamin B6)	Isoniazid toxicosis in dogs	Difficult to obtain; can be used 1 : 1 ratio (dose of isoniazid: dose of pyridoxine); 5%-10% IV infusion over 30-60 minutes; use in conjunction with diazepam to control CNS effects
Prussian blue	Thallium toxicosis	Used PO; difficult to obtain; thallium toxicosis not common anymore
Leucovorin	Methotrexate overdose	Leucovorin is active form of folic acid; 25-250 mg/m^2 q 6 h IV, IM for up to 72 h

Anticoagulant Rodenticides in Common Usage

Active Ingredient	Common Brand Names	Comments

Brodifacoum	• D-Con bait pellets
	• D-Con bait pellets II
	• D-Con bait pellets II place pack
	• D-Con Kills Rat
	• D-Con Lim-N8 Rat killer
	• D-Con Mouse Killing station
	• D-Con Mouse Prufe II
	• D-Con Ready Mixed Baitbits
	• De-Mize Kills Mice and Rats
	• Enforcer Mouse Kill II
	• Enforcer Mouse and Rat Bars
	• Enforcer Rat and Mouse Bars II
	• Enforcer Rat and Mouse Killer Pellets
	• Enforcer Rat Kill II with Bitrex
	• Final Blox All Weather
	• Final Blox All Weather Commercial (Canada)
	• Final Rodenticide Place Pack (Canada)
	• Final Rodenticide Ready to Use
	• Havoc Chunks
	• Havoc Rodenticide Bait Pellets
	• Havoc XT Blok
	• Jaguar 50 Bait Chunx (Canada)
	• Jaguar 50 Rodenticide place pack (Canada)
	• Jaguar 50 All Weather Blox (Canada)
	• Jaguar Rodenticide
	• Ratak Plus Rodenticide (Canada)
	• Ratak Plus Rodenticide Place pack (Canada)
	• Ropax Bars
	• Ropax Pellets
	• Ropax Rodenticide
	• Talon G Rodenticide bait pack
	• Talon G Rodenticide mini pellets
	• Talon Liquid Concentrate
	• Talon Plus Rodenticide
	• Talon-G mini pellets
	• Talon-G rodenticide bait pack
	• Talon-G Rodenticide with Bitrex
	• Weather Block bait
	• Weatherblok Bait with bitrex
	• Weatherblok XT bait (Canada)
	• Zep commercial rat and mouse bars
		• One of the most widely used anticoagulants
		• Available as 0.005% or 0.0025 % or 0.25% or 0.28% w/w bait
		• Available as pellets, blocks, bait chunks
		• Some baits also contain bitrex (denatonium benzoate, a bittering agent) to deter nontarget animals.
		• No toxicity concern from bittering agent
		• Mostly available as 1-oz blocks
		  ○ (28.5-g); 1.5-oz
		  ○ (45-g) or 3-oz
		  ○ (85-g) packages

Bromadiolone	• Boot Hill Kills Rats and Mice • Boot Hill Rat and Mice pellets • Boot Hill Rat and Mice place packs • Boot Hill mini block • Boot Hill pellets • Contrac all weather blox • Contrac all weather cake • Contrac blox all weather (Canada)	• A widely used anticoagulant available as 0.005% bait • Available as pellets, blocks, bars, cake, chunks, trays, meal bait • Sometimes baits impregnated with seeds • Some formulations contain bitrex (bittering agent) to deter nontarget species

Active Ingredient	Common Brand Names	Comments
	• Contrac II • Contrac II cake • Contrac Rat and Mouse Bait • Contrac Rodenticide (Canada) • Contrac Rodenticide Place Pac • Contrac Super Size Blox • Contrac Super Size Blox Commercial (Canada) • Enforcer Mouse Kill III • Green Cross Rodentex Block (Canada) • Green Cross Rodentex Pellets (Canada) • Hawk All Weather Rodent Block • Hawk Bait Chunx • Hawk Bait Chunx Commercial (Canada) • Hawk Integrator All Weather Block • Hawk Rodenticide • Hawk Rodenticide Domestic (Canada) • Hawk Rodenticide Ready To Use • Just One Bite II Bait Chunk • Just One Bite II Bait Pellets • Just One Bite Pellets • Just One Bite Place Pack • Just One Bite Mouse Bars • Maki Mini Block Rodenticide • Maki Paraffinized Pellets • Maki Rat and Mouse Meal Bait • Maki Rat and Mouse Place Packs • Maki Rodenticide Bait Packs • Maki Rodenticide Pellets Place Packs (Canada) • Purina Mouse A Rest Pellets • Purina Rat A Rest Pellets • Rat X Dura Block (Canada) • Rat XB Meal Bulk Rodenticide (Canada) • Rat XB Bait Pack (Canada) • Ratoxin Bromadiolone Rodenticide Bait Pack (Canada) • Ratoxin Dura Block Domestic (Canada) • Ratoxin Meal Bait Pack (Canada) • Rattoxin Mouse and Rat bait (Canada) • Sanex Brobone Meal bait (Canada) • Snare rodenticide (Canada) • Snare Rodenticide Bait Blox (Canada) • Tomcat All Weather Ultra Block bait (Canada) • Tomcat Ultra • Tomcat Ultra Block Bait • Tomcat Ultra Feeder Pack • Tomcat Ultra Pelleted Bait • Tomcat Ultra Prebaited Bait Station • Victor Bait Station • Victor Kills Mice and Rat Bait Block • Victor Kills Mice and Rat Pellets	

Active Ingredient	Common Brand Names	Comments
	• Victor Mouse and Rat Block with Bitrex (Canada) • Wilson Super Mouse Treat (Canada) • Wilson Super Rat and Mouse Killer (Canada) • Wilson Wilsarin Rat and Mouse Bait (Canada)	
Chlorophacinone	• AC Formula 90 place packs or ready-to-use bait • Bonide No Escape rat and mouse place packs • Enforcer rat and mouse killer • Enforcer rat bait • Enforcer rat and mice bait (indoor outdoor use) • Green Cross mouse bait (Canada) • Ground Force field rodent bait (Canada) • Ground Force rat and mouse pellets or place packs (Canada) • JT Eaton feeder box rat bait • JT Eaton Answer for mice • JT Eaton Answer for chipmunks • JT Eaton Rozol Bait blocks • Rat XC bait pack (Canada) • Ratol Superbags I rodenticide (Canada) • Rozol Canary Seed Mouse Bait • Rozol Liquid Rodenticide Concentrated (Canada) • Rozol Mineral Oil Concentrated Rodenticide (Canada) • Rozol Pellets for Voles • Rozol Gopher bait • Rozol Rat and Mouse Killer • Rozol Tracking Powder • Super Bloc II Rodenticide (Canada) • Super Bloc I Rodent Bait (Canada) • Wilco Ground Squirrel Bait • Wilson Bait Bloks (Canada) • Wilson Ready to Mice Rodenticide (Canada) • Wilson Riddex Rat and Mouse Killer Pellets (Canada) • Wilson Riddex Rat and Mouse Killer Meal (Canada)	• Mostly available as 0.005% w/w bait • Sometimes 0.01%, 0.07%, or 0.28% w/w rat or mouse bait • Occasionally used for gophers, moles, chipmunks, voles, and squirrels • Available as pellets, paraffin blocks, tracking powder, or feeder station • Can be used indoors or outdoors • Tracking powder can be more concentrated (up to 0.28%). • Bait sometimes may be impregnated with bird seeds.
Difethialone	• D-Con Bait Paste Pouch • D-Con Rat and Mouse Mini Block • D-Cease Mini Bars • Enforcer Mouse Max Killer • Enforcer Rat Max Killer • Generation Blue Max Meal Bait • Generation Blue Max Block • Generation Blue Max Mini Block (Canada) • Generation Blue Max Rodenticide Pellets (Canada)	• Relatively new compared to other anticoagulants • Available as 0.025% w/w bait • Available as pellets, mini blocks, bars, meal, paste • Sometimes bait available with bittering agent

Active Ingredient	Common Brand Names	Comments
	• Generation Mini Block • Generation Block Commercial (Canada) • Generation Pellets Placepacks • Hombre Block • Hombre Pellets Place Packs • Hombre Pellets Ready to Use • Ortho Home Defense Max Bait Block • Ortho Home Defense Max Bait Station • Sweeneys Bait Block Rodenticide • Sweeneys Mice Bait Pack Pellets • Sweeneys No Mess Paste Bait • Wilson Predator Rat and Mouse Blok (Canada) • Wilson Predator Rat and Mouse Pellets Place Pack (Canada)	
Diphacinone	• Black Jack Ratonicide Rat & Mouse Killer • Ditrac All Weather Blox • Ditrac All Weather Cake • Ditrac Rat & Mouse bait • Ditrac Rat and Mouse Bait Place Pack • Eatons All Weather Bait • Eatons All Weather Blocks • Eaton Answer for Pocket Gophers • Enforcer Rat & Mouse Killer II • Enforcer Rat & Mouse Weather Bars • Greenlight Gopher Killer • JT Eaton Bait Blocks • Promar Blox All Weather Rodenticide • Ramik Green • Ramik Green Bait Pack • Ramik Green Mini Bait • Tomcat All Weather Rodent Block • Tomcat All Weather Bait • Wilco Gopher Getter • Wilco Ground Squirrel	• Available for indoor/outdoor use • Used for rats, mice, gophers, and squirrels • Available as 0.005% w/w bait • Available as bars, pellets, blocks, cake, tracking powder, chunks • Also used with bitrex (bittering agent) • Baits sometimes flavored with peanut butter or molasses
Warfarin	• Apo Rat and Mouse Bait • Bolt Rodenticide (Canada) • Bonide Tomcat • Contrac Rodenticide Kills Rats (Canada) • D-Con Pellets • D-Con Pellets Kills Rats and Mice • D-Con Ready Mixed Kills Rats and Mice • Ferret Rodenticide • Final Pelleted Rat and Mouse Bait • Final Rat and Mouse Bait • Hopkins Rodex Blox I • Kaput Mole Gel Bait • Kaput Mouse Block • Rat Control Pellets	• Not used commonly anymore, owing to availability of second- generation anticoagulants • Available as 0.025% w/w bait • Used as bars, meal, cakes, pellets • Used for rats, mice, moles, and occasionally for wild ferrets

Active Ingredient	Common Brand Names	Comments
	• Rid-A-Rat Rat & Mouse Killer • Rodex Blox I • Rodex Mole Gel Formula • Rodex Pelleted Bait • Warfarin Rat & Mouse Killer Meal (Canada)	

Anorexia: Tips for Coax Feeding

- Minimize stress at mealtimes.
- Approximate the patient's routine feeding management as much as possible.
- Recognize the signs of food aversion and modify/temporarily suspend feeding accordingly.
- Choose complete and balanced, energy-dense foods that are appropriate for the patient's medical condition.
- When medically appropriate, choose foods the patient is familiar with.
- Warm the food slightly.
- Offer modest portions of fresh foods frequently.
- Offer one food item at a time.
- Do not leave food with the patient for extended periods of time.
- Try novel foods if the patient seems averse to his/her typical diet.
- Give clear feeding instructions that include the specific diet to be fed, portion size, and meal frequency.

AUTHOR: KATHRYN MICHEL

Anorexia

From Willard M, Tvedten H: Small animal clinical diagnosis by laboratory methods, ed 4, St Louis, 2004, Saunders.

- **Psychogenic (especially cats)**
- **Inability to smell food**
- **Dysphagia (especially when it causes pain)**
- **Inflammation**
  - Because of an infectious agent
  - Because of immune-mediated disease
  - Because of neoplasia
  - Because of necrosis
  - Because of drugs
- **Alimentary and abdominal diseases (especially those causing nausea or abdominal pain)**
- **Neoplasia**
  - Because of the neoplasm itself
  - Because of secondary bacterial infection when neoplasia impairs natural defense mechanisms
- **Toxins**
  - Exogenous (various ones)
  - Endogenous (e.g., renal failure, hepatic encephalopathy)
- **Endocrine disease**
  - Diabetic ketoacidosis
  - Hypoadrenocorticism
  - Hyperthyroidism
- **Central nervous system (CNS) disease**
  - Primary
  - Secondary

Anisocoria

Modified with permission from Oliver JE, Lorenz MD: Blindness, anisocoria, and abnormal eye movements. In Oliver JE, Lorenz MD: Handbook of veterinary neurology, Philadelphia, 1994, Saunders, p 261.

*Unilateral lesions of these structures are rare.†Possibly loss of sight in left visual field, with partial sparing of right visual field.

Anisocoria and Other Signs of Lesions in the Visual Pathways

	VISION	PUPIL SIZE	PUPILLARY LIGHT REFLEX IN CONTRALATERAL EYE			
Complete Lesion on Right Side	**Right Eye**	**Left Eye**	**Right Eye**	**Left Eye**	**Light in Right Eye**	**Light in Left Eye**
1. Retina or optic nerve	Absent	Normal	Slightly dilated	Normal	No response	Both constrict
2. Orbit (CN II, III)	Absent	Normal	Dilated	Normal	No response	Left constricts
3. Optic chiasm (bilateral)*	Absent	Absent	Dilated	Dilated	No response	No response
4. Optic tract	Normal	Absent† or slightly miotic	Normal or slightly dilated	Normal	Both constrict	Both constrict
5. Lateral geniculate nucleus	Normal	Absent†	Normal	Normal	Both constrict	Both constrict
6. Optic radiation	Normal	Absent†	Normal	Normal	Both constrict	Both constrict
7. Occipital cortex	Normal	Absent†	Normal	Normal	Both constrict	Both constrict
8. Parasympathetic nucleus of CN III (bilateral)*	Normal	Normal	Dilated	Dilated	No response	No response
9. Oculomotor nerve	Normal	Normal	Dilated	Normal	Left constricts	Left constricts
10. Sympathetic nerve	Normal	Normal	Constricted	Normal	Both constrict	Both constrict

Anemias: Characteristics

Modified from Willard M, Tvedten H: Small animal clinical diagnosis by laboratory methods, ed 4, St Louis, 2004, Saunders.

Conclusions That May Be Drawn from Hematologic Data

Hematologic Conclusion	Typical Evidence
Regenerative anemia	Appropriate degree of increased reticulocytes or polychromasia for severity of the anemia
Nonregenerative anemia	Insufficient increase in reticulocytes for the severity and duration of the anemia
Hemolytic anemia	Regenerative anemia with additional evidence such as hemoglobinuria, normal plasma protein, hyperbilirubinemia, and documentation of one of the causes of hemolysis
Blood-loss anemia	Regenerative anemia with normal to decreased plasma protein, evidence of iron deficiency, or proof of blood loss
Immune-mediated hemolytic anemia (IMHA)	Moderate to marked spherocytosis, autoagglutination, and/or positive Coombs' test
Oxidant-induced hemolytic anemia	Increased numbers of Heinz bodies, eccentrocytes, and methemoglobinemia
Fragmentation anemia	Increased number of keratocytes, schizocytes, or acanthocytes
Iron-deficiency anemia	Microcytic hypochromic anemia with variable regeneration

Anemias: Evaluation

Approach to Anemia Diagnosis

From Willard M, Tvedten H: Small animal clinical diagnosis by laboratory methods, ed 4, St Louis, 2004, Saunders.

I. **Determine severity of anemia.**
- Mild anemia (PCV > 30% dog, >20% cat)
  - Consider age, breed, and statistical chance of normality.
  - Check for laboratory or sample error; repeat venipuncture.
  - For a secondary problem, go to step IV.
- For moderate to severe anemia, go to step II.

II. **Determine bone marrow responsiveness.**
- No reticulocytosis or polychromasia expected during first 2-3 days or in mild anemia (PCV > 30% dog, >20% cat).
- Reticulocytosis and polychromasia peak at 4-5 days if bone marrow function normal.
  - Marked canine reticulocytosis > 500,000/mcL
  - Marked feline aggregate reticulocytosis > 200,000/mcL
- Later-stage responsiveness at 7-14 days:
  - Feline punctuate reticulocytosis, marked > 1,500,000/mcL
  - Dogs: increase in macrocytic hypochromic RBCs
- Classification by RBC indices and hematology instrument graphics
  - Macrocytic hypochromic: regenerative anemia
  - Normocytic normochromic: nonregenerative or preregenerative anemia
  - Microcytic hypochromic: iron-deficiency anemia
  - Macrocytic normochromic: regenerative or nonregenerative
- If adequately regenerative, go to step III; if inadequately regenerative, go to step IV.

III. **Regenerative anemia diagnosis**
- Blood smear analysis critical in hemolytic anemia diagnosis
  - Spherocytes, autoagglutination, Heinz bodies, polychromasia, blood parasites, eccentrocytes, RBC fragmentation
- Hemoglobinuria is best proof of intravascular hemolytic anemia.
- Internal blood loss resembles hemolytic anemia.
  - Document hemorrhage with gross evidence of melena, ultrasound evidence of blood in body cavities, etc.
- External blood loss
  - Often in history
  - Tendency toward hypoproteinemia, hypoalbuminemia, or both
  - Check for thrombocytopenia or bleeding tendency.

IV. **Nonregenerative anemia diagnosis**
- Way to a diagnosis varies with case presentation.
- Use history and severity of anemia to reevaluate reticulocyte numbers to see if anemia is truly nonregenerative; duration exceeding 3-4 days excludes preregenerative anemia; reticulocyte response is weak or absent 2 weeks after the cause of an anemia ceases; mild anemia will not stimulate much reticulocytosis.
- Evaluate rest of the hematology report.
  - Microcytic hypochromic RBCs usually indicate iron-deficiency anemia
    - RBC cytograms and histograms more sensitive than MCV and MCHC
    - Half of iron-deficiency anemia cases regenerative
  - Normocytic normochromic anemia most common but nonspecific
  - Macrocytic normochromic feline RBCs without reticulocytosis suggests FeLV-induced myelodysplasia (see text)
  - Evidence of inflammation; anemia of inflammatory diseases is very common (i.e., mild, normocytic normochromic anemia).
  - Evidence of leukemia or dysplastic hematopoiesis usually indicates bone marrow evaluation; go to H.
  - Thrombocytopenia; consider *Ehrlichia* or other infections.
  - Pancytopenia or bicytopenia indicates bone marrow disease and bone marrow evaluation; go to H.
- Clinical chemistry profile
  - Renal or hepatic failure causes secondary anemia.
  - Systemic diseases have variable causes of anemia.
- Virology, serology if infection is likely (e.g., fever, lymphadenopathy)
- Endocrinologic examination for hypothyroidism or other dysfunction (e.g., mild, normocytic normochromic anemia)
- Toxicosis
  - Check for testicular neoplasm or access to estrogen.
  - Withhold any current drug therapy and monitor for recovery.

        - Check for toxicants in environment.
    - Bone marrow examination reveals many diagnoses.
        - Myelofibrosis, aplastic pancytopenia, dyserythropoiesis, leukemia, myelodysplasia, refractory anemia with excessive blasts, etc.

FeLV, feline leukemia virus; *MCHC,* mean corpuscular hemoglobin concentration; *MCV,* mean corpuscular volume; *PCV,* Packed cell volume; *RBC,* red blood cell.

Anemia: Causes

Causes

Modified with permission from Bonagura J: Kirk's current veterinary therapy XII: small animal practice, ed 12, St Louis, 1995, Saunders, p 448.

Hemorrhage

- ***Surgery/Trauma***
- ***Bleeding Disorder:***
  - von Willebrand disease/thrombopathia
  - Thrombocytopenia
  - Hemophilia A, B; decreases in other factors
  - DIC
- ***Ectoparasitosis (fleas, ticks, lice)***
- ***GI (hookworms, neoplasia, ulceration)***
- ***Neoplasia (hemangiosarcoma)***

Hemolysis

- ***Antibody-Mediated:***
  - Neonatal isoerythrolysis
  - Warm-reactive IgG IHA
  - Cold-reactive IgM IHA
  - Transfusion reaction
- ***Congenital:***
  - Phosphofructokinase deficiency (English springer spaniels, American cocker spaniel)
  - Familial nonspherocytic, hemolytic anemia (poodles)
  - Elliptocytosis (one crossbred dog)
  - NADH methemoglobin reductase deficiency (several breeds of dogs)
  - Hemolytic anemia secondary to RBC membrane defect (beagles)
  - Pyruvate kinase deficiency (beagles, basenjis, West Highland white terriers, giant schnauzers, Abyssinians)
  - Vitamin B12 deficiency (giant schnauzers)
  - Predisposition to oxidant injury, high erythrocyte potassium and low glutathione levels (Akitas, Shiba Inus)
- ***Toxin/Drug-Induced:***
  - Propylthiouracil
  - Lead
  - dl-methionine
  - Cephalosporins
  - Fenbendazole
  - Dapsone
  - Gold salts
  - MLV vaccines
  - Oxidants
  - Onions
  - Acetaminophen
  - Methylene blue
  - Phenacetin
  - Propylene glycol
  - Phenol compounds (mothballs)
  - Benzocaine
  - Hydroxyurea
  - Vitamin K3
- ***Parasites:***
  - *Mycoplasma haemofelis* and *M. haemominutum* infection
  - *Cytauxzoon felis*
  - Babesiosis (*Babesia canis, B. gibsoni*)
  - Ehrlichiosis (*Ehrlichia canis*)
- ***Microangiopathic:***
  - Splenic torsion

- Cranial vena cava syndrome
- Hemangiosarcoma

Decreased Production

- ***Bone Marrow Disorder:***
  - Hematopoietic malignancy
  - Myelofibrosis
  - Idiopathic aplastic anemia
  - Irradiation
  - Myelodysplasia
- ***Systemic Disease:***
  - Anemia of chronic disease/inflammation
  - FeLV
  - Parvovirus
  - Renal failure
  - Liver disease
  - Endocrine disease (hypothyroidism, hypoadrenocorticism)
  - Neoplasia
- ***Toxin/Drug:***
  - Estrogen
  - Chemotherapy
  - Phenylbutazone
  - TMS
  - Griseofulvin
  - Quinidine
  - Thiacetarsemide
  - NSAIDs
- ***Nutritional:***
  - Mineral deficiency (iron)
  - Vitamin deficiency (B complex)
  - Inadequate protein intake

DIC, Disseminated intravascular coagulation; *FeLV,* feline leukemia virus; *GI,* gastrointestinal; *IHA,* immune-mediated hemolytic anemia; *MLV,* modified live virus; *NSAIDs,* nonsteroidal antiinflammatory drugs; *TMS,* trimethoprim/sulfadiazine.

Anemia, Immune-Mediated

Examples of Underlying Disorders and Triggers

From Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

Infectious

- Viral: FeLV, FIV, FIP infection, transient or chronic persistent upper respiratory or GI viral diseases
- Bacterial: leptospirosis, feline mycoplasmosis, various acute and chronic infections (e.g., abscess, pyometra, diskospondylitis)
- Parasitic: babesiosis, leishmaniasis, dirofilariasis, ehrlichiosis, *Ancylostoma caninum*
- Other emerging infectious diseases (e.g., bartonellosis), bee stings

Drugs

- Sulfonamides
- Cephalosporins
- Penicillins
- Vaccines
- Propylthiouracil (cats)
- Methimazole (cats)
- Procainamide

Neoplasia

- Hemolymphatic: leukemias, lymphoma, multiple myeloma
- Solid tumors

Immune Disorders

- SLE
- Hypothyroidism
- Primary and secondary immunodeficiencies

Genetic Predisposition

- American cocker spaniel (one-third of all cases)
- English springer spaniel
- Old English sheepdog
- Irish setter
- Poodle
- Dachshund

FeLV, Feline leukemia virus; *FIP,* feline infectious peritonitis; *FIV,* feline immunodeficiency virus; *GI,* gastrointestinal; *SLE*, systemic lupus erythematosus.

Anemia, Hemolytic

Adapted from Bonagura J, Twedt DC, editors: Kirk's current veterinary therapy XIV: small animal practice, St Louis, 2009, Saunders.

Causes of Hemolytic Anemia in Dogs and Cats

Inherited Causes

- Pyruvate kinase deficiency
- Phosphofructokinase deficiency
- Chondrodysplasia/anemia
- Nonspherocytic hemolytic anemia

Immune-Mediated Causes (Primary)

- Primary (idiopathic) immune-mediated hemolytic anemia (IMHA)
- IMHA associated with systemic lupus erythematosus
- Neonatal isoerythrolysis
- Incompatible transfusions

Metabolic Causes

- Hypophosphatemia

Neoplastic Causes

- Microangiopathic anemia associated with hemangiosarcoma or lymphoma

Infectious Causes

- *Babesia canis*
- *Babesia gibsoni*
- *Mycoplasma haemominutum*
- *Mycoplasma haemofelis*
- *Mycoplasma haemocanis*
- *Dirofilaria immitis*
- Bacterial endocarditis
- Feline leukemia virus
- Leptospirosis
- *Cytauxzoon felis*
- *Ehrlichia canis*

Toxin- or Drug-Related Causes

- Onion toxicity
- Zinc toxicity
- Methylene blue
- Copper toxicity
- Propylthiouracil
- Methimazole
- Sulfa drugs
- Penicillins and cephalosporins
- Quinidine
- Acetaminophen (cats > dogs)
- Benzocaine (cats)
- Dapsone
- Nitrofurantoin
- Phenacetin (cats > dogs)
- Phenazopyridine
- Propofol (cats)
- Vaccinations
- Vitamin K3 (cats)

Anemia, Aplastic

Modified with permission from Kirk R, Bonagura J, editors: Kirk's current veterinary therapy Xl: small animal practice, St Louis, 1993, Saunders, p 481. *D,* Dog; *C,* cat.

Causes

Cause	Dog/Cat	Type of Aplasia	Outcome
Idiopathic	D,C	Chronic	Irreversible
Drug-Associated			
Estrogen	D	Acute/chronic	Reversible/irreversible
Chemotherapy	D,C	Acute	Reversible
Phenylbutazone	D	Acute	Mostly irreversible
Meclofenamic acid	D	Acute	Irreversible
Trimethoprim/sulfadiazine (TMS)	D	Acute	Reversible
Quinidine	D	Acute	Reversible
Thiacetarsemide	D	Acute	Reversible
Griseofulvin	C	Acute	Reversible
Infectious			
Ehrlichia	D	Acute/chronic	Reversible/irreversible
Parvovirus	D,C	Acute	Reversible
Feline leukemia virus	C	Chronic	Irreversible

Anaphylaxis

Causes

Modified from Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

Venoms

- Insects of the *Hymenoptera* order: bees, wasps, ants
- Spiders: black widow, brown recluse
- Lizards: Gila monster, Mexican beaded lizard
- Snakes: pit vipers (rattlesnakes, copperheads, water moccasins), coral snakes

Hormones

- Insulin
- Corticotropin
- Vasopressin
- Parathyroid hormone
- Betamethasone
- Triamcinolone

Antibiotics

- Penicillins: amoxicillin, ampicillin, procaine penicillin
- Chloramphenicol
- Lincomycin
- Gentamicin
- Tetracycline
- Sulfonamides
- Cephalosporins
- Polymyxin B
- Doxorubicin

Nonsteroidal Antiinflammatory Drugs (NSAIDs)

- Aspirin
- Ibuprofen

Anesthetics and Sedatives

- Acepromazine
- Ketamine
- Barbiturates
- Lidocaine and other local anesthetics
- Narcotics
- Diazepam

Parasiticides

- Dichlorophen
- Levamisole
- Piperazine
- Dichlorvos
- Diethylcarbamazine
- Thiacetarsemide

Miscellaneous

- Blood products

- Aminophylline
- Asparaginase
- Calcium disodium edetate
- Iodinated contrast media
- Neostigmine
- Amphotericin B
- Vaccines
- Allergen extracts: pollens, molds, foods
- Enzymes: chymotrypsin and trypsin
- Vitamins: vitamin K, thiamine, and folic acid
- Dextrans and gelatins
- Sulfonamides

Foods

- Milk
- Egg white
- Shellfish
- Legumes
- Fruits: citrus
- Chocolate
- Grains

Physical Factors

- Cold
- Heat
- Exercise

Amyloidosis

Diseases Reported in Association With Amyloidosis in Dogs

Modified from Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

Systemic Disease (Glomerular Disease)

Infectious

- ***Bacterial***
  - Pyelonephritis (A)
  - Pyometra (A, G)
  - Pyoderma (A, G)
  - Other chronic bacterial infections (A, G)
- ***Protozoal***
  - Leishmaniasis (A, MN, P-E, and M)
- ***Rickettsial***
- ***Viral***
  - Canine adenovirus type 1 (P-M)
- ***Fungal***
  - Blastomycosis (A)
  - Coccidioidomycosis (A, G)

Inflammatory

- Chronic dermatitis (A, G)
- Pancreatitis (A, G)
- Periodontal disease (A, G)
- Polyarthritis (A, G)
- Shar-pei fever (A)
- Systemic lupus erythematosus (A, MN, P-E, and M)

Neoplastic

- Lymphoma (A, G)
- Primary erythrocytosis (MCD?)
- Other neoplasms (A, G, MN)

Miscellaneous

- Hyperlipidemia (?)
- Chronic insulin infusion (A)
- Cyclic hematopoiesis in gray collies (A)

Familial

Idiopathic (A, G, MN, MCD, P-E, or M)

A, Amyloidosis; *E,* endocapillary; G, glomerulonephritis, uncharacterized; *M,* mesangial; *MCD,* minimal change disease; *MN,* membranous nephropathy; *P,* proliferative.

American Society of Anesthesiologists Classification System

From Slatter D: Textbook of small animal surgery, ed 3, Philadelphia, 2003, Saunders.

CBC, Complete blood cell count; *PCV,* packed cell volume; *TP,* total protein; *U/A,* urinalysis.*Minor is duration less than 60 minutes.†Major is duration longer than 60 minutes or concerns patients older than 7 years.‡Surgical panel: urea, creatinine, alkaline phosphatase, alanine aminotransferase, glucose, sodium, potassium, chloride, total protein.§Biochemical panel: full panel includes surgical panel tests plus bicarbonate, anion gap, calcium, phosphorus, cholesterol, total bilirubin, γ-glutamyltransferase, and albumin.

American Society of Anesthesiologists: Classification System for Physical Status and Recommended Tests for Each Class

			RECOMMENDED LABORATORY TESTS		
Physical Status	**Definition**	**Examples**	**Minor***	**Major†**	**Prognosis**
I	Healthy with no organic disease	Elective procedures not necessary for health (e.g., ovariohysterectomy)	PCV, TP, urine specific gravity	CBC, U/A, surgical panel‡	Excellent
II	Local disease with no systemic signs	Healthy nonelective surgery (e.g., skin laceration, simple fracture)	PCV, TP, urine specific gravity	CBC, U/A, surgical panel‡	Good
III	Disease causes moderate systemic signs that limit function	Heart murmur, anemia, pneumonia, mild chest trauma, moderate dehydration	CBC, U/A, surgical panel‡	CBC, U/A, biochemical§ panel	Fair
IV	Disease causes severe systemic signs that threaten life	Gastric torsion, diaphragmatic hernia, severe chest trauma, severe anemia or dehydration	CBC, U/A, biochemical panel§	CBC, U/A, biochemical§ panel	Guarded
V	Moribund, not expected to live for more than 24 hours with or without surgery	Endotoxic shock, severe trauma, multiorgan failure	CBC, U/A, biochemical panel§	CBC, U/A, biochemical§ panel	Grave
E	Emergency	Qualifier of above classes	PCV, TP, urine specific gravity	Depends on facilities available	Variable

Alopecia, Canine Symmetrical

ACTH, Adrenocorticotropic hormone; *FSH,* follicle stimulating hormone; *GH,* growth hormone; *hrTSH,* human recombinant thyroid stimulating hormone; *LH,* luteinizing hormone; *PU/PD,* polyuria/polydipsia; *T4,* thyroxine; *TgAA,* antithyroglobulin antibodies; *TSH,* thyroid stimulating hormone.

Disorders Causing Symmetrical Alopecia in Dogs

Disorders	Cutaneous and Systemic Signs Apart from Alopecia	Common Clinicopathologic Abnormalities	Diagnostic Tests
Alopecia X	Skin hyperpigmentation, hair regrowth at the biopsy site	None	Signalment, rule out other causes, skin biopsies (large number of flame follicles suggestive)
Anagen defluxion	Related to severe systemic disease or to cytotoxic therapy	Related to the underlying disorder	History, trichogram
Breed-specific follicular dysplasia	Secondary pyoderma	None	Signalment, trichogram, skin biopsy
Canine recurrent flank alopecia	None	None	Signalment, history, skin biopsy
Color dilution alopecia	Comedones, secondary pyoderma	None	Signalment, trichogram, skin biopsy
Congenital alopecia	Anomalies of dentition	None	Signalment, skin biopsy
Hyperadrenocorticism	• Atrophic skin, calcinosis cutis, comedones, prominent cutaneous blood vessels, phlebectasia • PU/PD, polyphagia, panting, pot belly, muscle atrophy, lethargy, testicular atrophy, abnormal estrus	Stress leukogram, increased serum alkaline phosphatase, hypercholesterolemia, hyposthenuria, urinary tract infection	History, physical findings, ACTH stimulation test, low-dose dexamethasone suppression test, high-dose dexamethasone suppression test, ultrasonography, urine cortisol/creatinine ratio
Hyperestrogenism	• Skin hyperpigmentation, linear preputial dermatosis • Enlarged vulva, gynecomastia • Abnormal estrus, abnormal sexual behavior	Bone marrow suppression	Signalment, physical findings, ultrasonography/radiography, histopathology (gonads)
Hypothyroidism	Dull haircoat, scaling, myxedema, lethargy, obesity	Hypercholesterolemia, mild nonregenerative anemia	Total T4, free T4, TSH, (+/− TgAA, TSH stimulation test with hrTSH)
Pattern alopecia	None	None	Signalment, skin biopsy
Pituitary dwarfism	• Skin hyperpigmentation, secondary pyoderma • Proportionate dwarfism, clinical signs of hypothyroidism (if concomitant TSH deficiency), hypogonadism (if concomitant LH and FSH deficiency)	None	Signalment, physical findings, basal and poststimulation GH measurement, total T4 or free T4
Sebaceous adenitis	Scaling, follicular casts	None	Skin biopsy, trichogram

Disorders	Cutaneous and Systemic Signs Apart from Alopecia	Common Clinicopathologic Abnormalities	Diagnostic Tests
Telogen effluvium	Only if systemic disease or physiologic stress is present	None	History, trichogram, skin biopsy

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Alkalosis, Respiratory

Causes

From DiBartola S: Fluid, electrolyte, and acid-base disorders in small animal practice, St Louis, 2006, Saunders.

Hypoxemia (stimulation of peripheral chemoreceptors by decreased oxygen delivery)

- Right-to-left shunting
- Decreased Pio2 (e.g., residence at high altitude)
- Congestive heart failure (CHF)
- Severe anemia
- Hypotension
- Pulmonary diseases (causing ventilation/perfusion inequality)
    - Pneumonia
    - Pulmonary embolism
    - Pulmonary fibrosis
    - Pulmonary edema
    - Acute pulmonary distress syndrome (ARDS)

Pulmonary Disease (stimulation of nociceptive receptors independent of hypoxemia)

- Pneumonia
- Pulmonary embolism
- Interstitial lung disease
- Pulmonary edema
- ARDS

Central Nervous System (CNS)–Mediated Hypocapnia (direct stimulation of medullary respiratory center)

- Liver disease
- Gram-negative sepsis
- Drugs: salicylate intoxication, progesterone, xanthines (e.g., aminophylline)
- Recovery from metabolic acidosis
- Central neurologic disease
    - Trauma
    - Tumor
    - Infection
    - Inflammation (e.g., granulomatous meningoencephalitis)
    - Cerebrovascular accident
- Exercise
- Heatstroke

Mechanical Ventilation

Alkalosis, Metabolic

Causes

From DiBartola S: Fluid, electrolyte, and acid-base disorders in small animal practice, St Louis, 2006, Saunders.

Chloride Responsive

- Vomiting of stomach contents
- Diuretic therapy
- Post hypercapnia

Chloride Resistant

- Primary hyperaldosteronism
- Hyperadrenocorticism

Alkali Administration

- Oral administration of sodium bicarbonate or other organic anions (e.g., lactate, citrate, gluconate, acetate)
- Oral administration of cation exchange resin with nonabsorbable alkali (e.g., phosphorus binder)

Miscellaneous

- Refeeding after fasting
- High-dose penicillin
- Severe potassium or magnesium deficiency

Adrenal Mass/Nodule

List of Possibilities in the Differential Diagnosis of an Incidentally Discovered Mass in the Adrenal Region

From Bonagura J: Kirk's current veterinary therapy XIII, St Louis, 2000, Saunders.

Adrenal Cortex

- Nodular hyperplasia
- Adenoma
- Carcinoma

Adrenal Medulla

- Pheochromocytoma
- Ganglioneuroma

Extraadrenal Masses

- Extraadrenal pheochromocytoma (paraganglioma)

Other Adrenal Masses

- Myelolipoma
- Granulomatous disease (fungal, feline infectious peritonitis [FIP])
- Teratoma
- Adrenal cyst
- Hematoma

Metastasis

- Mammary gland tumors
- Lymphoma
- Leukemia
- Pulmonary adenocarcinoma
- Other carcinomas (prostate, bladder, gastric)

Pseudoadrenal Masses

- Arising from kidney, pancreas, lymph nodes, and blood vessels

Technical Artifacts

Acute Respiratory Distress Syndrome (ARDS)

Causes, Predispositions, and Risk Factors*

*Risk factors may apply to veterinary patients, human patients, or both.

- Electrocution
- Near drowning
- Neurologic insult (e.g., brain injury)
- Noxious gas inhalation (e.g., phosphine toxicosis)
- Oxygen toxicity
- Pneumonia (aspiration, other)
- Pulmonary contusions
- Pulmonary embolism
- Sepsis (e.g., secondary to parvoviral enteritis or other processes)
- Smoke inhalation
- Strangulation
- Trauma (massive)
- Upper airway obstruction (laryngeal paralysis, elongated soft palate, foreign body, mass)
- Vasculitis/systemic inflammatory response syndrome (SIRS) (e.g., secondary to necrotizing pancreatitis or other generalized inflammatory states)

Acute Renal Failure

Causes

Modified from Bonagura J: Kirk's current veterinary therapy XIII, St Louis, 2000, Saunders.

Prerenal

- Anesthesia
- Dehydration*
- Heatstroke
- Hemorrhagic shock
- Hypoadrenocorticism*
- Hypoalbuminemia
- Hypotensive shock
- Hypovolemic shock
- Septic shock
- Surgery
- Trauma
- Vasculitis

Intrinsic Renal

Nephrotoxins

- Aminoglycosides
- Amphotericin B
- Cisplatin
- Ethylene glycol
- Heavy metals
- Hemoglobinuria
- Lilies
- Myoglobinuria
- Nonsteroidal antiinflammatory drugs (NSAIDs)
- Radiocontrast agents
- Raisins/grapes
- Snake venom

Hemodynamic

- Anesthesia
- Cardiovascular shock
- Hemorrhagic shock
- Hypotensive shock
- Hypovolemic shock
- Septic shock
- Surgery

Other Conditions

- Borreliosis
- Glomerulonephritis
- Hemoglobin/myoglobin
- Hypercalcemia
- Leptospirosis
- Lymphoma
- Pyelonephritis
- Renal arterial thromboembolism
- Rickettsial infections
- Trauma

Postrenal

- Bilateral renal calculi
- Bilateral ureteral calculi
- Extraluminal obstruction
- Prostatic disease
- Rupture of outflow tracts
- Urethral calculi
- Urethral neoplasia

*Hypoadrenocorticism, diuretic treatment, and diabetes mellitus may cause azotemia with isosthenuria in the absence of kidney disease.

Acute Abdomen

Modified from Bonagura J: Kirk's current veterinary therapy XIII, St Louis, 2000, Saunders.

DE, Definitely requires emergent surgery; *DS,* definitely surgical; *NS,* nonsurgical (urgency of medical treatment depends on specific problem and condition of the patient; some nonsurgical acute abdomen cases may eventually require surgery on a nonemergent basis); *PE,* potentially requires emergent surgery; *PS,* potentially surgical (some conditions designated as PE may require surgery, although not on an emergent basis).

Differential Diagnoses and Immediate Triage Strategies for the Acute Abdomen

Body System: Cause of Acute Abdomen	**Treatment**
Gastrointestinal Digestive System	
Gastric dilatation	PS
Gastric dilatation/volvulus	DS, DE
Gastroduodenal ulceration	NS
Gastroduodenal perforation	DS, PE
Gastroduodenal rupture	DS, DE
Gastroduodenal dehiscence	DS, DE
Gastroenteritis (viral, bacterial, toxic; i.e., garbage)	NS
Hemorrhagic gastroenteritis	NS
Intestinal obstruction (foreign body, intussusception, neoplasia)	DS, PE
Functional intestinal obstruction; ileus	NS
Intestinal ulceration	NS
Intestinal perforation	DS, DE
Intestinal rupture	DS, DE
Intestinal dehiscence	DS, DE
Intestinal volvulus	DS, DE
Cecal inversion	DS, PE
Obstipation	NS
Colitis	NS
Colonic ulceration	NS
Colonic perforation	DS, DE
Colonic rupture	DS, DE
Colonic dehiscence	DS, DE
Hepatobiliary Digestive System	
Acute hepatitis (toxic, infectious)	NS
Hepatic abscess	DS, PE
Hepatic trauma	PS, PE
Hepatic rupture	PS, PE
Hepatobiliary neoplasia	PS, PE

Body System: Cause of Acute Abdomen	**Treatment**
Biliary obstruction (calculi, neoplasia, pancreatitis—abscess)	PS, PE
Biliary rupture	DS, DE
Cholecystitis	PS, PE
Cholangiohepatitis	NS
Pancreatic Digestive System	
Acute pancreatitis	NS
Pancreatic abscess	DS, PE
Pancreatic neoplasia	DS, PE
Urinary System	
Acute nephrosis (toxicosis)	NS
Acute nephritis-pyelonephritis	NS
Urinary calculi: renal	PS, PE
Urinary calculi: ureteral	PS, PE
Urinary calculi: cystic	PS, PE
Urinary calculi: urethral	PS, PE
Trauma-avulsion-rupture (renal, ureteral, cystic, urethral)	DS, PE
Obstruction (neoplasia, stricture): ureter	DS, PE
Obstruction (neoplasia, stricture): urethra	DS, PE
Renal artery thrombosis	PS, PE
Renal neoplasia	PS, PE
Reproductive System	
Female	
Acute metritis	PS, PE
Pyometra	DS, DE
Uterine torsion	DS, DE
Dystocia	PS, PE
Ovarian cyst	PS, PE
Ovarian neoplasia	DS, PE
Male	
Acute prostatitis	NS
Prostatic abscess	DS, PE
Prostatic cysts	DS, PE
Prostatic neoplasia	DS, PE
Testicular torsion	DS, DE
Hematopoietic System: Spleen	

Body System: Cause of Acute Abdomen	**Treatment**
Splenic mass (hematoma, extramedullary hema- topoiesis, neoplasia, nodular hyperplasia, abscess)	DS, PE
Splenic rupture (mass)	DS, DE
Splenic rupture (trauma)	PS, PE
Splenic torsion	DS, DE
Peritoneum and Mesentery	
Peritonitis: septic	DS, DE
Peritonitis: chemical (bile, urine, enzymes)	PS, PE
Parietal peritoneal trauma: blunt	NS
Parietal peritoneal trauma: penetrating	DS, DE
Mesenteric traction: large masses	DS, PE
Mesenteric lymphadenopathy	PS, PE
Mesenteric lymphadenitis	NS
Mesenteric volvulus	DS, DE
Mesenteric avulsion	DS, DE
Mesenteric artery thrombosis	DS, DE
Adhesions with organ entrapment: internal hernias	DS, PE
Abdominal Wall	
Trauma	PS, PE
Abscess	DS, PE
Hematoma	PS, PE
Strangulated hernias	DS, DE
Extraabdominal	
Intervertebral disk disease	PS, PE
Diskospondylitis	PS, PE
Intoxications (heavy metal)	NS
Thoracic wall disease	PS, PE
Steatitis	NS
Myositis	NS
Hypoadrenocorticism	NS

Acidosis, Respiratory

Causes

From DiBartola S: Fluid, electrolyte, and acid-base disorders in small animal practice, ed 3, St Louis, 2006, Saunders.

Airway Obstruction

- Aspiration (e.g., foreign body, vomitus)

Respiratory Center Depression

- Neurologic disease (e.g., brainstem, high cervical spinal cord lesion)
- Drugs (e.g., narcotics, sedatives, barbiturates, inhalation anesthetics)

Cardiopulmonary Arrest

Neuromuscular Defects

- **Myasthenia gravis**
- **Tetanus**
- **Botulism**
- **Polyradiculoneuritis**
- **Polymyositis**
- **Tick paralysis**
- **Hypokalemic myopathy in cats**
- **Hypokalemic periodic paralysis in Burmese cats**
- **Drug-induced (succinylcholine, pancuronium, aminoglycosides with anesthetics, organophosphates)**

Restrictive Defects

- **Diaphragmatic hernia**
- **Pneumothorax**
- **Pleural effusion**
- **Hemothorax**
- **Chest wall trauma**
- **Pulmonary fibrosis**
- **Pyothorax**

Pulmonary Disease

- **Acute respiratory distress syndrome**
- **Pneumonia**
- **Severe pulmonary edema**
- **Diffuse metastatic disease**
- **Smoke inhalation**
- **Pulmonary thromboembolism**
- **Chronic sterile bronchitis**
- **Pulmonary fibrosis**

Inadequate Mechanical Ventilation

Acidosis, Metabolic

Causes

From DiBartola S: Fluid, electrolyte, and acid-base disorders in small animal practice, ed 3, St Louis, 2006, Saunders.

- **Increased Anion Gap (Normochloremic)**
- Ethylene glycol intoxication
- Salicylate intoxication
- Other rare intoxications (e.g., paraldehyde, methanol)
- Diabetic ketoacidosis*
- Uremic acidosis†
- Lactic acidosis
- **Normal Anion Gap (Hyperchloremic)**
- Diarrhea
- Renal tubular acidosis
- Carbonic anhydrase inhibitors (e.g., acetazolamide)
- Ammonium chloride
- Cationic amino acids (e.g., lysine, arginine, histidine)
- Posthypocapnic metabolic acidosis
- Dilutional acidosis (e.g., rapid administration of 0.9% saline)
- Hypoadrenocorticism‡

Acidosis, Lactic

Causes*

*d-lactic acidosis occurs with short bowel syndrome in human beings and has been observed in cats fed propylene glycol.

From DiBartola S: Fluid, electrolyte, and acid-base disorders in small animal practice, ed 3, St Louis, 2006, Saunders.

Type A: Hypoxic

- Increased oxygen demand
  - Severe exercise
  - Convulsions
- Decreased oxygen availability
  - Reduced tissue perfusion
    - Cardiac arrest, cardiopulmonary resuscitation
    - Shock
    - Hypovolemia
    - Left ventricular failure
    - Low cardiac output
    - Acute pulmonary edema
  - Reduced arterial oxygen content
    - Hypoxemia (Po2 30 mm Hg)
    - Extremely severe anemia (packed cell volume [PCV] < 10%)

Type B: Nonhypoxic

- Drugs and toxins
  - Salicylates
  - Ethylene glycol
  - Many others
- Diabetes mellitus
- Liver failure
- Neoplasia (e.g., lymphoma)
- Sepsis
- Renal failure
- Hypoglycemia
- Hereditary defects
  - Mitochondrial myopathies
  - Defects in gluconeogenesis

Abortion, Canine

From Feldman E, Nelson R: Canine and feline endocrinology and reproduction, ed 3, St Louis, 2004, Saunders.

AGID, Agar gel immunodiffusion test; *RSAT,* rapid slide agglutination test; *TAT,* tube agglutination test; *TSH,* thyroid-stimulating hormone.

Causes and Methods for Diagnosis of Canine Abortions

Causative Agents	Clinical Findings	Necropsy Findings	Tests
Bacteria			
Brucella canis	Third-trimester abortion	Autolyzed fetuses	Culture (special media): vaginal discharge and blood serologic examination: RSAT, TAT, and AGID
B. abortus, *B. suis*, or *B. melitensis*	History of contact with infected livestock, third-trimester abortion	Autolyzed fetuses	Serologic testing: specific for organism
Salmonella spp.	Systemic disease in bitch, purulent vaginal discharge	Fetal septicemia	Culture: vaginal discharge and fetal tissues
Campylobacter spp.	History of diarrhea in bitch or contact with humans	Placentitis	Culture (special media): vaginal discharge and fetal tissues
Escherichia coli or *Streptococcus* spp.	Purulent vaginal discharge, systemic disease in bitch	Fetal septicemia	Culture: vaginal discharge and fetal tissues
Viruses			
Canine herpesvirus	Third-trimester abortion, bitch asymptomatic, vaginal vesicles, stillbirth, infertility	Fetal septicemia; multifocal petechiae; necrosis in fetal adrenal glands, kidney, liver, and lung	Serology in bitch: paired samples 2 weeks apart, run together
Canine distemper or canine adenovirus	Systemic involvement in bitch	Depends on virus involved	Depends on virus involved
Other Organisms			
Mycoplasmataceae (*Mycoplasma* or *Ureaplasma* spp.)	Asymptomatic bitch housed in overcrowded conditions, vaginal discharge, infertility	Fetal septicemia	Culture: vaginal discharge and fetal tissues
Toxoplasma gondii	Bitch may be asymptomatic or have multisystemic involvement	Placentitis, multiorgan involvement in fetus	Serology: paired samples 2 weeks apart, run together (fourfold increase significant)
Endocrine Causes			
Progesterone deficiency	Infectious causes ruled out	None	Serial progesterone assays during luteal phase
Hypothyroidism	Obesity, lethargy, symmetric hair loss	None	TSH stimulation test

Bronchial Disease, Chronic

Possible Causes of Chronic Bronchitis in Dogs

Modified with permission from Kuehn NF: Chronic bronchitis in dogs. In King L: In Textbook of respiratory disease in dogs and cats, 2004, Saunders, p 381.

- **Atmospheric pollution**
- **Passive smoking**
  - Chronic exposure to smoke in poorly ventilated confined spaces
- **Respiratory tract infections**
  - Chronic fungal infection
  - Chronic bacterial infection: *Bordetella bronchiseptica, Mycoplasma* spp.
  - Viral infection: canine distemper virus, adenovirus (types 1 and 2), herpesvirus
  - Parasites: *Filaroides milksi, F. hirthi, Crenosoma vulpis, Capillaria aerophila, Dirofilaria immitis*
- **Genetic or acquired defects**
  - α1-Antitrypsin deficiency
  - Mucociliary defects
  - Immunodeficiency
- **Hypersensitivity (allergic) lung disease**

Bradycardia

Causes of Bradycardia in Dogs and Cats

- **Arrhythmias**
  - Second-degree AV block
  - Third-degree AV block
  - SSS/sinus node dysfunction
  - Atrial standstill (hyperkalemia, atrial myopathy)
- **Hypothermia**
- **Hypothyroidism**
- **Organophosphate toxicosis**
- **Pharmacologic** (e.g., due to β-blockers, calcium channel blockers, digitalis, opiates, α2 blocking drugs)
- **Vagai tone high: normal**
  - Brachycephalic breed
  - Athletic animal at rest
  - Sleep
- **Vagai tone high: abnormal**
  - GI disturbances
  - Upper respiratory obstruction (e.g., foreign body, laryngeal paralysis, elongated soft palate, mass, anesthetic circuit problem)
  - Neurologic lesions (central and severe: usually coma)

AV, Atrioventricular; *GI,* gastrointestinal; *SSS,* sick sinus syndrome.

Notes: First-degree AV block does not affect the heart rate.

In critically ill or anesthetized animals, an acute transition from tachycardia to bradycardia may indicate an upcoming cardiac arrest.

Definition of bradycardia in the clinical setting: heart rate < 60 bpm (large-breed dogs), <70 bpm (medium-breed dogs), <90 bpm (small-breed dogs), <130 bpm (cats).

Bone Neoplasia

From Slatter D: Textbook of small animal surgery, ed 3, Philadelphia, 2003, Saunders.

Comparison of Primary Bone Tumors of the Appendicular Skeleton in Dogs

	Osteosarcoma	Chondrosarcoma	Fibrosarcoma	Hemangiosarcoma
Incidence of overall bone tumors	80%-85%	10%	<5%	<5%
Prevalence in appendicular versus axial skeleton	75%	11%	<40%	<50%
Age	Median 7-8 years	5-9 years	Mean 8.4 years	Young to middle-aged
Sex predilection	None (historically, male)	None	None	None
Breed predilection	Large and giant breeds	Medium to large breeds (golden retrievers)	Medium to large breeds	Medium to large breeds (German shepherds, boxers, Great Danes)
Radiographic findings	Osteolytic and osteoproductive	Osteolytic with periosteal reaction	Primarily lytic	Primarily lytic with considerable intramedullary extension
Histopathologic findings	Malignant spindle cells producing osteoid	Malignant spindle cells producing neoplastic chondroid in a fibrillar matrix	Malignant tumor of fibrous connective tissue	Malignant tumor of vascular endothelium
Sites	Metaphyseal; forelimb > hindlimb; distal radius primary	Primarily metaphyseal; hindlimb > forelimb	Metaphyseal and diaphyseal	Proximal and distal third of long bones; proximal humerus primary
Metastatic rate without treatment	90% before 1 year	20% (very slow)-100%	6%	Very high, at least 88%
Metastatic sites	Lungs > bone	Lung primary	Multiple	Multiple
Prognosis improved with tumor removal	Yes	Yes	Yes	Unknown
Prognosis improved with adjuvant chemotherapy	Yes	Unknown	Unknown	Unknown (possibly with doxorubicin)
Median survival without treatment	3-5 months	<2 months	Unknown	<3 months
Median survival with treatment	12 months	19 months	47% survival at 1 year	<5 months; <10% 1-year survival rate with amputation
Prognostic factors	Age, tumor size, percentage of tumor necrosis, tumor microvessel density, histologic grade, serum alkaline phosphatase	Histologic grade, location (i.e., if not resectable)	Degree of histologic differentiation	Unknown; all histologic grades carry a grave prognosis

	Osteosarcoma	Chondrosarcoma	Fibrosarcoma	Hemangiosarcoma

Bone Marrow Disorders

From Slatter D: Textbook of small animal surgery, ed 3, Philadelphia, 2003, Saunders.

FeLV, Feline leukemia virus; *FIV,* feline immunodeficiency virus; *IHA,* immune-mediated hemolytic anemia.

Causes Based on Blood and Bone Marrow Examination

PERIPHERAL BLOOD EXAMINATION			
Cytopenia	**Hematocytosis**	**Dysplastic Cells**	**Blast Cells**
BONE MARROW EVALUATION			
Aplasia or Hypoplasia	**Hyperplasia**	**Myelodysplasia**	**Neoplasia**
Infections:	Infections:	Myelodysplastic syndrome	Acute lymphoblastic leukemia
Viral	Bacterial	Drug-induced dysplasia	Acute myelogenous leukemia
Rickettsial	Mycoplasmal	Lead toxicosis	Metastatic neoplasm
Protozoal	Rickettsial	Infections:	
Fungal	Protozoal	FeLV	
Drugs or chemicals	FIV (early)	FIV	
Estrogen (neoplasm or iatrogenic)	Parasitic	Nutritional deficiencies	
Organ failure	Viral (recovery)	Pelger-Huët anomaly	
Chronic disease or inflammation	Immune-mediated damage	Macrocytosis (poodles)	
Endocrine disorders	Iron deficiency	Myeloid leukemia	
Irradiation	Oxidative injury	IHA	
Hereditary cytopenia	Zinc toxicosis	Lymphoma	
Nutritional deficiencies	Hereditary enzyme deficiency		
Myelophthisis	Allergic reactions		
Myelofibrosis	Inflammation or hypersensitivity		
Marrow necrosis	Chronic leukemias		
Immune-mediated damage	Paraneoplastic syndrome		

Bone Diseases, Congenital

Congenital Skeletal Disorders of Small Animals

Adapted from Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders, p 1970.

Generalized Bone Malformations

- Osteopetrosis—dense bones
- Osteogenesis imperfecta—osteopenia and bone fragility
- Mucopolysaccharidosis—lysosomal enzyme defects
- Dwarfism—osteochondrodysplasias (Scottish fold) and pituitary
- Congenital hypothyroidism
- Retained cartilage cores
- Craniomandibular osteopathy
- Multiple cartilaginous exostoses
- Avascular necrosis of the femoral head

Malformations of Individual Bones

- Hemimelia—radial or tibial agenesis
- Congenital amputation—absence of distal limb portion
- Phocomelia—missing segment of limb
- Amelia—absence of complete limb

Malformations of Bone Combinations

- Syndactyly—fused digits
- Polydactyly—extra digits
- Ectrodactyly—split or lobster claw deformity

Blood Type Frequencies, Dogs

From limited surveys in Giger U, Gelens J, Callan MB, et al: An acute hemolytic transfusion reaction caused by dog erythrocyte antigen 1.1 incompatibility in a previously sensitized dog. J Am Vet Med Assoc 206:9, 1995.

DEA, Dog erythrocyte antigen.*DEA 1.1 and 1.2 negative dogs.

	PERCENTAGE (%)	
Blood Type	**Positive**	**Negative**
DEA 1.1*		
1.1 (A1)	33–45	55–67
1.2 (A2)	7–20	35–60*
DEA 3 (B)	5–10	90–95
DEA 4 (C)	87–98	2–13
DEA 5 (D)	12–22	78–88
DEA 7 (Tr)	8–45	55–92

Blood Type Frequencies, Cats

With permission from Oxford University Press, adapted from Giger U, Bucheler J, Patterson DF: Frequency and inheritance of A and B blood types in feline breeds of the United States. J Hered 82:15, 1991. Also with permission, adapted from Giger U, Griot-Wenk M, Bucheler J, et al: Geographical variation of the feline blood type frequencies in the United States. Feline Pract 19:5, 1991.

*Breeds with isolated type AB cats.

	PEERCENTAGE (%)			PERCENTAGE (%)	
Domestic Shorthair*	**Type A**	**Type B**	**Purebred Cats**	**Type A**	**Type B**
USA			Abyssinian	84	16
Northeast	99.7	0.3	American shorthair	100	0
North central	99.6	0.4	Birman*	82	18
Southeast	98.5	1.5	British shorthair*	64	36
Southwest	97.5	2.5	Burmese	100	0
West Coast	95.3	4.7	Cornish rex	67	33
Other Countries			Devon rex	59	41
Australia (Brisbane)	73.7	26.3	Exotic shorthair	73	27
Argentina	97.3	2.7	Himalayan	94	6
Europe			Japanese bobtail	84	16
Austria	97.0	3.0	Maine coon	97	3
England	97.1	2.9	Norwegian forest cat	93	7
Finland	100	0	Oriental shorthair	100	0
France	85.1	14.9	Persian	86	14
Germany	94.0	6.0	Scottish fold*	81	19
Italy	88.8	11.2	Siamese	100	0
Netherlands	96.1	3.9	Somali*	82	18
Scotland	97.1	2.9	Sphinx* (Canadian hairless)	83	17
Switzerland	99.6	0.4	Tonkinese	100	0

Blindness

From Slatter D: Textbook of small animal surgery, ed 3, Philadelphia, 2003, Saunders.

Acute Blindness

Location	Diagnosis	Potential Causes
Cornea	Edema	Loss of endothelial function (glaucoma, trauma, uveitis)
Anterior chamber	Uveitis	Hyphema
		Hypopyon
		Lipemic flare
Lens	Cataract	Diabetes mellitus
Vitreous		Hemorrhage
Retina	Retinal detachment	Hypertension, hyperviscosity
		Trauma
		Uveodermatologic syndrome
		Other immune-mediated disease
		Collie eye anomaly
		Vitreoretinal dysplasia
		Infectious:
		Mycotic
		Ehrlichiosis
		Rocky Mountain spotted fever
		Protothecosis
		Toxoplasmosis
		Feline immunodeficiency virus
		Feline leukemia virus
		Other
		Rhegmatogenous (shih tzu)
		Neoplasia (primary versus secondary)
	Retinal degeneration	Sudden acquired retinal degeneration
		Glaucoma
		Toxic: enrofloxacin, ivermectin, others
		Glaucoma
Optic nerve, optic chiasm, optic tract		Optic neuritis (infectious and noninfectious)
		Reticulosis
		Neoplasia (primary versus secondary)
		Trauma
Lateral geniculate body, optic radiation, visual cortex		Inflammatory (infectious and noninfectious)
		Postanesthesia
		Elevated intracranial pressure
		Neoplasia

Location	Diagnosis	Potential Causes
		Postictal
		Reticulosis

Bleeding Disorders: Primary Versus Secondary

With permission from Bonagura J: Kirk's current veterinary therapy XII: small animal practice, St Louis, 1995, Saunders, p 459.

Clinical Manifestations of Primary and Secondary Hemostatic Defects

Primary Hemostatic Defect	Secondary Hemostatic Defect
Petechiae common	Petechiae rare
Hematomas rare	Hematomas common
Bleeding at mucosal membranes, bleeding from multiple sites	Bleeding into muscles, joints, and body cavities
Bleeding immediately after venipuncture	Delayed bleeding after venipuncture
Examples: immune-mediated thrombocytopenia, aspirin therapy, von Willebrand disease	Examples: anticoagulant rodenticide intoxication, coagulopathy of hepatic insufficiency, hemophilias

Bleeding Disorders

Modified from Willard M, Tvedten H: Small animal clinical diagnosis by laboratory methods, ed 4, St Louis, 2004, Saunders.

APTT, Activated partial thromboplastin time; *BMBT,* buccal mucosal bleeding time; *D,* decreased; *DIC,* disseminated intravascular coagulation; *FDP,* fibrin degradation products; *I,* increased; *N,* normal; *PT,* prothrombin time; *vWD,* von Willebrand disease. DIC can have widely variable results.*Initially stops in normal time period but may start bleeding again.†Mild thrombocytopenia may occur if patient is concurrently hypothyroid.‡Usually normal but may be increased.

Expected Hemostatic Test Results in Selected Diseases

	HEMOSTATIC PROFILE				
Disease	**BMBT**	**Platelet Count**	**APTT**	**PT**	**FDP**
Thrombocytopenia (e.g., ehrlichiosis)	I	D	N	N	N
Platelet dysfunction (e.g., aspirin treatment, vWD)	I	N	N	N	N
Intrinsic pathway defect (e.g., hemophilia A or B)	N*	N	I	N	N
Factor VII deficiency	N	N	N	I	N
Multiple factor defects (e.g., vitamin K antagonism)	N*	N	I	I	N
Common pathway defect (e.g., factor X deficiency)	N*	N	I	I	N
DIC	I	D	I	I	I
von Willebrand disease	I	N†	N‡	N	N

Behavioral Change: Primary Behavioral Versus Neurologic

Modified from Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 4, St Louis, 1994, Saunders.

Behavioral Signs Usually Caused by a Primary Behavioral Problem

- Aggression: dominance, competition, internal, fear, pain, learned, idiopathic
- Fear: fearful reactions to thunderstorms, gunshots, fireworks, separation anxiety, other animals, specific people
- Barking/hyperactivity: not true hyperkinesis
- Destruction: scratching, chewing, digging
- Roaming
- Inappropriate elimination: marking territory, urine spraying in cats, submissive
- Sexual: inappropriate mounting, lack of interest
- Maternal: cannibalism, anxiety, pseudopregnancy, indifference
- Predation feeding: aversions, coprophagy, pica, anorexia, wood chewing, grass and plant eating
- Attention-getting: self-mutilation; biting or chewing own feet, tail, or objects; barking; chasing shadows
- Stress response: self-mutilation, flank-sucking, head-bobbing or weaving, fly snapping, flank-staring, circling, face-rubbing, excessive grooming, tail and back twitching

Behavioral Signs Usually Caused by Neurologic Disease

- Persistent circling
- Aimless pacing
- Head pressing/getting stuck in corners
- Disorientation
- Nonrecognition of owners and familiar objects
- Dullness, depression, lethargy
- Hiding
- Seizures (episodic, untriggered behavioral abnormalities)
- Sudden idiopathic increase or loss of appetite
- Idiopathic polydipsia, sudden onset of frequent urination, unknowing dropping of fecal material in house, unexplained tremors, deafness, no response to sounds, bumping into objects

Bacteria Isolated from Sites of Infection

Data compiled from Greene CE, editor: Clinical microbiology and infectious diseases of the dog and cat, Philadelphia, 1998, Saunders.

Integument

- ***Pyoderma***
  - *Staphylococcus aureus/pseudintermedius*
  - *Proteus* spp.
  - *Pseudomonas* spp.
  - *Escherichia coli* (usually secondary to staphylococci)
- ***Ear***
  - *Pseudomonas* spp.
  - *S. aureus/intermedius*
  - *Proteus* spp.

Respiratory System

- ***Pneumonia***
  - *Pseudomonas* spp.
  - *E. coli*
  - *Klebsiella* spp.
  - *Pasteurella* spp.
  - *Bordetella* spp.
  - *Staphylococcus* spp.
  - *Streptococcus* spp.
  - *Mycoplasma* spp.
- ***Pleural Cavity***
  - *Nocardia* spp.
  - *Actinomyces* spp.
  - *Pasteurella* spp.
  - Anaerobes

Gastrointestinal Tract

- ***Intestine***
  - *Salmonella* spp.
  - *Campylobacter* spp.
  - *Clostridium perfringens*
  - *E. coli*

Genitourinary Tract

- *E. coli*
- *Proteus* spp.
- *Klebsiella* spp.
- *S. aureus/intermedius*

Eye (Conjunctiva and Cornea)

- *S. aureus* (coagulase positive and negative)
- *Streptococcus* spp.
- *S. epidermidis*
- *E. coli*
- *Proteus* spp.
- *Bacillus* spp.

Cardiovascular System

- ***Aerobes***
  - *S. aureus*
  - β-hemolytic streptococci
  - *E. coli*
  - *Klebsiella* spp.
  - *Pseudomonas* spp.
  - *Proteus* spp.
  - *Salmonella* spp.
- ***Anaerobes***
  - *Bacteroides* spp.
  - *Fusobacterium* spp.
  - *Clostridium* spp.

Cyanosis: Differentiation

From Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 5, St Louis, 2000, Saunders.

↓, Decreased; ↓↓, markedly decreased; ↑, increased; ↑↑, markedly increased.*Normal SaO2 (room air) = ~97%; normal PaO2 (room air) = ~100 mm Hg; normal PaCO2 (room air) = ~40 mm Hg; (−), no response.†Unless drawn from affected area.

Blood Gas Measurements, Oxygen Saturations, and Response to Oxygen Supplementation in Various Cyanotic Disorders

	Sao2	Pao2		Pao2
Problem	**Room Air***	**Room Air***	**PaCO2***	**Response to 100% O2**
Peripheral cyanosis	Normal†	Normal†	Normal	(−)
Right-to-left intracardiac shunt	↓↓	↓↓	Normal	(−)
Pulmonary parenchymal disease	↓↓	↓↓	↑	↑
Hypoventilation	↓	↓	↑↑	↑
Systemic hypoperfusion	↓	↓	Normal/↑	↑
Ventilation/perfusion mismatch	↓	↓	Normal/↓	↑
Methemoglobinemia	↓	Normal	Normal	(−)

Cyanosis

Causes of Central and Peripheral Cyanosis

Modified from Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

CENTRAL CYANOSIS

Cardiac (Right-to-Left Shunting)

Intracardiac:

- Tetralogy of Fallot
- Atrial or ventricular septal defect with pulmonic stenosis or pulmonary hypertension

Extracardiac:

- Reversed patent ductus arteriosus (PDA) (differential cyanosis)
- Pulmonary arteriovenous fistulas with pulmonary hypertension

Pulmonary

Hypoventilation:

- Pleural effusion, pneumothorax
- Respiratory muscle failure (e.g., fatigue, myopathy, or neuromuscular disease)
- Toxicity (e.g., sedative or anesthetic overdose)
- Primary neurologic disease (e.g., neoplasia, inflammatory)

Obstruction:

- Laryngeal paralysis
- Foreign body (e.g., laryngeal, tracheal)
- Mass lesion of large airways (e.g., neoplasia, parasitic, inflammatory)
- Inadequate oxygen concentration of inspired gas (e.g., high-altitude, anesthetic complication)

Ventilation-Perfusion Mismatch

- Pulmonary thromboembolism
- Pulmonary infiltration
- Edema
- Inflammation
- Neoplasia
- Acute respiratory distress syndrome (ARDS)
- Chronic obstructive pulmonary disease or pulmonary fibrosis

Non–Oxygen-Carrying Hemoglobin (e.g., methemoglobinemia)

PERIPHERAL CYANOSIS

- Central cyanosis (e.g., congestive heart failure)
- Decreased arterial supply (e.g., surgical ligation of artery)
- Peripheral vasoconstriction (e.g., hypothermia, shock)
- Arterial thromboembolism
- Low cardiac output
- Obstruction of venous drainage: tourniquet or foreign object (i.e., rubber band), venous thrombosis, right-sided heart failure

Cutaneous Neoplastic and Nonneoplastic Masses

Classification

Epithelial Neoplastic and Nonneoplastic Skin MassesEpidermal Origin

- Viral papilloma
- Squamous cell carcinoma
- Basal cell carcinoma
- Dermoid cyst (Rhodesian ridgeback)

Follicular Origin

- Follicular cyst (infundibular cyst)
- Follicular hamartoma
- Trichoblastoma
- Trichoepithelioma
- Trichofolliculoma
- Infundibular keratinizing acanthoma (intracutaneous cornifying epithelioma, keratoacanthoma)
- Pilomatricoma

Melanocytic Origin

- Melanocytoma
- Melanoma

Sebaceous Origin

- Sebaceous hamartoma/nevus
- Sebaceous gland hyperplasia/adenoma
- Sebaceous epithelioma
- Sebaceous carcinoma
- Perianal (hepatoid) gland hyperplasia and adenoma
- Perianal gland epithelioma
- Perianal gland carcinoma

Sweat Gland Origin

- Apocrine cyst
- Apocrine adenoma
- Apocrine adenocarcinoma
- Eccrine carcinoma

Mesenchymal Neoplastic and Nonneo-plastic Skin MassesFibrous Origin

- Collagenous hamartoma/nevus
- Canine nodular dermatofibrosis (German shepherd)
- Acrochordon (skin tag)
- Fibroma
- Fibrosarcoma

Vascular and Perivascular Origin

- Hemangioma
- Hemangiosarcoma
- Lymphangiosarcoma
- Hemangiopericytoma

Lipocytic Origin

- Lipoma
- Liposarcoma

Muscular Origin

- Leiomyoma
- Leiomyosarcoma

Neural and Perineural Origin

Merkel cell tumor

Lymphohistiocytic Skin MassesHistiocytic Origin

- Canine cutaneous histiocytoma
- Canine reactive histiocytosis (cutane-ous, systemic)
- Histiocytic sarcoma

Lymphocytic Origin

- Plasmacytoma
- Epitheliotropic lymphoma
- Nonepitheliotropic lymphoma
- Cutaneous lymphomatosis

Miscellaneous Origins

- Mast cell tumor
- Transmissible venereal tumor
- Cutaneous metastases

* For noninflammatory and infectious processes, see algorithm of Nodular Dermatitis, .

AUTHOR: MANON PARADIS

Cranial Nerve Deficits

With permission from Braund KG: Clinical syndromes in veterinary neurology, St Louis, 1994, Mosby.

Cranial Nerve Dysfunction

Nerve	Clinical Signs	Clinical Tests	Normal Response	Abnormal Response
I. Olfactory	Hyposmia or anosmia	Smell of food or nonirritating, volatile substance	Interest in food; sniff, recoil, or nose lick with volatile substance	No response
II. Optic	Visual impairment and hesitancy in moving	• Obstacle test • Visual placing reaction • Menace reaction • Following movement test	• Avoidance of obstacle • Visual placement of limbs • Eye blink • Eyes following objects	• Bumping objects • No response
III. Oculomotor	Ventrolateral strabismus	1. Ocular movement in horizontal and vertical planes	1. Normal ocular excursion	1. Impaired movements of affected eye
	Paralysis of upper eyelid (ptosis), mydriasis	2. Point source of light in each eye	2. Direct and consensual pupillary light reflexes	2. On affected side, direct pupillary reflex absent, consensual reflex present; on normal side, direct pupillary reflex present, consensual reflex absent
Sympathetic control of pupillary function	Constricted pupil (miosis), enophthalmos, prolapse of third eyelid, ptosis of upper lid			
IV. Trochlear	Usually not noted			
V. Trigeminal (motor and sensory)	• Atrophy of masticatory muscles • Inability to close mouth	• Jaw tone • Palpate and observe masticatory muscles • Palpebral reflex • Corneal reflex • Probe nasal mucosa • Touch face	• Resistance to opening jaws • Normal muscle contour and resilience • Eye blink • Eye blink and globe retraction • Recoil • No reaction	• Lack of resistance • Atrophy, hypotonia • No response • Intense discomfort
VI. Abducent	Medial strabismus	Ocular movements in horizontal plane	Normal ocular excursion	Impaired lateral movement of affected eye
VII. Facial	• Asymmetry of facial expression • Inability to close eyelids • Lip commissure paralysis • Ear paralysis	• Palpebral reflex • Corneal reflex • Menace reaction • Tickle ear	1-3. Eye blink • Ear flick	1-4. No response
VIII. Vestibulocochlear				

Nerve	Clinical Signs	Clinical Tests	Normal Response	Abnormal Response
Vestibular	• Nystagmus, head tilt, circling • Falling and rolling	• Ocular movements in horizontal and vertical planes • Caloric and rotatory test • Righting reactions	1-2. Normal physiologic nystagmus • Normal righting	1-3. No response, ventrolateral strabismus on dorsal extension of head
Cochlear	Deafness	Hand clap	Startle reaction, blink ear contraction	No response
IX. Glossopharyngeal	Dysphagia	Gag reflex	Swallowing response	No response
X. Vagus	• Dysphagia • Abnormal vocalizing • Inspiratory dyspnea • Megaesophagus	• Gag reflex • Laryngeal reflex • Oculocardiac reflex	• Swallow • Cough • Bradycardia	1-3. No response
XI. Spinal accessory	Usually not noted			
XII. Hypoglossal	Deviation of tongue	• Tongue stretch • Nose rub	• Retraction • Lick response	1-2. No response

Coughing

Modified with permission from King L: In Textbook of respiratory disease in dogs and cats, Philadelphia, 2004, Saunders, p 44.

COPD, Chronic obstructive pulmonary disease; *PIE,* pulmonary infiltrates with eosinophils.

Causes of Cough in Small Animals

Allergic Inflammatory

- Feline asthma
- Chronic bronchitis/COPD
- Eosinophilic bronchopneumopathy/PIE
- Eosinophilic pneumonitis

Cardiovascular

- Pulmonary edema
- Left atrial enlargement
- Pulmonary thromboembolism

Infectious

- Tracheobronchitis
- Pneumonia
- Bacterial
- Viral
- Fungal
- Protozoal

Neoplastic

- Primary
- Lung
- Trachea
- Larynx
- Metastatic
- Heart-base tumor
- Compression due to enlarged lymph nodes

Parasites

- *Filaroides*
- *Aelurostrongylus*
- *Paragonimus*
- *Capillaria*
- *Dirofilaria*, especially post adulticide treatment
- Larval migration (*Toxocara* spp., *Ancylostoma caninum*, *Strongyloides stercoralis*)
- Other

Trauma and Physical Abnormalities

- Foreign body
- Collapsing trachea
- Tracheal hypoplasia
- Tracheal stenosis
- Smoke inhalation
- Pulmonary hemorrhage

Corneal Ulcer

Underlying Causes of Corneal Ulceration in Dogs and Cats

Modified with permission from Kirk R: Kirk's current veterinary therapy XI: small animal practice, ed 11, Philadelphia, 1993, Saunders, p 1103.

- Entropion
- Other lid defects
- Distichiasis
- Ectopie cilia
- Lagophthalmos
- Exophthalmos
- Foreign body
- KCS
- Ocular trauma
- Qualitative tear film deficiencies (mucin and/or lipid)
- Severe debilitation
- Cranial nerve deficits; CN V and/or VII

CN, Cranial nerve; *KCS,* keratoconjunctivitis sicca.

Constipation

Differential Diagnosis of Constipation in the Cat

Adapted from Washabau RJ, Hasler AH: Constipation, obstipation, and megacolon In August JR, editor: Consultations in feline internal medicine, ed 3, Philadelphia, 1997, Saunders, p 106.

Neuromuscular Dysfunction

- Colonie smooth muscle: idiopathic megacolon, aging
- Spinal cord disease: lumbosacral disease, cauda equina syndrome, sacral spinal cord deformity (Manx cat)
- Hypogastric or pelvic nerve disorders: traumatic injury, malignant disease, dysautonomia
- Submucosal or myenteric plexus neuropathy: dysautonomia, aging

Mechanical Obstruction

- Intraluminal: foreign material (bones, plant material, hair), neoplasia, rectal diverticulum, permeai hernia, anorectal stricture
- Intramural: neoplasia
- Extraluminal: pelvic fracture, neoplasia, prostatic disease

Inflammation

- Perianal fistula, proctitis, anal sac abscess, anorectal foreign body, perianal bite wound

Metabolic and Endocrine

- Metabolic: dehydration, hypokalemia, hypocalcemia, hypercalcemia
- Endocrine: hypothyroidism (e.g., post-thyroidectomy), obesity, nutritional secondary hyperparathyroidism

Pharmacologic

- Opioid agonists, cholinergic antagonists, diuretics, barium sulfate, phenothiazines

Environmental and Behavioral

- Soiled litter box, inactivity, hospitalizaron, change in environment

Conjunctivitis, Feline

Modified from Kirk RW: Current veterinary therapy VI, ed 6, Philadelphia, 1971, Saunders, p 1284; Modified with permission from Panel report, colloquium on feline diseases. J Am Vet Med Assoc 158:838-839.

CF test, complement-fixing test; *CNS,* central nervous system; *FA test,* Fluorescent antibody test; *HA test,* hemagglutinating antibody test; *H&E,* hematoxylin and eosin stain; *MLV,* modified live vaccine; *SN test,* serum-neutralizing test.

Differential Diagnosis of Feline Conjunctivitis and Respiratory Disease Complex

	Rhinotracheitis	**Caliciviral Disease (FCV)**	**Reovirus Infection (FRI)**	**Chlamydiosis**	**Mycoplasma and Other Infections**
Agent	Feline herpesvirus	Feline caliciviruses (picornaviruses, numerous strains)	Reovirus	*Chlamydophila felis* (formerly *Chlamydia psittaci*)	*Mycoplasma* spp., *Staphylococcus pyogenes*, *Pasteurella multocida*, *Bordetella bronchiseptica*, and others
Signs:					
Severity	Regularly more severe	Mild to moderate, subclinical infections common	Mild	Mild	Subclinical infections common
Ocular	Lacrimation, conjunctivitis, chemosis, occasionally keratitis	Lacrimation, sometimes conjunctivitis	Lacrimation	Conjunctivitis (can be follicular)	Conjunctivitis
Nasal	Serous or mucopurulent discharge, sneezing	Serous discharge, occasional sneezing, ulceration of external nares	Nasal discharge rare	Nasal discharge rare	None or purulent
Oral	Occasional small vesicles and ulcers in buccal epithelium	Frequent ulceration on anterior dorsal margin of tongue and hard palate, gingivitis	None	None	None
Other	Coughing, abortion, skin ulcers, CNS signs	Paw erosions	None	None	None
Course	2-4 weeks	7-10 days	1-26 days	Often chronic or recurrent	May be chronic
Incubation (natural infection)	2-10 days	1-9 days	4-19 days	6-15 days	Usually secondary
Immunity	Initially low and transient, can be boosted and become persistent	Some strains produce broad cross-protection clinically but allow reduced viral multiplication	Unknown	Weak, transient	Weak, transient

	Rhinotracheitis	Caliciviral Disease (FCV)	Reovirus Infection (FRI)	Chlamydiosis	Mycoplasma and Other Infections
Diagnosis	Demonstration of intranuclear inclusions in H&E-stained biopsy specimens, tissue culture isolation, FA test	Tissue culture isolation, FA test	Tissue culture isolation, SN test, HA test	Conjunctival smears Giemsa-stained to show elementary bodies, CF tests	Culture
Inclusions	Intranuclear inclusions in respiratory epithelial cells, conjunctiva, and other such areas	None	Paranuclear cytoplasmic	Intracytoplasmic elementary bodies in conjunctival epithelial cells	None
Carrier state	Latent phase with periodic excretion after stress	Continuous shedding until self-clearance	Probable	Yes	Yes
Morbidity	High	High	50%	Variable	Variable
Mortality	High in kittens, aged, or immunocompromised	Variable; may be moderate in young kittens	Very low	Very low	Very low
Maternal antibody	<9 weeks	<11 weeks	Unknown	Unknown	Unknown
Prophylaxis	MLV	MLV	None	MLV	None
Treatment	Symptomatic, supportive with antibiotics; oral L-lysine as needed	Symptomatic, supportive with antibiotics	Symptomatic	Tetracyclines locally and systemically	Antibiotics

Congestive Heart Failure: Classification

Functional Classification of CHF

New York Heart Association Classification*

I. Normal activity does not produce undue fatigue, dyspnea, or coughing.
II. The dog or cat is comfortable at rest, but ordinary physical activity causes fatigue, dyspnea, or coughing.
III. The dog or cat is comfortable at rest, but minimal exercise may produce fatigue, dyspnea, or coughing. Signs may also develop while the animal is in a recumbent position (orthopnea).
IV. CHF, dyspnea, and coughing are present even when the dog or cat is at rest. Signs are exaggerated by any physical activity.

International Small Animal Cardiac Health Council†

I. Asymptomatic patient
    - Signs of heart disease but no cardiomegaly
    - Signs of heart disease and evidence of compensation (cardiomegaly)
II. Mild to moderate CHF
    - Clinical signs of CHF are evident at rest or with mild exercise and adversely affect the quality of life
III. Advanced CHF
    - Clinical signs of CHF are immediately obvious.
        - Home care is possible.
        - Hospitalization is recommended (cardiogenic shock, life-threatening edema, large pleural effusion, refractory ascites).

Consensus Panel of the Specialty of Cardiology, American College of Veterinary Internal Medicine, 2009‡

Stage A. Propensity to develop structural heart disease with or without overt clinical signs (phenotype) but no detectable abnormality on physical examination or clinical diagnostic testing.

- Example: Cavalier King Charles spaniel dog destined to develop myxomatous mitral valve disease, examined months/years before developing a heart murmur. Normal physical examination and echocardiogram.

Stage B. Physical exam abnormality consistent with cardiovascular disease but no overt clinical signs.

- Stage B1. No secondary changes on diagnostic investigation
    - Example: Cavalier King Charles spaniel dog with incidentally discovered heart murmur due to myxomatous mitral valve disease. No overt clinical signs. No left atrial enlargement on echocardiogram.
- Stage B2. Evidence of secondary changes on diagnostic tests.
    - Example: Cavalier King Charles spaniel dog with incidentally discovered heart murmur due to myxomatous mitral valve disease. No overt clinical signs. Moderate left atrial enlargement on echocardiogram.

Stage C. Decompensation of the underlying cardiovascular lesion, causing overt clinical signs

- Stage C1. Acute congestive heart failure. Overt clinical signs are present.
    - Example: Cavalier King Charles spaniel dog with dyspnea, cough, and orthopnea due to cardiogenic pulmonary edema
- Stage C2. Chronic controlled congestive heart failure. Overt clinical signs are absent while appropriate treatment is being administered, typically at home.
    - Example: Cavalier King Charles spaniel dog with a history of cardiogenic pulmonary edema, now home and feeling well with daily medications.

Stage D. Refractory congestive heart failure. Despite increases in oral medications, signs of decompensation persist.

- Stage D1. Acute, refractory congestive heart failure. In-hospital treatment.
    - Example: Cavalier King Charles spaniel dog reevaluated because of severe dyspnea due to recurrent pulmonary edema.
- Stage D2. Chronic, persistently overt congestive heart failure.
    - Example: Cavalier King Charles spaniel dog previously in stage D1, with improved but not fully resolved overt clinical

signs, discharged to home/palliative care.

CHF, Congestive heart failure.

Congestive Heart Failure: Physical Signs

Physical Signs Associated With CHF

Modified from Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 4, St Louis, 1994, Saunders.

Pulmonary Signs (Left-Sided CHF)

- Rales/crackles on auscultation (alveolar edema)
- Frothy, pink sputum
- Shortness of breath, tachypnea
- Dyspnea and discomfort during recumbency (orthopnea)
- Cough

Signs Attributable to Either Left or Right CHF

- Weakness and fatigue (general exercise intolerance)
- Exertional dyspnea
- Gallop sound/"gallop rhythm" (accentuated third heart sound)
- Poor peripheral perfusion: pale mucous membranes, slow capillary refill time, mild cyanosis, cool extremities
- Tachycardia
- Weight loss (cachexia)

Systemic Signs (Right-Sided CHF)

- Generalized venous engorgement
- Hepatomegaly
- Body cavity effusions (modified transudate): ascites, pleural effusion, pericardial effusion
- Dependent peripheral edema
- Weight gain (retained fluid)

CHF, Congestive heart failure.

Congestive Heart Failure: Causes

From DiBartola S: Fluid, electrolyte, and acid-base disorders in small animal practice, St Louis, 2000, Saunders.

Causes

Valvular Heart Disease

- Congenital malformations: aortic or subaortic stenosis, mitral valve malformation, pulmonic stenosis, tricuspid valve malformation
- Acquired diseases: myxomatous atrioventricular valvular disease, ruptured chordae tendineae, bacterial endocarditis

Myocardial Diseases

- Malformations: defects of the atrial and ventricular septum
- Dilated cardiomyopathy
- Hypertrophic cardiomyopathy
- Restrictive cardiomyopathy (endomyocardial. brosis)
- Unclassified feline cardiomyopathies
- Atrial muscle degeneration
- Right ventricular cardiomyopathy
- Myocarditis
- Secondary myocardial diseases: hyperthyroidism, acromegaly, hypertension

Pericardial Diseases

- Idiopathic pericardial hemorrhage/pericarditis
- Cardiac neoplasia leading to pericardial effusion
- Infectious

Vascular Diseases

- Malformation: patent ductus arteriosus, arteriovenous. stula
- Heartworm disease

High-Output States

- Anemia
- Thyrotoxicosis

Cardiac Arrhythmia

- Chronic bradyarrhythmia
- Chronic tachyarrhythmia

Congenital Heart Disease: Breed Predilections

With permission from Kirk R, Bonagura J, editors: Kirk's current veterinary therapy XI: small animal practice, St Louis, 1993, Saunders, p 650. Data from Veterinary Medical Data Base (VMDB) at Purdue University, 1987-1989: 1320 dogs with congenital heart disease (CHD) out of 154,233 dogs. Numbers 1, 2, and 3 identify predisposed breeds represented by four or more affected dogs in which relative risk for the indicated abnormality was significantly elevated in this series (P 0.05 to P 0.0001):

- 1: Mildly increased risk (odds ratio 1.5-2.9 times all other dogs)
- 2: Moderate risk (odds ratio 3-4.9 times others)
- 3: Marked risk (odds ratio 5 times others)

*Breed-associated diseases were not confirmed in this study but suggested or confirmed by others.Sex predominance: PDA (females 3:1), PS in English bulldogs (males 4:1), mitral and tricuspid dysplasia (males 2:1).

Breed Predilections in Dogs With CHD

Breed	Condition
Airedale terrier	Pulmonic stenosis (PS)-2
Beagle	PS*
Bichon frise	Patent ductus arteriosus (PDA)-2
Boxer	Aortic stenosis (AS)-3
Boykin spaniel	PS*
Bull terrier	Mitral dysplasia (MD)*
Chihuahua	PS,* PDA*
Cocker spaniel	PDA-1, PS-1
Collie	PDA-1
Doberman pinscher	Atrial septal defect (ASD)*
English bulldog	PS-3, ventricular septal defect (VSD)-3, AS-1, tetralogy of Fallot (TF)*
English springer spaniel	PDA-2
German shepherd	Tricuspid dysplasia (TD)-3, AS-1, persistent right aortic arch (PRAA)-2, MD,* PDA*
German shorthaired pointer	AS*
Golden retriever	AS-3, TD*
Great Dane	AS-1, PRAA-3, MD,* TD*
Irish setter	PRAA*
Keeshond	PDA-2, TF*
Kerry blue terrier	PDA-3
Labrador retriever	TD-3
Maltese	PDA-3
Mastiff	PS-3
Miniature schnauzer	PS-2
Newfoundland	AS-3
Pomeranian	PDA-3

Breed	Condition
Poodles	PDA-2
Rottweiler	AS-3
Samoyed	PS-3, AS-1, ASD*
Scottish terrier	PS-2
Shetland sheepdog	PDA-3
West Highland white terrier	PS-3
Weimaraner	TD,* peritoneopericardial hernia*
Yorkshire terrier	PDA-1

Coma, Stupor

Causes of Stupor and Coma

From Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 5, St Louis, 2000, Saunders.

Congenital or Familial Disorders

- Hydrocephalus
- Lysosomal storage disorders
- Lissencephaly

Metabolic Disorders

- Hepatic encephalopathy
- Hypoadrenocorticism
- Diabetes mellitus
- Hypoglycemia
- Hypothyroidism
- Uremia
- Hypoxemia
- Acid-base imbalance
- Osmolality imbalance
- Heatstroke
- Hyperlipidemia

Nutritional Disorders

- Thiamine deficiency (end-stage)

Neoplasia

- Primary lesions
- Metastatic lesions

Inflammation

- Canine distemper
- Rabies
- Rocky Mountain spotted fever
- *Ehrlichia* infection
- Feline infectious peritonitis
- Fungal, protozoal, and bacterial infections
- Granulomatous meningoencephalitis

Toxins/Drugs

- Ethylene glycol
- Lead
- Barbiturates
- Mushroom poisoning
- Alcohol
- Cannabinoids
- Hallucinogens

Trauma

- Cranial trauma

Vascular

- Coagulopathies
- Hypertension
- Cardiomyopathy
- Bacterial emboli
- Feline ischemic encephalopathy
- Ischemia

Other

- Status epilepticus

Chronic Kidney Disease: Complications

Complications and Comorbid Conditions in Animals With Chronic Kidney Disease

Adapted from Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

Complications of Chronic Kidney Disease

- Anemia
- Systemic hypertension
- Dehydration
- Hyperparathyroidism
- Hypermagnesemia
- Hyperphosphatemia
- Hypocalcemia and hypercalcemia
- Hypokalemia
- Malnutrition
- Metabolic acidosis
- Uremic encephalopathy
- Uremic gastritis
- Uremic pneumonitis
- Uremic stomatitis

Comorbid Conditions: Common

- Cardiac disease
- Degenerative joint disease
- Dental and oral diseases
- Hyperthyroidism (cats)
- Nephroliths and ureteroliths
- Urinary tract infections

Chronic Kidney Disease: Stages

From Ettinger SJ, Feldman, EC: Textbook of veterinary internal medicine, ed 7, St Louis, 2010, Saunders.

Stages of Chronic Kidney Disease in Dogs and Cats

SERUM CREATININE VALUES (mg/dL/µmol/L)		
Stage	**Dogs**	**Cats**
Stage 1	<1.4 / <125	<1.6 / <140
Stage 2	1.4-2.0 / 125-179	1.6-2.8 / 140-249
Stage 3	2.1-5.0 / 180-439	2.9-5.0 / 250-439
Stage 4	>5.0 / >440	>5.0 / >440

Cerebrospinal Fluid Abnormalities

Modified from de Lahunta A: Veterinary neuroanatomy and clinical neurology, St Louis, 1983, Saunders.

cmm, Cubic millimeter; *CSF*, cerebrospinal fluid; *WBC*, white blood cell.

CSF Determinations and Diseases of the Nervous System

	DISEASE	
Determination	**Meningitis**	**Parenchymal Disease**
	Bacterial disease: suppurative inflammation	Tissue necrosis: neoplasia, degenerations Viral disease: nonsuppurative inflammation
Physical	Turbid, clot	Clear, colorless
Cytologic (WBC)		
Quantitative	Large increase: >100/cmm	Small increase: <100/cmm
Differential	Mostly neutrophils	Mostly mononuclear cells
Chemical		
Protein, Quantitative (total)	Large increase: >100 mg/dL	Small increase: <100 mg/dL
Glucose: normally about 80% of blood level	Normal or decreased to below 50% of blood level	Normal

Central Nervous System Disorders, Multifocal

Modified from Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

CNS, Central nervous system; *FIP,* feline infectious peritonitis virus; *FIV,* feline immunodeficiency virus; *GME,* granulomatous meningoencephalitis; *RMSF,* Rocky Mountain spotted fever.

Diseases That Typically Result in Multifocal or Diffuse CNS Signs

Degenerative

- Storage disease
- Multineuronal degeneration

Anomalous

- Hydrocephalus/syringomyelia/hydromyelia complex

Metabolic

- Hepatic
- Renal
- Hypoglycemia
- Hyperthyroidism
- Hypothyroidism
- Hyperadrenocorticism
- Hyperosmolar syndromes
    - Adipsia

Neoplastic

- Lymphoma
- Leukemias
- Metastatic tumors

Nutritional

- Thiamine

Inflammatory

- ***Infectious***
- Viral
    - Distemper
    - Herpes
    - Parvovirus
    - Parainfluenza
    - FIP
    - FIV
- Bacterial
    - Bacterial encephalitis
    - Tetanus
- Fungal
    - Cryptococcosis
    - Blastomycosis
    - Coccidioidomycosis
    - Candidiasis
    - Aspergillosis
- Protozoal
    - Toxoplasmosis
    - Neosporosis
- Parasitic
    - *Toxocara*
    - *Cuterebra*
- Rickettsial
    - RMSF
    - *Ehrlichia*
- Unclassified
    - Protothecosis

Noninfectious

- GME
- Breed-associated CNS inflammation (necrotizing encephalitis): pug, Maltese, Yorkshire terrier
- Spinal cord vasculitis
- Nonclassified
    - Steroid-responsive meningoencephalitis

Idiopathic

- Dysautonomia

Toxins

Vascular disease

- Intracranial hemorrhage
- Thromboembolism
- Hypertension
- Spinal hemorrhage

Dystocia: Causes

From Feldman EC, Nelson RW: Canine and feline endocrinology and reproduction, ed 3, St Louis, 2004, Saunders.

Causes in Bitches and Queens

Cause	Bitch (%)	Queen (%)
Maternal	**75.3**	**67.1**
Primary complete inertia	48.9	36.8
Primary partial inertia	23.1	22.6
Birth canal too narrow	1.1	5.2
Uterine torsion	1.1	—
Uterine prolapse	—	0.6
Uterine strangulation	—	0.6
Hydrallantois	0.5	—
Vaginal septum formation	0.5	—
Fetal	**24.7**	**29.7**
Malpresentations	15.4	15.5
Malformations	1.6	7.7
Fetal oversize	6.6	1.9
Fetal death	1.1	1.1

Dystocia Versus Other Periparturient Phenomena

Modified from Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

Reasons for Seeking Veterinary Assistance for Reproductive Disorders

Presenting Complaint	Disorder(s)
No signs of labor >24 hours after temperature decrease to <37.8°C	Normal or dystocia
More than 1 week overdue	
Fetal membranes in vulva >15 minutes	
Strong contractions >30 minutes without delivery	
No fetus produced after 4-6 hours of onset of stage II labor	Dystocia
More than 3 hours between fetal delivery	Dystocia in canine
Vaginal discharge	Dystocia, metritis, pyometra
Temperature >39.7°C in the bitch	Dystocia, metritis, pyometra, uterine torsion, mastitis
Profuse vomiting, diarrhea, and toxemia in the bitch	
Incessant crying of offspring	
Anorexia, lethargy, depression >24 hours postpartum	Metritis, mastitis
Hot, painful, swollen mammary glands	Mastitis
Extreme restlessness, panting, tremors, and stiff gait	Eclampsia

Dyspnea

Causes

From Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 5, St Louis, 2000, Saunders.

Upper Airway Disorders

- Nasal cavity*
  - Stenotic nares
  - Obstruction (infection, inflammation, neoplasia, trauma, bleeding disorders)
- Pharynx, larynx
  - Elongated or edematous soft palate
  - Pharyngeal polyp (cat)
  - Laryngeal edema, collapse, foreign body, inflammation, trauma, paralysis, spasm, neoplasia, vocal-fold webbing
  - Everted laryngeal saccules
- Cervical trachea
  - Collapse, stenosis
  - Trauma, foreign body
  - Neoplasia, osteochondral dysplasia
  - Parasites (*Oslerus osleri*)

Lower Airway Disorders

- Thoracic trachea (see Cervical Trachea, above)
  - Extraluminal compression (lymphadenopathy, heart-based tumors, enlarged left atrium)
- Bronchial disease (allergic, infectious, parasitic, chronic obstructive pulmonary disease)

Pulmonary Parenchymal Disorders

- Edema (cardiogenic, noncardiogenic)
- Pneumonia (infectious, parasitic, inhalation)
- Neoplasia
- Allergy (allergic pneumonitis, including heartworm; eosinophilic granuloma; eosinophilic bronchopneumopathy)
- Embolism (dirofilariasis, hyperadrenocorticism, disseminated intravascular coagulation)
- Trauma, bleeding disorders

Pleural/Body Wall Disorders

- Pneumothorax
- Pleural effusion
- Congenital body wall disorders (pectus excavatum)
- Thoracic wall trauma
- Thoracic wall neoplasia
- Thoracic wall paralysis
- Diaphragmatic hernia (congenital, acquired)

Mediastinal Disorders

- Infection
- Trauma, including pneumomediastinum
- Neoplasia

Peritoneal Cavity Disorders

- Organomegaly, obesity
- Effusion
- Gastric torsion, dilatation/volvulus

Hemoglobin Disorders

- Anemia
- Methemoglobinemia
- Cyanosis

Miscellaneous

- Central nervous system (brain, spinal cord)
- Peripheral nerve, neuromuscular, muscular
- Metabolic (acidemia; severe hypokalemia in cats)
- Anxiety
    - Fear
    - Pain

Dysphagia

Causes

From Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

Anatomic or Mechanical Lesions

- Pharyngeal inflammation (e.g., abscess, inflammatory polyp, oral eosinophilic granuloma)
- Foreign-body obstruction (oral, pharyngeal, nasopharyngeal, proximal esophagu)
- Neoplasia
- Retropharyngeal lymphadenomegaly
- Sialocele
- Mandibular fracture
- Lingual frenulum disorder
- Cricopharyngeal achalasia or asynchrony
- TMJ disorder (e.g., luxation, fracture)
- Cleft palate
- Pharyngeal trauma

Pain

- Stomatitis/glossitis/pharyngitis (FIV, FeLV, immune-mediated disease, uremic glossitis, ingestion of a caustic substance)
- Tooth-related problems (tooth root abscess, fracture, periodontitis)
- Trauma
- Electric cord burns
- Retrobulbar abscess

Neuromuscular Disorders

- Myasthenia gravis (focalized or generalized)
- Acute polyradiculoneuritis
- Masticatory myositis
- Tick paralysis
- Botulism
- Polymyositis
- TMJ disease

Neurologic Disorders

- Rabies
- Trigeminal paralysis or neuritis
- Neuropathies of CN VII, IX, X, or XII
- CNS disease (brainstem lesion)

CN, Cranial nerve; *CNS,* central nervous system; *FeLV,* feline leukemia virus; *FIV,* feline immunodeficiency virus; *TMJ,* temporomandibular joint.

Disseminated Intravascular Coagulation (DIC)

Associated Conditions

Modified from Bonagura J: Kirk's current veterinary therapy XIII, St Louis, 2000, Saunders.

Intravascular Hemolysis

- Hemolytic transfusion reaction
- Hemolytic anemia

Septicemia

- Gram-negative bacteria (endotoxin)
- Gram-positive bacteria (bacterial coat mucopolysaccharide)

Viremia

Parasitic Infections

- Protozoal infection
- Metazoal infection

Obstetric Complications

Miscellaneous

- Gastric dilatation/volvulus
- Diabetes mellitus

Neoplasia

Massive Tissue Injury

- Burns
- Trauma
- Surgical procedures
- Heatstroke

Venoms and Toxins

- Snakebites
- Insect stings
- Aflatoxin

Hepatic Disease

Pancreatitis

While a cause-and-effect relationship has not been established for most cases of DIC in dogs and cats, the conditions listed here are suspected to contribute to the onset, perpetuation, or both, of DIC.

Diskospondylitis: Microorganisms

Infectious Agents Associated With Diskospondylitis in Dogs and Cats

Modified from Greene C: Infectious diseases of the dog and cat, ed 2, St Louis, 1999, Saunders.

Dogs

- Bacterial
  - *Staphylococcus pseudintermedius*
  - *Bruceila canis*
  - *Nocardia*
  - *Actinomyces*
  - *Streptococcus canis*
  - *Escherichia coli*
  - *Alcaligenes*
  - *Micrococcus*
  - *Proteus*
  - *Mycobacterium*
  - *Corynebacterium*
- Fungal
  - *Aspergillus terreus*
  - *Paecilomyces varioti*
  - *Fusarium*
  - *Mucor*

Cats

- *S. canis*
- *Actinomyces*
- *E. coli*

Discolored Urine

From Willard M, Tvedten H: Small animal clinical diagnosis by laboratory methods, ed 4, St Louis, 2004, Saunders.

RBCs, Red blood cells.

Potential Causes in Dogs and Cats

Urine Color	Causes
Dark yellow	Concentrated urine
Pale yellow	Normal urochromes, urobilin
Yellow-brown	Bile pigments
Yellow-orange	Bilirubin
	Fluorescein
	Concentrated urine
	Phenazopyridine
Red	Hemoglobin
	RBCs
	Myoglobin
	Dyes
	Phenazopyridine
	Phenolsulfonphthalein
Green-blue	Methylene blue
	Dithiazanine
	Biliverdin
Brown-black	Bile pigments
	Myoglobin
	Methemoglobin
Milky	Pyuria
	Lipiduria
	Phosphate crystals
Colorless	Dilute

Dilated Cardiomyopathy Differential Diagnosis: Myocardial Failure

Modified with permission from Kittleson M: Small animal cardiovascular medicine, St Louis, 1998, Mosby, p 320.

†These causes constitute less than 10% of the clinical cases of severe myocardial failure seen clinically. The remainder are idiopathic.

*Clinically documented causes of myocardial failure in veterinary medicine.

Potential Causes of Ventricular Dilation and Poor Contractility (Myocardial Failure)

Viral

- Parvovirus*
- Distemper virus
- Canine herpesvirus

Fungal

Rickettsial

- *Ehrlichia canis*
- *Rickettsia rickettsii*
- *Bartonella elizabethae*

Spirochetal

- *Borrelia burgdorferi**

Parasitic

- *Trypanosoma cruzi**
- *Toxoplasma gondii*
- *Toxocara canis*

Endocrinologic

- Severe hypothyroidism
- Hyperthyroidism*
- Pheochromocytoma

Drugs and Toxins

- Adriamycin*
- Cobalt
- Gossypol

Physical Injury

- Electric shock
- Trauma
- Heatstroke

Nutritional Deficiencies

- Taurine*
- Carnitine*

Ischemia/Infarction

- Septic coronary artery embolus*
- Atherosclerosis*

Muscular Dystrophy

Diet: Assessment

Relevant Considerations

- Inquire about specific varieties and amounts of what the patient is typically fed and what it is currently being fed, including:
  - Commercial pet foods
  - Home-prepared diets
  - Table foods or scraps
  - Treats
  - Dietary supplements
  - Foods used to deliver medications or supplements
- Establish who lives in the household and whether there have been any recent changes, including:
  - People and other pets
- Inquire about how the patient is fed and whether there have been any recent changes, including:
  - Who feeds the pet
  - Timing of meals
  - Free choice versus meal feeding
- Ask about the patient's feeding behavior.

AUTHOR: KATHRYN MICHEL

Diarrhea

Major Categories and Causes for Acute Diarrhea in Dogs and Cats

From Willard M, Tvedten H: Small animal clinical diagnosis by laboratory methods, ed 4, St Louis, 2004, Saunders.

Intestinal Parasites

- Hookworms
- Roundworms
- Whipworms
- Coccidia
- *Giardia intestinalis* (sometimes difficult to diagnose)
- Strongyloides
- Trichomoniasis

Dietary Problems

- Poor-quality food or food poisoning
- Sudden dietary change (especially in young animals)
- Food intolerance or allergy

Acute Viral or Bacterial Enteritis

- Parvovirus (canine and feline)
- Coronavirus (canine and feline)
- *Clostridium perfringens*–associated enteritis
- Campylobacteriosis
- Salmonellosis
- *Escherichia coli*–associated enteritis (verotoxin-producing strains)

Intussusception

Intoxication

- Garbage
- Food poisoning
- Heavy metal
- Organophosphate

Hemorrhagic Gastroenteritis

Diarrhea, Small Versus Large Intestine

Modified from Willard M, Tvedten H: Small animal clinical diagnosis by laboratory methods, ed 4, St Louis, 2004, Saunders.

Differentiation of Chronic Small-Intestinal from Chronic Large-Intestinal Diarrhea

	Small-Intestinal Diarrhea	Large-Intestinal Diarrhea
Weight loss (most important criterion)	Expected	Uncommon except with histoplasmosis, pythiosis, or cancer
Polyphagia	Often present	Uncommon
Vomiting	Common	Occurs in 10%-20% of animals
Volume of feces	May be normal or larger than normal	May be normal or smaller than normal
Frequency of defecation	Normal to slightly increased	Normal to markedly increased; may have many small defecations per bowel movement
Slate-gray feces (steatorrhea)	Occasionally	No
Hematochezia	No	Sometimes present
Melena	Sometimes	No
Mucoid stools	Rare (unless ileum is diseased)	Often present
Tenesmus/dyschezia	Rarely present	Sometimes present

Diarrhea, Neonatal

Modified from Bonagura J: Kirk's current veterinary therapy XIII, St Louis, 2000, Saunders.

FeLV, Feline leukemia virus; *FIP,* feline infectious peritonitis; *FIV,* feline immunodeficiency virus.

Causes of Neonatal Diarrhea in Puppies and Kittens

Dietary

- Abrupt change in diet
- Overfeeding
- Indiscretion: garbage ingestion
- Ingestion of abrasive or indigestible material
- Food intolerance
- Intolerance of lactose ingested as milk

Endoparasitic

- Helminths: ascarids, hookworms, whipworms, *Strongyloides*
- Others: cestodes, trematodes, *Trichinella*
- Protozoa: coccidia (*Cystoisospora*), *Cryptosporidium*, *Giardia lamblia*
- Others: *Pentatrichomonas*, *Entamoeba*, *Balantidium*, rickettsial organisms
- Salmon poisoning disease

Obstructive

- Intestinal foreign body
- Intussusception
- Intestinal volvulus

Idiopathic Chronic Diarrhea in Young Cats

Drug- and Toxin-Induced

- Antiinflammatory drugs
- Antimicrobials
- Anthelmintics
- Heavy metals: lead, arsenic, thallium
- Insecticides: organophosphates
- Plants

Infectious

- Viral: parvoviruses, coronaviruses, rotaviruses, canine distemper, FeLV, FIV, FIP
- Bacterial: *Salmonella* spp., *Campylobacter* spp., *Yersinia enterocolitica*, *Bacillus piliformis*, *Escherichia coli*, *Clostridium* spp.

Extraintestinal

- Renal failure
- Hepatic disease
- Hypoadrenocorticism
- Acute pancreatitis
- Diabetes mellitus

Diarrhea, Chronic Large Intestinal: Causes

From Bonagura J: Kirk's current veterinary therapy XIII, St Louis, 2000, Saunders.

Diagnosis in 74 Cases of Chronic Large-Bowel Diarrhea

Diagnosis	Number of Cases
Idiopathic	19
Plasmacytic lymphocytic colitis	15
Clostridium perfringens enterotoxicosis	10
Malignant neoplasia	10
Pyogranulomatous colitis	6
Histiocytic ulcerative colitis	3
Eosinophilic granulomatous colitis	2
Trichuris vulpis	1
Histoplasmosis	1
Miscellaneous	7

Diabetes, Ketoacidosis

Triggers and Predisposing Conditions

- Acromegaly
- Chronic kidney disease
- Congestive heart failure
- Epinephrine release
- Glucagonoma
- Glucocorticoid treatment
- Hepatitis/cholangiohepatitis
- Hyperadrenocorticism
- Infection
    - Abscess (subcutaneous, other)
    - Periodontal/oral
    - Pneumonia
    - Pyoderma
    - Pyometra
    - Urinary tract infection
- Pancreatitis
- Progesterone (diestrus; progestagen treatment)

Diabetes Mellitus

Complications in Dogs and Cats

Modified from Feldman E, Nelson R: Canine and feline endocrinology and reproduction, ed 3, St Louis, 2004, Saunders.

Common

- Iatrogenic hypoglycemia
- Persistent polyuria and polydipsia (PU/PD)
- Weight loss
- Cataracts (dogs)
- Bacterial infections, especially in the urinary tract
- Pancreatitis
- Ketoacidosis
- Hepatic lipidosis
- Peripheral neuropathy (cat)

Uncommon

- Peripheral neuropathy (dog)
- Glomerulonephropathy, glomerulosclerosis
- Retinopathy
- Systemic hypertension
- Exocrine pancreatic insufficiency
- Gastric paresis
- Diabetic diarrhea
- Diabetic dermatopathy (dog) (i.e., superficial necrolytic dermatitis/hepatocutaneous syndrome)

Diabetes Insipidus, Nephrogenic

Causes

From DiBartola S: Fluid, electrolyte, and acid-base disorders in small animal practice, St Louis, 2000, Saunders.

Congenital (Primary)

Acquired (Secondary)Functional

- Drugs
  - Glucocorticoids
  - Lithium
  - Demeclocycline
  - Methoxyflurane
  - *Escherichia coli* endotoxin (e.g., pyelonephritis, pyometra)
  - Diuretics
- Electrolyte/mineral disturbances
  - Hypokalemia
  - Hypercalcemia
- Altered medullary hypertonicity
  - Hypoadrenocorticism
- Multifactorial or unknown mechanism
  - Hepatic insufficiency
  - Hyperthyroidism
  - Hyperadrenocorticism
  - Postobstructive diuresis
  - Acromegaly

Structural

- Medullary interstitial amyloidosis (e.g., in cats, shar-pei dogs)
- Polycystic kidney disease
- Chronic pyelonephritis
- Chronic interstitial nephritis

Dermatosis, Periocular

Dogs

- Parasitic:
  - Demodicosis
  - Sarcoptic acariasis
  - Trombiculiasis
- Fungal:
  - Dermatophytosis
  - *Malassezia* dermatitis
- Bacterial:
  - Staphylococcal folliculitis
  - Mucocutaneous pyoderma
- Protozoal:
  - Leishmaniasis
- Allergic:
  - Atopic dermatitis
  - Food allergy
  - Contact allergic dermatitis
  - Angioedema
- Autoimmune/immune-mediated:
  - Pemphigus (foliaceus, erythematosus, vulgaris)
  - Lupus erythematosus (cutaneous, systemic)
  - Bullus pemphigoid
  - Canine familial dermatomyositis
  - Erythema multiforme
  - Uveodermatologic syndrome
  - Vitiligo
- Neoplastic:
  - Epitheliotropic lymphoma
- Miscellaneous:
  - Juvenile cellulitis
  - Superficial necrolytic dermatitis (hepatocutaneous syndrome)
  - Zinc-responsive dermatosis
  - Actinic dermatitis

Cats

- Parasitic:
  - Notoedric acariasis
  - Demodicosis
  - Trombiculiasis
- Fungal:
  - Dermatophytosis
- Bacterial:
  - Staphylococcal folliculitis
- Allergic:
  - Atopic dermatitis
  - Food allergy
  - Contact allergic dermatitis
- Autoimmune/immune-mediated:
  - Pemphigus (foliaceus, erythematosus, vulgaris)
  - Cutaneous lupus erythematosus
  - Systemic lupus erythematosus
  - Erythema multiforme
  - Periocular leukotrichia (Siamese)
- Miscellaneous:
  - Actinic dermatitis
  - Idiopathic facial dermatitis (Persian, Himalayan, exotic short hair)

Dermatoses, Scaling and Crusting

Modified from Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

BC, Bacterial culture; *Bx,* skin biopsy; *C,* common; *CS,* clinical signs; *Cyt,* cytology; *DTM,* dermatophyte test medium fungal culture; *Hx,* history; *IDST,* intradermal skin test; *IgE,* allergen-specific serum IgE assay; *MDB,* minimum database; *NSF,* no significant findings; *R,* rare; *SS,* skin scraping; *U,* uncommon; +, positive; −, negative.

Scaling and Crusting Dermatoses of Dogs and Cats

Disease	Lesions	Species	Signalment	Lesion Distribution	Frequency	Pruritus	Diagnosis
Bacterial							
Superficial folliculitis	Crusts, scales, collarettes, pustules	Dog > cat	Varies	Trunk	C	− to + +	CS, Cyt, BC, Bx
Deep pyoderma	Crusts, ulcers	Dog > cat	Varies	Trunk, feet	C	+	CS, Cyt, BC, Bx
Mucocutaneous pyoderma	Crusts, ulcers	Dog	German shepherd or others	Lips, peribuccal	U	+ (painful)	CS, Bx
Acute moist dermatitis	Moist crust, exudation, erythema	Dog	Any (often flea related)	Face, neck, caudal trunk	C	+ + +	CS
Fungal							
Dermatophytosis	Crusts, scales, alopecia, erythema	Cat > dog	Young most frequently	Head, extremities, trunk	C	− to + +	DTM, Wood's light
Malassezia dermatitis	Crusts, scales, erythema, lichenification	Dog > cat	Adult most frequently	Axillary, groin, interdigital, facial	C	+ + +	Cyt
Parasitic							
Ctenocephalides felis (flea)	Scales, erythema	Dog > cat	Any	Lumbosacral, neck	C	+	CS, parasite exam
Sarcoptes scabiei	Crusts, scales, excoriations, alopecia, erythema	Dog	Any	Pinnal margins, lateral elbows, ventrum	C	+ + +	SS, response to therapy
Demodex canis	Crusts, scales, exudation, alopecia, erythema	Dog	Young or immunocompromised adults	From single lesions on the head to generalized	C	− to +	SS
Cheyletiella spp.	Scales	Dog, cat	Young, most frequently	Dorsal trunk to generalized	U	− to + + +	SS, tape impression
Notoedres cati	Crusts, scales	Cat	Any	Head, feet, generalized	U	− to + + +	SS
Viral							
Feline leukemia virus (FeLV)	Crusts, scales, erosions	Cat	Any	Face, pinnae, perioral, feet, trunk	U	++	Serology, Bx
Allergic Reaction							

Disease	Lesions	Species	Signalment	Lesion Distribution	Frequency	Pruritus	Diagnosis
Atopic dermatitis	Erythema, alopecia, crusts (excoriation), scales, and others	Dog > cat	All, dogs often 1-5 years old	Face, ears, feet, ventrum	C	+ to + + +	CS, IDST, IgE
Food hypersensitivity	Erythema, crusts (excoriation), and others	Dog, cat	All, any age	Any	C	+ to + + +	Food trial
Flea bite hypersensitivity	Erythema, crusts (excoriation), and others	Dog, cat	All	Caudal dorsum, ventrum, thighs	C	+ + to + + +	Response to flea control
Miliary dermatitis	Small hemorrhagic crusts	Cat	All (often associated with fleas)	Dorsum	C	+ +	CS
Endocrine and Metabolic							
Hyperadrenocorticism	Alopecia, cutaneous atrophy, calcinosis cutis, crusts (pyoderma)	Dog > cat	Middle-aged, older animals	Trunk	C	− (occ. +)	MDB, hormone assays, imaging, Bx
Hypothyroidism	Scaling, dry skin, pyoderma, ± alopecia	Dog	Middle-aged, often large breeds	Generalized	C	−	MDB, thyroid assay
Superficial necrolytic dermatitis (hepatocutaneous syndrome)	Severe adherent crusting	Dog (cat)	Old	Muzzle, footpads, pressure points	R	+ to ++ (painful)	Bx, MDB, liver assays, imaging
Immune-Mediated Disease							
Pemphigus foliaceus	Crusts, pustules	Dog, cat	Any age and sex; Akita, chow chow, and others	Nasal planum, muzzle, pinnae, footpads, trunk	U	− to +	Bx
Discoid lupus erythematosus (DLE)	Crusts, depigmentation, erosions, ulcers	Dog, cat	Collies, Shetland sheepdog, and others	Nasal planum, muzzle	U	−	Bx
Exfoliative cutaneous lupus erythematosus	Excessive scaling	Dog	German short-haired pointer	Generalized	U		Bx
Erythema multiforme	Crusts, vesicles erythema, target lesions, erosions, ulcers	Dog, cat	Any	Axillae, groin, mucocutaneous junctions	U	−	Bx
Congenital and Hereditary							
Primary seborrhea	Excessive scaling or greasy skin	Dog (cat)	Onset before 6 months of age; American cocker spaniel and others	Generalized	U	− to + +, especially with secondary infections	Bx

Disease	Lesions	Species	Signalment	Lesion Distribution	Frequency	Pruritus	Diagnosis
Ichthyosis	Excessive scaling	Dog	Golden retriever, Norfolk terrier, American Bulldog and others	Generalized	U		Bx
Schnauzer comedo syndrome	Comedones that may become crusted	Dog	Miniature schnauzer	Dorsum	C	−	CS, Bx
Familial canine dermatomyositis	Alopecia, scaling, depigmentation	Dog	Onset before 6 months of age, collie, Shetland sheep dog, and others	Face, pressure points	U	−	Cx, Bx
Cornification Defects							
Secondary seborrhea	Excessive scaling or greasy skin	Dog, cat	Any age	Depends on primary cause	C	− to + + + depending on cause	CS, any appropriate tests for primary disease
Vitamin A–responsive dermatosis	Marked follicular plugging, hyperkeratotic plaques	Dog	Cocker spaniel and others; Adult onset	Generalized, more pronounced on ventrum	U	− to + +	CS, Bx
Ear margin dermatosis	Follicular casts and scaling	Dog	Dachshund and others	Ear margins, lateral and medial	U	− may become painful	CS, Bx
Environmental							
Solar dermatitis	Erythema, scaling, may progress to exudation and crusting	Dog > cat	Light-haired animals, outdoor exposure	Pinnae, nasal planum (cat), bridge of nose, ventrum (dog)	C	− to +	CS, Bx
Nutritional							
Zinc-responsive dermatosis	Crusts, scales, erythema, alopecia	Dog	Siberian husky, Alaskan malamute; young adults	Periocular, perioral mucocutaneous junctions, pressure points	U	− to +	Bx
Fatty acid deficiency	Scales	Dog, cat	Any	Generalized	U	− to + +	Dietary hx
Others							
Cutaneous lymphoma	Lesions highly variable but may include severe scaling	Dog > cat	Older animals	Generalized or localized	U	− to + + +	Bx
Granulomatous sebaceous adenitis	Hyperkeratosis, alopecia, follicular casts, may be erythematous	Dog (cat)	Young to middle-aged, standard poodle, Akita, vizsla, and others	Face, trunk, pinnae, become generalized	C	− to + +	CS, Bx

Disease	Lesions	Species	Signalment	Lesion Distribution	Frequency	Pruritus	Diagnosis
Otitis externa	Scale, erythema otic exudate	Dog > cat	Any	Pinnae, ear canal	C	+ +	Otoscopic examination, Cyt, BC

Eosinophilia

Potential Causes of Eosinophilia in Dogs and Cats

From Feldman E, Nelson R: Canine and feline endocrinology and reproduction, ed 3, St Louis, 2004, Saunders, 2004.

- Parasitism
  - Heartworm disease
  - GI
  - Dermatologic
  - Other
- Asthma
- Nonparasitic dermatologie disease
- Mast cell tumor
- Hypoadrenocorticism (Addison's disease)
- Uterine disease
- Eosinophilic myositis
- Eosinophilic pneumonitis/rhinitis/conjunctivitis
- Eosinophilic enterocolitis (allergic colitis)
- Eosinophilic leukemia
- Eosinophilic granuloma complex
- Eosinophilic vasculitis
- Drug reaction

GI, Gastrointestinal.

Enteropathies: Breed-Related

Modified from Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

Suspected and Confirmed Breed Susceptibilities for Small-Intestinal Disease in Dogs and Cats

Breed	Condition
Basenji	Lymphocytic-plasmacytic enteritis (also called immunoproliferative disease)
Beagle	Cobalamin deficiency
Border collie	Cobalamin deficiency
Boxer	Histiocytic ulcerative colitis
German shepherd	Idiopathic antibiotic-responsive, inflammatory bowel disease (lymphoplasmacytic, eosinophilic)
Giant schnauzer	Defective cobalamin absorption
Irish setter	Gluten-sensitive enteropathy
Lundehund	Lymphangiectasia
Retrievers	Dietary allergy
Rottweiler	Susceptibility to parvovirus
Soft-coated wheaten terrier	Protein-losing enteropathy/nephropathy
Shar-pei	Lymphocytic-plasmacytic enteritis, cobalamin deficiency
Toy breeds	Hemorrhagic gastroenteritis
Yorkshire terrier	Lymphangiectasia

Endocarditis

Modified with permission from Greene C: Infectious diseases of the dog and cat, ed 2, St Louis, 1999, Saunders, p 568.

Frequency of Isolation of Bacteria from Positive Blood Culture

Bacteria	Canine Endocarditis (% of Cases)
Gram Positive	
Staphylococcus intermedius	6–33
Streptococcus spp.	12–26
Gram Negative	
Escherichia coli	6–30
Anaerobic	
Propionibacterium acnes	6
Erysipelothrix rhusiopathiae	19
Corynebacterium spp.	19
Other	
Bartonella spp.	28

Electrocardiogram (ECG) Abnormalities

Common Associations

Baseline

- Sawtooth: atrial flutter versus artifact (panting, purring, electrical interference).

P waves

- Tall (>0.4 mV [dog], >0.2 mV [cat]): P pulmonale. Rule out right atrial enlargement. Tall P waves are normal if R-R interval is short (i.e., normal during sinus tachycardia), but P wave height should normalize when heart rate slows.
- Wide (>0.05 sec [dog], >0.04 sec [cat]): P mitrale. Rule out left atrial enlargement.
- Cyclical increase and decrease in P-wave amplitude: wandering pacemaker.
- Absent: isoelectric to that lead (P waves are present but visible only in other leads), atrial standstill due to hyperkalemia, atrial standstill due to atrial myocardial disorder (rare), atrial fibrillation (fine, wavy baseline and irregularly irregular R-R interval must be present also).

PR Association

- Long PR interval (>0.13 sec [dog], >0.09 sec [cat]): first-degree atrioventricular (AV) block.
- Progressive lengthening of PR interval until longest one is followed by P wave without QRS complex: second-degree AV block, Mobitz type I.
- Two or more consecutive P waves without QRS complexes, then a P wave triggers a QRS complex: second-degree AV block, Mobitz type II.
- P waves and QRS complexes occur independently: third-degree AV block (normal or high atrial [P wave] rate, ventricular escape rhythm [wide, bizarre QRS complexes] slower than atrial rate) or ventricular tachycardia (wide, bizarre QRS complexes occur at a faster rate than P waves, which are often buried within the QRS complexes).
- Short PR interval (<0.06 sec [dog], <0.05 sec [cat]): preexcitation/Wolff-Parkinson-White syndrome (PR interval is short at any heart rate) or sinus tachycardia (PR interval normally shortens as heart rate increases).

QRS Complexes

- Wide (>0.06 sec [dogs], >0.04 sec [cats]): diagnostic of left bundle branch block. Strongly suggests left ventricular enlargement; also occurs with severe hyperkalemia, quinidine toxicity.
- Small (low amplitude): rule out hypothyroidism, pericardial effusion, pleural effusion, ascites, obesity, pneumothorax, intrathoracic mass, hypothermia (dogs); rule out normal (cats).

Q Waves (Lead II)

- Deep: generally normal, especially in young, large-breed dogs; has been loosely associated with interventricular septal hypertrophy in dogs.

R Waves (Lead II)

- Tall (>2.5 mV [dogs that are small or medium breeds], >3.0 mV [dogs that are large breeds], >0.9 mV [cats]): left ventricular enlargement.

S Waves (Lead II)

- Deep: rule out right ventricular enlargement.
- S1S2S3 (S wave present in leads I, II, and III): strongly suggests right ventricular enlargement.

ST Segment

- Elevation (>0.15 mV [dog], any [cat]) or depression (>0.2 mV [dog], any [cat]): myocardial hypoxia, electrolyte disturbances.
- Slurring/coving: myocardial hypoxia.

T Waves

- Tall (>1 mV or >¼ of height of R wave [dog]; >0.3 mV [cats]): commonly normal. If onset of tall T waves is noted during ECG monitoring over time: rule out hyperkalemia, myocardial hypoxia, movement artifact (change in limb position).
- Different from rest of T waves: indicates abnormal repolarization, which in turn suggests abnormal ventricular depolarization of that heartbeat (e.g., premature ventricular complex).

Widespread availability of echocardiography has demonstrated that ECG is of limited accuracy for inferring cardiac structure. Indications of abnormal cardiac chamber size based on ECG features should be considered tentative and are best confirmed or ruled out using echocardiography.

Effusions

Modified with permission from Kittleson MD, Kienle RD, editors: Pericardial disease and cardiac neoplasia. In Small animal cardiovascular medicine, St Louis, 1998, Mosby, p 420.

FIP, Feline infectious peritonitis; *GI,* gastrointestinal.

Characteristics of Effusions

Parameter	Transudate	Modified Transudate	Exudate	Hemorrhage
Specific gravity	<1.018	1.018-1.025	>1.025	>1.025
Protein (g/dL)	<2.5	2.5-6.0	>2.5	>2.5
Appearance	Clear and watery	Clear to serosanguineous	Turbid, serosanguineous, serofibrinous	Serosanguineous, sanguineous
Cellularity (cells/mm^3)	<1000	>2500	>5000	>5000
Cytologic examination	Macrophages, mesothelial cells, and occasional neutrophils	Macrophages, mesothelial cells, and occasional neutrophils and erythrocytes	Variable	Primarily erythrocytes
Examples	Hypoalbuminemia (renal loss, GI loss, hepatic synthetic failure, massive skin wound/burn loss), prehepatic congestion/obstruction (e.g., portal vein thrombosis)	Heart failure, posthepatic vascular obstruction (e.g., caudal vena caval thrombosis), neoplasia, chyle	Septic (bacterial infection [aerobic, anaerobic]), nonseptic (e.g., FIP)	Anticoagulant rodenticide toxicosis, ruptured neoplasm, trauma

Effusions, Bicavitary*

Conditions Associated With Bicavitary Effusions

Modified from Willard M, Tvedten H: Small animal clinical diagnosis by laboratory methods, ed 4, St Louis, 2004, Saunders.

- Cardiovascular conditions
  - Pericardial effusion of any cause (neoplastic, idiopathic, toxic [anticoagulant], other) causing cardiac tamponade
  - Constrictive pericardial disease
  - Right-sided congestive failure: dilated cardiomyopathy, tricuspid regurgitation of any cause (tricuspid dysplasia, myxomatous tricuspid valve disease/endocardiosis, other), severe pulmonic stenosis, cor pulmonale of any cause (heartworm disease/caval syndrome, idiopathic pulmonary hypertension, other), tricuspid valve stenosis
  - Caudal vena cava thromboembolism
- Congenital obstruction: caudal vena cava
- Hypoalbuminemia: protein-losing nephropathy, protein-losing enteropathy, advanced hepatic disease, pancreatitis, extensive burns
- Bile peritonitis
- Vasculitis (e.g., FIP)
- Neoplastic conditions
  - Right atrial fibroma
  - Metastatic adenocarcinoma
  - Lymphoma
  - Hemangiosarcoma
  - Mesothelioma
  - Cholangiocellular carcinoma
  - Chemodectoma
  - Prostatic adenocarcinoma
  - Diffuse carcinomatosis

FIP, Feline infectious peritonitis.

Edema

Modified from Mitchell RN, Cotran RS: Hemodynamic disorders, thrombosis, and shock. In Cotran RS, et al, editors: Robbins pathologic basis of disease, ed 6, Philadelphia, 1999, Saunders.

Cause	Contributing Factor	Specific Clinical Syndromes
Increased hydrostatic pressure	Impaired venous return	Congestive heart failure (CHF)
		Pericardial disease (pericardial effusion, constrictive pericarditis, pericardial cyst or neoplasm)
		Portal hypertension
		Venous obstruction or compression (thrombosis, external pressure, extremity inactivity)
	Small-caliber arteriolar dilation	Heat
		Neurohumoral dysregulation
Reduced plasma oncotic pressure	Hypoproteinemia	Protein losing nephropathy (amyloidosis, glomerulonephritis)
		Synthetic failure (chronic liver disease)
		Malnutrition
		Protein-losing gastroenteropathy
Lymphatic obstruction	Decreased lymphatic drainage of interstitium	Various inflammatory conditions
		Congenital (lymphedema)
		Neoplastic
		Postsurgical
		Postirradiation
Sodium retention	Excess dietary intake with renal insufficiency	
	Increased tubular sodium resorption	Renal hypoperfusion
		Increased renin-angiotensin-aldosterone secretion
Inflammation	Acute inflammation	
	Chronic inflammation	
	Angiogenesis	

Fever of Unknown Origin

Associated Conditions

Modified with permission from Greene C: Table 96-3: Conditions associated with fevers of unknown origin. In Greene C, editor: Infectious diseases of the dog and cat, ed 2, St Louis, 1999, Saunders, p 696.

Systemic Infections

Dogs

- Bacterial endocarditis, bacteremias from an inapparent focus (e.g., secondary to persistent neutropenia or a congenital/acquired immunodeficiency syndrome); Lyme borreliosis (acute); leptospirosis; brucellosis; mycobacterial infections; rickettsial disease (e.g., ehrlichiosis, RMSF); protozoal infections (e.g., babesiosis, leishmaniasis, disseminated toxoplasmosis, neosporosis); disseminated mycotic infections (e.g., histoplasmosis, blastomycosis, cryptococcosis, coccidioidomycosis, aspergillosis)

Cats

- FIV infection; FeLV infection; feline hemotropic mycoplasma infection; feline infectious peritonitis; bacteremias from an inapparent focus; systemic mycoses (e.g., histoplasmosis, cryptococcosis); mycobacterial infections (often atypical); atypical calicivirus infection

Localized Infections

Dogs

- Bacterial endocarditis; urogenital infections (e.g., pyelonephritis, chronic prostatitis/prostatic abscess, stump pyometra); pyothorax and lung infections (e.g., inhaled pulmonary foreign bodies/pulmonary abscess, bronchopneumonia); occult hepatic abscess or cholangitis; localized peritonitis; diskospondylitis; juvenile metaphyseal osteomyelitis; retrobulbar or tooth root abscess; oropharyngeal stick injuries, septic thrombi

Cats

- Pyothorax and lung infections (e.g., pulmonary abscess, bronchopneumonia), upper respiratory infections; occult hepatic abscess or cholangiohepatitis; urogenital infections (e.g., pyelonephritis); localized peritonitis; osteomyelitis; cat bite abscess/cellulitis

Immune-Mediated Diseases

Dogs

- SLE; immune-mediated polyarthropathies: rheumatoid arthritis (erosive); nonerosive, nonseptic polyarthritis; idiopathic diseases; polyarthritis-meningitis complex (weimaraner, Newfoundland, German shorthaired pointer, boxer, beagle); polyarthritis-polymyositis complex (spaniel breeds); polyarthritis of Akitas; polyarthritis and amyloidosis of the Chinese shar-pei (shar-pei hock/fever); polyarteritis nodosa; autoimmune hemolytic anemia and immune-mediated thrombocytopenia; steroid-responsive meningitis; immunodeficiency syndromes

Cats

- SLE (rare in cats); chronic progressive polyarthropathy, including the ankylosing (periosteal proliferative) and luxating (erosive) forms; autoimmune hemolytic anemia (uncommon; may be FeLV associated); immune-mediated thrombocytopenia (rare; may be FeLV associated)

Neoplasia

Dogs

- Solid neoplasms (especially those that are necrotic, elicit an inflammatory response or have widespread metastases); lymphoproliferative or myeloproliferative disease

Cats

- FeLV-related lymphoproliferative and myeloproliferative disorders

Miscellaneous

Dogs

- Metaphyseal osteopathy, panosteitis; inflammatory-granulomatous bowel disease; liver disease (e.g., hepatic necrosis, cirrhosis, portosystemic shunts); pulmonary emboli; nodular panniculitis; drug reactions (tetracyclines, penicillin, sulfonamides, amphotericin B, quinidine)

Cats

- Pansteatitis (cats on fish-rich diets); hypervitaminosis A; drug reactions (e.g., tetracycline, levamisole)

FeLV, Feline leukemia virus; *FIV,* feline immunodeficiency virus; *RMSF,* Rocky Mountain spotted fever; *SLE,* systemic lupus erythematosus.

Feline Leukemia Virus and Feline Immunodeficiency Virus: Associated Disorders

Associated Diseases

From Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 5, St Louis, 2000, Saunders.

- Immunosuppression with opportunistic infections
- Gingivitis/stomatitis (FIV > FeLV)
- Myeloproliferative disease/erythroleukemia (FeLV ≫ FIV)
- Lymphosarcoma/lymphoid leukemias (FeLV ≫ FIV)
- Diarrhea/panleukopenia-like syndrome
- Weight loss/cachexia
- Chronic fever
- Glomerulonephritis
- Anterior uveitis/pars planitis/glaucoma (FIV ≫ FeLV)
- Behavioral changes/dementia/peripheral neuropathies
- Hypergammaglobulinemia (FIV > FeLV)
- Hemolytic anemias/aplastic anemias (FeLV ≫ FIV)
- Lymphopenia/neutropenia
- Thrombocytopenia (FeLV ≫ FIV)
- Abortion/fetal resorption/thymic atrophy (FeLV ≫ FIV)
- Chronic progressive polyarthritis
- *FeLV,* Feline leukemia virus; *FIV,* feline immunodeficiency virus.

Glucosuria

From Willard M, Tvedten H: Small animal clinical diagnosis by laboratory methods, ed 4, St Louis, 2004, Saunders.

Causes in Dogs and Cats	
Blood glucose concentration exceeding renal threshold (common)	• Diabetes mellitus • Stress (especially in cats) • Infusion of dextrose-containing fluids • Hyperadrenocorticism (rarely causes glucose >180 mg/dL) • Pheochromocytoma (rare)
Abnormal proximal renal tubular function	• Aminoglycoside toxicity • Acute renal failure • Fanconi syndrome • Primary renal glucosuria
Contamination	• Urinary hemorrhage in an animal with mild hyperglycemia

Glomerular Diseases, Dogs

Associated Diseases Reported in Dogs

Modified from Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

Infectious

- Bacterial
  - Bartonellosis (G)
  - Borreliosis (G)
  - Brucellosis (G)
  - Endocarditis (G)
  - Pyometra (A, G)
  - Pyoderma (A, G)
  - Other chronic bacterial infections (A, G)
- Protozoal
  - Babesiosis (MPGN)
  - Hepatozoonosis (G)
  - Leishmaniasis (A, MN, P-E, and P-M)
  - Trypanosomiasis (G)
- Rickettsial
  - Ehrlichiosis (G)
- Viral
  - Canine adenovirus type 1 (P-M)
- Parasitic
  - Dirofilariasis (A, MN)
- Fungal
  - Coccidioidomycosis (A, G)
  - Blastomycosis (G)

Inflammatory

- Chronic dermatitis (A, G)
- Inflammatory bowel disease (G)
- Pancreatitis (A, G)
- Periodontal disease (A, G)
- Polyarthritis (A, G)
- SLE (A, MN, P-E, and P-M)
- Other immune-mediated diseases (G)

Neoplastic

- Leukemia (G)
- Lymphosarcoma (A, G)
- Mastocytosis (G)
- Primary erythrocytosis (MCD?)
- Systemic histiocytosis (G)
- Other neoplasms (A, G, MN)

Miscellaneous

- Corticosteroid excess (G)
- Trimethoprim-sulfa therapy (G)
- Hyperlipidemia (?)
- Congenital C3 deficiency

Familial

Idiopathic (A, G, MN, MCD, P-E, or M)

A, Amyloidosis; G, glomerulonephritis, uncharacterized; *MCD,* minimal change disease; *MN,* membranous nephropathy; *MPGN,* membranoproliferative (mesangiocapillary) glomerulonephritis; *P*, proliferative (*E*, endocapillary; *M,* mesangial); *SLE,* systemic lupus erythematosus; *?*, association uncertain.

Glomerular Diseases, Cats

Associated Diseases Reported in Cats

From Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

Systemic Disease (Glomerular Disease)

Infectious

- Bacterial
  - Chronic bacterial infections (G)
  - Mycoplasmal polyarthritis (G)
- Viral
  - FIV (G)
  - FIP (MN)
  - FeLV (G, MN)

Inflammatory

- Pancreatitis (G)
- Cholangiohepatitis (G)
- Chronic progressive polyarthritis (G)
- SLE (MN)
- Other immune-mediated diseases (G)

Neoplastic

- Leukemia (MN)
- Lymphosarcoma (MN)
- Mastocytosis (G)
- Other neoplasms (G)

Miscellaneous

- Acromegaly (?)
- Mercury toxicity (MN)

Familial (MN)

Idiopathic (MN)

FeLV, Feline leukemia virus; *FIP,* feline infectious peritonitis; *FIV,* feline immunodeficiency virus; *G*, glomerulonephritis, uncharacterized; *MN,* membranous nephropathy; *SLE,* systemic lupus erythematosus; γ, uncertain association.

Gastrointestinal Ulceration

Conditions and Drugs Associated With GI Ulceration in Small Animals

From Bonagura J: Kirk's current veterinary therapy XII: small animal practice, St Louis, 1995, Saunders.

Impaired Mucosal Defense

- Drugs
  - NSAIDs*
  - Corticosteroids
- Stress
  - Shock
  - Sepsis
  - Trauma
  - Major surgery
- Neurologic disease
  - Head trauma
  - Intervertebral disk disease†
- Metabolic disorders
  - Liver disease
  - Renal disease
  - Pancreatitis
- Inflammatory bowel disease
- GI neoplasia
- Mastocytosis
- Gastric motility disorders

Hyperacidity

- Gastrinoma
- Mastocytosis

GI, Gastrointestinal; *NSAIDs,* nonsteroidal antiinflammatory drugs.

* NSAIDs that have been associated with GI ulcers in small animals include aspirin, indomethacin, phenylbutazone, flunixin, ibuprofen, deracoxib, meloxicam, naproxen, and piroxicam.

† Treated with corticosteroids.

Gastrointestinal Endocrine Diseases

Disease	Main Clinical Abnormality
Glucagonoma	Persistent hyperglycemia; hepatocutaneous syndrome possible
Gastrinoma	Gastric ulceration
Carcinoma	Liver; lethargy, anorexia; metastasis; no vasoactive amine signs
Pancreatic polypeptidoma	Chronic vomiting

Gastric Outflow Obstruction

From Slatter D: Textbook of small animal surgery, ed 3, Philadelphia, 2003, Saunders.

AAPH, Acquired antral pyloric hypertrophy; *CHPG,* chronic hypertrophic pyloric gastropathy.*Condition is secondary to CHPG/AAPH, gastric motility disorders, chronic gastritis, gastric or duodenal ulcers, gastric neoplasia, or extragastric causes.

History, Physical Findings, and Laboratory Findings in Animals With Gastric Retention or Outflow Obstruction*

	CHPG/AAPH	Motility Disorder	Chronic Gastritis Related	Ulcer Related or Gastric Neoplasia	Extragastric
History	Vomiting present: variable chronicity	Vomiting present: variable chronicity	Vomiting present: variable chronicity; intermittent occurrence	Vomiting present: progressive increase in frequency	Vomiting present
	Partially digested food	Partially digested food	Partially digested food or bile-stained fluid	Partially digested food or bile-stained fluid	
	Occurs anytime after eating	Occurs anytime after eating	Exacerbated by eating or drinking	Hematemesis common	
			Hematemesis may be present		
	Dietary modifications affect frequency				
	Abdominal distention present	Abdominal distention present	Abdominal distention present	Abdominal distention present	Abdominal distention present
	Appetite good	Appetite good	Appetite variable to poor	Appetite variable to poor	Appetite variable to poor
	Body weight variable	Body weight variable	Weight loss, unthrifty	Weight loss, unthrifty	Body weight variable
		May have history of acute or gastric dilatation with volvulus or other gastric disease or surgery	Melena may be present	Melena common; abdominal pain present	History compatible with specific extragastric disease
				Appetite variable to poor	
Physical Examination	Normal to decreased body condition	Normal to decreased body condition	Slight to significant decreased body condition	Slight to significant decreased body condition	Signs consistent with extragastric disease
	Bright, responsive	Bright, responsive	Normal to depressed	Normal to depressed	
	No abdominal pain	No abdominal pain	Variable cranial abdominal pain	Variable cranial abdominal pain	
	Cranial abdominal distention	Cranial abdominal distention	Cranial abdominal distention	Cranial abdominal distention	Cranial abdominal distention

	CHPG/AAPH	Motility Disorder	Chronic Gastritis Related	Ulcer Related or Gastric Neoplasia	Extragastric
Laboratory Findings	No abnormalities unless severe vomiting	No abnormalities unless severe vomiting	Variable acid-base status	Variable acid-base status	Variable acid-base status
	Alkalosis	Alkalosis	Hypokalemia	Hypokalemia	Laboratory findings consistent with extragastric disease
	Hypokalemia	Hypokalemia	Anemia (chronic disease, blood loss, or iron deficiency)	Anemia (chronic disease, blood loss, or iron deficiency)	
	Hypochloremia	Hypochloremia	Hypoproteinemia	Hypoproteinemia	
	Hemoconcentration	Hemoconcentration			

Hypoxemia

Causes

Hypoventilation*

- Acute barbiturate toxicosis, CNS lesion, neuromuscular disease (e.g., botulism, polyradiculoneuritis), pneumothorax, flail chest, pleural effusion, upper airway obstruction (e.g., laryngeal paralysis, foreign body, large airway trauma, large airway mass), anesthetic circuit problems

Diffusion/Gas Exchange Disorder*

- Pneumonia, pulmonary edema, pulmonary hemorrhage

Ventilation/Perfusion Mismatch*

- Pulmonary thromboembolism, prolonged recumbency

Right-to-Left Cardiovascular Shunt

- Tetralogy of Fallot, right-to-left shunting patent ductus arteriosus, other forms of Eisenmenger's physiology

CNS, Central nervous system.

Hypothyroidism

Neurologic Associations (Confirmed or Suspected)

- Neuromuscular weakness (slowly progressive)
- Muscle atrophy (scapular, masticatory)
- Facial nerve paralysis
- Vestibular signs (peripheral)
- Laryngeal paralysis
- Megaesophagus

Hypothermia

Causes

Modified with permission from Bonagura J: Kirk's current veterinary therapy XII small animal practice, St Louis, 1995, Saunders, p 159.

Iatrogenic

- Surgery
- Anesthesia
- Overzealous treatment of hyperthermia

Systemic Disease

- Cardiac
- Hypothyroidism
- Sepsis
- Chronic kidney disease
- Hypoadrenocorticism
- Malnutrition
- Hypoglycemia
- Neurologic:
    - Head trauma
    - Neoplasia
    - Cerebrovascular accident

Environmental

- Exposure
- Trauma

Hypotension, Systemic

Causes

Modified from Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

Decreased PreloadHypovolemia

- Hemorrhage
- Trauma
- Gastrointestinal losses
- Polyuria
- Hypoadrenocorticism
- Effusions or other third spacing of fluid
- Burns
- Heatstroke
- Pulmonary arterial hypertension (severe)

Decreased Venous Return

- Pericardial effusion/cardiac tamponade
- Constrictive pericarditis
- Severe pneumothorax
- Positive-pressure ventilation
- Gastric dilatation/volvulus
- Heartworm disease (cavai syndrome)

Decreased Cardiac Function

- Cardiomyopathy
- Valvular disease
- Bradyarrhythmias
- Tachyarrhythmias
- Electrolyte abnormalities
- Acid-base disturbances
- Severe hypoxemia

Decreased Vascular Tone

- SIRS
- Anaphylaxis
- Neurogenico
- Drug-induced (anesthetic agents, vasodilators, β-blockers, calcium channel blockers)
- Electrolyte abnormalities
- Acid-base disturbances
- Severe hypoxemia

SIRS, Sepsis/systemic inflammatory response syndrome.

Hypophosphatemia

Causes

Modified from DiBartola S: Fluid, electrolyte, and acid-base disorders in small animal practice, St Louis, 2000, Saunders.

Maldistribution (Translocation)

- Treatment of diabetic ketoacidosis
- Carbohydrate load or insulin administration
- Respiratory alkalosis or hyperventilation
- Parenteral nutrition or nutritional recovery
- Hypothermia

Increased Loss (Reduced Renal Resorption)

- Primary hyperparathyroidism
- Renal tubular disorders (e.g., Fanconi syndrome)
- Proximally acting diuretics (e.g., carbonic anhydrase inhibitors) *(?)
- Eclampsia
- Hyperadrenocorticism (?)

Decreased Intake (Reduced Intestinal Absorption)

- Dietary deficiency (?)
- Vomiting (?)
- Malabsorption (?)
- Phosphate binders
- Vitamin D deficiency

Laboratory Error

- Example: mannitol administration

Hyponatremia

Causes

From DiBartola S: Fluid, electrolyte, and acid-base disorders in small animal practice, St Louis, 2000, Saunders.

With Normal Plasma Osmolality

- Hyperlipidemia
- Hyperproteinemia

With High Plasma Osmolality

- Hyperglycemia
- Mannitol infusion

With Low Plasma Osmolality

- Including Hypervolemia
  - Severe liver disease
  - Congestive heart failure
  - Nephrotic syndrome
  - Advanced renal failure
- Including Normovolemia
  - Psychogenic polydipsia
  - Syndrome of inappropriate antidiuretic hormone secretion
  - Antidiuretic drugs
  - Myxedema coma of hypothyroidism
  - Hypotonie fluid infusion
- Including Hypovolemia
  - Gastrointestinal loss:
    - Vomiting
    - Diarrhea
  - Third-space loss:
    - Pancreatitis
    - Peritonitis
    - Uroabdomen
    - Pleural effusion (e.g., chylothorax)
    - Peritoneal effusion
  - Cutaneous loss:
    - Burns
  - Hypoadrenocorticism
  - Diuretic administration

Hypomagnesemia

Causes of Magnesium Depletion in Humans

Modified from DiBartola S: Fluid, electrolyte, and acid-base disorders in small animal practice, St Louis, 2000, Saunders.

Inadequate Dietary Intake

- Protein-calorie malnutrition
- Magnesium-free fluids and total parenteral nutrition

Gastrointestinal Disorders

- Prolonged nasogastric suction
- Chronic diarrhea
- Malabsorption syndromes
- Extensive bowel resection
- Intestinal and biliary fistulas
- Primary infantile hypomagnesemia

Renal Loss

- Chronic parenteral fluid therapy with magnesium-free fluids
- Intrinsic tubular disorders:
    - Chronic interstitial nephritis, pyelonephritis, glomerulonephritis
    - Acute tubular necrosis (diuretic phase)
    - Postobstructive diuresis
    - Renal tubular acidosis
    - Congenital magnesium wasting
    - Drug injury:
        - Aminoglycosides
        - Amphotericin B
        - Cisplatin
        - Cyclosporine
    - Loop diuretics
    - Osmotic diuretics: glucose, mannitol, urea
    - Hypercalcemia
    - Hypokalemia
    - Alcohol

Metabolic

- Hypercalcemia
- Hypophosphatemia

Endocrine

- Diabetes mellitus
- Hyperthyroidism
- Primary hyperparathyroidism
- Hyperadrenocorticism
- Syndrome of inappropriate antidiuretic hormone secretion

Redistribution

- Pancreatitis
- Hyperadrenergic states
- Massive blood transfusion
- Insulin therapy
- Refeeding syndrome

- Hypothermia
- Acute respiratory alkalosis
- Sepsis
- Cardiopulmonary bypass

Miscellaneous

- Severe burns
- Excessive lactation
- Excessive sweating

Hypokalemia: Associated Disorders (Cats)

Conditions Associated With Hypokalemia in Cats

Modified from Bonagura J: Kirk's current veterinary therapy XIII, St Louis, 2000, Saunders.

- Thyrotoxicosis
- Chronic kidney disease
- Metabolic acidosis
- Dietary
  - Potassium deficient
  - Acidified diets
- Insulin overdose
- Diuretic therapy (furosemide)
- Metabolic alkalosis
- Chronic vomiting/diarrhea
- Fluid administration (plasma dilution and volume-induced diuresis)
- Idiopathic (Burmese breed)
- Systemic diseases
  - Hepatic disease
  - Infectious disease
- Hyperaldosteronism (adrenocortical tumor)
- Renal tubular acidosis

Hypokalemia: Causes

Causes

Modified from DiBartola S: Fluid, electrolyte, and acid-base disorders in small animal practice, St Louis, 2000, Saunders.

Decreased Intake

- Alone, unlikely to cause hypokalemia unless diet is aberrant
- Administration of potassium-free fluids (e.g., 0.9% NaCl, 5% dextrose in water)

Translocation (ECF to ICF)

- Alkalemia
- Insulin/glucose-containing fluids
- Catecholamines
- Hypothermia (?)
- Hypokalemic periodic paralysis (Burmese cats)

Increased LossGI (FEk < 4%-6%)

- Vomiting of stomach contents
- Diarrhea

Urinary (FEk > 4%-6%)

- Chronic kidney disease in cats
- Diet-induced hypokalemic nephropathy in cats
- Distal (type I) RTA
- Proximal (type II) RTA after NaHco3 treatment
- Postobstructive diuresis
- Dialysis
- Mineralocorticoid excess:
    - Hyperadrenocorticism
    - Primary hyperaldosteronism (adenoma, hyperplasia)

Drugs

- Loop diuretics (e.g., furosemide, ethacrynic acid)
- Thiazide diuretics (e.g., chlorothiazide, hydrochlorothiazide)
- Amphotericin B
- Penicillins
- Albuterol overdosage

ECF, Extracellular fluid; *FEk,* urinary fractional excretion of potassium; *GI,* gastrointestinal; *ICF,* intracellular fluid; *RTA,* renal tubular acidosis.

Hypoglycemia

Causes

Modified from Willard M, Tvedten H: Small animal clinical diagnosis by laboratory methods, ed 4, St Louis, 2004, Saunders.

- Beta-cell tumor (insulinoma)*
- Extrapancreatic neoplasia
  - Hepatocellular carcinoma, hepatoma
  - Leiomyosarcoma, leiomyoma
  - Hemangiosarcoma (rarely)
- Hepatic insufficiency*
  - Portocaval shunts*
  - Chronic fibrosis, cirrhosis
- Sepsis*
- Hypoadrenocorticism
- Hypopituitarism
- Idiopathic hypoglycemia*
  - Neonatal hypoglycemia
  - Juvenile hypoglycemia (esp. toy breeds)
  - Hunting dog hypoglycemia
- Renal failure (rarely)
- Exocrine pancreatic neoplasia
- Hepatic enzyme deficiencies
  - von Gierke's disease (type 1 glycogen storage disease)
  - Cori's disease (type 3 glycogen storage disease)
- Severe polycythemia
- Prolonged starvation
- Prolonged sample storage*
- Iatrogenic*
  - Insulin therapy
  - Sulfonylurea therapy
  - Ethanol
  - Ethylene glycol
- Artifact
  - Glucometers
  - Laboratory error

Hypochloremia

Causes

Adapted from de Morais: Chloride ion in small animal practice: the forgotten ion. J Vet Emerg Crit Care 2:11-24, 1992.

- Pseudohypochloremia
  - Lipemic samples (titrimetric methods)
- Excessive loss of chloride relative to sodium
  - Vomiting of stomach contents*
  - Therapy with thiazides or loop diuretics*
  - Chronic respiratory acidosis
  - Hyperadrenocorticism
  - Exercise
- Therapy with solutions containing high sodium concentration relative to chloride
- Sodium bicarbonate
- Sodium penicillin (extremely high doses)

Hypocapnia

Causes

Modified with permission from King L: Textbook of respiratory disease in dogs and cats, St Louis, 2004, Saunders, 183.

- Hypotension
- Fever
- Sepsis
- Excitement
- Exercise
- Pain
- Pulmonary thromboembolism
- Early pulmonary parenchymal disease
- Cytokine release in the systemic inflammatory response syndrome
- Inappropriate ventilator settings
- Compensation for metabolic acidosis

Definition of hypocapnia: abnormally decreased arterial carbon dioxide tension (e.g., in dogs: Pco2 <33 mm Hg [venous], <36 mm Hg [arterial]; in cats: Pco2 <33 mm Hg [venous], <28 mm Hg [arterial]).

Hypocalcemia

Conditions Associated With Hypocalcemia

From DiBartola S: Fluid, electrolyte, and acid-base disorders in small animal practice, St Louis, 2000, Saunders.

Common

- Hypoalbuminemia
- Chronic kidney disease
- Puerperal tetany (eclampsia)
- Acute kidney disease
- Acute pancreatitis
- Undefined cause (mild hypocalcemia)

Occasional

- Soft-tissue trauma or rhabdomyolysis
- Hypoparathyroidism:
    - Primary:
        - Idiopathic or spontaneous
        - Postoperative bilateral thyroidectomy
    - After sudden reversal of chronic hypercalcemia
- Ethylene glycol intoxication
- Phosphate enema
- After NaHco3 administration

Uncommon

- Laboratory error
- Improper sample anticoagulant (EDTA)
- Infarction of parathyroid gland adenoma
- Rapid IV infusion of phosphates
- Acute calcium-free IV infusion (dilutional)
- Intestinal malabsorption or severe starvation
- Hypovitaminosis D
- Blood transfusion (citrated anticoagulant)
- Hypomagnesemia
- Nutritional secondary hyperparathyroidism
- Acute tumor lysis syndrome

Human

- Pseudohypoparathyroidism
- Drug-induced
- Hypercalcitoninism
- Osteoblastic bone neoplasia (prostate cancer)

EDTA, Ethylenediamine tetraacetic acid.

Hypoalbuminemia

Causes

From Willard M, Tvedten H: Small animal clinical diagnosis by laboratory methods, ed 4, St Louis, 2004, Saunders.

Decreased Production or Uptake

- Chronic hepatic insufficiency*
- Inadequate protein intake†‡
- Maldigestion†
- Malabsorption†

Hypergammaglobulinemia

Sequestration

- Body cavity effusion
- Vasculopathy

Increased Loss

- PLN due to glomerular disease*
- GI: PLE*
- Cutaneous
- Whole blood loss

Dilution

GI, Gastrointestinal; *PLE,* protein-losing enteropathy; *PLN,* protein-losing nephropathy.

Hyperthyroid Therapy

From Bonagura J: Kirk's Current veterinary therapy XIII, St Louis, 2000, Saunders.

Adverse Reactions Associated With Drugs Used Therapeutically in Feline Hyperthyroidism

Drug	Reaction	Approximate Percentage of Cats Affected	Time of Occurrence	Treatment Required
Methimazole	Vomiting, anorexia, depression	15	<4 weeks	Usually transient
	Eosinophilia, leukopenia, lymphocytosis	15	<8 weeks	Usually transient
	Self-induced excoriations	2	<4 weeks	Withdrawal and glucocorticoid therapy
	Agranulocytosis, thrombocytopenia	<5	<3 months	Withdrawal and supportive therapy
	Hepatopathy (anorexia, alanine aminotransferase, alkaline phosphatase elevations)	<2	<2 months	Withdrawal and supportive therapy
	Positive antinuclear antibody (ANA)	>50	>6 months	Decrease daily dosage
	Acquired myasthenia gravis	Rare	<16 weeks	Withdrawal or glucocorticoid therapy
Carbimazole	Vomiting, anorexia, depression	10	<3 weeks	Usually transient
	Eosinophilia, leukopenia	5	<2 weeks	Usually transient lymphocytosis
	Self-induced excoriations	Rare	<4 weeks	Withdrawal and glucocorticoid therapy
Stable iodine	Salivation and anorexia	Occasional	Immediate	Change formulation

Hyperthermia: Nonfebrile

Causes of Increased Body Temperature Excluding Fever

Modified with permission from Greene C: Infectious diseases of the dog and cat, ed 2, St Louis, 1999, Saunders, p 694.

Impaired Heat Loss

- Exposure to high ambient temperatures in a closed, poorly ventilated environment (heatstroke)
- Strenuous exercise, especially if concurrent respiratory embarrassment (e.g., if animal is brachycephalic or has laryngeal paralysis)

Hypermetabolic Disorders

- Malignant hyperthermia
- Hyperthyroidism
- Pheochromocytoma

Increased Muscle Activity

- Tetanus
- Seizure activity
- Metaldehyde intoxication
- Hypocalcemia

Miscellaneous Causes

- Hypothalamic tumor
- Certain drugs (phenothiazines, cholinergics)

Hypertension, Systemic

Diseases/Clinical Findings Commonly Associated With Systemic Hypertension

From Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

Dogs

- Ocular findings consistent with hypertensive choroidopathy, hypertensive retinopathy, or intraocular hemorrhage
- Chronic or acute renal failure
- Hyperadrenocorticism
- Diabetes mellitus
- Neurologic signs unexplained by other causes
- Pheochromocytoma
- Unexplained left ventricular hypertrophy (uniform/symmetrical)

Cats

- Ocular findings consistent with hypertensive choroidopathy, hypertensive retinopathy, or intraocular hemorrhage
- Chronic or acute renal failure
- Hyperthyroidism
- Diabetes mellitus
- Any neurologic signs
- Age >10 years
- Heart murmur caused by uniform/symmetrical left ventricular hypertrophy (reversible with long-term control of hypertension)

A complete funduscopic examination and BP measurement are indicated in animals known to have or suspected of having these disease conditions. Conditions that are rare in the species (e.g., hyperthyroidism in dogs) are not included. BP measurement is often included in routine cardiac evaluations. Idiopathic hypertrophic cardiomyopathy cannot be diagnosed without excluding hypertension.

Hypersensitivity

Types and Examples

Features: Type and Mechanism	Examples	Pathophysiology	Signs
Type I Immediate (anaphylactic)	• Food allergy • Atopy • Insect bite hypersensitivity • Adverse vaccine reaction • Adverse drug reaction	Acute, systemic inflammation is triggered by IgE-mediated degranulation of mast cells and basophils; degranulation releases histamine, leukotrienes, interleukins, and other vasodilatory and inflammatory substances.	• Urticaria (plaques of skin swelling) • Angioedema (regional or diffuse cutaneous or visceral swelling) • Pruritus • If severe: hypotension and shock (dogs) or dyspnea (cats)
Type II Cytotoxic	• Immune-mediated hemolytic anemia • Immune-mediated thrombocytopenia • Hypothyroidism (lymphocytic thyroiditis) • Hemolytic reaction (incompatible transfusion donor-recipient match; neonatal isoerythrolysis) • Pemphigus • Adverse drug reaction	• Antibody (IgM or IgG) binds to surface molecules (rightly or wrongly perceived as antigenic) on cells of body tissues. • The antibody-tagged cells are destroyed by the mononuclear-phagocytic (reticuloendothelial) system.	• Signs depend on body tissue cells involved. • Examples include hemolysis and cutaneous lesions.
Type III Immune complex–mediated	• Systemic lupus erythematosus • Rheumatoid arthritis • Feline infectious peritonitis	• Complexing of antibody with soluble antigen (slight excess of antigen causes the most intense reactions). Deposition of antigen-antibody complexes in tissues elicits neutrophil release of enzymes and free radicals, causing tissue damage. • Common sites of tissue damage include glomeruli, synovium, and vascular endothelium.	Signs of protein-losing nephropathy, polyarthritis, polyarteritis
Type IV Delayed cell-mediated	• Contact hypersensitivity • Transplanted organ rejection	• T lymphocyte–mediated (rather than primarily antibody-mediated) interaction with antigen. • “Delay” refers to late onset of reaction (>12 hours after beginning of exposure) due to mobilization and infiltration of T lymphocytes, usually “memory T cells” from prior or ongoing exposure to antigen. These T lymphocytes secrete inflammatory substances and attract macrophages and more lymphocytes, leading to tissue destruction.	Signs depend on body tissue involved. Examples include cutaneous lesions (contact hypersensitivity) and organ dysfunction (transplant rejection).

Hyperphosphatemia

Causes

From DiBartola S: Fluid, electrolyte, and acid-base disorders in small animal practice, St Louis, 2000, Saunders.

Maldistribution (Translocation)

- Tumor cell lysis
- Tissue trauma or rhabdomyolysis
- Hemolysis
- Metabolic acidosis

Increased Intake

- Gastrointestinal
  - Phosphate enemas
  - Vitamin D intoxication
- Parenteral
  - IV phosphate

Decreased Loss

- Acute or chronic kidney disease
- Uroabdomen or urethral obstruction
- Hypoparathyroidism
- Acromegaly(?)*
- Hyperthyroidism

Physiologic: young growing animal

Laboratory Error (e.g., lipemia, hyperproteinemia, depending on methodology)

Hypernatremia

Causes

From DiBartola S: Fluid, electrolyte, and acid-base disorders in small animal practice, St Louis, 2000, Saunders.

Pure Water Deficit

- Primary hypodipsia (e.g., in miniature schnauzers)
- Diabetes insipidus:
  - Central
  - Nephrogenic
- High environmental temperature
- Fever
- Inadequate access to water

Impermeable Solute Gain

- Salt poisoning
- Hypertonic fluid administration
  - Hypertonic saline
  - Sodium bicarbonate
  - Parenteral nutrition
  - Sodium phosphate enema
- Hyperaldosteronism
- Hyperadrenocorticism

Hypotonic Fluid LossExtrarenal

- Gastrointestinal
  - Vomiting
  - Diarrhea
  - Small-intestinal obstruction
- Third-space loss
  - Peritonitis
  - Pancreatitis
- Cutaneous
  - Burns

Renal

- Osmotic diuresis
  - Diabetes mellitus
  - Mannitol infusion
- Chemical diuretics
- Chronic renal failure
- Nonoliguric acute renal failure
- Postobstructive diuresis

Hyperlipidemia

Diseases and Conditions That Cause Hypertriglyceridemia and Hypercholesterolemia

Data from Stockham FL, Scott MA: Lipids. In: Fundamentals of veterinary clinical pathology, Ames, Iowa, 2002, Iowa State Press, pp 521–537.

Causes of HypertriglyceridemiaIncreased Triglyceride Production

- By hepatocytes
- By enterocytes:
    - Postprandial hyperlipidemia

Decreased Lipolysis or Intravascular Processing of Lipoproteins

- Hypothyroidism
- Nephrotic syndrome
- Lipoprotein lipase deficiency (rare in cats, very rare in dogs)

Other, Unknown, or Multiple Mechanisms

- Acute pancreatitis
- Diabetes mellitus
- High-lipid diet
- Hyperadrenocorticism or excess glucocorticoids
- Hyperlipidemia in a Brittany spaniel
- Idiopathic hyperlipidemia of miniature schnauzers

Causes of HypercholesterolemiaIncreased Cholesterol Production

- By hepatocytes:
    - Nephrotic syndrome or protein-losing nephropathy
- By enterocytes:
    - Postprandial hyperlipidemia

Decreased Lipolysis or Intravascular Processing of Lipoproteins

- Hypothyroidism
- Nephrotic syndrome or protein-losing nephropathy
- Lipoprotein lipase deficiency (very rare in dogs)

Other, Unknown, or Multiple Mechanisms

- Acute pancreatitis
- Cholestasis (obstructive)
- Diabetes mellitus
- Hyperadrenocorticism
- Hypercholesterolemia in briards
- Idiopathic hyperlipidemia of miniature schnauzers

Hyperkalemia

Causes

Modified from DiBartola S: Fluid, Electrolyte and acid-base disorders in small animal practice, St Louis, 2006, Saunders.

Pseudohyperkalemia

- Platelet activation (blood clotting in vitro)
- Thrombocytosis
- Hemolysis in susceptible breeds (Akita, Shiba Inu, Tosa Inu)

Increased Intake

- Unlikely to cause hyperkalemia in presence of normal renal function unless iatrogenic (e.g., continuous infusion of excessive amounts of potassium)

Translocation (ICF to ECF)

- Acute mineral acidosis (e.g., HCl, NH_4Cl)
- Insulin deficiency (e.g., diabetic ketoacidosis)
- Acute tumor lysis syndrome
- Reperfusion of extremities after aortic thromboembolism in cats with cardiomyopathy
- Hyperkalemic periodic paralysis (one case report in a pit bull)
- Drugs: nonspecific beta-blockers (e.g., propranolol)*

Decreased Urinary Excretion

- Urethral obstruction
- Ruptured bladder
- Anuric or oliguric renal failure
- Hypoadrenocorticism
- Selected GI disease (e.g., trichuriasis, salmonellosis, perforated duodenal ulcer)
- Chylothorax with repeated pleural fluid drainage
- Hyporeninemic hypoaldosteronism

Drugs

- Angiotensin-converting enzyme inhibitors (e.g., captopril, enalapril, benazepril, ramipril, lisinopril)*
- Potassium-sparing diuretics (e.g., spironolactone, amiloride, triamterene)*
- Prostaglandin inhibitors (e.g., indomethacin)*
- Heparin*

ECF, Extracellular fluid; *GI,* gastrointestinal; *ICF,* intracellular fluid.

Hyperglycemia

Causes of Altered Blood Glucose in Dogs and Cats

Modified from Willard M, Tvedten H: Small animal clinical diagnosis by laboratory methods, ed 4, St Louis, 2004, Saunders.

- Diabetes mellitus*
- "Stress" (cat)*
- Postprandial
- Hyperadrenocorticism*
- Acromegaly (cat)
- Diestrus (bitch)
- Pheochromocytoma (dog)
- Pancreatitis
- Exocrine pancreatic neoplasia
- Renal insufficiency
- Drug therapy*
    - Glucocorticoids
    - Progestogens
    - Megestrol acetate
    - Thiazide diuretics
    - Parenteral nutrition

Hyperglobulinemia

Causes

Modified from Willard M, Tvedten H: Small animal clinical diagnosis by laboratory methods, ed 4, St Louis, 2004, Saunders.

Polyclonal

Infections

- Bacterial[*†]
  - Brucellosis
  - Pyoderma
  - Bacterial endocarditis
- Viral
  - FIP[‡]
  - FIV
  - FeLV
- Fungal[*†]
  - Systemic fungal infections (e.g., blastomycosis, histoplasmosis, coccidioidomycosis)
- Rickettsial[†‡]
  - Ehrlichiosis
- Parasitic
  - Dirofilariasis[*†]
  - Demodicosis
  - Scabies

Immune-Mediated Disease

- Infections (immune complex)
  - Dirofilariasis[*†]
  - Feline cholangitis/cholangiohepatitis
  - Pyometra
- SLE, including glomerulonephritis, IMHA, IMT, and polyarthritis[*]
- IMHA, IMT (not because of SLE)[*]
- Pemphigus complex, bullous pemphigoid[*]
- Rheumatoid arthritis[*]

Neoplasia[†‡]

Monoclonal

Infection

- Ehrlichiosis[†‡]
- Leishmaniasis[†‡]
- FIP (rare)

Idiopathic[†‡]

- Benign monoclonal gammopathy

Neoplasia[†‡]

- Multiple myeloma[‡]
- Macroglobulinemia

- Lymphoma
- Chronic lymphocytic leukemia
- Extramedullary plasmacytoma (rare)

Miscellaneous

- Cutaneous amyloidosis
- Plasmacytic gastroenterocolitis*

Effect of age should be considered when assessing globulin value.

FeLV, Feline leukemia virus; *FIP,* feline infectious peritonitis; *FIV,* feline immunodeficiency virus; *IMHA,* immune-mediated hemolytic anemia; *IMT,* immune-mediated thrombocytopenia; *SLE,* systemic lupus erythematosus.

*Mild (4−5 g/dL).

†Moderate (5−6 g/dL).

‡Severe (>6 g/dL).

Hyperchloremia

Adapted from de Morais: Chloride ion in small animal practice: the forgotten ion. J Vet Emerg Crit Care 2:11–24, 1992.

*May be associated with corrected hypochloremia in cats.

Causes of Corrected Hyperchloremia

Pseudohyperchloremia

- Lipemic samples (colorimetric methods)
- Potassium bromide therapy

Excessive Loss of Sodium Relative to Chloride

- Diarrhea

Excessive Gain of Chloride Relative to Sodium

- Therapy with chloride salts (NH_4Cl, KCl)
- Total parenteral nutrition
- Fluid therapy (e.g., 0.9% NaCl, hypertonic saline, KCl-supplemented fluids)
- Salt poisoning

Renal Chloride Retention

- Renal failure
- Renal tubular acidosis
- Hypoadrenocorticism*
- Diabetes mellitus*
- Chronic respiratory alkalosis
- Drug-induced: acetazolamide, spironolactone

Hypercapnia

Causes

Hypoventilation

Neuromuscular disorder

Medullary dysfunction (excessive depth of anesthesia, intracranial disease)

Cervical disease or neuromuscular disease

Airway Obstruction

Large-airway obstruction (laryngeal paralysis, tracheal collapse)

Small-airway obstruction (chronic airway disease, bronchoconstriction)

Thoracic Wall Problems

Open pneumothorax

Flail chest

Anterior displacement of the diaphragm by abdominal space filling disorders

Pleural space filling disorder (air, fluid, diaphragmatic hernia)

Pleural fibrosis

Pulmonary Parenchymal Disease (Late)

Inappropriate Ventilator Settings

Dead-Space Rebreathing

Recent Bicarbonate Therapy (in Ventilatory Compromised Animals)

Compensation for Metabolic Acidosis

Malignant Hyperthermia

With permission from King L: Textbook of respiratory disease in dogs and cats. St Louis, 2004, Saunders, 184.

Definition of hypercapnia (synonym: hypercarbia): abnormally increased arterial carbon dioxide tension (e.g., in dogs: Pco2 >50 mm Hg [venous], >44 mm Hg [arterial]; in cats: PCO2 >45 mm Hg [venous], >32 mm Hg [arterial]).

Hypercalcemia: Lab

Modified from Slatter D: Textbook of small animal surgery, ed 3, Philadelphia, 2003, Saunders.

BUN, Blood urea nitrogen; *N,* normal blood concentration; *PTH,* parathyroid hormone; *PTHrP,* PTH-related protein; (−), below normal blood concentration; (+), greater than normal blood concentration.

Relative Values of Selected Hematologic Parameters in Dogs and Cats With Hypercalcemia-Associated Diseases

	PTH	PTHrP	Ionized Calcium	Phosphorus	Vitamin D	BUN
Parathyroid adenoma	N to +++	−	+++	−	N/++	N/+
Hypercalcemia of malignancy	−	++	++	−	N	N/+
Hypoadrenocorticism	N	N	+	N/+	N	N
Vitamin D toxicosis	−	−	+++	++	+++	N/+
Renal secondary hyperparathyroidism	++	N/++	+	++	N	+++
Inflammatory disease	−/N	?	+	N	N/+	N
Parathyroid hyperplasia	N to +++	−	+++	−	N/++	N/+

Hypercalcemia: Causes

Causes

Adapted from Dibartola S: Fluid, electrolyte, and acid-base disorders in small animal practice, St Louis, 2006, Saunders.

Nonpathologic

- Nonfasting (minimal increase)
- Physiologic growth of young
- Laboratory error
- Spurious:
  - Lipemia
  - Detergent contamination of sample or tube

Transient or Inconsequential

- Hemoconcentration
- Hyperproteinemia
- Hypoadrenocorticism
- Severe environmental hypothermia

Pathologic or Consequential—Persistent

- Associated with malignancy:
  - Humoral hypercalcemia of malignancy:
    - Lymphoma (common)
    - Anal sac apocrine gland adenocarcinoma (common)
    - Carcinoma (sporadic): squamous cell (cats; common), lung, pancreas, skin, nasal cavity, thyroid, mammary gland, adrenal medulla
    - Thymoma (rare)
  - Hematologic malignancies (bone marrow osteolysis):
    - Lymphoma
    - Multiple myeloma
    - Myeloproliterative disease (rare)
    - Leukemia (rare)
  - Metastatic or primary bone neoplasia (very uncommon)
- Chronic kidney disease
- Hypervitaminosis D:
  - Iatrogenic
  - Plants (calcitriol glycosides)
  - Vitamin D3 ointments
  - Rodenticide
- Granulomatous disease:
  - Blastomycosis
  - Cryptococcosis (cats)
  - Schist osomiasis
  - Dermatitis
- Primary hyperparathyroidism:
  - Adenoma (common)
  - Adenocarcinoma (rare)
  - Hyperplasia (uncommon)
- Acute renal failure
- Skeletal lesions (nonmalignant, uncommon):
  - Osteomyelitis (bacterial or mycotic)
  - Hypertrophie osteodystrophy
  - Disuse osteoporosis (immobilization)
- Excessive calcium-containing intestinal phosphate binders
- Excessive calcium supplementation (calcium carbonate)
- Hypervitaminosis A
- Hypercalcemic conditions in human medicine:

    - Milk-alkali syndrome (rare in dogs)
    - Thiazide diuretics
    - Acromegaly
    - Thyrotoxicosis
    - Postrenal transplantation
- Aluminum exposure (dogs?)
- Idiopathic (cats)

Horner's Syndrome

Modified from Delahunta A: Veterinary neuroanatomy and clinical neurology, St Louis, 1983, Saunders.

Summary of Lesions

Location	Example of Lesion	Associated Neurologic Deficit
Cervical spinal cord	• External injury • Focal leukomyelomalacia, embolic infarct, disk compression	• Tetraplegia-spastic; dyspnea • Hemiplegia-ipsilateral, spastic
T1–T3 spinal cord	• External injury • Neoplasm • Focal poliomyelomalacia (embolic infarct) • Diffuse myelomalacia (ascending and pelvic limbs, descending)	• Pelvic and thoracic limb or paresis or paralysis with lower motor neuron deficit in thoracic limbs and upper motor neuron deficit in pelvic limbs • Lower motor neuron deficit; analgesia of tail, anus, abdomen, and thorax with paretic thoracic limbs
T1–T3 ventral roots	Avulsion of roots of brachial plexus	Lower motor neuron paresis or paralysis of the thoracic limb on the same side
Proximal spinal nerves	Lymphoma	None if confined to the trunk
Cranial thoracic sympathetic trunk	Neurofibroma	None if confined to the trunk
Cervical sympathetic trunk	Injury from surgical intervention in the area or from dog bites	None if unilateral; bilateral lesions interfere with laryngeal and esophageal function because of vagal involvement
Middle ear cavity (small animals)	• Otitis media • Neoplasia	Signs of peripheral vestibular disturbance; ipsilateral ataxia, head tilt, nystagmus, and sometimes facial palsy or hemifacial spasm
Retrobulbar	• Contusion • Neoplasia	Varies with degree of contusion to the optic and oculomotor nerves, which also influence pupillary size and vision

Hepatotoxic Agents

Adapted from Khan SA: Intoxication versus acute nontoxicologic illness: differentiating the two. In Ettinger SJ, Feldman EC, editors: Textbook of veterinary internal medicine, St Louis, 2010, Saunders, pp 549–554.

GI, Gastrointestinal; *NSAID,* nonsteroidal antiinflammatory drug.

Agent	Comments/Notes
Anticonvulsants (primidone; phenytoin; phenobarbital)	Dogs; occurs after repeated use for weeks, months
Diazepam	Cats; idiosyncratic reaction after repeated use for 5-11 days or more
NSAID-induced hepatopathy	Dogs; reported from carprofen; can occur from any NSAID following repeated use (days to weeks)
Corticosteroids (steroid hepatopathy)	Occurs from long-term use
Mushroom (*Amanita* type)	Mostly dogs; delayed onset of GI signs (12 hours); acute hepatic damage within 1-3 days
Acetaminophen	Cats more prone to methemoglobinemia within a few hours of exposure; dogs can have both hepatic damage and methemoglobinemia; hepatic damage in 1-3 days
Iron (multivitamin ingestion)	Dogs; prenatal multivitamins have more elemental iron; initial GI signs followed by shock and liver damage in 1-2 days
Sago palm or cycad palm toxins	Dogs; all parts toxic; seeds contain more toxin; GI signs, liver damage, seizures; mortality 33%
Blue-green algae toxins	Dogs; shock and acute hepatic damage
Aflatoxins (contaminated commercial dog food)	Dogs very sensitive; several outbreaks reported in the United States; can occur with acute exposure (large dose) or with repeated exposure (low doses)
Copper storage disease	Dogs; certain breeds can accumulate copper in the liver over a period of time
Xylitol (sugar alcohol present in gums, bakery products, confectionery)	Dogs; hypoglycemia within 12 hours; hepatic damage and coagulopathy in 1-3 days
Zinc metal	Dogs; zinc-containing objects (pennies, nuts); affects multiple organs; hemoglobinuria, anemia, increased liver enzymes, azotemia, pancreatitis
Castor beans (ricinus)	All parts toxic; seeds more toxic; affects multiple organs such as GI, kidney, and liver
Joint chews (containing glucosamine, chondroitin sulfate, dimethylsulfone, and other ingredients)	Dogs; recently reported with accidental overdose; elderly dogs appear at higher risk

Hepatopathy, Vacuolar

Differential Diagnoses for Canine Vacuolar Hepatopathy

Modified from Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

Hyperadrenocorticism

- Spontaneous disease
- Pituitary or adrenal origin

Iatrogenic, Glucocorticoid Therapy:

- **PO, IM, SQ, topical (skin, eye, ear)**

Adrenal Hyperplasia Syndrome

- Abnormal sex hormone production (aberrant adrenocortical disease)

Superficial Necrolytic Dermatitis (Hepatocutaneous Syndrome)

Chronic Stress

- Illness > 4 weeks

Severe Dental Disease

- Infection

Chronic Infections or Inflammation

- Pyelonephritis, chronic dermatitis (examples)

Inflammatory Bowel Disease (IBD)

- Lymphoplasmacytic
- Eosinophilic

Neoplasia

- Lymphoma, other

Disorders Influencing Lipid Metabolism

- Diabetes mellitus
- Idiopathic hyperlipidemia (e.g., schnauzer, Shetiland sheepdog, other)

Pancreatitis, Chronic

Hypothyroidism, Severe

Congestive Heart Failure (CHF)

Hepatic Neoplasia

From Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

Dogs

- **Primary Hepatic Tumors (26%)*
  - Hepatocellular carcinoma
  - Hepatocellular adenoma
  - Hepatic hemangiosarcoma
  - Biliary carcinoma
- *Other*
  - Leiomyosarcoma
  - Liposarcoma
  - Myxosarcoma
  - Fibrosarcoma
  - Biliary adenoma
  - Hepatic carcinoid
- *Hemolymphatic Neoplasia (28%)*
  - Lymphoma
  - MCT
  - Plasma cell tumor
- *Metastatic Neoplasia (46%)*

Cats

- **Primary Hepatic Tumors (20%)*
  - Biliary carcinoma
  - Hepatocellular carcinoma
  - Hepatic hemangiosarcoma
- *Other*
  - Biliary cystadenoma
  - Myelolipoma
  - Hepatic carcinoid
- *Hemolymphatic Neoplasia (60%)*
  - Lymphoma
  - MCT
  - Plasma cell tumor
- *Metastatic Neoplasia (20%)*

MCT, Mast cell tumor

Primary tumors: in order of prevalence.

Hepatic Infections and Abscesses

Bacteria Isolated from Hepatobiliary Suppurative Inflammation and Abscesses

Modified with permission from Greene C: Infectious diseases of the dog and cat, ed 2, St Louis, 1999, Saunders, p 616.

Aerobic Cultures (Positive Cultures: n = 54)

- n ≥ 3 each
  - *Escherichia coli*
  - *Staphylococcus pseudintermedius*
  - *S. aureus*
  - *S. epidermidis*
  - *Streptococcus* group D enterococci
  - *Streptococcus* β-hemolytic
  - *Enterococcus*
  - *Enterobacter aerogenes*
  - *E. agglomerans*
  - *Pseudomonas aeruginosa*
- n = 1 each
  - *Pseudomonas fluorescens*
  - *Klebsiella pneumoniae*
  - *Bacillus spp.*
  - *Acinetobacter calcoaceticus*
  - *Citrobacter freundii*
  - *Moraxella phenylpyruvica*
  - *Pasteurella multocida*
  - *Bordetella bronchiseptica*
  - *Nocardia*
  - *Salmonella*
  - *Campylobacter jejuni*

Anaerobic Cultures (Positive Cultures: n = 26)

- *Propionibacterium acnes*
- *Clostridium perfringens*
- *Clostridium*
- *Bacteroides melaninogenicus*
- *Corynebacterium* spp.
- *Actinomyces*
- *Peptostreptococcus*
- *Fusobacterium*
- Anaerobic streptococci

Additional Microbes Reported Elsewhere

- *Bacillus piliformis*
- *Corynebacterium* spp.
- *Proteus* spp.
- *Francisella tularensis*
- *Listeria monocytogenes*
- Eugenic fermenter-4 bacilli

In order from most to least common. Data acquired from case records, Companion Animal Hospital, College of Veterinary Medicine, Cornell University, Ithaca, NY, 1985–1996.

Hepatic Fibrosis

Causes in Dogs

From Bonagura J: Kirk's current veterinary therapy XIII, St Louis, 2000, Saunders.

- Chronic hepatitis
  - Hepatic copper accumulation
    - Primary (Bedlington terriers, West Highland white terriers)
    - Secondary (Doberman pinschers, Skye terriers)
  - Infectious
  - Drug-induced Primidone
  - Metabolic
    - α1-Antitrypsin deficiency
  - Others
    - Lobular dissecting hepatitis
    - Idiopathic chronic hepatitis
- Toxins, chemicals
  - Pyrrolizidine alkaloids, CCl_4
- Postnecrotic fibrosis
- Chronic congestive heart failure
- Chronic cholangiohepatitis
- Chronic biliary obstruction
- Idiopathic hepatic fibrosis
  - Perivenous
  - Diffuse pericellular
  - Periportal

Hepatic Failure, Acute

Clinically Relevant Causes

Modified from Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 4, St Louis, 1994, Saunders.

Category of Injury	Examples
Trauma	• Automobile accident • High-rise syndrome

Toxin	• Environmental agents:
	  ○ Aflatoxin
	  ○ *Amanita pantherina*, *Amanita phalloides*
	  ○ Cycadaceae
	  ○ Heavy metals
	• Drugs:
	  ○ Thiacetarsemide
	  ○ Mebendazole
	  ○ Diethylcarbamazine-oxibendazole
	  ○ Acetaminophen
	  ○ Methoxyflurane, halothane
	  ○ Diethylcarbamazine
	  ○ Tetracycline
	  ○ Trimethoprim-sulfadiazine
	  ○ Griseofulvin
	  ○ Diazepam (cats)

Infectious agents	• Infectious canine hepatitis • Leptospirosis • Toxoplasmosis • Heartworm caval syndrome • Bacterial sepsis
Thermal	Heatstroke
Extension of abdominal inflammation	• Pancreatis • Peritonitis • Inflammatory bowel disease
Metabolic disorder	Lipidosis (cats)

Hemothorax

Causes of Hemothorax and Sanguineous Pleural Effusion

Modified with permission from King L: Textbook of respiratory disease in dogs and cats. St Louis, 2004, Saunders, p 611.

- Trauma
- Malignancy
- Coagulopathy
- Diaphragmatic hernia
- Lung lobe torsion
- Pulmonary infarction
- Pulmonary abscessation
- Recent surgery
- Aortic aneurysm
- Swan-Ganz catheter placement*
- Tube thoracostomy*
- Hemopneumothorax*
- Costal exostosis*
- Endometriosis*
- Foreign body
- Heartworm disease
- Central venous catheter placement

* Reported only in human literature.

Hemoptysis

Causes

From Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

Pulmonary

- Pulmonary thromboembolism: secondary to neoplastic, endocrine, cardiac, metabolic disease
- Pulmonary hypertension: secondary to heartworm disease; congenital or acquired cardiac defects that result in shunting of blood
- Chronic bronchitis/bronchiectasis
- Bacterial pneumonia
- Nocardiosis
- Pulmonary abscess
- Kennel cough (rarely causes hemoptysis)
- Fungal pneumonia: blastomycosis, histoplasmosis, coccidioidomycosis
- Parasites: *Paragonimus kellicotti, Capillaria aerophila*, *Aelurostrongylus abstrusus*
- Eosinophilic bronchopneumopathy
- Neoplasia, lung: primary adenocarcinoma, undifferentiated carcinoma, SCC, chondrosarcoma; metastatic; primary tracheal tumors
- Lung lobe torsion

Cardiovascular

- Heartworm disease
- Cardiogenic pulmonary edema
- Arteriovenous fistula
- Bacterial endocarditis

Systemic

- Bleeding disorder: primary (quantitative or qualitative platelet defects) or secondary hemostatic (factor deficiencies, anticoagulant rodenticide toxicity, DIC) abnormalities
- Trauma: pulmonary contusion, tracheal rupture, FB
- Iatrogenic: endotracheal intubation; complication of lung biopsy/aspirate, transtracheal wash, or bronchoscopy

DIC, Disseminated intravascular coagulopathy; *FB,* foreign body; *SCC,* squamous cell carcinoma.

Hematuria

Causes

Modified from Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

Urinary Tract Origin (Kidneys, Ureters, Bladder, Urethra)

- Trauma
  - Traumatic collection (e.g., catheter, cystocentesis)
  - Renal biopsy
  - Blunt trauma (e.g., automobile accident)
- Urolithiasis
- Neoplasia
- Inflammatory disease
- Urinary tract infection
- Feline lower urinary tract signs/disease/interstitial cystitis
- Chemically-induced inflammation (e.g., cyclophosphamide-induced cystitis)
- Parasites
  - *Dioctophyma renale*
  - *Capillaria plica*
- Bleeding disorder
  - Warfarin intoxication
  - Disseminated intravascular coagulation
  - Hemophilia
  - Thrombocytopenia
- Renal infarction
- Renal pelvic hematoma
- Vascular malformation
  - Renal telangiectasia (Welsh corgi)
  - Idiopathic renal hematuria

Genital Tract Contamination (Prostate, Prepuce, Vagina)

- Estrus
- Inflammatory, neoplastic, and traumatic lesions of the genital tract

Hematochezia

Causes

Modified from Tams TR: Gastrointestinal symptoms. In: Handbook of small animal gastroenterology, Philadelphia, 1996, Saunders.

Anal Disease

- Perianal fistulas
- Anal sacculitis or abscess
- Stricture
- Neoplasia (e.g., anal sac tumor)
- Trauma (e.g., bite wound)
- Perianal hernia
- Foreign body

Rectum and Colon

- Proctitis (inflammation of the rectal mucosa)
- Colitis
    - Idiopathic
    - Inflammatory bowel disease
    - Stress
    - Infectious
        - *Campylobacter spp.*
        - *Clostridium perfringens*
- Parvovirus
- Parasitism
    - Hookworms
    - Whipworms
    - Coccidia
    - Roundworms
- Neoplasia
    - Rectal polyp
    - Adenocarcinoma
    - Lymphoma
- Rectal prolapse
- Mucosal trauma
    - Movement of foreign material (e.g., hairballs)
    - Iatrogenic (e.g., thermometers, enemas, fecal loops)
- Automobile trauma
- Ileocecocolic area: intussusception
- Bleeding disorder

Constipation often can cause excessive straining which can result in formed stools with blood on the surface.

Hematemesis

Causes

Modified with permission from Kirk RW, Bonagura JD, editors: Kirk's current veterinary therapy XI: small animal practice, St Louis, 1992, Saunders, p 133.

Bleeding Disorders

- Disseminated intravascular coagulation
- Anticoagulant rodenticide toxicity
- Thrombocytopenia
- Congenital or acquired coagulation factor deficiencies/defects

Heavy Metal Toxicity

- Arsenic
- Lead
- Zinc

Infectious Disorders

- GI parasitism
- Viral gastroenteritis
- Bacterial gastroenteritis

Perioperative Hemorrhage

- Gastric dilatation/volvulus
- Gastrectomy
- Gastrostomy

Gastric/Duodenal Erosions/UlcerationsInfiltrative Disease

- Neoplasia
- Inflammatory bowel disease
- Phycomycosis

Metabolic Disorders

- Renal disease
- Liver disease
- Hypoadrenocorticism

Stress Erosions/Ulcerations

- Burns (Curling's ulcer)
- Neurologic disorders
    - Head trauma (Cushing's ulcer)
    - Spinal cord disorders
- Sepsis/septic shock
- Hypovolemic shock
- Multiple trauma

Drug AdministrationGlucocorticoids

NSAIDs

- Aspirin
- Indomethacin
- Phenylbutazone
- Naproxen
- Sulindac
- Deracoxib
- Ibuprofen
- Flunixin meglumine
- Meclofenamic acid
- Piroxicam

Gastric/Duodenal Foreign Bodies

Neoplasia

- Mast cell tumor
- Gastrinoma (Zollinger-Ellison syndrome)
- Pancreatic polypeptide–secreting tumor
- Basophilic leukemia

Hemorrhagic Gastroenteritis

Esophageal Disorders

- Esophagitis
- Esophageal neoplasia
- Esophageal foreign bodies

GI, Gastrointestinal: *NSAIDs,* nonsteroidal antiinflammatory drugs.

Heartworm: Clinical Severity

With permission from Fox P: Textbook of canine and feline cardiology: principles and practice, St Louis, 2000, Saunders, p 707.

Classification of Heartworm Disease Severity Based on Signs, Physical Examination, and Radiographic Findings

Class	Clinical Signs	Examination Findings	Radiographic Findings
1	None to occasional cough	Normal examination	No lesions
2	Occasional cough and mild-to-moderate exercise intolerance	Increased lung sounds	Slight pulmonary arterial enlargement
		Fair general condition	Circumscribed perivascular density plus mixed alveolar- interstitial lesions
3	Persistent cough, moderate to severe exercise intolerance	Increased lung sounds	Moderate-to-severe pulmonary arterial enlargement
Caval syndrome	Weight loss, cachexia	Accentuated or split S2	RV enlargement
	Respiratory distress	Right apical gallop	Diffuse and severe pulmonary infiltrates
	Overt right heart failure	Tachypnea, dyspnea	
	General loss of condition		

Heartworm Disease: Complications

Complications

Untreated

- Eosinophilic granulomatosis
- Eosinophilic pneumonitis
- Right-sided congestive heart failure*
- Hemoglobinuria, "pigment nephropathy"*
- Hemolytic anemia*
- Pulmonary thromboembolism

During or Shortly After Treatment Period

- Acute (Surgical Removal)
  - Anaphylaxis
  - Hypotension
  - Cardiac arrest
- Subacute (Medical Treatment)
  - Eosinophilic pneumonitis
  - Pain at injection site (melarsomine)
  - Pulmonary thromboembolism (possibly massive, especially if inadequate exercise restriction)
  - Sudden death (especially if inadequate exercise restriction)

* Together, comprise the "caval syndrome" of heartworm disease

Heartworm *Dirofilaria* Versus *Acanthocheilonema*

Modified from Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

Differentiating Characteristics of *Acanthocheilonema* (formerly *Dipetalonema*) *reconditum* and *Dirofilaria immitis*

	Number in Blood	Motion	Shape	Length (Modified Knott Test)
Acanthocheilonema reconditum	Usually few	Progressive	Curved body Blunt head Curved or “buttonhook” tail	263 µm (250-288 µm)
Dirofilaria immitis	Usually many	Stationary	Straight body and tail Tapered head	308 µm (295-325 µm)

Heart Murmurs: Congenital Heart Defect-Associated

Modified with permission from Kittleson M: Small animal cardiovascular medicine, St Louis, 1998, Mosby, p 197.

PDA, Patent ductus arteriosus; *VSD,* ventricular septal defect.

Auscultatory Abnormalities in Dogs With Congenital Cardiac Disease

Abnormality	Timing of Murmur	Quality of Murmur	Point of Maximal Intensity	Comments
Aortic regurgitation	Diastolic	Decrescendo; usually soft	Left base	May occur in association with a VSD
Atrial septal defect	Systolic	Soft	Left base	Result of relative pulmonic stenosis
Eisenmenger's syndrome (right-to-left shunting PDA or VSD)	Absent (a systolic murmur may still be present in a PDA with bidirectional shunting)	—	Left axillary region for a bidirectional PDA	Split second heart sound may be present
Mitral dysplasia	Systolic	Holosystolic or pansystolic; plateau	Left apex	May radiate widely
Left-to-right shunting PDA	Continuous	Wind tunnel	Cranial to the left base	Peaks in intensity at S2
Pulmonic stenosis	Systolic	Crescendo-decrescendo	Left base	Possible ejection sound
Subaortic stenosis	Systolic	Crescendo-decrescendo	Left-base (occasionally right base and occasionally apex)	May radiate up into carotid arteries
Tetralogy of Fallot	Systolic	Crescendo-decrescendo	Left base	Murmur may rarely be absent
Tricuspid dysplasia	Systolic	Holosystolic or pansystolic; plateau	Right apex	May be soft or absent in cats with severe disease
VSD	Systolic	Holosystolic or pansystolic; plateau	Cranial to or at right apex; left base	Second heart sound may be split
VSD and aortic regurgitation	Systolic and diastolic (to-and- fro murmur)	Pansystolic murmur followed by a diastolic decrescendo murmur	Left base or cranial to right apex	May sound as if it is continuous and may be confused with a PDA murmur

Heart Murmurs

Characteristics and Clinical Signs Associated With "Innocent" Murmurs Versus Murmurs Associated With CHD

Modified from Bonagura J: Kirk's current veterinary therapy XIII, St Louis, 2000, Saunders.

Innocent Murmur

- Grade usually <III/VI
- Systolic
- PMI: usually left base
- Murmur characteristics may change with animal position
- Murmur intensity may increase or decrease with increasing heart rate
- Decreased intensity with age
- Generally inaudible after ~16 weeks of age
- Animal clinically normal

Congenital Heart Disease

- Any grade
- Any timing possible
- PMI: any possible
- Similar murmur characteristics in all body positions
- Murmur intensity increases with increase in heart rate
- Same or increasing intensity up to and beyond 16 weeks of age
- Persists after ~16 weeks of age
- Stunting, unthriftiness, cyanosis, or signs of heart failure may be present.

CHD, Congenital heart disease; *PMI,* point of maximal murmur intensity.

Halitosis

Causes

Oral Diseases

- Periodontal disease (gingivitis, periodontitis, abscessation)
- Neoplasia (melanoma, fibrosarcoma, SCC)
- Foreign body or trauma (fractures, electrical cord injury)
- Pharyngitis
- Stomatitis, lymphocytic-plasmacytic feline stomatitis

Respiratory Diseases

- Rhinitis and/or sinusitis
- Neoplasia
- Pneumonia or pulmonary abscess

Dermatologic Diseases

- Lip fold pyoderma
- Ulcerative mucocutaneous pyoderma
- Feline or canine eosinophilic granulomas
- Pemphigus complex, bullous pemphigoid, systemic lupus erythematosus
- Drug eruptions
- Cutaneous lymphoma
- Exposure to DMSO

Metabolic Diseases

- Renal failure/uremia
- Diabetic ketoacidosis

Gastrointestinal Diseases

- Megaesophagus
- Inflammatory bowel disease
- Exocrine pancreatic insufficiency
- Neoplasia
- Constipation

Dietary

- Aromatic foods (onions, garlic)
- Fetid foodstuffs (e.g., ingestion of carrion)
- Coprophagy

Grooming Behavior

- Anal sacculitis
- Vaginitis/balanoposthitis
- Lower UTI

Adapted from Veterinary clinical guide to odor and disease: the oral cavity and dermatology, Yardley, Penna., 1997

DMSO, Dimethyl sulfoxide; SCC, squamous cell carcinoma; *UTI,* urinary tract infection.

Iron Abnormalities

N, Normal; *TIBC,* total iron-binding capacity (equivalent to saturated transferrin concentration).*Concurrent inflammation or other disorders may raise ferritin level into normal range.

	Serum [Iron]	TIBC	Ferritin
Normal	N	N	N
Hemolytic anemia	↑	↑	↑
Anemia of chronic disease	N or ↓	N or ↓	N or ↑
Iron deficiency (= chronic blood loss)	↓	N or ↑	↓*
Inflammation	↓	↓	↑
Glucocorticoid treatment/excess	↑	N	—
Iron overload/toxicosis	↑	↓	↑
Artifact (sample contamination)	↑ (serum Fe > TIBC)	↓ or N	—

Insulin Resistance

Recognized Causes of Insulin Ineffectiveness or Insulin Resistance in Diabetic Dogs and Cats

From Feldman E, Nelson R: Canine and feline endocrinology and reproduction, ed 3, St Louis, 2004, Saunders.

Caused by Insulin Therapy

- Inactive insulin
- Diluted insulin
- Improper administration technique
- Inadequate dose
- Somogyi effect
- Inadequate frequency of insulin administration
- Impaired insulin absorption, especially Ultralente insulin
- Antiinsulin antibody excess

Caused by Concurrent Disorder

- Diabetogenic drugs
- Hyperadrenocorticism
- Diestrus (bitch)
- Acromegaly (cat)
- Infection, especially of oral cavity and urinary tract
- Hypothyroidism (dog)
- Hyperthyroidism (cat)
- Renal insufficiency
- Liver insufficiency
- Cardiac insufficiency
- Glucagonoma (dog)
- Pheochromocytoma
- Chronic inflammation, especially pancreatitis
- Pancreatic exocrine insufficiency
- Severe obesity
- Hyperlipidemia
- Neoplasia

Inflammatory Bowel Diseases

Causes of Chronic Small Bowel Inflammation

From Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

Chronic Infection

- *Giardia* sp.
- *Histoplasma* sp.
- *Toxoplasma* sp.
- *Mycobacteria* sp.
- Protothecosis
- Pythiosis
- Pathogenic bacteria (*Campylobacter, Salmonella* spp., pathogenic *Escherichia coli*)

Food Allergy

Small Bowel Inflammation Associated With Other Primary Gastrointestinal Diseases

- Lymphoma
- Lymphangiectasia

Idiopathic Causes

- Lymphocytic-plasmacytic enteritis (LPE)
- Eosinophilic gastroenterocolitis (EGE)
- Granulomatous enteritis (same as regional enteritis?)

Infertility, Male

Based on Inability to Sire a Litter

Modified from Feldman E, Nelson R: Canine and feline endocrinology and reproduction, ed 3, St Louis, 2004, Saunders.

Congenital InfertilityHormonal

- Hypopituitarism
- Hypothyroidism

Chromosomal aberration

Developmental

- Cryptorchidism
- Penis, prepuce, os penis anomaly
- Testicular hypoplasia
- Duct aplasia

Motility defect

- Kartagener's syndrome
- Retrograde ejaculation

Acquired InfertilityHormonal

- Hypopituitarism
- Hypothyroidism
- Hyperadrenocorticism

Metabolic

- Uremia
- Hepatic

Neoplasia

- Compression
- Hormonal secretion

Stress

Infection

Fever

Duct obstruction

Immune-mediated orchitis

Drugs, exogenous hormone therapy

Retrograde ejaculation

Idiopathic testicular degeneration

Sexual overuse?

Psychological?

Infertility With Preserved Libido

Drugs and Exogenous Hormones That Affect Fertility in Humans and Possibly Dogs

From Feldman E, Nelson R: Canine and feline endocrinology and reproduction, ed 3, St Louis, 2004, Saunders.

Chemotherapeutic Drugs

- Busulfan
- Chlorambucil
- Cisplatin
- Cyclophosphamide
- Methotrexate
- Vinblastine
- Vincristine

Miscellaneous Drugs

- Amphotericin B*
- Alloxan
- Cimetidine*
- Clomipramine
- Ketoconazole*
- Spironolactone
- Sulfasalazine

HormonesAnabolic Steroids

- Methyltestosterone*
- Testosterone esters*

Estrogens

- Estradiol 17B*
- Diethylstilbestrol*
- KABI 1774*

Progestogens

- Medroxyprogesterone acetate*
- Megestrol acetate*
- Delmadinone acetate*

Others

- Glucocorticoids*
- Tamoxifen citrate*
- Gossypol*
- GnRH antagonists*
- GnRH agonists*

Incontinence, Urinary

Causes

Modified from Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

- Urethral sphincter mechanism incompetence
- Ectopie ureters
- Neurologic disorders
- Urge incontinence (secondary to urinary tract infection [UTI] or uroliths)
- Idiopathic detrusor instability
- Paradoxic (overflow) incontinence
- Ureterocele
- Pelvic bladder
- Ureterovaginal or urethrorectal fistula
- Patent urachus

Incontinence, Fecal

Causes

From Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

Neurologic DiseaseSacral Spinal Cord

- Congenital vertebral malformation
- Meningomyelocele
- Sacrococcygeal hypoplasia of Manx cats
- Sacral fracture
- Sacrococcygeal subluxation
- Lumbosacral instability
- Viral meningomyelitis
- Diskospondylitis
- Degenerative myelopathy
- Neoplasia

Peripheral Neuropathy

- Trauma
- Repair of perineal hernia
- Perineal urethrostomy
- Penetrating wounds
- Dysautonomia
- Hypothyroidism
- Diabetes mellitus

Nonneurologic DiseaseColorectal Causes

- Inflammatory bowel disease
- Neoplasia
- Constipation

Anorectal Causes

- Trauma
- Surgery (anal sac, perineal hernia, rectal resection)
- Perianal fistula
- Neoplasia

Miscellaneous Causes

- Severe diarrhea
- Irritable bowel syndrome
- Decreased mentation
- Old age/cognitive disfunction

Immunodeficiency-Related Complications

Organisms and Medical Problems Commonly Implicated in Immunocompromised Hosts

Modified with permission from Greene C: Infectious diseases of the dog and cat, ed 2, St Louis, 1999, Saunders, p 684.

Opportunistic Organisms

- Viruses: feline herpesvirus, feline infectious peritonitis, feline calicivirus, canine papillomavirus, canine herpesvirus
- Rickettsia: *Haemobartonella*
- Bacteria: Citrobacter sp., *Escherichia coli, Enterobacter, Klebsiella pneumoniae, Mycobacterium* spp., *Nocardia asteroides, Proteus, Pseudomonas aeruginosa, Serratia marcescens, Staphylococcus pseudintermedius*
- Fungi: *Aspergillus* sp., *Candida* sp., *Cryptococcus, Histoplasma, Mucor*
- Protozoa: *Pneumocystis carinii, Toxoplasma gondii, Cryptosporidium*
- Metazoa: *Demodex canis, Otodectes, Notoedres, Sarcoptes scabiei*

Medical Problems

- Recurrent skin infections
- Recurrent mucosal infections
- Neonatal sepsis and mortality
- Reactive amyloidosis
- Vasculitis, arteritis, polyarthritis
- Recurrent bacteremia
- Granulomatous infections
- Chronic hypersensitivity reactions
- Autoimmune diseases
- Persistent intracellular rickettsial or bacterial infections
- Disproportional leukocytosis
- Persistent lymphopenia

Immunodeficiency Syndromes: Congenital

With permission from Greene C: Infectious diseases of the dog and cat, ed 3, St Louis, 2006, Saunders, p 1015–1016. In addition to the listed syndromes, bone marrow dyscrasia has been described in miniature and toy poodles and transient hypogammaglobulinemia in Samoyeds, but less is known of these disorders.

AD, autosomal dominant; *AR,* autosomal recessive; *GI,* gastrointestinal; *HOD,* hypertrophic osteodystrophy; *Ig,* immunoglobulin; *IL,* interleukin; *RAMP,* resistance against mycobacterial protein; *U,* unknown; *XR,* X-linked recessive; γ, suspected.*(E.g., springer spaniel, Old English sheepdog, English setter, West Highland white terriers, pointers.)

Primary or Hereditary Immunodeficiencies

Disease (Synonyms)	Inheritance	Breeds	Defect	Characterization
Dog				
Ciliary dyskinesia (immotile cilia syndrome)	AR	Many breeds*	Functional/morphologic cilia abnormalities	Rhinosinusitis, bronchopneumonia with bronchiectasis, situs inversus
Respiratory infections	U	Irish wolfhound	Unknown, IgA defect?	Rhinitis, pneumonia
Bactericidal neutrophil defect	U	Doberman pinscher	Unknown	Upper respiratory tract infections, reduced bactericidal activity, ciliary dyskinesia not excluded
Cyclic hematopoiesis (cyclic neutropenia)	AR	Gray collie	Hematopoietic growth factors	Severe neutropenia every 12-14 days, reactive amyloidosis
Leukocyte adhesion deficiency (canine granulocytopathy)	AR	Irish setter	CD11/18 deficiency, B-chain (CD18) deficiency	Severe leukocytosis, limited pus formation, lack of neutrophil adhesion
Complement component 3 (C3) deficiency	AR	Brittany spaniel	C3 deficiency	Pyogenic infections, lack of C-mediated phagocytosis in colony of dogs with neuromuscular disease
Selective cobalamin malabsorption	AR	Giant schnauzerBorder collie	Ileal cobalamin receptor defect	Weight loss, inappetence, leukopenia with hypersegmentation, megaloblastic bone marrowMethylmalonic aciduria
Increased susceptibility to avian mycobacteriosis	U	Basset hound	RAMP deficiency?	
Increased susceptibility to	XR	Dachshund	Unknown	
Pneumocystis carinii pneumonia				
Pelger-Huët anomaly	AD	Australian shepherd, foxhound, others	Unknown	No immunodeficiency, hyposegmented granulocytes
Susceptibility to fungal and rickettsial infections, pyoderma	U	German shepherd	Macrophage? T cell?	

Disease (Synonyms)	Inheritance	Breeds	Defect	Characterization
Severe combined immunodeficiency	XR	Basset hound, Cardigan, Welsh corgi	Common gamma chain of IL-2 and other cytokines	Severe bacterial/viral infections, no IgG and IgA, deficient lymphocyte blastogenesis
Selective IgA deficiency	U	Beagle, shar-pei, German shepherd	IgA deficiency	Respiratory and GI infections
Thymic abnormalities and dwarfism	U	Weimaraner	Unknown	Reduced growth (thymosin responsive)
Recurrent infections	U	Weimaraner	Reduced IgG	Pyoderma, severe abscess formation, bleeding tendency (HOD)
Combined immunodeficiency	U	Shar-pei	T cell, B cell, low IL-6 and IL-2	Skin, respiratory, and GI infections
Amyloidosis	U	Shar-pei	Elevated IL-6	Arthritis, amyloidosis, renal failure, hepatic rupture, hypoproteinemia
Lethal acrodermatitis	AR	Bull terrier	Zinc metabolism defect	Zinc deficiency, hyperkeratosis
Increased susceptibility to parvoviral infection	U	Rottweiler, Doberman	Unknown	
Vaccine-exacerbated immunity	U	Akita	Unknown	Variable meningitis, polyarthritis
Cat				
Hypotrichosis, congenital and thymic aplasia	AR	Birman	Unknown	Nude kittens, neonatal death, no thymus
Thymic and lymphoid atrophy	U	Ragdoll	Unknown	Neonatal death or fatal infections at weaning, lack of lymph nodes and thymus
Leukocyte granulation	U	Birman	Unknown	No immunodeficiency, acidophilic granules
Pelger-Huët anomaly	AD	Domestic shorthair	Unknown	No immunodeficiency, hyposegmented granulocytes
Chédiak-Higashi syndrome	AR	Persian	Unknown	No immunodeficiency, large granules in phagocytes, bleeding tendency
Reactive AA amyloidosis	U	Abyssinian, Siamese, Oriental shorthair	Unknown	Reactive AA amyloidosis, renal or hepatic failure

Immunodeficiency Syndromes: Acquired

Common Acquired Causes of Compromised Immune System Function

From Bonagura J: Kirk's current veterinary therapy XIII, St Louis, 2000, Saunders.

Drugs

- Antineoplastics
- Corticosteroids
- Other immunosuppressive agents (e.g., azathioprine, gold salts)

Malnutrition

- Intestinal parasitism
- Inflammatory bowel disease
- Protein-calorie deficiency
- Obesity

Infections

- Viral infection (FeLV, FIV, FIP, CDV, parvovirus)
- *Ehrlichia canis*

Endocrine Disease

- Hyperadrenocorticism
- Diabetes mellitus

Neoplasia

Miscellaneous

- Neonatal colostrum deprivation

CDV, Canine distemper virus; *FeLV,* feline leukemia virus; *FIP,* feline infectious peritonitis; *FIV,* feline immunodeficiency virus.

Ileus

Causes

From Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

Physical

- Intestinal obstruction
- Overdistention by aerophagia

Neuromuscular

- Anticholinergic drugs
- Dysautonomia
- Spinal cord injury
- Visceral myopathies

Metabolic

- Hypokalemia
- Uremia
- Endotoxemia

Functional

- Abdominal surgery
- Ischemia
- Inflammatory causes
- Peritonitis
- Pancreatitis
- Parvovirus

Icterus

Modified from Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 4, St Louis, 1994, Saunders.

DIC, Disseminated intravascular coagulation; *FeLV,* feline leukemia virus; *FIP,* feline infectious peritonitis; *ICH,* infectious canine hepatitis; *SLE,* systemic lupus erythematosus.

Differential Diagnosis of Icterus

Prehepatic or Hemolytic Icterus	**Extrahepatic Icterus**	**Hepatic Icterus**	
Hemolytic Anemias	**Bile Duct Occlusion**	**Miscellaneous Disorders**	Hemolytic disease → cholestasis
Erythrocyte parasitemia:	Cholecystitis	Endotoxemia/sepsis	
Babesia	Cholangitis	Shock	Anoxia → cholestasis
Mycoplasma haemofelis	Secondary peribiliary disease	Chronic passive congestion	DIC
Incompatible blood transfusion	Congenital malformations	Hyperthyroidism (cat, rare)	
Neonatal isoerythrolysis	Choledochal cysts		
Microangiopathic hemolytic anemia	Multiple biliary cysts (cat)	**Intrahepatic Cholestasis**	
DIC	Intraluminal bile duct occlusion	Infectious	
Vasculitis	Inspissated bile syndrome (cat)	Neoplasia:	
Dirofilariasis	Cholelithiasis	Mechanical infiltrative-sinusoids, peribiliary	
Vascular neoplasia (hemangiosarcoma)	Trauma → blood clots		
Congenital erythrocyte defects	Neoplasia:	Paraneoplastic effects	
Pyruvate kinase deficiency (basenji dog)	Primary and secondary biliary involvement	Viral (FIP, ICH, parvovirus)	
Phosphofructokinase deficiency		Bacterial (leptospirosis, septicemia)	
Hereditary stomatocytosis (malamute)	Pancreatic disease	Mycotic	
Immune-mediated hemolytic anemia	Parasitic infection (flukes)	Drug associated:	Diltiazem (sustained-release formulation)
SLE	Ruptured biliary tract (bile duct or gallbladder)	Methyltestosterone	
Infectious disease associated		Impeded androgens (danazol)	Carprofen
Idiopathic	Trauma	Sulfa antibiotics	Mebendazole
Drug associated	Cholelithiasis	Anticonvulsants (phenytoin, primidone, phenobarbital)	Thiacetarsemide
Infectious:	Cholangitis/cholecystitis		
FeLV	Iatrogenic: hepatic biopsy	Acetaminophen	

Prehepatic or Hemolytic Icterus	**Extrahepatic Icterus**	**Hepatic Icterus**	
Ehrlichia		Specific hepatic disorders:	
Dirofilariasis		Cholangitis	Cholangiohepatitis syndrome (cat)
Leptospirosis		Cirrhosis	
Septicemia		Chronic idiopathic hepatitis of dogs	Lobular dissecting hepatitis
Heinz body anemia			
Onion toxicity, zinc toxicity		Hepatic lipidosis (cat)	Breed-specific disorder:
Benzocaine (cat), methionine		Idiopathic lipidosis secondary to other disorders	Bedlington terrier
Cetacaine (cat), methylene blue			
Vitamin K1, acetaminophen		Diabetes mellitus	Doberman pinscher
Phenazopyridine		Hepatic necrosis: many causes	West Highland white terriers
Propylene glycol		Infiltrative disease (neoplasia, amyloid, infectious agents)	
Increased Hemoprotein Liberation			Cocker spaniels
Body cavity hemorrhage			Severe steroid hepatopathy (dogs only)
Large hematoma formation and absorption			
Ineffective erythropoiesis			
Congenital porphyria (cat, rare)			

Joint Effusion

From Willard M, Tvedten H: Small animal clinical diagnosis by laboratory methods, ed 4, St Louis, 2004, Saunders. *LE,* Lupus erythematosus; *RBC,* red blood cell; *WBC,* white blood cell.

Analysis of Joint Effusions

	NONINFLAMMATORY JOINT DISEASE	**INFLAMMATORY JOINT DISEASE**				
	Degenerative Joint Disease	**Neoplastic Joint Involvement**	**Hemarthrosis**	**Infectious Inflammation**	**Noninfectious Inflammation**	**NORMAL**
Color	Light yellow	Light yellow, blood-tinged	Bloody, xanthochromic	Variable: yellow, blood-tinged, bloody	Variable: yellow, blood-tinged	Straw-colored
Turbidity	Clear, slightly turbid	Mild to moderate turbidity	Turbid	Turbid to purulent	Variable: slight to moderate turbidity	Clear
Viscosity	Normal	Normal to reduced	Reduced	Reduced	Reduced	Viscous
Mucin clot test	Normal firm	Normal firm	Normal to slightly friable	Friable	Friable	Firm
Cytologic Analysis						
RBC	Few	Few to many	Many, erythrophagocytosis	Moderate	Few to moderate	Rare
WBC/µL	<3000	Variable	Variable	40,000-250,000	Many but variable	0-2900
Neutrophils	Few (<20%)	Moderate	Moderate	Many (usually >90%)	Many but variable	0%-10%
Degenerative WBC changes	Absent	Absent	Absent	May be present	None to mild	None
Lymphocytes	Few to moderate	Few to moderate	Rare	Few	Few to moderate	Few
Synoviocytes	Common	Few	Rare	Few to moderate	Few to moderate	Few
Macrophages	Few to moderate	Few to moderate	Moderate if chronic	Few to moderate	Few to moderate	Rare
Microorganisms	None	None	None	May be present	None	None
Neoplastic cells	None	Variable	None	None	None	None
Others					May see LE cells	

Ketonuria

Causes

- Diabetes mellitus/diabetic ketoacidosis
- Starvation
- Lactation
- Pregnancy
- Fever
- Renal glucosuria
- Severely carbohydrate-restricted diet
- Glycogen storage disease

Keratoconjunctivitis Sicca (KCS)

Causes

Modified with permission from Bonagura J: Kirk's current veterinary therapy XII: small animal practice, Philadelphia, 1995 WB Saunders, p 1232.

- Imune-mediated adenitis: most common (dogs)
- Breed predisposition
- Congenital anomaly
- Drug induced (transient KCS): general anesthesia, topical anesthesia, atropine
- Drug toxicosis (transient or permanent KCS): sulfa drugs, phenazopyridine, aminosalicylic acid, etodolac
- Iatrogenic:
    - Removal of the gland of the third eyelid
- Idiopathic
- Infectious agents:
    - Canine distemper virus
    - Feline herpesvirus
- Metabolic disease (hypothyroidism, hyperadrenocorticism, diabetes mellitus)
- Chronic blepharoconjunctivitis (chemosis/ascending infection from lacrimal gland, causing lacrimal ductile obstruction)
- Neurogenic
- Radiation therapy for nasal or intracranial neoplasms
- Trauma to orbit or eye

Lymphoma Staging Classification

The World Health Organization (WHO) Clinical Staging System for Lymphoma

Modified from Slatter D: Textbook of small animal surgery, ed 3, Philadelphia, 2003, Saunders.

- Stage I Single lymph node involved
- Stage II Multiple lymph nodes involved on one side of the diaphragm
- Stage III Generalized peripheral lymph node involvement
- Stage IV Liver and/or splenic involvement with or without stages I-III
- Stage V Blood and/or bone marrow involvement and/or extranodal involvement; with or without stages I-IV
- Substage A: no signs of systemic illness
- Substage B: signs of systemic illness, hypercalcemia, uveitis, fever
- Substage E: designation used for extranodal tumors

Lymphoma and Lymphoid Neoplasia

Modified from Slatter D: Textbook of small animal surgery, ed 3, Philadelphia, 2003, Saunders. *FeLV,* Feline leukemia virus; *FIV,* feline immunodeficiency virus; *GI,* gastrointestinal.

Anatomical Classification of Lymphoid Neoplasms

Name	Incidence in Dogs	Incidence in Cats (FeLV status)	Selected Clinicopathologic Characteristics
Lymphoma			
Multicentric	80%-85%	20%-40% (commonly FeLV+)	In cats, spleen and liver are virtually always affected; feline lymphoid hyperplasia is a common cause of generalized lymphadenopathy; in dogs, diffuse pulmonary infiltrates are in 25%-35% of cases.
Alimentary	<7%	15%-45% (uncommonly FeLV+)	Regional lymph nodes are commonly affected; late-stage disease affects kidneys; in some cats, the condition may be associated with FIV.
Mediastinal (thymic)	<5%	20%-50% (commonly FeLV+)	Sternal lymph nodes are affected in dogs, and nodes and thymus are affected in cats; pleural effusion and hypercalcemia are common (40%).
Extranodal sites	7%	5%-10%	B-cell tumors are termed *cutaneous lymphoma*; T-cell tumors are termed *mycosis fungoides*.
Nervous system		(commonly FeLV+)	This is the most common cause of posterior paresis in cats; the bone marrow is often affected; in dogs, the condition usually reflects late-stage multicentric disease. Late-stage disease affects CNS; patients are often presented in renal failure.
Renal			
Plasma Cell Tumors			
Multiple myeloma	Uncommon	Rare (no association with FeLV)	75% of dogs have immunoglobulin or monoclonal gammopathy, and 10% have circulating plasmacytes; immunoglobulin M-producing tumor termed *macroglobulinemia* (Waldenstrom's).
Cutaneous	Infrequent	Extremely rare	Rarely metastasize (<5%)
GI	Infrequent	Unreported	Uncommonly metastasize
Osseous	Rare	Unreported	Often progress to systemic myeloma within 6 months

Lymphatic Drainage

From Slatter D: Textbook of small animal surgery, ed 3, Philadelphia, 2003, Saunders.

Normally Palpable Lymph Nodes and Body Regions That Nodes Drain

Lymph Node	Area Drained
Mandibular	All parts of the head not drained by parotid node (parotid node drains cutaneous area of caudal half of dorsum of muzzle and lateral cranium, parotid gland, and muscles of mastication)
Superficial cervical (prescapular)	Skin on caudal part of head, including pharynx, part of pinna, lateral surface of neck and thoracic limb except shoulder, and medial side of brachium and antebrachium
Axillary and accessory axillary	Mammary glands, thoracic wall, and deep structures of thoracic limb
Superficial inguinal	Ventral half of abdominal wall, including abdominal and inguinal mammary glands as well as efferent vessels from popliteal lymph nodes, penis, prepuce, and scrotum in the male
Popliteal	All parts of pelvic limb distal to node

Lymphatic Disorders

Causes

From Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

Lymphangitis, Lymphedema, Lymphadenitis, Lymphadenopathy

- Infection
- Neoplasia
- Reactive hyperplasia
- Granuloma

LymphedemaPrimary Developmental Abnormality of Lymphatics

- Hypoplasia
- Aplasia
- Lymphangiectasia
- Hyperplasia

Secondary Acquired Abnormality of Lymphatics

- Surgical excision of lymphatics or lymph nodes
- Posttraumatic lymphangiopathy
- Neoplastic invasion
- Extrinsic compression of lymph vessels or tissue
- Acute obstructive lymphadenitis
- Chronic sclerosing lymphadenitis/lymphangitis
- Lymphatic atrophy with interstitial fibrosis
- Radiation therapy

Lymphocysts

- Cystic hygroma, lymphoceles, pseudocyst

Lymphangiomas

Liver Enzyme Elevations

Conditions That Cause Liver Enzyme Elevations in the Absence of Primary Liver Disease

ALP, Alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transpeptidase.

Modified from Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 5, St Louis, 2000, Saunders.

Drug Induction

Corticosteroids (dogs):↑↑↑ALP,↑↑GGT,↑ALT,↑AST

Anticonvulsants (phenobarbital, phenytoin, primidone):↑ALT,↑ALP,↑AST,↑GGT

Endocrinopathies

Hyperthyroidism (cats):↑ALP,↑ALT

Hypothyroidism (dogs):↑ALP

Diabetes mellitus:↑ALP

Hyperadrenocorticism (dogs):↑↑↑ALP,↑ALT,↑GGT,↑AST

Hypoxemia/Hypotension: ↑↑↑ ALT, ↑ ALP, ↑ GGT, ↑ AST

Congestive heart failure

Severe acute blood loss

Status epilepticus

Hypotensive crisis

Surgery

Septic shock

Hypoadrenocorticism

Hypovolemic shock

Muscle Injury: ↑ AST

Acute muscle necrosis/trauma

Malignant hyperthermia

Myopathies

Neoplasia

Adenocarcinomas: pancreatic, intestinal, adrenocortical, mammary

Sarcomas: hemangiosarcoma, leiomyosarcoma

Hepatic metastasis: ↑ AST,↑ALT,↑ ALP

Unique enzyme induction: ↑↑ ALP, ↑↑ GGT

Miscellaneous

Systemic infections

Pregnancy (cats): ↑ placental ALP

Colostrum-fed neonates (dogs): ↑ GGT

Bone Disorders: ↑ ALP

Young animals (up to 7 months)

Osteosarcoma

Osteomyelitis

Laryngeal Neoplasia

Malignant Tumors of the Canine and Feline Larynx

Modified from Bonagura J: Kirk's current veterinary therapy XIII, St Louis, 2000, Saunders.

- Lymphoma
- Squamous cell carcinoma
- Mast cell tumor
- Osteosarcoma
- Melanoma
- Oncocytoma
- Rhabdomyosarcoma
- Plasmacytoma
- Adenocarcinoma
- Chondrosarcoma
- Granular cell myoblastoma
- Fibrosarcoma
- Anaplastic carcinoma
- Leiomyoma

Lactate: Elevated Serum Levels

Major Causes

From Bonagura J: Kirk's current veterinary therapy XIII, St Louis, 2000, Saunders.

Type A: Clinical Evidence of Absolute or Relative Tissue HypoxiaShock (Systemic Hypoperfusion)

- Hypovolemic
- Cardiogenic
- Septic

Local Hypoperfusion

- Gastric necrosis and other causes of splanchnic ischemia
- Aortic thromboembolism

Severe Hypoxemia (Pao2 < 30-40 mm Hg)

- Severe anemia (packed cell volume < 15%)
- Carbon monoxide toxicity
- Excessive muscular activity:
  - Exercise
  - Trembling
  - Seizures

Type B: No Clinical Evidence of Tissue HypoxiaType B1 (In Association With Underlying Disease)

- Diabetes mellitus
- Severe liver disease
- Malignancy
- Sepsis
- Pheochromocytoma
- Thiamine deficiency

Type B2 (Due to Drugs and Toxins)

- Acetaminophen
- Cyanide
- Epinephrine
- Ethanol
- Ethylene glycol
- Insulin
- Methanol
- Morphine
- Nitroprusside
- Propylene glycol
- Salicylates
- Terbutaline

Type B3 (Due to Inborn Metabolic Defects)

- Mitochondrial myopathy

Miscellaneous

- Alkalosis: hyperventilation
- Hypoglycemia

Lacrimation/Epiphora, Chronic

CAT

- Chronic conjunctivitis due to feline herpesvirus
- Lacrimal punctal atresia
- Feline corneal sequestration
- Entropion
- Painful corneal lesion (e.g., corneal ulcer)
- Punctal scarring after conjunctivitis
- Dacryocystitis
- Feline proliferative (eosinophilic) keratoconjunctivitis

DOG

- Entropion
- Painful corneal lesion (e.g., corneal ulcer)
- Dacryocystitis
- Lacrimal punctal atresia
- Distichiasis
- Ectopic cilia
- Tear-staining syndrome (e.g., medioventral entropion and caruncular trichiaisis in brachycephalic breeds of dogs)
- Allergic inhalant dermatitis (atopy)
- Uveitis
- Chronic conjunctivitis as a result of concurrent tear film deficiency (e.g., KCS; mucin and/or lipid deficiency), ectropion or allergic inhalant dermatitis (atopy)

Modified from Slatter D: Fundamentals of veterinary ophthalmology, St Louis, 2001, Saunders.

Myositis

Microorganisms Associated With Musculoskeletal Infections

Modified with permission from Greene C: Infectious diseases of the dog and cat, ed 2, St Louis, 1999, Saunders, p 555; and Morgan R: Handbook of small animal practice, ed 5, St Louis, 2008, Saunders, p 800.

Causes of Myositis Infection

- *Hepatozoon*
- *Toxoplasma gondii*
- *Neospora caninum*
- *Leptospira*
- *Borrelia*
- Numerous bacteria (e.g., *Staphylococci* [dogs], *Pasteurella multocida* [cats])
- Toxigenic *Streptococcus canis*

Myopathies

Classification

From Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders; and Shelton D: What's new in muscle and peripheral nerve disease. Vet Comp Orthop Traumatol 20:249-255, 2007.

Inflammatory

- Infectious
  - Bacterial: leptospirosis
  - Protozoal: toxoplasmosis/neosporosis
  - Parasitic: *Toxocara*, others
- Immune-mediated
  - Masticatory myositis
  - Polymyositis
  - Dermatomyositis
- Degenerative
  - Acquired
    - Endocrine:
      - Hyperadrenocorticism
      - Hypothyroidism
      - Hypokalemic polymyopathy (cats)
    - Fibrotic/ossifying myopathies
    - Ischemic
    - Nutritional
    - Neoplastic
    - Toxic
  - Inherited
    - Muscular dystrophy:
      - Exercise-induced collapse in Labrador retrievers
      - X-linked muscular dystrophy (dystrophin deficient)
      - Other muscular dystrophies (dystrophin positive)
    - Myotonia
    - Metabolic:
      - Pyruvate dehydrogenase phosphatase 1 deficiency in Clumber and Sussex spaniels
      - Glycogen storage disease
        - Mitochondrial myopathy
        - Lipidic myopathy
        - Malignant hyperthermia
    - Centronuclear myopathy (Labrador retriever)
    - Hypertonicity in Cavalier King Charles spaniels
    - Inherited myopathy of Great Danes

Myopathies, Feline Congenital

From Gaschen F, Jaggy A, Jones B: Congenital diseases of feline muscle and neuromuscular junction. J Feline Med Surg 6:355–366, 2004.

ACH, Acetylcholine; *AUS,* Australia; *CH,* Switzerland; *DSH,* domestic shorthair; *GB,* Great Britain; *GBE,* glycogen branching enzyme; *MG,* myasthenia gravis; *NL,* Netherlands; *NZ,* New Zealand; *US,* United States.

Characteristics

Disease	Affected Breeds and Geographical Provenance	Mode of Inheritance	Underlying Defect	Clinical Signs	Prognosis
Congenital myotonia	DSH (NZ, US)	Autosomal recessive	Probable defect in chloride channels	Stiff gait, hyperactivity of selected muscle groups when startled, percussion dimple	Fair to good (nonprogressive condition, cats enjoy a normal quality of life)
Devon rex myopathy	Devon rex (AUS, GB)	Autosomal recessive	Unknown	Cervical ventroflexion; generalized muscle weakness; abnormal gait; megaesophagus	Poor (many cats die of asphyxiation)
Dystrophin-deficient myopathy	DSH (US, NL, CH)	X-linked recessive	Dystrophin deficiency	Skeletal muscle hypertrophy with possible complications, sensitivity to stress, stiff gait	Guarded to fair (cats can have an almost normal quality of life but may require more frequent veterinary visits)
Glycogen storage disease type IV	Norwegian forest cats (US, Europe)	Autosomal recessive	GBE deficiency	Stillbirth, muscle tremor, muscle atrophy; cardiomyopathy	Poor (all cats eventually die from the condition)
Hypokalemic myopathy	Burmese (AUS, NZ, GB, NL)	Probably autosomal recessive	Unknown	Transient, paroxysmal clinical signs with generalized muscle weakness, cervical ventroflexion	Good response to potassium supplementation
Malignant hyperthermia	DSH	Unknown	Unknown	Severe hyperthermia during anesthesia (halothane)	Poor (two reported cases in which cats died)
Merosin-deficient myopathy	DSH, Siamese (US)	Unknown	Merosin (laminin-2) deficiency	Hind limb weakness from 6 months old, worsening to muscle atrophy and contractures at 1 year old	Poor (both cats in the two reported cases were euthanized before 2 years of age)
MG	DSH	Unknown	Lack of ACH receptors	Generalized muscle weakness	Fair, generally good response to therapy
Nemaline myopathy	DSH (US)	Possibly autosomal recessive	Unknown	Progressive weakness (6–18 months); rapid, choppy, hypermetric gait; tremor, exercise intolerance	Poor (five reported cats died or were euthanized)

Myocarditis

Causes

Modified with permission from Greene C: Infectious disease of the dog and cat, ed 2, St Louis, 1999, Saunders, p 580.

Viral

- Canine distemper virus (neonate)
- Canine parvovirus (prenatal, neonate)

Rickettsial

- *Rickettsia rickettsii*

Bacterial

- Numerous genera
- *Borrelia burgdorferi*

Algal

- *Prototheca* spp.

Fungal

- *Cryptococcus neoformans*
- *Coccidioides immitis*
- *Aspergillus terreus*
- *Paecilomyces variotii*

Protozoal

- *Trypanosoma cruzi*
- *Toxoplasma gondii*
- *Hepatozoon canis*
- *Neospora caninum*

Traumatic

- Automobile trauma
- Injury from falling
- Penetrating trauma
- Cardiac catheterization

Immune-Mediated Conditions

- Rarely reported in veterinary medicine

Unknown

- Transmissible myocarditis-diaphragmitis of cats

Myocardial Diseases, Feline

Causes

From Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 5, St Louis, 2000, Saunders.

Idiopathic

- Hypertrophic cardiomyopathy
- Restrictive cardiomyopathy
- Dilated cardiomyopathy
- Arrhythmogenic right ventricular cardiomyopathy

Secondary (Including Specific Cardiomyopathies)

- Inflammatory
  - Viral (panleukopenia?)
  - Bacterial
  - Protozoal
  - Fungal
  - Algal
  - Parasitic
- Metabolic
  - Nutritional:
    - Taurine deficiency
  - Endocrine:
    - Thyrotoxicosis
    - Acromegaly
    - Diabetes mellitus
  - Toxic:
    - Anthracyclines (doxorubicin)
- Vascular
  - Systemic hypertension
- Infiltrative
  - Neoplastic
  - Glycogen storage disorders
  - Mucopolysaccharidosis
- Fibroplastic
  - Endomyocardial fibrosis
  - Endocardial fibroelastosis
- Genetic
  - Hypertrophic cardiomyopathy
- Physical Agents
  - Heatstroke
- Unclassified Cardiomyopathies
  - Idiopathic unclassified cardiomyopathy
  - Persistent atrial standstill
- Miscellaneous
  - Ischemia
  - Excessive left ventricular moderator bands

Monoclonal Gammopathy

Associated Conditions

With permission from Bonagura J: Kirk's current veterinary therapy XII: small animal practice, St Louis, 1995, Saunders, p 525.

- Multiple myeloma
- Waldenstrom's macroglobulinemia
- Plasma cell leukemia
- Nonsecretory myeloma
- Extramedullary plasmacytoma
- Monoclonal gammopathy of undetermined significance
- Chronic lymphocytic leukemia
- Lymphoma
- Feline infectious peritonitis
- Ehrlichiosis
- Amyloidosis
- Lymphocytic enteritis

Melena

Causes

Modified from Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

Ingested Blood

- Oral lesions
- Nasopharyngeal lesions
- Pulmonary lesions
- Diet

Parasitism

- Hookworms

Neoplasia

- Adenocarcinoma
- Lymphoma
- Leiomyoma or leiomyosarcoma
- Mast cell tumor
- Gastrinoma

Coagulopathies

- DIC
- Rodenticide intoxication

Drug Administration

- NSAIDs
- Glucocorticoids

Miscellaneous

- Liver failure
- Pancreatitis
- Renal failure
- Inflammation (e.g., foreign body, acute gastritis, hemorrhagic gastroenteritis, inflammatory bowel disease)
- Hypoadrenocorticism
- GI ischemia (e.g., shock, volvulus, intussusception)
- Foreign bodies
- GI blood vessel malformations (e.g., arteriovenous fistula)
- Polyps

DIC, Disseminated intravascular coagulation; *GI*, gastrointestinal; *NSAIDs*, nonsteroidal antiinflammatory drugs.

Note: Melena occurs as a result of oxidization of heme in blood in the GI tract, a time-dependent process. Since transit time is longer from the small intestine than from the large intestine, melena is considered a sign of small-intestinal disease. However, melena may occur with large-intestinal bleeding if there is a delay or stoppage of colonic motility, allowing heme oxidation.

Megaesophagus

Associated Diseases and Causes in Dogs

Modified from Bonagura J: Kirk's current veterinary therapy XIII, St Louis, 2000, Saunders., γ, Cause-and-effect relationship not established.

Central Nervous System

- Canine distemper
- Cervical spondylomyelopathy with leukomalacia
- Brainstem lesions
- Neoplasia
- Trauma

Peripheral Neuropathies

- Polyneuritis
- Polyradiculoneuritis
- Ganglioradiculitis
- Dysautonomia
- Giant cell axonal neuropathy
- Spinal muscular atrophy
- Intoxication:
  - Lead
  - Thallium
  - Acrylamide
- Bilateral vagal damage

Neuromuscular Junction

- Myasthenia gravis
- Botulism
- Tetanus
- Anticholinesterase toxicity

Esophageal Musculature

- Esophagitis
- Systemic lupus erythematosus
- Glycogen storage disease
- Polymyositis
- Dermatomyositis
- Cachexia
- Trypanosomiasis
- Hypoadrenocorticism
- Hypothyroidism?

Miscellaneous

- Pyloric stenosis
- Gastric dilatation/volvulus
- Pituitary dwarfism
- Thymoma
- Mediastinitis

Mediastinal Enlargement

From Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

Differential Diagnoses for Lesions Associated With Focal Mediastinal Enlargement

Region	Diseases
Cranioventral	Lymphadenopathy; abscess; thymic mass; ectopic thyroid; hematoma; granuloma; obesity; vascular mass (aorta, cranial vena cava); esophageal mass, foreign body, or dilatation; tracheal mass
Craniodorsal	Esophageal mass, foreign body, or dilatation; heart base mass; neurogenic tumor; paraspinal or spinal mass; hematoma; lymphadenopathy; aortic stenosis; patent ductus arteriosus; abscess; tracheal mass
Perihilar	Lymphadenopathy; left atrial enlargement; esophageal mass, foreign body, or dilatation; main pulmonary artery mass (poststenotic dilatation); heart base or right atrial mass; spinal or paraspinal mass
Caudodorsal	Esophageal mass, foreign body, or dilatation; hiatal hernia; diaphragmatic hernia or mass; spirocercosis; spinal or paraspinal mass; aortic aneurysm; gastroesophageal intussusception
Caudoventral	Diaphragmatic hernia; peritoneopericardial diaphragmatic hernia; abscess; granuloma; hematoma

Neutrophil Dysfunction

Modified from Bonagura J: Kirk's current veterinary therapy XIII, St Louis, 2000, Saunders.

FeLV, Feline leukemia virus; FIP, feline infectious peritonitis.*Neutrophil chemotaxis was tested in only one of four English-American (Walker) foxhounds with Pelger-Huët anomaly; defective chemotaxis has not been found in other dogs, including foxhounds, with the anomaly.

Causes of Congenital and Acquired Neutrophil Dysfunction

Dysfunction	Species
Chemotactic Factor Generation	
Congenital	
C3 deficiency (Brittany spaniel)	Dog
Adherence	
Congenital	
CD11–CD18 adhesion protein deficiency (Irish setter)	Dog
Acquired	
Diabetes mellitus (poorly regulated)	Dog
Chemotaxis	
Congenital	
C3 deficiency (Brittany spaniel)	Dog
CD11–CD18 adhesion protein deficiency (Irish setter)	Dog
Chédiak-Higashi syndrome (Persian)	Cat
Pelger-Huët anomaly? (foxhound)	Dog*
Primary ciliary dyskinesia (pointer)	Dog
Recurrent infections (weimaraner)	Dog
Acquired	
Bacterial pyoderma	Dog
Demodicosis (serum inhibitor?)	Dog
FeLV infection	Cat
FIP	Cat
Hyperalimentation-induced hypophosphatemia	Dog
Protothecosis (serum inhibitor?)	Dog
Phagocytosis	
Congenital	
C3 deficiency (Brittany spaniel)	Dog
CD11–CD18 adhesion protein deficiency (Irish setter)	Dog
Recurrent and persistent infections (weimaraner)	Dog
Acquired	

Dysfunction	Species
Continuous-flow centrifugation and filtration-leukapheresis	
Collected neutrophils (few hours after pheresis)	Dog
Hyperalimentation-induced hypophosphatemia	Dog
Bacterial Killing	
Congenital	
CD11–CD18 adhesion protein deficiency (Irish setter)	Dog
Cyclic neutropenia (Gray collies)	Dog
Recurrent and persistent infections (weimaraner)	Dog
Rhinitis-pneumonia syndrome (Doberman pinscher)	Dog
Acquired	
FeLV infection	Cat
Hyperalimentation-induced hypophosphatemia	Dog
Lead toxicosis	Dog
Turpentine-induced inflammation	Dog

Neutropenia

Courtesy M.D. Willard from Willard M, Tvedten H: Small animal clinical diagnosis by laboratory methods, ed 4, St Louis, 2004, Saunders.

FeLV, Feline leukemia virus; *FIV,* feline immunodeficiency virus.*Incomplete list of other drugs is in text.

Consumption of Neutrophils	**Affected Animals**
Overwhelming sepsis/endotoxemia (important)	Dogs/Cats
Parvovirus enteritis (important)	Dogs/Cats
Salmonellosis	Dogs/Cats
Immune-mediated destruction (rare)	Dogs
Bone Marrow Suppression	**Affected Animals**
FeLV (important)	Cats
FIV	Cats
Parvovirus (important)	Dogs/Cats
Ehrlichiosis	Dogs
Bone marrow toxicosis	Dogs/Cats
Estrogen (endogenous/exogenous)	Dogs
Phenylbutazone*	Dogs/Cats
Cancer chemotherapy	Dogs/Cats
Irradiation	Dogs/Cats
Leukemia (important)	Dogs/Cats
Myelophthisis/myelonecrosis	Dogs/Cats
Immune-mediated destruction of neutrophil precursors (rare)	Dogs/Cats

Neuromuscular Diseases

From de Lahunta A: Veterinary neuroanatomy and clinical neurology, St Louis, 1983, Saunders.

Diseases of the Lower Motor NeuronNeuromuscular Junction

- Botulism
- Tick paralysis
- Myasthenia gravis
- Organophosphate intoxication

Peripheral Nerve

- Trauma
- Neoplasia
- Ischemia—caudal aortic thrombosis-embolism

Spinal Roots and Nerves

- Trauma—root avulsion
- Lumbosacral stenosis—cauda equina syndrome
- Neoplasia—neurofibroma
- Inflammation

Spinal Roots and/or Nerves and Peripheral Nerves

- Inflammation:
  - Acute polyneuritis/polyneuropathy:
    - Dog: idiopathic polyradiculoneuritis/coonhound paralysis
    - Acute idiopathic polyneuropathy
    - Postrabies vaccination
    - Distal denervating disease
    - Brachial plexus neuritis
  - Chronic polyneuritis/polyneuropathy:
    - Dog: chronic polyneuritis
    - Inherited hypertrophic neuropathy
    - Giant axonal neuropathy
    - Distal symmetric polyneuropathy
    - Metabolic neuropathy

Spinal Cord

- Focal myelopathy from compression
- Acute ischemic myelopathy: fibrocartilaginous emboli
- Diffuse myelomalacia
- Inflammations: viral, protozoal
- Hereditary neuronal abiotrophy in Swedish Lapland dogs
- Hereditary spinal muscular atrophy in Brittany spaniels
- Stockard's paralysis

Muscle Disease

- Myositis:
  - Infectious
  - Idiopathic—immune mediated:
    - Masticatory
    - Polymyositis
- Myotonia:
  - Hereditary myopathic myotonia of young animals
  - Acquired myopathic myotonia of old dogs

- Other myopathies

Neurologic Signs and Underlying Causes

From de Lahunta A: Veterinary neuroanatomy and clinical neurology, St Louis, 1983, Saunders.

CN, Cranial nerve; *CNS,* central nervous system; *LMN,* lower motor neuron; *UMN,* upper motor neuron; γ, may occur with lesion in this location.

Relationship of Clinical Signs to Anatomic Site of Lesion

Clinical Signs	Functional System	Anatomic Location
Inability to prehend	Masticatory and tongue muscles	CN V, XII, pons-medulla
Dysphagia	Tongue, palatal, pharyngeal, and esophageal muscles	CN IX, X, XI, XII, medulla
Drooling	Facial paralysis, dysphagia	• CN VII, middle ear, medulla • CN IX, X, medulla
Head tilt, nystagmus, loss of balance, rolling	Vestibular system	CN VIII: inner ear, medulla, cerebellum
Strabismus	CN to extraocular muscles, vestibular system	• CN III, IV, VI, midbrain-medulla • Inner ear-medulla-cerebellum
Circling		
With loss of balance	Vestibular system	Inner ear, medulla, cerebellum
Without loss of balance	Limbic system (?)	Frontal lobe, rostral thalamus
Head and eye deviation-turning to one side	Limbic system (?)	Frontal lobe, rostral thalamus
Pacing, head pressing	Limbic system	Frontal lobe, rostral thalamus
Opisthotonos	Upper motor neuron	Rostral cerebellum, midbrain
Blindness	Visual system	
	Dilated unresponsive pupils	Eyeball, optic nerves
	Normal pupils	Visual cortex-cerebrum, (midbrain)
Depression, semicoma, coma	Ascending reticular activating system	Pons to thalamus-cerebral cortex
Seizures	Cerebrum, thalamus-hypothalamus	
Hyperesthesia, hyperactivity to external stimuli	Ascending reticular activating system	Thalamus, cerebrum
Aggressive behavior, mania-hysteria, odontoprisis	Limbic system	Thalamus, cerebrum
Tremor		
Associated with movements, head, and neck	Cerebellar system	Cerebellum
Associated with movements, head, trunk, limbs	Multiple systems	Diffuse CNS

Clinical Signs	Functional System	Anatomic Location
Episodic, not associated with movements, head, trunk, limbs		Thalamus, cerebrum
Bradycardia, hypothermia, hyperthermia	UMN for general visceral efferent system	Hypothalamus
Irregular-ataxic respirations	UMN for respiratory muscle LMN	Pons-medulla

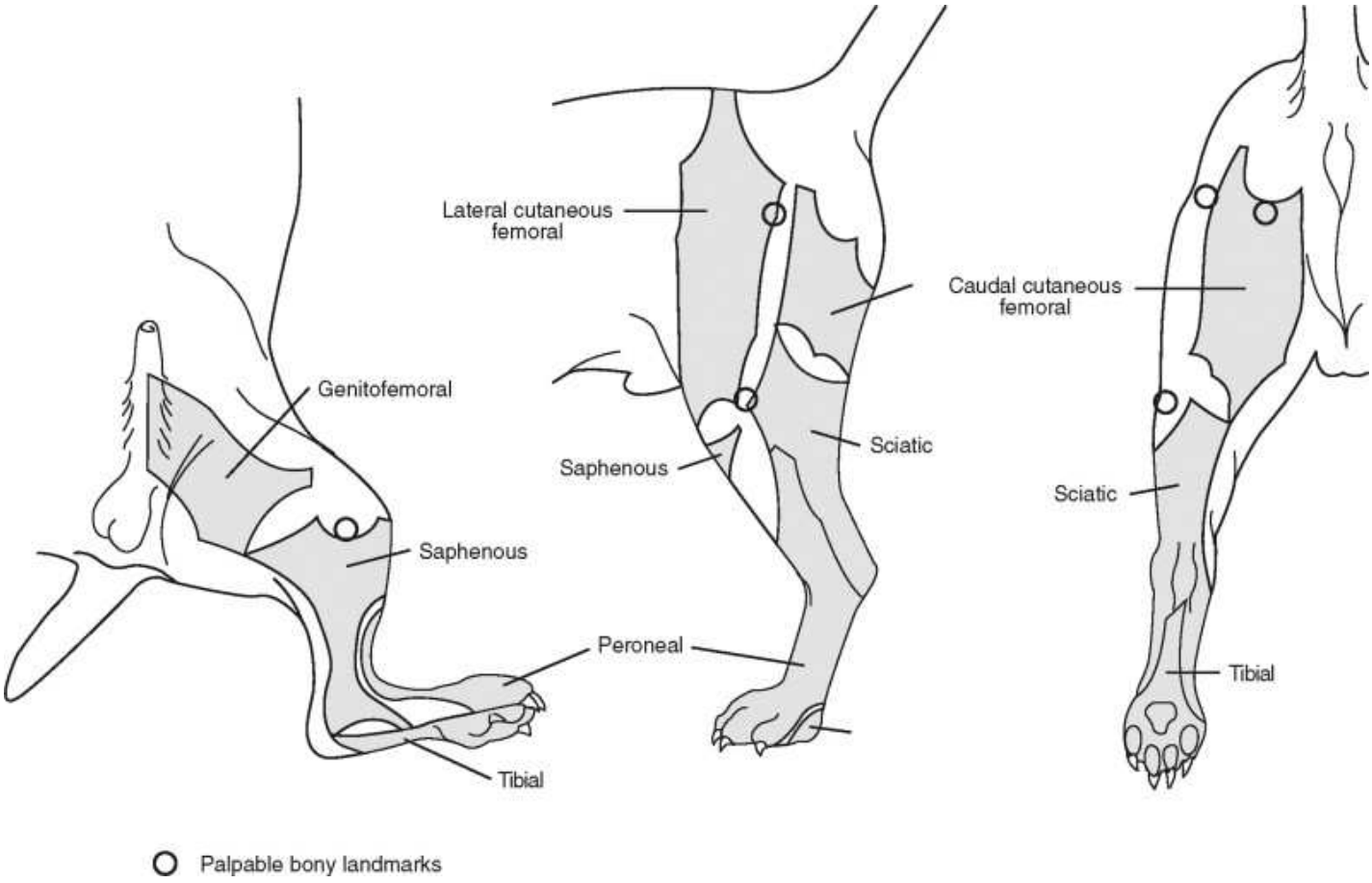
Nerves of the Hind Limb: Localization of Contributing Spinal Cord Segments

Nerves of the Hind Limb

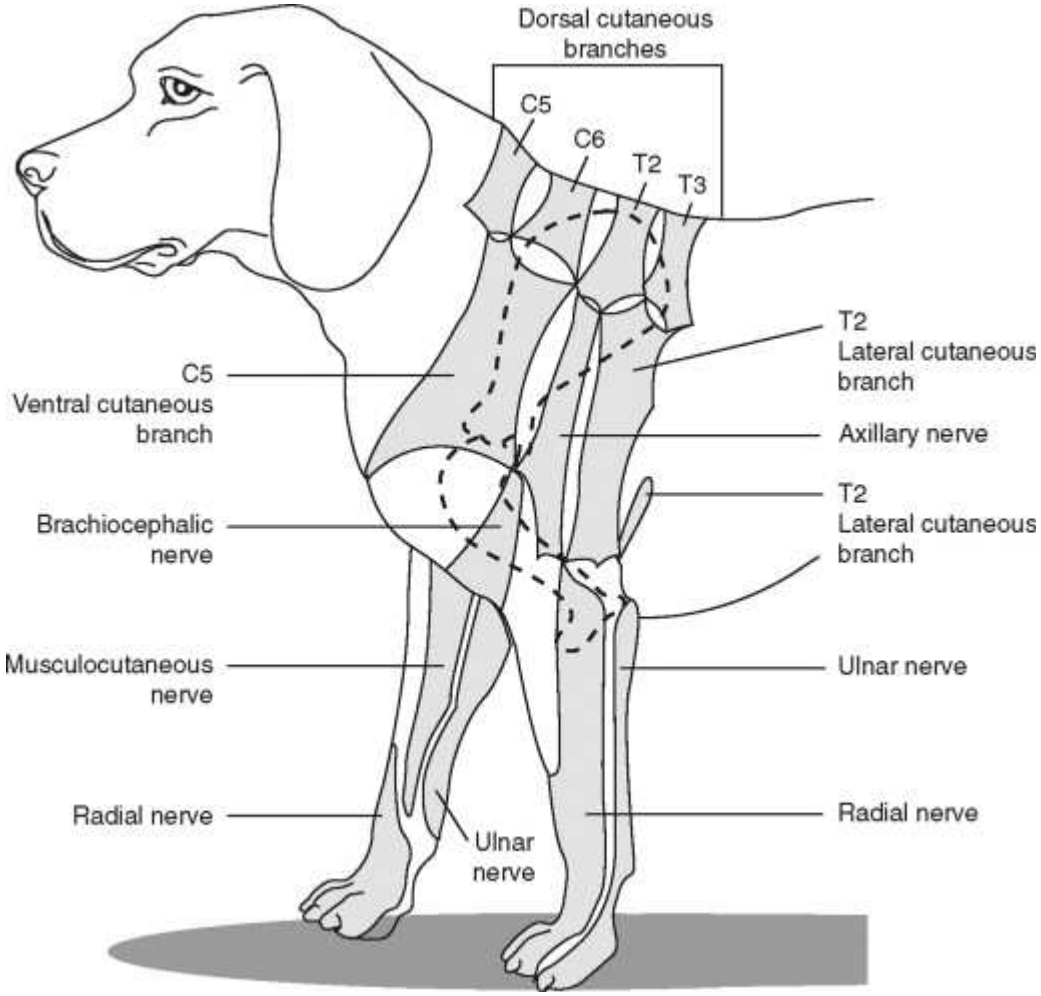
From Evans H, de Lahunta A: Guide to the dissection of the dog, ed 6, St Louis, 2004, Saunders.

Nerve	Spinal Cord Segments
Femoral	L4, 5, 6
Obturator	L(4), 5, 6
Cranial gluteal	L6, 7, S1
Caudal gluteal	L7, S1, 2
Sciatic	L6, 7, S1, 2
Pudendal	S1, 2, 3

Nerves of the Hind Limb: Cutaneous Distribution



Nerves of the Forelimb: Cutaneous Distribution



Nerves of the Forelimb: Localization of Contributing Spinal Cord Segments

Nerves of the Forelimb

From Evans H, de Lahunta A: Guide to the dissection of the dog, ed 6, St Louis, 2004, Saunders.

Nerve	Spinal Cord Segments
Phrenic	C5, 6, 7
Cranial pectoral	C6, 7, 8
Suprascapular	C6, 7
Subscapular	C6, 7
Musculocutaneous	C6, 7, 8
Axillary	C7, 8
Thoracodorsal	C8
Lateral thoracic	C8, T1
Radial	C7, 8, T1, 2
Median and ulnar	C8, T1, 2
Caudal pectoral	C8, T1, 2
Sympathetics (Horner's)	T1, 2, 3

Nephrotoxic Agents in Dogs and Cats

Adapted from Khan SA: Intoxication versus acute nontoxicologic illness: differentiating the two. In Ettinger SJ, Feldman EC, editors: Textbook of veterinary internal medicine, St Louis, 2010, Saunders, pp 549–554.

CNS, Central nervous system; *CV,* cardiovascular; *GI,* gastrointestinal; *NSAIDs,* nonsteroidal antiinflammatory drugs.

Agent	Comments/Notes
Aminoglycoside antibiotics like neomycin, kanamycin, gentamicin, amikacin, and tobramycin	Dogs, cats; not common anymore; mostly seen with parenteral use with repeated dosing, especially if dehydration has not been corrected first
Tetracyclines	Dogs; reported with intravenous use; rare
Sulfonamides	Crystalluria leading to nephrotoxicity; used less commonly such that toxicity not common anymore
NSAIDs such as carprofen, deracoxib, naproxen, ibuprofen, nabumetone, ketoprofen, oxaprozin, etodolac, piroxicam, flurbiprofen, sulindac, diclofenac, meloxicam, tepoxalin	Cats generally more sensitive than dogs; renal toxicosis can occur with acute single large overdose or with repeated use; adverse GI effects more common
Ethylene glycol (antifreeze)	Cats more sensitive than dogs (require less amount to be toxic), but more cases seen in dogs
Melamine and cyanuric acid (contamination)	Cats, dogs; outbreak in United States from contaminated dog and cat food in 2007; crystalluria, azotemia, GI signs
Grapes and raisins ingestion	Dogs only; initial GI signs followed by evidence of renal damage/failure, azotemia > 24 hours
Plants: Easter lily (*Lilium longiflorum*), tiger lily (*Lilium tigrinum*), day lily (*Hemerocallis* spp.), rubrum or Japanese show lilies (*Lilium speciosum*)	Cats only; initially vomiting, anorexia, and lethargy followed by evidence of renal damage within 24–72 hours
Cholecalciferol and other vitamin D3 analogs such as calcipotriene and calcitriol	Dogs and cats; mostly reported in dogs; initial GI signs followed by hyperphosphatemia, hypercalcemia, azotemia, CV and CNS effects
Zinc (pennies, zinc-plated nuts, wires)	Dogs; affects multiple organs; hemoglobinuria, anemia, azotemia, increased liver enzymes, pancreatitis
Heavy metals such as lead, mercury, arsenic	These affect multiple organs; GI signs, CNS effects, increased liver enzymes, azotemia; profuse diarrhea and shock from arsenic

Nasal Obstruction/Discharge in Cats, Chronic

Causes

- Viral rhinitis with or without secondary bacterial infection
  - Herpesvirus (feline viral rhinotracheitis)
  - Calicivirus
- Nasopharyngeal stenosis
- Esophageal motility dysfunction
- Foreign body (typically blade of grass)
- Allergic rhinitis
- Nasopharyngeal polyp
- Neoplasia (nasal lymphoma, other)
- Cryptococcal rhinitis
- Cleft palate (congenital) (uncommon)

Nasal Neoplasia

Malignant Tumors of the Canine and Feline Nasal and Paranasal Sinuses

Modified from Bonagura J: Kirk's current veterinary therapy XIII, St Louis, 2000, Saunders.

Canine

- Adenocarcinoma
  - Differentiated
  - Undifferentiated
- Squamous cell carcinoma
- Chondrosarcoma
- Fibrosarcoma
- Lymphosarcoma

Feline

- Adenocarcinoma
- Lymphoma

Infrequently Reported

- Osteosarcoma
- Hemangiosarcoma
- Rhabdomyosarcoma
- Leiomyosarcoma
- Nerve sheath tumors
- Neuroblastoma

Nasal Discharge and Sneezing

Causes of Concurrent Nasal Discharge and Sneezing

From Willard M, Tvedten H: Small animal clinical diagnosis by laboratory methods, ed 4, St Louis, 2004, Saunders.

Structural Anomalies

- Cleft palate
- Oronasal fistula
- Cricopharyngeal achalasia
- Megaesophagus

Allergic/Immunologic

- Allergic rhinitis
- Lymphoplasmacytic rhinitis

Bleeding Disorder

- Factor deficiency (congenital and acquired)
- Thrombocytopenia (infectious and immune mediated)
- Vessel wall (trauma and vasculitis)
- Foreign bodies/trauma

Infections

- Viral: distemper, parainfluenza, adenovirus type 2 (dogs); her-pesvirus, calicivirus (cats)
- Bacterial: including dental disease, chronic feline rhinosinusitis
- Fungal: *Aspergillus* spp., *Penicillium* spp., *Cryptococcus neoformans, Rhinosporidium seeberi*; other opportunistic fungi are rare (e.g., *Trichosporon*)
- Rickettsial (*Ehrlichia canis*, Rocky Mountain spotted fever)
- Parasitic (*Pneumonyssoides caninum, Linguatula serrata, Capil-laria aerophila, Syngamus ierei, Cuterebra* spp.)
- Other (*Chlamydia* spp.)

Neoplasia/Polyps

- Carcinomas, sarcomas, transmissible venereal tumor
- Polyp (nasopharyngeal in cats)

Ototoxic Agents

Agents With Potential to Cause Cochlear or Vestibular Damage

Ototoxic Agents	Comments
Aminoglycoside antibiotics (streptomycin, neomycin, kanamycin, amikacin, gentamicin, tobramycin)	Affects cochlear or vestibular apparatus; can be unilateral or bilateral; ototoxicity occurs mostly with repeated use; affects higher-frequency range first, followed by lower-frequency range
Other antibiotics (erythromycin; chloramphenicol; polymyxin B; minocycline; vancomycin, hygromycin B)	IV or large oral doses of erythromycin reversible; minocycline reversible; topical administration of polymyxin or some aminoglycosides in patients with perforated tympanic membrane; hygromycin B fed to 3 collies for 10 months
Tea tree oil	Possible if concentrated oil administered in the ear for treating otitis externa; high risk in patients with perforated tympanic membrane
Chemotherapeutic agents such as cisplatin or carboplatin	Likely with repeated doses or high acute administration
Salicylate analgesics	Possible with large acute ingestion; reversible
Diuretics (furosemide, ethacrynic acid)	Can affect stria vascularis in cochlea; possible with rapid IV use, especially in human renal failure patients; toxicosis not reported in small animals
Antiseptics (quaternary ammonium compounds such as benzethonium chloride, benzalkonium chloride, and cetrimide; ethanol, iodine or iodophors in 70% alcohol; chlorhexidine)	Possible with topical use; higher risk in patients with perforated tympanic membrane
Heavy metals (lead, mercury, arsenic)	Directly toxic to neural tissues; may affect hearing; ototoxicity not well documented in small animals
Quinine (antimalarial)	Likely not an issue in small animals
Propylene glycol	Possible with 100% solution used topically

Osteomyelitis

Causes in Dogs

Bacterial Aerobes

- *Escherichia coli*
- *Klebsiella* spp.
- *Pasteurella* spp.
- *Proteus* spp.
- *Pseudomonas* spp.
- *Staphylococcus* spp. (most common of the bacteria that cause osteomyelitis)
    - *S. pseudintermedius*
- *Streptococcus* spp.

Anaerobes

- *Actinomyces* spp.
- *Bacteroides* spp.
- *Clostridium* spp.
- *Fusobacterium* spp.
- *Nocardia* spp.
- *Peptostreptococcus* spp.

Viral

- Canine distemper virus

Fungal

- *Aspergillus* spp.
- *Blastomyces dermatitidis Candida* spp.
- *Coccidioides immitis*
- *Cryptococcus neoformans*
- *Histoplasma capsulatum*

Orbital Disorders

From Maggs DJ, Miller PE, Ofri R: Slatter's fundamentals of veterinary ophthalmology, ed 4, St Louis, 2008, Saunders, p 362.

Type of Disorder	Condition	Clinical Signs
Developmental abnormalities	Shallow orbit (brachycephalic breeds)	Exophthalmos, exposure keratitis, corneal ulceration, pigmentation
	Microphthalmos, anophthalmia	Small or absent globe, narrow palpebral fissure, prominent third eyelid, epiphora, blindness
	Hydrocephalus with orbital malformation	Exotropia, hypotropia, poor vision
	Euryblepharon	Long palpebral fissure resulting in apparent exophthalmos
	Orbital arteriovenous malformation or venous varices	Exophthalmos may be pulsatile, sometimes varies with position of varices; fremitus, pulse detectable; arteriovenous malformation has audible bruit
Trauma	Hemorrhages	Subconjunctival and episcleral hemorrhages; retrobulbar hemorrhage with exophthalmos or proptosis
	Penetrating foreign bodies (e.g., grass awns, needles, from mouth)	Discharging sinus fluid through the conjunctiva, periocular skin, buccal mucosa; exophthalmos, periorbital swelling, pain on opening of mouth
	Orbital fractures	Pain, crepitus; skin abrasions, displacement of globe
	Acquired vascular shunts	Pulsatile exophthalmos, may vary with position; audible bruit, fremitus
Infections	Bacterial, fungal	Ocular discharge usually secondary to penetrating foreign bodies from conjunctiva or oral cavity; sinusitis, rhinitis, or infections of roots of teeth
	Parasites (*Dirofilaria immitis*; *Pneumonyssoides caninum*)	Granulomatous lesions due to wandering larvae (*Dirofilaria* [rare]) or extension of infection from nasal cavity (*Pneumonyssoides*)
Neoplasia	Primary orbital neoplasms and neoplasia extending from adjacent area: sarcoma, meningioma, adenocarcinoma from orbital glands or nasal cavity, lymphosarcoma in cats	Exophthalmos, exposure keratitis, strabismus, displacement of globe, usually not painful; possible nasal or neurologic signs
	Metastatic: includes lymphosarcoma	Localized signs as already listed; possible systemic signs
Miscellaneous conditions	Zygomatic mucocele/sialocele	Exophthalmos, strabismus, swelling in any part of orbit or behind upper last molar tooth
	Infections of roots of teeth (especially carnassial)	Discharging fistula beneath eye in dogs
	Dehydration	Enophthalmos, protrusion of third eyelid

Type of Disorder	Condition	Clinical Signs
	Masticatory myositis	Exophthalmos, pain with dysphagia in acute stage; enophthalmos potentiated by opening of mouth in chronic stage when temporal muscles have atrophied
	Extraocular polymyositis	Exophthalmos, often bilateral, may be accentuated with exercise and stress
	Horner's syndrome	Enophthalmos, miosis, ptosis, protrusion of nictitating membrane, dermal vasodilation, local hypothermia

Oral Ulcers

Modified with permission from Greene C: Infectious diseases of the dog and cat, ed 3, St Louis, 2006, Saunders, p 888.

B, Both cat and dog; *C,* cats; *D,* dogs; *FeLV,* feline leukemia virus; *FIV,* feline immunodeficiency virus; *RMSF,* Rocky Mountain spotted fever.

Comparison of Ulcerative Lesions in Oral Cavities of Dogs and Cats

Cause	Species	Lesion Location
Excessive licking (eosinophilic ulcer)	C	Upper incisor or carnassial area of lip, near philtrum, roof of mouth (hard palate)
Autoimmune diseases, bullous pemphigoid	D	Roof of mouth, lips, cheeks, often symmetric; other mucocutaneous regions, footpads
Irritants, uremia	B	Tip of tongue
Viral (parvoviral), rickettsial (RMSF)	D	Multifocal lingual
Maltese terrier stomatitis	D	Ulcerative lesions, lateral tongue, and buccal mucosa
Dental tartar, periodontal disease	B	Periodontal regions (gingival margins)
Herpesvirus	C	Tongue, palate, multifocal
Calicivirus	C	Acute: tongue, palate, multifocal
		Chronic: fauces (glossopharyngeal reflection, upper last molar region), occasionally extends rostrally, occasionally roof of mouth (hard palate)
Immunosuppression; hyperadrenocorticism, leukopenia, FeLV, FIV, Abyssinian, Persian	B	Periodontal region, may spread to gums and cheeks
Electrocution	C	Tongue, often in linear pattern (electrical cord bite)

Optic Nerve Disorders

From Slatter D: Fundamentals of veterinary ophthalmology, St Louis, 2001, Saunders.

Feature	Optic Neuritis	Papilledema	Myelination of the Nerve Fiber Layer
Age	Middle-aged dogs	No specific age group unless associated with cerebral neoplasia, which is more common in older dogs	Present from birth, nonprogressive, and not pathologic
Vision	Severely affected or absent	No effect	No effect
Direct pupillary light reflex	Depressed or absent	Present	Present
Disc hemorrhages	Usually present	Rarely present	Absent
Peripapillary chorioretinitis	Often present	Absent (edema may be present)	Absent
“Kink” in vessels at disc margin	Often present	Often present	Absent
Vitreous haze	Often present	Absent	Absent

Obesity, Causes of/Contributors to

- Excess caloric intake
- Insufficient physical activity
- Neutering
- Hypothyroidism
- Hyperadrenocorticism
- Hypothalamic disorders
- Chronic steroid or antiepileptic drug use
- Orthopedic disease

AUTHOR: DR. KATHRYN MICHEL

Pyoderma

Differential Diagnosis of Canine Pyoderma

Surface Pyoderma

Pyotraumatic dermatitis (acute moist dermatitis, hot spots):

- Pyotraumatic folliculitis and furunculosis, demodicosis, dermatophytosis, neoplasia, cutaneous metastasis, fixed drug eruption, early necrotizing form of idiopathic nodular panniculitis, early localized vasculitis

Intertrigo (skinfold pyoderma):

- Localized demodicosis, mucocutaneous pyoderma, dermatophytosis, *Malassezia* dermatitis, candidiasis, superficial necrolytic dermatitis, zinc-responsive dermatosis

Bacterial overgrowth:

- *Malassezia* dermatitis, atopic dermatitis, food allergy

Superficial Pyoderma

Impetigo (puppy pyoderma):

- Superficial bacterial folliculitis, demodicosis, dermatophytosis, early scabies

Superficial bacterial folliculitis:

- Impetigo, superficial spreading pyoderma, dermatophytosis, demodicosis, sarcoptic acariasis, flea allergy dermatitis, pemphigus foliaceus, urticaria, drug eruption, erythema multiforme, sterile eosinophilic pustulosis, leishmaniasis

Superficial spreading pyoderma:

- Superficial bacterial folliculitis, dermatophytosis, demodicosis, pemphigus foliaceus

Mucocutaneous pyoderma:

- Intertrigo, *Malassezia* dermatitis, localized demodicosis, early discoid lupus erythematosus, zinc-responsive dermatosis, autoimmune skin diseases (DLE, SLE, PV, BP), epitheliotropic lymphoma (mycosis fungoides)

Deep Pyoderma

Pyotraumatic folliculitis:

- Pyotraumatic dermatitis/acute moist dermatitis (hot spot), demodicosis, neoplasia, cutaneous metastasis, fixed drug eruption, idiopathic nodular panniculitis, localized vasculitis

Muzzle folliculitis and furunculosis (canine acne):

- Localized demodicosis, dermatophytosis, early juvenile cellulitis, eosinophilic furunculosis, contact dermatitis

Pedal folliculitis and furunculosis:

- Pelodera dermatitis, dermatophytosis, subcutaneous and systemic mycoses, opportunistic fungal diseases, mycobacterial diseases, interdigital pyogranulomas, neoplasia
- Callus/pressure-point pyoderma: acral lick dermatitis, focal actinic comedones, sarcoptic acariasis

German shepherd dog pyoderma:

- Demodicosis with secondary deep pyoderma, subcutaneous and deep mycoses, opportunistic fungal infection, idiopathic

nodular panniculitis, vasculitis

DLE, Discoid lupus erythematosus; *SLE,* systemic lupus erythematosus; *PV,* pemphigus vulgaris; *BP,* bullous pemphigoid.

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Pulmonary Markings

Differential Diagnoses for the Various Lung Patterns on Thoracic Radiographs

From Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

Bronchial Pattern

- Chronic bronchitis (irritant, allergic, parasitic)
- Calcification
- Peribronchial cuffing (edema, bronchopneumonia, eosinophiliic bronchopneumopathy)

Interstitial Pattern Nodular

- Neoplasia
- Granuloma (eosinophilic, fungal, parasitic- or heartworm-associated, foreign body)
- Bulla with fluid
- Hematoma, abscess, cyst
- Mucus-filled bronchus
- Bronchiectasis

Hazy and Unstructured, Diffuse

- Artifact (underexposure, obesity, end-expiratory film)
- Degenerative changes (“old dog lung”)
- Neoplasia (lymphoma, metastasis)
- Pneumonitis (toxic, inhalant, metabolic, viral, parasitic)
- ARDS
    - Transitional stages of disease, such as edema, hemorrhage, bronchopneumonia

Hazy and Unstructured, Localized

- Hemorrhage
- PTE
- Foreign body
- Partial atelectasis
- Transitional stages of disease, such as edema, bronchopneumonia, hemorrhage, or parasites

Alveolar PatternDiffuse

- Edema (cardiogenic or noncardiogenic)
- Bronchopneumonia
- Hemorrhage
- Smoke inhalation
- Near-drowning incident
- Acute respiratory distress syndrome

Localized

- Edema
- Bronchopneumonia
- Hemorrhage
- Primary lung tumor or metastasis
- Lobar collapse or atelectasis
- Heartworm disease
- Infarct

ARDS, Acute respiratory distress syndrome; *PTE,* pulmonary embolism.

Pulmonary Hypertension

Causes

- Airway or pulmonary parenchymal disease (chronic)
- Branch pulmonary artery stenosis (congenital)
- Congestive heart failure (chronic left-sided)
- Heartworm disease
- Hypoxia (chronic): high altitude, chronic airway obstruction
- Idiopathic/"primary"
- Left-to-right shunting congenital malformations
- Persistently underdeveloped/"fetal" pulmonary circulation
- Pulmonary thromboembolism

Pruritic Feline Dermatoses

Modified by Manon Paradis from Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

C, Common; *L,* less common; *R,* regional; *S,* seasonal; *U,* uncommon.

Disease	Site	Lesions
Flea allergy dermatitis C, R, S	Neck, dorsum, lumbosacral, caudal and medial thighs, groin, ears	"Miliary dermatitis," erythema, alopecia, eosinophilic plaques
Eosinophilic plaque C, R, S	Ventral abdomen, medial thighs, anywhere	Raised, ulcerated, erythematous alopecic plaques secondary to allergy (primarily flea allergy dermatitis)
Otodectic acariosis (ear mites) C	Ears, head, neck, rarely generalized	Otitis externa, excoriations, "miliary dermatitis"
Food allergy C	Head, neck, ears, generalized	Erythema, excoriations, alopecia, lack of primary lesions, "miliary dermatitis," eosinophilic plaque
Self-induced pruritic hair loss (atopic dermatitis, food allergy, flea allergy) L	Bilaterally symmetric, caudal and lateral thighs, ventral abdomen, perineum	Alopecia, hair stubble, erythema, papules, underlying skin may be normal
Atopic dermatitis L, S	Head, neck, ears, generalized	"Miliary dermatitis," erythema, excoriations, alopecia, eosinophilic plaque
Self-induced psychogenic hair loss L	Bilaterally symmetric, stripe(s) on dorsal thorax, caudal and lateral thighs, ventral abdomen, perineum, forelegs	Alopecia, hair stubble, normal underlying skin
Cheyletiellosis L, R	Dorsum of thorax, generalized	Large scales, crusts, seborrhea, "miliary dermatitis"
Demodicosis L, R	Trunk, ventral, generalized	Alopecia, scaling
Mosquito-bite hypersensitivity U, R, S	Bilaterally symmetric, dorsal muzzle, planum nasale	Papules, crusts, alopecia, erosion, exudation, periorbital, pinnae, paw pad margins fistulation
Pediculosis U, R, S	Dorsum, generalized	Scales, crusts, alopecia
Notoedric acariosis (feline scabies) U, R	Head, ears, neck, generalized	Erythema, papules, crusts, excoriations, partially bilaterally symmetric alopecia
Harvest mites (chiggers, trombiculiasis) U, R, S	Ventrum, legs, anywhere	Erythema, scales, crusts, papules, alopecia
Pruritic dermatophytosis U	Head, neck, ears, generalized	Erythema, alopecia, hair stubble, "miliary dermatitis," hyperpigmentation
Drug eruptions U	Anywhere, localized or generalized, pinnae, face	Pleomorphic, erythema, papules, coalescing target lesions
Pemphigus foliaceus U	Bilaterally symmetric, face, planum nasale, ears, interdigital webs, nipples, generalized	Pustules, epidermal collarettes, crusts, alopecia

Pruritic Canine Dermatoses

Modified from Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

C, Common; *L,* less common; *R,* regional (geographically variable); *S,* seasonal; *U,* uncommon.

Disease	Site	Lesions
Flea allergy dermatitis C, R, S	Bilaterally symmetric, dorsal lumbosacral, caudal thighs, groin, axilla, caudal half of body	Papules, macules, alopecia, erythema, lichenification, hyperpigmentation, excoriations, fibropruritic nodules
Canine scabies C	Ventrum, pinnae margins, face, elbows, partially bilaterally symmetric	Macules, papules, erythema, alopecia, crusts, excoriations
Demodicosis C	Periorbital, commissures of mouth, forelegs, generalized	Alopecia, erythema, crusts, follicular plugging, hyperpigmentation, secondary pyoderma
Pyoderma C	Groin, axilla, ventrum, interdigital webs, generalized, pressure points	Pustules, crusted papules, erythema, alopecia, target lesions, coalescing collarettes, hyperpigmentation
Atopic dermatitis C, S	Face, periorbital, ears, caudal carpi and tarsi, feet (dorsum), otitis externa, axillae, generalized	Erythema, alopecia, excoriations, lack of primary lesions, lichenification, hyperpigmentation
Malassezia dermatitis C, R, S	Ventral neck, groin, skin folds, face, feet, ventrum	Erythema, exudative or dry, alopecia, hyperpigmentation, lichenification
Otodectic acariosis (ear mites) C	Ear canal, pinnae	Erythema, brown otic discharge, excoriation, alopecia
Food allergy L	Face, feet, ears, generalized	Erythema, alopecia, excoriations, lack of primary lesions
Cheyletiellosis L, R	Dorsum of thorax, generalized	Large scales, crusts, alopecia, erythema
Cornification defects L	Generalized, ears, preen body	Scales, crusts, alopecia, erythematous plaques
Acral lick dermatitis L	Anterior carpal, metacarpal, radial, metatarsal, tibial regions	Firm alopecic plaque, central irregular ulcer, hyperpigmented halo
Contact dermatitis U	Hairless areas, feet (ventrum), genitals, groin, axilla, generalized	Erythema, exudation, lichenification, hyperpigmentation, papules
Drug eruptions U	Anywhere, localized or generalized, face ears, scrotum	Pleomorphic, erythema, papules, coalescing target lesions
Pediculosis U, R, S	Dorsum, generalized	Scales, crusts, alopecia, papules
Harvest mites (chiggers, trombiculiasis) U, R, S	Ventrum, legs, anywhere	Erythema, scales, crusts, papules, alopecia
Endoparasitic migration in puppies U	Face, feet, generalized	Erythema, alopecia, excoriations, lack of primary lesions
Pelodera dermatitis U, R, S	Ventrum, legs, groin	Erythema, papules, alopecia, crusts
Superficial necrolytic dermatitis (hepatocutaneous syndrome) U	Footpads, face, mucocutaneous junctions, genitals, groin	Adherent crusts, ulcers, erythema, excoriations, fissured pads
Epitheliotropic lymphoma U	Mucocutaneous, generalized	Erythema, alopecia, scaling, ulcers, nodules

Disease	Site	Lesions
Calcinosis cutis U	Dorsal neck, anywhere	Papules, plaques, erythema, crusting
Tail-dock neuroma U	Previously docked tail	Erythema, excoriations, alopecia

Proteinuria

Modified with permission from Bonagura J: Kirk's current veterinary therapy XII: small animal practice, St Louis, 1995, Saunders, p 938.

PreglomerularPhysiologic

- Stress
- Extreme temperatures
- Strenuous exercise
- Renal venous congestion

Overload

- Hyperproteinemia (total protein > 9 g/dL)
- Hemoglobinemia
- Myoglobinemia
- Paraproteinemia

GlomerularGlomerulonephritis

- Infectious:
  - Dirofilariasis
  - *Ehrlichia canis* infection
  - Chronic bacterial infections
  - Bacterial endocarditis
  - Brucellosis
  - Leishmaniasis
  - Borreliosis
  - Septicemia
- Inflammatory:
  - SLE
- Neoplastic
- Familial
- Idiopathic

Amyloidosis

- Familial
- Inflammatory:
  - SLE
- Neoplastic
- Idiopathic

Glomerulosclerosis

- Diabetes mellitus
- Hyperadrenocorticism
- Hyperfiltration
- Hypertension

PostglomerularTubular Dysfunction

- Fanconi syndrome
- Acute tubular necrosis
- Genitourinary inflammation

Hemorrhage

UTI

Urolithiasis

Trauma

Neoplasia

SLE, Systemic lupus erythematosus; *UTI,* urinary tract infection.

Protein-Losing Enteropathies

From Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

HGE, Hemorrhagic gastroenteritis.

Causes	Examples
Lymphangiectasia	Primary lymphatic disorder, venous hypertension (e.g., right heart failure, hepatic cirrhosis)
Infectious	Parvovirus, salmonellosis, histoplasmosis, phycomycosis
Structural	Intussusception
Neoplasia	Lymphoma
Inflammation	Lymphocytic-plasmacytic, eosinophilic, granulomatous
Endoparasites	*Giardia*, *Ancylostoma* spp.
Gastrointestinal hemorrhage	HGE, neoplasia, ulceration

Prostatomegaly

- Abscess (asymmetric, often painful)
- Benign prostatic hyperplasia (symmetric, nonpainful; uncommon in castrated dogs)
- Cyst (prostatic, paraprostatic; asymmetric, nonpainful)
- Neoplasia (adenocarcinoma, others; asymmetric, usually nonpainful)
- Prostatitis (asymmetric; painful [acute prostatitis] or nonpainful [chronic])

Preputial Discharge

Urine

- PU/PD
- Ectopie ureters
- Urethral sphincter dysfunction
- UTI
- Urolithiasis

Hemorrhagic

- Bleeding disorder (thrombocytopenia, coagulopathy)
- Neoplasia (bladder, urethra, prostate, testicle)
- Inflammation/infection (bladder, urethra, prostate, testicle, penis/prepuce [balanoposthitis])
- Foreign body (bladder, urethra, prepuce)
- Trauma
- Urolithiasis

Mucopurulent

- Penile and preputial inflammation/infection (balanoposthitis)
- Neoplasia
- Foreign body (preputial, urethral)
- Phimosis

PU/PD, Polyuria/polydipsia; *UTI,* urinary tract infection.

Portosystemic Shunts

Breeds

- More commonly single, intrahepatic in large-breed dogs
- More commonly single, extrahepatic in small-breed dogs and cats

Multiple Shunts

- Multiple shunts are extrahepatic and are most commonly acquired rather than congenital. They occur secondary to portal hypertension induced by chronic hepatopathies or surgical intervention in an animal with hepatic microvascular dysplasia.

Location on Portogram

- If shunt is cranial to T13, more likely intrahepatic
- If any part of the shunt is caudal to T13, more likely extrahepatic

Polyuria and Polydipsia: Drug-Induced

Modified from Feldman E, Nelson R: Canine and feline endocrinology and reproduction, ed 3, St Louis, 2004, Saunders.

PU/PD, Polyuria and polydipsia; *WBC/HPF,* white blood cells counted per high-power field.

Urinalysis Results in Dogs With Selected Disorders Causing PU/PD

URINE SPECIFIC GRAVITY					
Disorder	**Number of Dogs**	**Mean**	**Range**	**Proteinuria**	**WBC (>5/HPF)**
Central diabetes insipidus	20	1.005	1.001-1.012	5%	0%
Psychogenic polydipsia	18	1.011	1.003-1.023	0%	0%
Hyperadrenocorticism	20	1.012	1.001-1.027	48%	0%
Chronic kidney disease	20	1.011	1.008-1.016	90%	25%
Pyelonephritis	20	1.019	1.007-1.045	70%	75%

Polyuria and Polydipsia: Differential Diagnosis

From Feldman E, Nelson R: Canine and feline endocrinology and reproduction, ed 3, St Louis, 2004, Saunders.

ACTH, Adrenocorticotropic hormone; *BP,* blood pressure; *BUN,* blood urea nitrogen; *CBC,* complete blood count; *PD,* polydipsia; *PU/PD,* polyuria and polydipsia.

Differential Diagnosis for PU/PD and Useful Diagnostic Tests

Disorder	Diagnostic Aids
Diabetes mellitus	Fasting blood glucose, urinalysis
Renal glycosuria	Fasting blood glucose, urinalysis
Chronic kidney disease	BUN, creatinine, Ca:P, urinalysis
Postobstructive diuresis	History, monitoring urine output
Pyometra	History, CBC, abdominal radiography, abdominal ultrasonography
Escherichia coli septicemia	Blood, urine, or other bacterial cultures
Hypercalcemia	Serum calcium
Hepatic insufficiency	Biochemistry panel, bile acids, ammonia tolerance test, abdominal radiography and ultrasonography
Hyperadrenocorticism	History, ACTH stimulation test, dexamethasone suppression test, urine cortisol/creatinine ratio
Primary hyperaldosteronism	Serum sodium and potassium, BP, abdominal ultrasonography, ACTH stimulation test (aldosterone)
Bacterial pyelonephritis	Urine culture, abdominal ultrasonography, excretory urography
Hypokalemia	Serum potassium
Hyponatremia	Serum sodium
Hypoadrenocorticism	Na:K, ACTH stimulation test
Hyperthyroidism	Serum thyroxine
Diabetes insipidus	Modified water deprivation test
Psychogenic PD	Modified water deprivation test
Polycythemia	CBC
Acromegaly	Serum GH and IGF-I, CT scan
Paraneoplastic disorders:	
Intestinal leiomyosarcoma	Abdominal ultrasonography, biopsy
Iatrogenic disorders	History
Very low-protein diet	History

Polyphagia

Modified from Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

Primary PolyphagiaDestruction of Satiety Center

- Trauma
- Mass lesion (e.g., neoplasia)
- Infection

Psychogenic Causes

- Stress
- Introduction of a more palatable diet
- Gluttony

Drug-Induced Polyphagia

- Glucocorticoids
- Anticonvulsants
- Antihistamines
- Progestins
- Benzodiazepines
- Amitraz
- Cyproheptadine

Reported Specific Disorders

Associated With Polyphagia

- FIP
- Lymphocytic cholangitis (feline)
- Spongiform encephalopathy (feline)
- Foreign body encephalitis (feline)

Secondary PolyphagiaPhysiologic Increase in Metabolic Rate

- Cold temperature
- Lactation
- Pregnancy
- Growth
- Increased exercise

Pathologic Increase in Metabolic Rate

- Hyperthyroidism
- Acromegaly

Decreased Energy Supply

- Diabetes mellitus
- Malassimilation syndromes:
    - Pancreatic exocrine insufficiency
    - Infiltrative bowel disease
    - Parasites
    - Lymphangiectasia

Decreased Intake

- Megaesophagus (congenital)
- Low-calorie diet
- Hypoglycemia

Unknown

- Hyperadrenocorticism
- Portosystemic shunt/hepatoencephalopathy
- SARDS

FIP, Feline infectious peritonitis; *SARDS,* sudden acquired retinal degeneration.

Polycythemia

Relative

- Dehydration
- Splenic contraction

Absolute

- Hypoxemia (respiratory disease, obesity, high altitude)
- Renal neoplasm
- Pyelonephritis
- Renal cyst
- Hydronephrosis
- Hepatoma
- Right-to-left shunting cardiovascular malformation (Eisenmenger's physiology)
    - Tetralogy of Fallot
    - Right-to-left patent ductus arteriosus
    - Septal defect with concurrent severe pulmonic stenosis or pulmonary hypertension
    - Double outlet right ventricle
    - Transposition of the great arteries
- Polycythemia vera

NOTE: Strictly speaking, the correct term is *erythrocytosis* (an increase in number of red blood cells). However, the term *polycythemia* (increase in numbers of all blood cell lines) is used interchangeably and in this table, refers to erythrocytosis specifically.

Polyarthritis

Classification of Immune-Based Arthritis

Modified with permission from Bonagura J: Kirk's current veterinary therapy XII: small animal practice, St Louis, 1995, Saunders, p 1189.

Erosive

- Rheumatoid arthritis
- Periosteal proliferative polyarthritis
- Polyarthritis of greyhounds

Nonerosive

- Systemic lupus erythematosus
- Polyarthritis/polymyositis
- Polyarthritis/meningitis
- Calicivirus-associated (cats)
- Arthritis of Akita dogs
- Amyloidosis of shar-pei
- Polyarteritis nodosa
- Idiopathic
    - Type I (uncomplicated)
    - Type II (reactive)
    - Type III (enteropathic)
    - Type IV (malignancy)

Miscellaneous

- Vaccination “reactions”
- Plasmacytic/lymphocytic synovitis
- Drug induced

Pneumonia, Bacteria Isolated in Tracheal Aspirates from Dogs

From pharyngeal isolates, *Mycoplasma* are isolated 85.7%-100% of the time, representing normal microflora; from transtracheal washings, 34%-69%; from bronchiolar washings, 7.1%-26.9% (Jameson et al., 1995; Randolph et al., 1993). A range is not listed for anaerobes because data are from one study of 203 dogs (Angus et al., 1997); Data taken from

- Creighton SR, Wilkins RJ: Bacteriologic and cytologic evaluation of animals with lower respiratory tract disease using transtracheal aspiration biopsy.
- J Am Anim Hosp Assoc 10:227–232, 1974 (30 dogs); Harpster NK: The effectiveness of the cephalosporins in the treatment of bacterial pneumonias in the dog.
- J Am Anim Hosp Assoc 17:766–772, 1981 (30 dogs); Thayer GW, Robinson SK: Bacterial bronchopneumonia in the dog: a review of 42 cases.
- J Am Anim Hosp Assoc 20:731–735, 1984 (42 dogs); Hirsh DC: Bacteriology of the lower respiratory tract. In Kirk RW (ed), Current veterinary therapy IX. Philadelphia, 1986, WB Saunders, pp 247–250 (105 dogs); Jameson PH, King LA, Lappin MR, et al: Comparison of clinical signs, diagnostic findings, organisms isolated, and clinical outcome in dogs with bacterial pneumonia: 93 cases (1986-1991).
- J Am Vet Med Assoc 206:206–209, 1995 (48 dogs); Angus JC, Jang SS, Hirsh DC: Microbiological study of trans-tracheal aspirates from dogs with suspected lower respiratory tract disease: 264 cases (1989-1995).
- J Am Vet Med Assoc 218:55–58, 1997 (203 dogs); With permission from Greene C: Infectious diseases of the dog and cat, ed 3, St Louis, 2006, Saunders, p 870.

Bacteria	Range Percentage (%)
Gram Negative	
Escherichia coli	17–43
Klebsiella	3.9–23
Bordetella	3–23
Pseudomonas	4.9–33
Pasteurella	0–45
Enterobacter	0–5
Acinetobacter	0–7
Moraxella	2–26
Other gram-negative rods	4.4–12
Gram Positive	
Staphylococcus	5.4–27
Streptococcus	13.8–47
Nonhemolytic	0–13
α-Hemolytic	3–30
β-Hemolytic	0–16
Corynebacterium	0–5
Mycoplasma	2.9–100
Anaerobes	
Total	18.7
Bacteroides	23.7
Clostridium perfringens	5.3

Bacteria	Range Percentage (%)
Eubacterium	2.6
Fusobacterium	15.8
Peptostreptococcus	23.7
Prevotella	5.3
Porphyromonas	15.8
Propionibacterium	2.6

Pneumonia, Aspiration

Conditions Predisposing an Animal to Aspiration of Stomach Contents

With permission from King L: Textbook of respiratory disease in dogs and cats, St Louis, 2004, Saunders, p 423.

Impairment of Protective Airway Reflexes

- Coma
- Head trauma
- Metabolic derangements
- Central depressant medications (sedation, general anesthesia)
- Muscle relaxants
- Seizures
- Airway trauma
- Laryngeal/pharyngeal dysfunction

Large Volumes of Intragastric Food/Fluid

- Delayed gastric emptying:
  - Ileus
  - Bowel obstruction
  - Pain
  - Anxiety
  - Opioid medication
  - Peristaltic abnormalities
  - Pregnancy
  - Obesity
- Overfeeding by enteral tube
- Recent meal (before emergency anesthesia/surgery)

Impaired Function of Gastroesophageal Sphincter

- Presence of a nasogastric feeding tube
- Achalasia
- Esophageal obstruction
- Abnormalities of esophageal function:
  - Megaesophagus
  - Reflux esophagitis
  - Myasthenia gravis

Pleural Effusion

Modified with permission from King L: Textbook of respiratory disease in dogs and cats, St Louis, 2004, Saunders, p 16.

C&S, Culture and sensitivity; *FIP,* feline infectious peritonitis; *PCR,* polymerase chain reaction; *RBCs,* red blood cells.*Occasionally translucent; definitive diagnosis via triglyceride concentration, which is higher in chylous effusions than in blood.

Cause, Appearance, Total Protein, and Cytologic Examination Findings of Pleural Effusions

Cause	Appearance	Total Protein	Cytologic Examination	Other Tests
Pyothorax *(septic exudate)*	Cloudy, tomato soup, malodor	>4 g/dL	Degenerative neutrophils, intracellular and extracellular bacteria, macrophages, RBCs	Aerobic and anaerobic C&S
Idiopathic chylothorax *(modified transudate)*	Milky white*	3 g/dL	Mature lymphocytes, few RBCs, few macrophages, few neutrophils	Effusion and serum triglyceride levels
Right-sided (±left-sided in cats) heart failure *(modified transudate)*	Clear	2 g/dL	Very few cells: RBCs, lymphocytes	Echocardiogram
Lymphoma *(modified transudate or nonseptic exudate)*	Clear, milky, serosanguineous	2-4 g/dL	Immature lymphoblasts, few mature lymphocytes, few RBCs	Thoracic radiographs, thoracic ultrasound, aspirate/cytologic examination of mass
Thymoma *(modified transudate or nonseptic exudate)*	Clear, milky, serosanguineous	2-4 g/dL	Mesothelial cells, mature lymphocytes, few RBCs, few macrophages	Thoracic radiographs, thoracic ultrasound, aspirate/cytologic examination of mass
Other neoplasia (e.g., carcinoma) *(modified transudate or nonseptic exudate)*	Clear, cloudy, serosanguineous, bloody	2-4 g/dL	Clumps of neoplastic cells	Thoracic radiographs, thoracic ultrasound
Hypoalbuminemia *(pure transudate)*	Clear, watery	<2.5 g/dL	Mononuclear cells (mesothelial cells, lymphocytes, macrophages)	Serum albumin, urine protein/creatinine ratio, bile acids
FIP (cats) *(nonseptic exudate)*	Straw-colored, cloudy	>4 g/dL	Macrophages, lymphocytes, RBCs, fibrin	FIP PCR on fluid, serum FIP titer

Petechiae, Ecchymosis

From Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 5, St Louis, 2000, Saunders.

Thrombocytopenia

- ***Decreased Platelet Production***
- Drug:
  - Albendazole (D)
  - Azathioprine (D,C)
  - Chemotherapeutic agents (D,C)
  - Chloramphenicol (D,C)
  - Estrogen (D)
  - Griseofulvin (C)
  - Meclofenamic acid (D)
  - Phenobarbital (D)
  - Phenylbutazone (D)
  - Trimethoprim-sulfadiazine (D)
- Infection:
  - *Ehrlichia* spp.
  - FeLV
  - FIV
  - Disseminated histoplasmosis
- Myelophthisis
- Myelofibrosis
- Immune-mediated disorder (antimegakaryocytic)
- ***Increased Platelet Destruction***
- Primary IMT:
  - ITP
  - SLE
- Secondary IMT:
  - Infection
  - Neoplasia
  - Vaccine
  - Drug:
    - Sulfonamides (D)
    - Cephalosporins (D)
    - Gold salts (D)
    - Methimazole (C)
    - Propylthiouracil (C)
    - Dextrans (D)
- *Ehrlichia* spp. infection
- ***Increased Platelet Consumption***
- Disseminated intravascular coagulation
- Vasculitis:
  - Sepsis
  - *Rickettsia rickettsii*
  - *Leptospira* spp.
  - *Ehrlichia* spp.
  - FIP
- Neoplasia
- Inflammation
- Immune-mediated disorder
- Drug reaction

Thrombopathia

- ***Inherited***
- Chédiak-Higashi syndrome of Persian cats
- Thrombasthenia of otterhounds
- Delta storage–pool disease of American cocker spaniel

- Other thrombopathias:
  - Basset hound
  - Spitz
  - Grey collies with cyclic hematopoiesis
  - Domestic shorthair
- ***Acquired***
- Drug:
  - Aspirin
  - Cephalothin
  - Acepromazine
- Systemic disease:
  - Uremia
  - Liver disease
- Hematologic disorders:
  - IMT
  - Myelo-/lymphoproliferative disorders
  - Dysproteinemia (e.g., multiple myeloma)

Vascular Disorders

- Vasculitis (see Increased Platelet Consumption)
- Hyperadrenocorticism
- Dysproteinemia

C, Cats; *D,* dogs; *IMT,* immune-mediated thrombocytopenia; *FeLV,* feline leukemia virus; *FIP,* feline infectious peritonitis; *FIV,* feline immunodeficiency virus; *ITP,* idiopathic thrombocytopenic purpura; *SLE,* systemic lupus erythematosus.

Peritonitis

Causes of Peritonitis

From Slatter D: Textbook of small animal surgery, ed 3, Philadelphia, 2003, Saunders.

Aseptic Peritonitis

- Chemical peritonitis:
  - Bile peritonitis
  - Uroperitoneum
- Peritoneal foreign body
- Starch granulomatous peritonitis
- Sclerosing encapsulating peritonitis
- Mechanical peritonitis

Septic Peritonitis

- Leakage of gastrointestinal contents:
  - Perforating intestinal foreign body
  - Gastric rupture in gastric dilation/volvulus
  - Perforating gastric or intestinal ulcers
  - Colonic perforation (steroidal or nonsteroidal antiinflammatory drug induced)
  - Dehiscence of intestinal surgical wound
- Iatrogenic perforation:
  - Intraperitoneal alimentation
- Penetrating abdominal wounds
- Blunt abdominal trauma
- Ischemic intestinal injury
- Pancreatitis
- Ruptured pyometra
- Uterine torsion
- Ruptured prostatic abscess
- Liver abscess or hepatitis
- Splenic abscess or splenitis
- Splenic torsion
- Mesenteric lymph node abscess
- Ruptured gallbladder or bile duct with bacterobilia
- Ruptured bladder with cystitis
- Umbilical abscess
- Surgical peritoneal contamination
- Peritoneal dialysis

Pericardial Effusion in the Dog

BUN, Blood urea nitrogen; *C&S,* culture and sensitivity; *FIP,* feline infectious peritonitis; *PT,* prothrombin time.

	Gross Appearance of Effusion	Echocardiographic Appearance	Next Test
Hemangiosarcoma	Hemorrhagic; "port wine" color; usually does not clot (rarely, may clot if brisk hemorrhage); cytologic examination unhelpful	Small, medium, or large amount of anechoic effusion; right atrial/right atrioventricular epicardial mass may or may not be seen; diastolic right atrial and/or right ventricular collapse may be seen.	Serum troponin Central venous pressure elevated
Idiopathic benign pericarditis	Hemorrhagic; "port wine" color; does not clot; cytologic examination unhelpful	Small, medium, or large amount of anechoic effusion; diastolic right atrial and/or right ventricular collapse may be seen.	Serum troponin Central venous pressure elevated
Mesothelioma	Generally hemorrhagic; does not clot; cytologic examination unhelpful	Small, medium, or large amount of anechoic effusion; diastolic right atrial and/or right ventricular collapse may be seen; rarely, pericardium is noted to be thickened; rarely, forms a heart base mass.	Pericardial biopsy/pericardiectomy Central venous pressure elevated
Heart base tumor (chemodectoma; rarely ectopic thyroid carcinoma, mesothelioma, or other)	Generally hemorrhagic; does not clot	Small, medium, or large amount of anechoic effusion; mass generally seen between aortic root and either atrium; diastolic right atrial and/or right ventricular collapse may be seen.	Central venous pressure elevated
Hemorrhage/hemopericardium (coagulopathy, left atrial rupture)	Frank blood; erroneous centesis from the ventricle(s) produces a similar appearance.	Typically small to medium volume of effusion; spontaneous contrast (particulate specks or swirling waves of echogenic material) may be present, representing small clots; diastolic atrial and/or right ventricular collapse may be seen with left atrial rupture or with anticoagulant rodenticide toxicosis; marked atrial enlargement is always present if atrial rupture is the cause.	Platelet count, PT
Inflammatory (e.g., FIP, bacterial pericarditis)	Serosanguineous, rarely grossly purulent (exudate); because of small volume of effusion, pericardiocentesis is often challenging or dangerous and should not	Generally small volume of effusion; echogenic particles may be seen in the effusion, representing small clumps of inflammatory cells, bacteria, and fibrin (bacterial infection) or clumps of proteins/globulin	C&S, aerobic and anaerobic, of pericardial effusion

	Gross Appearance of Effusion	Echocardiographic Appearance	Next Test
	be performed unless clinical (right heart failure signs) and echocardiographic (atrial collapse) signs of tamponade are present.	(such as in FIP).	Surgical exploration if effusion is septic
Hypoalbuminemia	Serosanguineous and watery (pure transudate); because of small volume and low pressure of effusion, pericardiocentesis is challenging or dangerous, is of little additional diagnostic value, and generally is contraindicated.	Generally very small volume of effusion; anechoic	Serum albumin level Central venous pressure normal
Uremia	Serosanguineous and watery (pure transudate); because of small volume and low pressure of effusion, pericardiocentesis is challenging or dangerous, is of little additional diagnostic value, and generally is contraindicated.	Generally very small volume of effusion; anechoic	Serum/blood BUN, creatinine urinalysis Central venous pressure normal
Lymphoma	Serosanguineous or hemorrhagic	Small to medium volume of effusion	Pericardial biopsy rarely indicated
Pericardial cyst	Hemorrhagic	Small, medium, or large volume of effusion Intrapericardial mass distinctly attached to apical aspect of pericardium (not attached to heart)	Thoracotomy and biopsy
Right heart failure	Serosanguineous (modified transudate)	Right heart abnormality (tricuspid valve insufficiency causing marked right atrial enlargement, pulmonic stenosis, right ventricular hypertrophy, etc.); no diastolic collapse of right atrium or ventricle (unless [rarely] right atrial rupture is present)	Thoracic radiographs Abdominal ultrasound should identify enlarged hepatic veins.

Pericardial Diseases

With permission from Kittleson M, Kienle R: Small animal cardiovascular medicine, St Louis, 1998, Mosby, p 417.

Congenital Disorders Pericardial Defects

- Peritoneopericardial diaphragmatic hernia
- Pericardial cyst

Acquired Disorders Pericardial Effusion

- Hydropericardium (transudate)*
  - Congestive heart failure
  - Hypoalbuminemia
  - Peritoneopericardial diaphragmatic hernia
- Pericarditis (exudates)
  - Infectious (bacterial, fungal)
  - Sterile (idiopathic, metabolic, viral)
- Hemopericardium (hemorrhage)
  - Neoplastic
  - Traumatic
  - Cardiac rupture (especially left atrial)
  - Idiopathic

Pericardial Mass Lesions *(± Effusion)*

- Neoplastic
- Granulomatous (actinomycosis, coccidioidomycosis)
- Pericardial abscess

Constrictive Pericardial Disease

- Idiopathic
- Infectious
- Pericardial foreign body
- Neoplastic

Paraneoplastic Syndromes

With permission from Bonagura J: Kirk's current veterinary therapy XII: small animal practice, St Louis, 1995, Saunders, p 531.

Paraneoplastic Disorder	Clinical Features	Associated Neoplasms in Companion Animals
Malignancy-associated hypercalcemia	Dehydration, depression, muscular weakness, anorexia, polyuria and polydipsia, vomiting, arrhythmias	Lymphoma (thymic, multicentric, extranodal leukemia), carcinomas (nasal, pulmonary, mammary, squamous cell, thyroid, apocrine gland of anal sac, gastric, pancreatic, testicular, parathyroid gland), thymomas, multiple myeloma, epidermoid carcinoma of the lung
Extrapancreatic hypoglycemia	Weakness, seizures	Hepatocellular carcinoma, hepatoma, hemangiosarcoma, leiomyosarcoma, splenic hemangiosarcoma, salivary gland adenocarcinoma, metastatic oral melanoma, mammary carcinoma, pulmonary carcinoma, plasma cell tumor, lymphocytic leukemia, renal carcinoma
Hyperhistaminemia, mast cell degranulation	Gastrointestinal ulceration with melena and hematemesis, urticaria, erythema, pruritus, poor wound healing, anaphylactoid reaction, hypotension/arrhythmias, altered coagulation	Mast cell tumor
Cancer anorexia/cachexia syndrome	Weight loss >5%-10% body weight, anorexia >2-3 days' duration, early satiety	Any tumors
Syndrome of inappropriate antidiuretic hormone secretion	Hyponatremia, polyuria and polydipsia, edema	Pulmonary carcinoma (dog)
Fever	Persistent pyrexia >39.7°C (103°F) without infection	Lymphoproliferative and myeloproliferative neoplasms; mast cell, hepatic, and brain tumors
Polycythemia	Exercise intolerance, seizures, red mucous membranes, packed cell volume >60	Renal tumors, lymphoma, polycythemia vera, hepatic tumors
Hypertrophic osteopathy	Painful, hard, swollen distal limbs, reluctance to walk	Primary lung tumors, rhabdomyosarcoma (bladder), esophageal sarcomas, pulmonary metastasis, carcinoma, renal carcinomas, hepatic adenocarcinoma, renal papillary adenoma (cat), Sertoli cell tumor, transitional cell carcinoma of bladder, adrenocortical carcinoma
Dermatologic disorders	Nodular dermatofibrosis, erythema, flushing, necrolytic migratory erythema	Renal cystadenocarcinoma, mast cell tumor, pheochromocytoma, pancreatic adenocarcinoma
Renal disorders	Amyloid deposition, glomerulonephritis, concentrating defects, proteinuria, nephrotic syndrome	Many tumors, including lymphoma, plasma cell tumors, mast cell tumors

Paraneoplastic Disorder	Clinical Features	Associated Neoplasms in Companion Animals
Central nervous system dysfunction	Tissue hypoxia with or without thromboembolism, due to hyperviscosity syndrome (seizures, dementia)	Lymphoma, plasma cell tumors
Peripheral nervous system disorders:		
Neuromuscular junction	Myasthenia gravis (weakness with exercise that improves with rest)	Thymoma, hepatocellular carcinoma, osteosarcoma, mammary adenocarcinoma, pheochromocytoma, pulmonary adenocarcinoma
Neuropathy	Weakness, cranial nerve abnormalities	Lymphoma, bronchogenic carcinoma, insulinoma, leiomyosarcoma, hemangiosarcoma, and undifferentiated sarcomas
Neuromyopathy	Weakness, muscle pain, proprioception deficits	Pulmonary carcinoma
Myopathy	Myositis	Thymoma

Panting

Causes

Modified with permission from King L: Textbook of respiratory disease in dogs and cats, St Louis, 2004, Saunders, p 47.

- Elevated ambient temperature
- Overweight/obesity
- Fever, hyperthermia
- Anxiety, nervousness
- Pain
- Hyperadrenocorticism
- Glucocorticosteroid therapy
- Pheochromocytoma
- Hyperthyroidism
- Hypocalcemia
- Narcotic administration
- Cardiac disease/tachyarrhythmias
- Brain disease

Retinopathies

Common Systemic Disorders Affecting the Retina

Modified from Slatter D: Fundamentals of veterinary ophthalmology, St Louis, 2001, Saunders.

Dog

- Blastomycosis
- Coccidioidomycosis
- Cryptococcosis
- Distemper
- Ehrlichiosis
- Rocky Mountain spotted fever
- Histoplasmosis
- Systemic hypertension
- Larva migrans *(Toxocara* spp.)
- Leishmaniasis
- Lymphoma
- Multiple myeloma
- Toxoplasmosis
- Uveodermatologic syndrome

Cat

- Blastomycosis
- Cryptococcosis
- FIP
- Histoplasmosis
- Multiple myeloma
- Systemic hypertension
- Lymphoma (both FeLV positive and negative)
- Toxoplasmosis
- Tuberculosis

FeLV, Feline leukemia virus; *FIP*, feline infectious peritonitis.

Respiratory Parasites

Parasite (Host)	Comment
Aelurostrongylus abstrusus (cats)	Coughing, sneezing, lethargy possible but usually no signs
Capillaria aerophila (dogs, cats)	Chronic cough or no clinical signs
Crenosoma vulpis (wild canids; rarely dogs)	Chronic cough clinically mimicking chronic sterile bronchitis
Eucoleus boehmi (dogs, cats)	Chronic sneezing, nasal discharge, facial rubbing
Filaroides hirthi (dogs only)	Breeding kennels; zinc sulfate flotation is best (not Baermann)
Oslerus osleri (wild canids; rarely dogs)	Nodules in large airway mucosa; treatment difficult
Paragonimus kellicotti (dogs, cats)	Chronic cough ± pneumothorax; rust-colored pharyngeal phlegm
Pneumonyssoides caninum (dogs)	Nasal mite; sensitive to parenteral (and presumably oral) ivermectin

Renal Failure, Acute

Causes of Intrinsic Acute Renal Failure

From Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

Renal Ischemia

- Progression of prerenal azotemia
- Renal vascular disease (avulsion, thrombosis, stenosis)

Nephrotoxicosis

- Exogenous toxins
- Endogenous toxins
- Drugs

Primary Renal Diseases

- Infections: pyelonephritis, leptospirosis, infectious canine hepatitis
- Immune-mediated disease: acute glomerulonephritis, SLE, renal transplant rejection
- Neoplasia: lymphoma
- Miscellaneous: “Alabama rot”

Systemic Diseases With Renal Manifestations

- Infections: FIP, borreliosis, babesiosis, leishmaniasis, bacterial endocarditis
- Pancreatitis
- SIRS, sepsis, multiple organ failure, DIC
- Heart failure
- SLE
- Hepatorenal syndrome
- Malignant hypertension
- Hyperviscosity syndrome: polycythemia, multiple myeloma

DIC, Disseminated intravascular coagulopathy; *FIP*, feline infectious peritonitis; *SIRS*, systemic inflammatory response syndrome; *SLE*, systemic lupus erythematosus.

Renal Failure, Acute Versus Chronic

From Bonagura J: Kirk's current veterinary therapy XIII, St Louis, 2000, Saunders.

ARF, Acute renal failure; *CKD,* chronic kidney disease; *PCV,* packed cell volume; *PU/PD,* polyuria and polydipsia.*The clinician should be aware that there are many caveats to using these aids.

Diagnostic Aids for the Differentiation of Acute Renal Failure and Chronic Kidney Disease*

	Acute Renal Failure	Chronic Renal Failure	Caveats
History	Ischemic episode, toxicant exposure, nephrotoxic drug use, acute illness	Long-standing signs of weight loss, PU/PD, nocturia, vomiting, diarrhea; prior episodes of illness; prior renal disease/insufficiency	Animals with ARF developing secondary to another disease may have long-standing signs; urine output does not differentiate ARF from CKD.
Body condition	Good	Poor	Some animals with ARF have a poor body condition from another disease process; some animals with CKD look fine.
Kidneys	Normal to large, smooth contour, may be painful	Small, irregular contour	Some chronic renal diseases cause renal enlargement.
Osteodystrophy	Absent	Sometimes present	
PCV	Normal to increased	Decreased (nonregenerative)	Animals with ARF may have nonregenerative anemia.
Urine sediment	May be active	Often inactive	Many animals with ARF have inactive urine sediments.
Serum creatinine	Recently within reference range	Previously increased	Previous prerenal and postrenal factors could also have caused increase.
Serum potassium	Normal to increased	Normal to decreased	Urine output is a major determinant of serum potassium concentration.
Metabolic acidosis	More severe	Less severe	
Histopathologic features	Acute tubular necrosis, acute inflammation	Interstitial fibrosis, glomerulosclerosis, chronic inflammation	Chronic renal lesions can be an incidental finding.
Carbamylated hemoglobin	Normal to mild increase	Increased	

Regurgitation

Causes

From Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders. *AChE*, Acetylcholinesterase; *SLE*, systemic lupus erythematosus.

Esophageal Disease

- Megaesophagus (primary or secondary)
- Esophagitis
- Mechanical obstruction (foreign body, stricture, vascular ring anomaly)

Alimentary Disorders

- Pyloric outflow obstruction
- Gastric dilatation/volvulus
- Hiatal hernia

Neuropathies

- Peripheral (polyradiculitis, giant-cell axonal neuropathy, polyneuritis, lead poisoning)
- Central (distemper, brainstem lesion, neoplasia, trauma)

Neuromuscular Junction Abnormalities

- Myasthenia gravis (focal or generalized)
- Botulism
- Tetanus
- AChE toxicity

Immune-Mediated Causes

- SLE
- Polymyositis
- Dermatomyositis

Endocrine

- Hypothyroidism
- Hypoadrenocorticism

Red Eye: Differential Diagnosis

With permission from Lavignette AM: Differential diagnosis and treatment of anterior uveitis. Vet Clin North Am 3:504, 1973. Modified from Slatter D: Fundamentals of veterinary ophthalmology, St Louis, 2001, Saunders.

Note: These disorders often do not exist in isolation, and features of two or more disorders may be present simultaneously, may negate each other, or may be additive.

Parameter	Anterior Uveitis	Conjunctivitis	Superficial Keratitis	Glaucoma
Conjunctiva	Not thickened, vessels easily seen	Thick, folded, and hyperemic, vessels concealed	Not thickened	Not thickened
Conjunctival vessels	Circumcorneal and straight, not movable with conjunctiva	Superficial, diffuse, and tortuous	Diffuse, vessels form fine network in vicinity of cornea	Diffuse, superficial and prominent
Secretion or discharge	None	Moderate to copious	Serous to purulent	None
Pain	Moderate	Severe	Moderate to severe	Severe to acute
Photophobia	Moderate	None	Severe	Slight
Cornea	Clear to steamy	Clear	Clouded to opaque	Steamy
Pupil size	Small, sluggish, irregular, or fixed	Normal	Normal	Dilated, moderate to complete, and fixed
Pupillary light reflex	Poor	Normal	Normal	Absent
Intraocular pressure	Variable; typically low/diminished acutely	Normal	Normal	Elevated

Systemic Inflammatory Response and Multiple Organ Dysfunction

With permission from Fox P: Textbook of canine and feline cardiology: principles and practice, St Louis, 2000, Saunders, p 275.

MODS, Multiple organ dysfunction syndrome; *SIRS,* systemic inflammatory response syndrome; *Y,* yes, usually present; +, possibly present; +/++/+++, mild, moderate, severe.

Clinical Manifestations of SIRS and MODS

	SIRS	MODS
Historic Abnormalities		
Anorexia	+/++	++/+++
Lethargy	+/++	++/+++
Diarrhea (hemorrhagic)		+
Physical Examination		
Mental depression	+/++	+++
Fever	Y	
Hypothermia		Y
Vasodilation (red mucous membranes, accelerated capillary refill time)	Y	
Vasoconstriction (pale mucous membranes, prolonged capillary refill time)		Y
Heart murmur	Y	+
Arterial pulse quality:		
“Bounding”	Y	
Normal or decreased		Y
Tachycardia, arrhythmias	+	Y
Tachypnea, hyperventilation	Y	Y
Petechiae or bleeding	+	+/Y
Clinical Pathologic Findings		
Hyperglycemia	+/Y	
Hypoglycemia		+/Y
Leukocytosis (possibly following transient leukopenia; left shift, mild toxic changes)	Y	
Leukopenia or rapid decrease in leukocytes, with marked left shift, toxic neutrophils		Y
Coagulation parameters:		
Normal to hyperactive	Y	
Hypoactive		Y
Increased liver enzymes (particularly alkaline phosphatase)		Y
Hyperbilirubinemia		+/Y
Hypoalbuminemia	+/Y	+/Y
Azotemia	+/++	+/++/+++
Acidosis (lactic/metabolic)	+	+/++

	SIRS	MODS
Hemodynamic Changes		
Cardiac output:		
Normal to high	Y	
Low		Y
Arterial blood pressure; central venous pressure:		
Normal	+/++	+
Low	+/++/+++	+/++

Syncope

Differential Diagnoses for Syncope and Episodic Weakness

From Fox P: Textbook of canine and feline cardiology: principles and practice, St Louis, 2000, Saunders, 447.

Primary Cardiac Causes

- Arrhythmias
- Obstruction to cardiac filling
- Obstruction of ventricular ejection

Hypotension

- Inadequate cardiac output (e.g., dilated cardiomyopathy)
- Inadequate vascular tone (e.g., vasodilators, b-blockers)
- Inadequate blood volume:
    - Blood loss:
        - Internal (e.g., splenic hemangiosarcoma, GI blood loss)
        - External (e.g., trauma)
    - Diuresis (e.g., furosemide)
    - Hypoadrenocorticism
    - Fluid loss (e.g., emesis, diarrhea)

Hypoxemia

- Respiratory failure
- Pulmonary thromboembolism

Abnormalities of Blood Constituents

- Hypoglycemia
- Hypokalemia
- Anemia
- Hepatoencephalopathy

Neurologic and Neuromuscular Disorders

- Epilepsy
- Structural CNS disorders:
    - Neoplasia
    - Cerebral arterial disease
    - Thromboembolism
- Narcolepsy
- Myasthenia gravis

Syncope, Disease Associations

With permission from Fox P: Textbook of canine and feline cardiology: principles and practice, St Louis, 2000, Saunders, p 451.

Cardiovascular Causes of Syncope and Breed Predispositions

Causes of Syncope	**Breed Predispositions**
Structural Heart Diseases	
Dilated cardiomyopathy	Doberman pinscher, boxer, cocker spaniel, giant-breed dogs
Chronic valvular disease	Small-breed dogs (middle-aged to geriatric)
Pulmonic stenosis	English bulldog, Samoyed, beagle, Chihuahua, cocker spaniel, others
Subaortic stenosis	Newfoundland, boxer, golden retriever, German shepherd, others
Right-to-left shunting congenital defects	English bulldog
Hypertrophic cardiomyopathy	Cats (Maine coon, Ragdoll, Sphynx, Himalayan)
Pericardial effusion	
Intracardiac mass lesions (neoplasia; thrombus)	German shepherd, golden retriever, others
Cardiac Arrhythmias	
Sick sinus syndrome	Miniature schnauzer, dachshund, West Highland white terrier, cocker spaniel
Advanced AV block	German shepherd, dachshund, pug, Doberman pinscher
Asystole	
Sinus bradycardia	
Supraventricular tachycardia	Labrador retriever
Ventricular tachycardia	German shepherd, boxer, Doberman pinscher, cocker spaniel
Cor Pulmonale	
Pulmonary embolism	
Pulmonary hypertension	
Heartworm disease	
Tussive “Cough Drop” Syncope	Small-breed dogs with combined cardiopulmonary disease
Vasovagal Syncope	Boxer, brachycephalic breeds?

Stunted Growth

Potential Causes of Small Stature in Dogs and Cats

From Feldman E, Nelson R: Canine and feline endocrinology and reproduction, ed 3, St Louis, 2004, Saunders.

Endocrine

- Hyposomatotropism
- Hypothyroidism
- Hyperadrenocorticism
- Hypoadrenocorticism
- Diabetes mellitus

Nonendocrine

- Malnutrition
- Gastrointestinal:
  - Maldigestion
  - Pancreatic exocrine insufficiency
  - Malabsorption
  - Heavy intestinal parasitism
- Hepatic:
  - Portosystemic vascular shunt
  - Glycogen storage disease
- Renal disease
- Cardiovascular disease (especially congenital heart defects)
- Skeletal dysplasia; chondrodystrophy
- Mucopolysaccharidosis
- Hydrocephalus

Storage Disorders

From Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 5, St Louis, 2000, Saunders.

CNS, Central nervous system; *DSH,* domestic shorthair; *PNS,* peripheral nervous system.

Lysosomal Storage Disorders

Species/Breed	Age of Onset	Duration	Signs/Pathologic Examination
Neuronal Disorders			
GM1 Gangliosidosis (Betagalactosidase Deficiency)			
Feline Siamese, Korat, mixed breeds	4-6 months	6-10 months	Ataxia, tremors, paresis, visual loss, seizures, behavioral changes; corneal and retinal lesions; CNS, liver, pancreatic acinar cells involved
Canine Beagle/mixed	2-4 months	4-6 months	Visual signs, tremors, dysmetria, paresis, behavioral changes; CNS, liver, kidney, spleen, lymph nodes
Canine German shorthaired pointers	6 months	18 months	Behavioral changes, seizures, ataxia, weakness, visual signs, coma; CNS
Feline DSH	4-10 weeks		Tremors, dysmetria, ataxia, paresis; dwarfism, corneal opacity; CNS, liver, endothelium, bone marrow, spleen, kidney
Sphingomyelin Lipidosis (Sphingomyelinase Deficiency)			
Feline Siamese, DSH	3-6 months	3-6 months	Stunted growth, ataxia, dysmetria, tremors; CNS, liver, lung, spleen, lymph nodes, kidney, bone marrow, adrenal gland
Sphingomyelin in Lipidosis (Glucocerebrosidase Deficiency)			
Canine Sidney silkie	7 months	1 month	CNS, liver
Mannosidosis (α-Mannosidase Deficiency)			
Neuronal Ceroid Lipofuscinosis			
Canine English setters	14-18 months	8-12 months	Visual, mental, behavioral changes, cerebellar signs, seizures; CNS, lymph nodes, salivary gland, prostate, kidney
Leukodystrophies: Globoid Cell			
Canine Cairn and West Highland white terriers, beagles, blue tick hound, poodles	11-30 weeks	2-3 months	Tremor, dysmetria, paresis, muscle atrophy, visual changes, mental changes
Feline			CNS, PNS
Metachromatic Leukodystrophy: Cavitating leukodystrophy			
Canine Dalmatians	3-6 months		Decreased vision, ataxia, paresis

Stomatitis

Modified from Slatter D: Textbook of small animal surgery, ed 3, Philadelphia, 2003, Saunders.

FeLV, Feline leukemia virus; *FIV,* feline immunodeficiency virus.

Causes of Stomatitis

Conditions associated with immune system depression or dysfunction	• Necrotizing ulcerative gingivostomatitis • Mycotic infections (commonly candidiasis) • Neutrophil dysfunction, gray collie syndrome, drug therapy, viral infection (e.g., FeLV)
Autoimmune disorders	• Vesiculobullous skin diseases (e.g., pemphigus and pemphigoid) • Systemic or discoid lupus erythematosus • Sjögren-like syndrome
Hypersensitivity	• Drug eruptions • Insect stings
Viral infections	• FeLV • FIV • Calicivirus
Miscellaneous conditions	• Eosinophilic granuloma complex • Feline chronic gingivostomatitis

Splenomegaly

Causes of Splenomegaly

Modified from Bonagura J: Kirk's current veterinary therapy XIII, St Louis, 2000, Saunders.

Generalized SplenomegalyInflammation

- Infectious
- Granulomatous condition

Neoplasia

- Primary:
  - Lymphoma
  - Mastocytosis
  - Histiocytosis
  - Leukemias (acute, chronic)
- Metastatic

Hyperplasia

- Extramedullary hematopoiesis

Amyloidosis

Congestion

- Pharmacologic:
  - Phenothiazine tranquilizer
  - Barbiturates
- Torsion of splenic pedicle:
  - Isolated
  - With gastric dilatation/ volvulus
- Portal vein/caudal vena cava hypertension:
  - Vascular anomaly
  - Congestive heart failure
  - Hepatic cirrhosis
  - Neoplasia

Localized SplenomegalyNeoplasia

- Hemangiosarcoma
- Hemangioma
- Lymphoma
- Leiomyosarcoma
- Fibrosarcoma
- Osteosarcoma

Other

- Hematoma
- Nodular hyperplasia
- Abscess

Splenic Diseases: Infectious

Infectious Causes of Splenomegaly/Splenitis*

*Infectious disease may affect the spleen directly or indirectly cause splenomegaly by causing chronic anemia, chronic antigen stimulation, or disturbances in blood flow (e.g., endotoxemia).

From Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

Viral Diseases

- FIP (C)
- FeLV (C)
- FIV (C)
- Infectious canine hepatitis (D)

Rickettsial and Mycoplasmal Diseases

- Ehrlichiosis (canine and feline)
- RMSF (*Rickettsia rickettsii*)
- Q fever (*Coxiella burnetii*)
- Hemotropic mycoplasmosis (*Mycoplasma haemofelis*)

Bacterial Infections

- Canine brucellosis
- Mycoplasmosis
- Florida borreliosis
- Plague
- Tularemia
- Streptococcosis
- Staphylococcosis
- Salmonellosis
- *Francisella* infection
- Endotoxemia

Fungal Diseases

- Cryptococcosis
- Histoplasmosis
- Blastomycosis

Protozoal Diseases

- Toxoplasmosis
- Cytauxzoonosis (C)
- Babesiosis (*Babesia canis* and *B. gibsoni*)
- Leishmaniasis (D)

C, Cats; *D*, dogs; *FeLV*, feline leukemia virus; *FIP*, feline infectious peritonitis; *FIV*, feline immunodeficiency virus; *RMSF*, Rocky Mountain spotted fever.

Shock

With permission from Fox P: Textbook of canine and feline cardiology: principles and practice, St Louis, 2000, Saunders, p 273.

Clinical Classification of Shock: Mechanism or Primary Cause

Shock Classification	Primary Mechanism	Examples
Cardiogenic	Poor ventricular contractility	Dilated cardiomyopathy
		Toxins/drugs
		Myocardial infarction
		Pericardial effusion/cardiac tamponade
Distributive	Vasomotor dysfunction	Arteriovenous shunting
		Hypotension (expanded venous capacitance)
		High or normal resistance
		Hypodynamic late septic shock
Hypoxemic	Lack of oxygen	Anemia
		Hypoxemia
Metabolic	Inability to utilize energy substrates	Sepsis
		Cyanide poisoning
		Heatstroke
		Hypoglycemia
Obstructive	Inadequate cardiac preload	Pericardial tamponade
		Restrictive pericarditis
		Intracardiac masses
Hypovolemic	Inadequate circulating blood volume	Dehydration (any cause)
		Hypoproteinemia
		Blood loss
Septic	Bacteremia	Sepsis
	Endotoxemia	

Serotonin Syndrome–Inducing Agents

From Crowell-Davis SL, Poggiagliolmi S: Understanding behavior: serotonin syndrome. Compend Contin Educ Vet 30:490–493, 2008 and Mohammad-Zadeh LF, Moses L, Gwaltney-Brant SM: Serotonin: a review. J Vet Pharmacol Ther 31:187–199, 2008.

Substances That Potentially May Cause Serotonin Syndrome

Agent	General Comments for Each Category of Agent
• *Foods or supplements:* • L-5-HTP, L-tryptophan, *Griffonia* seed extract • Aged cheese, chicken liver	• L-5-HTP is an OTC supplement used in humans for depression, insomnia; serotonin syndrome (SS) reported as a result of accidental ingestion in dogs. • Tyramine present in certain foods can interfere with MAO inhibitors' action and enhance their toxicity.
• *Medications that increase presynaptic release of serotonin:* • Amphetamine • Methylphenidate • Ecstasy (MDMA; 3,4 methylenedioxymethamphetamine) • Bromocriptine • l-dopa	• In addition to CNS excitation from amphetamine, signs of confusion, disorientation, hallucination, and rigidity may be due to SS. • Cyproheptadine, 1.1 mg/kg for dogs and 2-4 mg/cat PO or per rectum q 6-8 h, can be used for treating signs of SS; discontinue after 2-3 treatments if no relief. • Chlorpromazine and other phenothiazines possess some antiserotonin effects.
• *Presynaptic reuptake inhibitors, selective serotonin reuptake inhibitors (SSRIs), and tricyclic antidepressants:* • Fluoxetine • Bupropion • Duloxetine • Fentanyl • Pethidine • Paroxetine • Sertraline • Citalopram • Fluvoxamine • Amitriptyline • Clomipramine (Clomicalm) • Tramadol • Chlorpheniramine • Venlafaxine • Dextromethorphan • Meperidine	• SS is a clinical entity characterized by presence of some GI signs, CNS signs (hyperreflexia, tremors, rigidity, confusion, agitation, excitation, seizures), and mydriasis, tachycardia, hyperthermia. • SS can be seen with acute large overdose or with repeated therapeutic treatment. • Cyproheptadine, 1.1 mg/kg for dogs and 2-4 mg/cat PO or per rectum q 6-8 h, can be used for treating signs of SS; discontinue after 2-3 treatments if no relief. • Chlorpromazine and other phenothiazines possess some antiserotonin effects.
• *Serotonin metabolism inhibitors:* • Selegiline (MAO-B inhibitor; Anipryl) • Amitraz	• Selegiline recommended for use in dogs for cognitive dysfunction • Interaction likely when selegiline used concurrently with tricyclic antidepressants, amitraz, meperidine, and SSRIs
• *Serotonin agonists at postsynaptic membrane:* • Buspirone • Lithium • LSD (lysergic acid diethylamide)	

Seizures: Characteristics and Differentiation

Modified from Ettinger SJ, Feldman EC: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders, p 27.

Convulsive syncope (anoxic or anoxic-epileptic seizures) are syncopal events generally caused by cardiac arrhythmias that produce profound syncope, temporary cerebral hypoxia, and seizures. Therefore, clarification of the type of event observed by the owner (syncope versus seizure) may be difficult and generally rests on the observation of an episode, the presence of heart disease, and the documentation of a severe bradycardia or tachycardia during the event. Videotaping of an episode by the owner and cardiac event monitoring (pager-size portable electrocardiographic [ECG] unit that is triggered by the owner when an event occurs) can be invaluable in clarifying whether an animal is experiencing seizures versus syncope.

Seizures, Differentiation from Other Events

	Seizure (Grand Mal)	Seizure (Partial)	Syncope	Episodic Weakness	Narcolepsy/Cataplexy
Precipitating event	Usually none	Usually none	Exertion, pain, micturition, defecation, cough, stressful event	Exertion or none	Excitement, feeding
Prodrome	Minutes to days; atypical behavior (e.g., anxious, more withdrawn, attention-seeking) ± vomiting		Seconds; acute weakness, staggering, vocalization, autonomic stimulation	None (disorder is neuromuscular)	None
Aura	None	Marks onset of partial seizure	None	None	None
Event features	Chomping, hypersalivation, tonic-clonic limb motion; duration often 1-2 minutes; duration > 5 minutes is consistent with seizure and highly inconsistent with syncope	Localized signs	Motionlessness; flaccid or rigid extension of limbs; opisthotonos possible; no tonic-clonic activity; duration generally transient (<1 minute)	Gradual or sudden loss of muscle tone, causing recumbency; mentation and consciousness remain normal; no tonic-clonic activity	Instantaneous loss of muscle tone; animal is immobile (sleeping) but appears to be aware of its surroundings.
Recovery	Slowness returning to consciousness; disorientation (commonly 10 minutes or longer); blindness, circling, and other signs of central nervous system dysfunction common	Varies	Rapid recovery of normal mentation; often able to walk (and considered back to normal by owner) within minutes	Highly variable; generally reflective of course of onset (gradual onset associated with slow recovery); in some cases, rapid onset disorders may have a protracted course.	Fairly rapid (several seconds to 1 minute), with appearance of waking from sleep

Seizures: Causes Grouped According to Age

Prevalence of Common Seizure Disorders in Relation to Patient's Age at Time of Onset of First Seizure

Modified with permission from Braund KB: Clinical syndromes in veterinary neurology, St Louis, 1994, Mosby, p 242.

Age at Onset: Before 8 Months

Rare: **Idiopathic Epilepsy**
Mainly:

- Developmental disorders (e.g., malformations, hydrocephalus)
- Encephalitis or meningitis
- Trauma
- Extracranial causes:
    - Hepatic encephalopathy (e.g., portocaval shunt)
    - Hypoglycemia
    - Intoxications
    - Intestinal parasitism

Age at Onset: 8 Months to 4 Years

Mainly: **Idiopathic Epilepsy**
Seldom:

- Developmental disorders (e.g., malformations, hydrocephalus)
- Trauma
- Encephalitis or meningitis
- Acquired hydrocephalus
- Neoplasia
- Extracranial causes:
    - Hepatic encephalopathy (e.g., portacaval shunt, liver disease)
    - Hypocalcemia
    - Electrolyte disturbances
    - Hypothyroidism
    - Intoxications

Age at Onset: More Than 4 Years

Seldom:

- Idiopathic epilepsy
- Trauma
- Encephalitis or meningitis
- Acquired hydrocephalus
- Extracranial causes:
    - Hepatic encephalopathy (e.g., serious liver disease)
    - Hypocalcemia
    - Electrolyte disturbances
    - Hypothyroidism

Increasing:

- Neoplasia
- Degenerative disorders
- Vascular disorders
- Extracranial causes:
    - Hypoxia
    - Hypoglycemia

Seizures

Causes

Modified from de Lahunta A: Veterinary neuroanatomy and clinical neurology, St Louis, 1983, Saunders.

Extracranial

- Hypoglycemia:
  - Glycogen storage diseases
  - Beta-cell neoplasm of pancreas/insulinoma
  - Youth and malnutrition (especially small or toy breeds)
  - Youth and GI disease (especially small or toy breeds)
  - Insulin excess during treatment for diabetes mellitus
  - Intestinal leiomyosarcoma
- Hypoxemia:
  - Cardiorespiratory disease (e.g., severe bradycardia or severe tachycardia, disorders producing polycythemia)
- Hepatoencephalopathy
- Renal disease, especially nephrotic syndrome (embolism)
- Hypocalcemia
- Hyperkalemia
- Hyperlipoproteinemia
- GI disease:
  - Parasitism
  - “Garbage intoxication”
- Polycythemia:
  - Right-to-left shunt (e.g., reversed patent ductus arteriosus, tetralogy of Fallot, atrial or ventricular septal defect with concurrent pulmonic stenosis or pulmonary hypertension)
  - Renal neoplasm (erythropoietin-producing)
  - Chronic lung disease
  - Polycythemia vera

Intracranial

- Inflammation:
  - Canine distemper encephalitis, toxoplasmosis, cryptococcosis, neosporosis
  - Other viral encephalitides: rabies FIP meningoencephalitis in cats
- Neoplasia:
  - Primary or metastatic
- Malformation:
  - Hydrocephalus, lissencephaly-pachygyria
- Injury
- Degeneration:
  - Thiamine deficiency in cats
  - Cerebral infarction in cats
  - Intoxications: lead, mercury, arsenic, chlorinated hydrocarbons, organophosphates, hexachlorophene, ethylene glycol, radiopaque media for myelography, metaldehyde, tremorgenic mycotoxins (penitrem A, roquefortine), blue-green algae, chocolate, marijuana, ethanol/ methanol/fermented materials (e.g., bread dough), prescription human medications

Idiopathic Epilepsy

FIP, Feline infectious peritonitis; *GI*, gastrointestinal.

Seizures, Refractory or Poorly Controlled

Factors Responsible for Inadequate Control of Seizures

Modified with permission from Kirk RW, Bonagura JD, editors: Kirk's current veterinary therapy XI: small animal practice, St Louis, 1993, Saunders, p 986.

Medication and Dosage

- Improper choice of drug
- Insufficient drug dosage
- Delayed increase in dosage
- Inadequate increase in dosage
- Too rapid change of medication
- Too rapid reduction of dosage
- Excessive fluctuations in serum concentrations
- Inappropriately combined drugs
- Failure to monitor serum levels
- Noncompliance
- Drug-drug interactions

Other Precipitating Factors

- Additional medications
- Additional diseases
- Physical or psychological stress

Diagnostic Failures

- Extracerebral causes of seizures
- Progressive brain lesions
- Misidentification of episodes
- Syncope
- Myasthenia gravis
- Narcolepsy/cataplexy

Salter-Harris Fracture Classification

Modified from Piermattei D, Flo G: Brinker, Piermattei, and Flo's handbook of small animal orthopedics and fracture repair, ed 3, St Louis, 1997, Saunders.

Salter-Harris Classification of Separations or Fracture-Separations Involving a Growth Plate and the Adjacent Metaphysis and Epiphysis

Type of Fracture	Radiographic Findings	Principal Anatomic Region Involved
Type 1	Physeal separation, displacement of the epiphysis from the metaphysis at the growth plate	Proximal humerus and femur, distal femur
Type 2	Small corner of the metaphyseal bone fractured, with displacement of the epiphysis from the metaphysis at the growth plate	Distal femur and humerus, proximal humerus, proximal tibia
Type 3	Fracture through the epiphysis and part of the growth plate, with the metaphysis unaffected	Distal humerus
Type 4	Fracture through the epiphysis, growth plate, and metaphysis; several fracture lines possible	Distal femur, distal humerus
Type 5	Compression of the growth plate. Soft-tissue swelling but no bony abnormalities seen following the injury.	Distal ulna, distal radius, distal femur

Tracheal Neoplasia

Malignant Tumors of the Canine and Feline Trachea

Modified from Bonagura JD: Kirk's current veterinary therapy XIII, ed 13, 1999, Saunders, p 503.

- Lymphoma
- Squamous cell carcinoma
- Mast cell tumor
- Chondrosarcoma
- Adenocarcinoma
- Osteosarcoma
- Anaplastic carcinoma
- Leiomyoma

Toxicants, Radiopaque

Differential Diagnosis for Radiopaque Objects in the Gastrointestinal Tract

Name of Substance/Toxicant	Comments
Zinc	Pennies minted after 1987; zinc-coated wires, nuts, bolts, screws
Lead	Fishing sinkers, some curtain weights, slug shots, pet toys (some)
Cadmium	Batteries (metal poisoning unlikely)
Mercury	Uncommon occurrence; difficult to see, since mercury from a broken thermometer can evaporate
Iron	Multivitamin pills containing iron; helpful for determining if exposure has occurred or not
Bismuth subsalicylates and other bismuth salts	Pills containing bismuth salts; pills may resemble pennies on radiograph.
Copper	Pennies (outer coating); copper-containing metallic objects (systemic copper poisoning from copper objects not likely; could see gastrointestinal (GI) signs)
Enteric-coated pills (e.g., aspirin)	May help confirm exposure on plain radiograph
Paradichlorobenzene-type moth balls	Naphthalene types are not radiopaque.
Barium sulfate or other barium salts	Used for contrast radiography
Iodine crystals	Sometimes used for contrast studies
Some sustained-release or extended-release medications (e.g., tricyclic antidepressants, phenothiazines)	Ingestion of large amounts can be seen on the plain radiograph early on; this can help determine exposure.
Chloral hydrate	Crystals; no longer commonly used or available
Expandable polyurethane glue	Glues containing cyanates or isocyanates as active ingredients; glue can expand and cover entire stomach; glue not radiopaque but will be visible as a foreign-body object
Aluminum	Could see GI signs; systemic aluminum toxicosis from aluminum-containing products not likely
Nickel	U.S. coins (nickel, dime, quarter); could see GI signs; systemic nickel poisoning not expected
Calcium, magnesium, or aluminum-containing salts (antacids)	Antacid pills containing calcium carbonate, aluminum hydroxide, or magnesium hydroxide may be visible on radiograph early on.

Total Protein Elevation, Serum

Modified from Cowell R: Veterinary clinical pathology secrets, St Louis, 2004, Mosby, 56.

Inflammation

-

Infectious

- Bacterial (e.g., deep pyoderma)
- Viral (e.g., feline infectious peritonitis)
- Protozoal (e.g., leishmaniasis)
- Fungal (e.g., blastomycosis)
- Rickettsial (e.g., ehrlichiosis)

Noninfectious

- Neoplasia (especially if necrotic areas are present)
- Foreign-body granuloma
- Antigenic response (e.g., inflammatory bowel disease)

Paraneoplastic Protein Synthesis

- Multiple myeloma
- Lymphoma

Dehydration

- Hemoconcentration can elevate both albumin and globulin fractions.
- Dehydration/hemoconcentration is the only differential diagnosis to explain hyperalbuminemia.

Thyroid Hormone Alterations

From Nelson RW, Couto GC: Small animal internal medicine, ed 3, St Louis, 2003, Mosby.

T3, Triiodothyronine; *T4,* thyroxine; *TSH,* thyroid-stimulating hormone.*There is a direct correlation between the severity and systemic nature of illness and suppression of serum T4 and free T4 concentrations.

Variables That May Affect Baseline Serum Thyroid Hormone Function Test Results in Dogs

Age	Inversely proportional effect
Neonate (<3 months)	Increased T4
Aged (>6 years)	Decreased T4
Body size	Inversely proportional effect
Small (<10 kg)	Increased T4
Large (>30 kg)	Decreased T4
Breed:	
Sight hounds (e.g., greyhound)	T4 and free T4 lower than normal range established for dogs; no difference for TSH
Gender	No effect
Time of day	No effect
Weight gain/obesity	Increased
Weight loss/fasting	Decreased T4, no effect on free T4
Strenuous exercise	Increased T4, decreased TSH, no effect on free T4
Estrus (estrogen)	No effect on T4
Pregnancy (progesterone)	Increased T4
Surgery/anesthesia	Decreased T4
Concurrent illness*	Decreased T4 and free T4; depending on illness, TSH may increase, decrease, or not change
Drugs:	
Carprofen	Decreased T4, free T4, and TSH
Etodolac	No effect on T4, free T4, or TSH
Glucocorticoids	Decreased T4 and free T4; decreased or no effect on TSH
Furosemide	Decreased T4
Methimazole	Decreased T4 and free T4; increased TSH
Phenobarbital	Decreased T4 and free T4; delayed increase in TSH
Phenylbutazone	Decreased T4
Potassium bromide	No effect on T4, free T4, or TSH
Progestogens	Decreased T4
Propylthiouracil	Decreased T4 and free T4; increased TSH
Sulfonamides	Decreased T4 and free T4; increased TSH
Ipodate	Increased T4, decreased T3

Dietary iodine intake	If excessive, decreased T4, and free T4; increased TSH
Thyroid hormone autoantibodies	Increased or decreased T4; no effect on free T4 or TSH

Thromboembolism

Causes and Predisposing Factors of Thrombosis and Thromboembolism

From Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

Vascular Endothelial Damage	Hypercoagulability	Abnormal Blood Flow
• Arteriosclerosis • Atherosclerosis • Vasculitis • Heartworm disease • Catheterization • Injection of irritating substances • Neoplasia • Vascular incarceration/compression • Hyperhomocysteinemia • FIE • Fibrocartilaginous embolism	• Infection/sepsis/abscess • Neoplasia • Hyperadrenocorticism • PLN • PLE • DIC • Thrombocytosis • Platelet hyperreactivity • IHA • Parvovirus infection	• Neoplasia • Cardiomyopathy • CHF • Endocarditis • Hypovolemia • Shock • Anemia • Polycythemia • Dehydration • Hyperviscosity

CHF, Congestive heart failure; *DIC*, disseminated intravascular coagulation; *FIE*, feline ischemic encephalopathy; *IHA*, immune-mediated hemolytic anemia; *PLE*, protein-losing enteropathy; *PLN*, protein-losing nephropathy.

Third Eyelid (Nictitating Membrane) Abnormalities

Differential Diagnosis of Prominent Third Eyelid/Third Eyelid Protrusion, and Treatment Approaches

From Slatter D: Textbook of small animal surgery, ed 3, Philadelphia, 2003, Saunders.

Prominent Third Eyelid With Focal Abnormality

- Curled or scrolled leading edge: excise abnormal cartilage
- Pink, fleshy mass protruding between globe and third eyelid in a young dog (“cherry eye”): surgically reposition the gland
- Pink, fleshy mass protruding between globe and third eyelid in an old dog: possible neoplasia; biopsy or complete excision of third eyelid
- Mass within or on anterior surface of third eyelid: biopsy or local excision with or without adjunctive therapy; larger masses may require complete excision of third eyelid.

Generalized Enlargement of Third Eyelid

- Thickened and depigmented; may have corneal involvement (chronic superficial keratoconjunctivitis; “pannus”): conjunctival scraping or biopsy; treat with topical corticosteroids, cyclosporine.
- Thickened and inflamed with firm, fibrous nodules; cornea, episclera, and bulbar conjunctiva are also often involved: biopsy; treat on basis of breed and biopsy results (collie: nodular granulomatous episclerokeratitis; other breeds: ocular nodular fasciitis)
- Diffuse, generalized enlargement of third eyelid or gland of the third eyelid: aspiration or biopsy; lymphoma or other systemic neoplasia

Prominent Third Eyelid Only

- Nonpigmented leading edge: appears prominent but needs no therapy
- Secondary to pain: check for corneal ulcer, foreign body, or other source of ocular or intraocular pain.
- Horner's syndrome: look for other signs of miosis, ptosis, and enophthalmos; attempt to localize lesion and treat if needed.
- Secondary to orbital disease: enophthalmos may lead to passive protrusion or orbital mass; cellulitis or myositis may displace third eyelid, causing protrusion.
- Systemic disease, such as tetanus Nonpigmented leading edge/margin (seen congenitally as a normal variant): appears prominent but needs no therapy

Testicular Dimension Abnormalities

Diseases That Cause Change in Testicular Size

From Bonagura J: Kirk's current veterinary therapy XIII, St Louis, 2000, Saunders.

Large Testes	Small Testes
Neoplasia	Hypoplasia
Acute infection	Chronic inflammation
Testicular torsion	Cryptorchidism
Inguinoscrotal hernia	Degeneration
Sperm granuloma	Intersex

Tenesmus/Dyschezia

Causes

From Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

Colorectal Disease

- Constipation
- Colitis-proctitis:
  - Inflammatory bowel disease
  - *Histoplasma capsulatum* (histoplasmosis)
  - *Clostridium perfringens* (enterotoxicosis)
  - *Prototheca zopfii* (protothecosis)
- Rectal stricture
- Neoplasia: polyps
- Foreign material
- Irritable bowel syndrome

Perineal-Perianal Disease

- Anal sacculitis, impaction, or abscess
- Anal sac neoplasia
- Perianal fistula
- Perineal hernia

Urogenital Disease

- Cystitis-urethritis-vaginitis
- Obstructive material—urethral calculi, foreign body
- Prostatitis-prostatic abscess
- Parturition
- Neoplasia of the urethra, bladder, prostate, or vagina

Miscellaneous Causes

- Caudal abdominal cavity mass
- Pelvic fracture: neoplasia

Tachycardia

Differential Diagnosis for a Rapid Heart Rate

- Sinus tachycardia:
  - Excitement
  - Pain
  - Toxicosis (e.g., chocolate; digitalis; aminophylline/theophylline; pseudoephedrine, phenylpropanolamine, and related compounds)
  - Sepsis
  - Hypotension
  - Congestive heart failure
  - Systemic illness (e.g., hyperthyroidism, fever, anemia)
- Atrial flutter
- Atrial fibrillation
- Atrial/junctional tachycardias
- Preexcitation (Wolff-Parkinson-White syndrome, others)
- Ventricular tachycardia
- Ventricular flutter
- Torsade de pointes

Uveitis

Causes of Anterior Uveitis in Cats and Dogs

From Bonagura JD, Twedt DC, editors: Current veterinary therapy XIV, St Louis, 2009, Saunders. *C*, Cat; *D*, dog.

Systemic InfectionBacterial

- Bacteremia or septicemia (e.g., pyometra, abscess) (D, C)
- Brucellosis (D)
- Bartonellosis (D, C)
- Leptospirosis (D)
- Borreliosis (Lyme disease) (D)

Rickettsial

- Ehrlichiosis (D, C)
- Rocky Mountain spotted fever (D)

Viral

- Canine adenovirus 1 (D)
- Feline leukemia virus (C)
- Feline immunodeficiency virus (C)
- Feline infectious peritonitis (C)

Mycotic

- Blastomycosis (D, C)
- Histoplasmosis (D, C)
- Coccidiomycosis (D, C)
- Cryptomycosis (D, C)
- Aspergillosis (D)

Algal

- Protothecosis (D)

Parasitic

- Aberrant nematode larval migration
- *Toxocara* (ocular larval migrans) (D, C)
- *Dirofilaria* larvae (D)
- Others

Protozoan

- Toxoplasmosis (D, C)—primarily cats
- Leishmaniasis (D, C)

Immune Mediated

- Lens-induced uveitis (D, C)
- Canine adenovirus vaccine (CAV-1 or CAV-2) reaction (D)
- Uveodermatologic syndrome (D)—primarily Akita and Arctic breeds of dogs
- Pigmentary uveitis (D) primarily golden retrievers
- Idiopathic anterior uveitis (D, C)

Neoplasia

- Primary (D, C)
- Metastatic—lymphoma most common (D, C)

Metabolic

- Diabetes mellitus—primarily through cataract and lens-induced uveitis (D)
- Hyperlipidemia (D)

Trauma

- Blunt or sharp trauma to the globe

Miscellaneous Causes of Blood-Eye Barrier Disruption

- Hyperviscosity syndrome (D, C)
- Hypertension (D, C)
- Scleritis (D)
- Ulcerative keratitis (D, C)

Uroliths

From Slatter D: Textbook of small animal surgery, ed 3, Philadelphia, 2003, Saunders.

*Not observed as a primary mineral in cats.

Radiographic Characteristics of Common Uroliths

Mineral Type	Degree of Radiopacity	Shape
Cystine	+ to ++	Smooth, usually small, round to oval
Calcium oxalate dihydrate	++++	Often rough, round to oval (occasionally jackstone)
Calcium oxalate monohydrate	+++	Often smooth, round (occasionally jackstone)
Struvite	+ to ++++	Smooth, round or faceted; sometimes assumes shape of renal pelvis, ureter, bladder, or urethra; sometimes laminated
Calcium phosphate	++++	Smooth, round or faceted
Ammonium urate and uric acid	0 to ++	Smooth but occasionally irregular; round or oval
Silica*	++ to ++++	Typically jackstone
Mixed and compound	+ to ++++	Varies with composition; may have detectable nucleus and shell
Matrix	0 to +	Usually round but may be influenced by location

Urinary Tract Infections, Recurrent and Persistent

Modified from Willard M, Tvedten H: Small animal clinical diagnosis by laboratory methods, ed 4, St Louis, 2004, Saunders.

C&S, Culture and sensitivity; *PU/PD,* polyuria and polydipsia; *UTI,* urinary tract infection; *WBC,* white blood cell.

Underlying Causes of a Recurrent or Persistent Urinary Tract Infection

Cause	Means of Diagnosis
Lack of owner compliance in drug administration	History (count remaining doses of medication)
Upper UTI	Abdominal ultrasound showing dilated renal pelvis, culture urine from renal pelvis, urinalysis demonstrating WBC casts
Calculi	Survey and/or contrast radiographs, ultrasonography, cystoscopy
Prostatitis	Rectal palpation, ejaculate cytologic examination and culture, prostatic aspirate, prostatic biopsy, ultrasonography
Neoplasm	Rectal palpation, vaginal palpation, cytologic examination of urine sediment, contrast radiographs, biopsy, ultrasonography, urethrocystoscopy
Diverticulum	Positive-contrast radiographs
Granuloma	Contrast radiographs, urethrocystoscopy, biopsy
Urinary incontinence or urine retention due to any cause	History, physical examination, determination of residual urine volume
Decreased resistance to infection	History, physical exam, medical evaluation to detect hyperadrenocorticism, diabetes mellitus, retroviral infection in cats, or other causes of immune compromise
Incorrect antibiotic selection	Urine C&S
Urinary catheterization	History, physical examination
Antibiotic resistance	Urine C&S
Foreign body	Ultrasound, cystoscopy
PU/PD (severe): antibiotic fails to attain adequate concentration in urine	Measure water intake; urinalysis
Vaginal or preputial conformational abnormalities (common, and commonly overlooked)	Physical exam

Urinary Crystals

Modified from Willard M, Tvedten H: Small animal clinical diagnosis by laboratory methods, ed 4, St Louis, 2004, Saunders.

Note: See for composite diagram of crystals found in urinary sediment.

Name	Description	Significance
Struvite (magnesium ammonium phosphate)	Colorless prisms with three to six sides (coffin lid)	Common in mildly acidic to alkaline urine in normal dogs and cats; may be associated with struvite calculi and infection with urease-producing bacteria
Calcium oxalate (monohydrate)	Dumbbells or small spindles	May be normal (especially if delay in analysis after urine collection) or due to ethylene glycol intoxication; may be associated with oxalate calculi
Calcium oxalate (dihydrate)	Colorless envelopes or small stars	May be normal (especially if delay in analysis after urine collection) or due to ethylene glycol intoxication; may be associated with oxalate calculi
Calcium phosphate	Prisms (long) or amorphous	May be normal or associated with calculi
Ammonium urate	Yellow-brown “thorn apples”	Normal in dalmatians and English bulldogs; associated with hepatic insufficiency and portosystemic shunts; may be associated with urate calculi
Uric acid	Yellow to yellow-brown prisms, diamonds, or rosettes	Same as ammonium urate
Bilirubin	Golden yellow to brown needles or granules	May be present in normal dogs with concentrated urine or may be due to bilirubinuria
Cystine	Colorless, flat hexagonal plates	Due to cystinuria; may be associated with calculi
Cholesterol	Colorless flat, notched plates	May be found in normal dogs and cats
Hippuric acid	Prisms (four to six sides with rounded corners)	Uncertain; have been confused with calcium oxalate monohydrate crystals
Sulfonamide	Clear to brown eccentrically bound needles in sheaves	Associated with sulfonamide administration

Upper Respiratory Infection, Feline

Adapted from Gaskell RM, Bennett M: Feline and canine infectious diseases. Oxford, 1996, Blackwell Science, p 8.

Blackwell Science *Bb, Bordetella bronchiseptica* infection; *FCh, Chlamydophila felis* (formerly *Chlamydia psittaci*) infection; *FCV,* feline calicivirus infection; *FVR,* feline viral rhinotracheitis (feline herpesvirus infection; (+), uncommon but may occur; ±, lesions may be present but are not usually seen clinically.*Strain variation.†Often persistent.‡Slight wetness may be seen around the mouth if ulcers present.

Essential Clinical Features of Respiratory Disease Related to Pathogen Involved

Feature	FVR	FCV*	FCh	Bb
Lethargy	+++	+	+	+
Sneezing	+++	+	+	++
Conjunctivitis	++	++	+++†	–
Hypersalivation	++	–‡	–	–
Ocular discharge	+++	++	+++	(+)
Nasal discharge	+++	++	+	++
Oral ulceration	+	+++	–	–
Keratitis	+	–	–	–
Coughing	(+)	–	–	++
Pneumonia	(+)	+	±	+
Lameness	–	++	–	–

Ulcers and Erosions (Cutaneous), Distribution

Distribution of Ulcers and Erosions as a Diagnostic Clue

Modified from Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

Axillary/Inguinal

- Fungal (*Malassezia pachydermatis*, *Candida* spp.) (D)
- Vesicular cutaneous lupus erythematosus (D)
- Intertrigo (D)
- Urine scald (D)

Focal/Multifocal

- Calcinosis cutis (D)
- Demodicosis (D)
- Eosinophilic plaque (C)
- Indolent ulcer (C)
- Intertrigo (D)
- Neoplasia (D, C)
- Pyoderma (principally pyotraumatic dermatitis or folliculitis) (D)
- Systemic/subcutaneous mycosis (D, C)

Facial

- Arthropod bites (D, C)
- Bullous pemphigoid (D, C)
- Deep pyoderma (D)
- Demodicosis (D)
- Dermatomyositis (D)
- Discoid lupus erythematosus (D)
- Linear immunoglobulin A (IgA) bullous disease (D)
- Pemphigus foliaceus/erythematosus (D, C)
- Solar injury (D, C)
- Squamous cell carcinoma (C)
- Systemic/subcutaneous mycosis (D, C)
- Uveodermatologic syndrome (D)

Mucocutaneous

- Bacteria (aerobic/anaerobic) (D, C)
- Bullous pemphigoid (D, C)
- Bullous systemic lupus type 1
- Epidermolysis bullosa acquisita (D)
- Epitheliotropic lymphoma (D)
- Fungal (*M. pachydermatis*, *Candida* spp.) (D)
- Mucocutaneous pyoderma (D)
- Mucocutaneous pemphigoid (D)
- Pemphigus vulgaris (D)
- Toxic epidermal necrosis/erythema multiforme (D, C)
- Uremia (D, C)
- Viral infection (calicivirus/herpesvirus) (C)

Generalized/Extensive

- Bullous pemphigoid (D)
- Deep pyoderma (D)
- Demodicosis (D)
- Drug reaction (D, C)

- Epitheliotropic lymphoma (D)
- *Malassezia* dermatitis (D)
- Pemphigus group (D, C)
- Thermal injury (D, C)
- Toxic epidermal necrolysis/erythema multiforme (D, C)

C, Cat; *D,* dog.

Ulcerative/Erosive Skin Lesions

Differential Diagnosis of Ulcers and Erosions Affecting Skin and Mucous Membranes

Modified from Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

Canine Diseases

Infectious

Bacterial pyoderma:

- Surface:
  - Acute moist dermatitis (pyotraumatic dermatitis)
  - Intertrigo
- Deep:
  - Folliculitis/furunculosis (including pyotraumatic folliculitis)
  - Oral bacterial infections (aerobic/anaerobic)
- Fungal:
  - Yeast infections (*Malassezia pachydermatis*, *Candida* spp.)
  - Systemic/subcutaneous
- Parasitic:
  - Demodicosis

Metabolic

Calcinosis cutis (hyperadrenocorticism)

Uremia/renal failure

Necrolytic migratory erythema/metabolic epidermal necrosis/hepatocutaneous syndrome

Neoplastic

Epitheliotropic lymphoma

Squamous cell carcinoma

Physical, Chemical

Drug reactions

Solar injury

Thermal injury (freeze or burn)

Urine scald

Immune Mediated/Autoimmune

Discoid lupus erythematosus

Vesicular cutaneous lupus erythematosus

Pemphigus group

Uveodermatologic syndrome

Miscellaneous autoimmune subepidermal vesiculobullous diseases:

- Bullous pemphigoid
- Epidermolysis bullosa acquisita

- Linear immunoglobulin A (IgA) bullous disease
- Mucocutaneous pemphigoid
- Bullous systemic lupus type 1

Miscellaneous

Arthropod bites

Dermatomyositis

Dystrophic epidermolysis bullosa

Junctional epidermolysis bullosa

Toxic epidermal necrolysis/erythema multiforme

Acral mutilation syndrome (French spaniel, German and English pointers)

Cutaneous asthenia (Ehlers-Danlos syndrome)

Feline Diseases

Infectious

Viral:

- Calicivirus and herpesvirus

Bacterial:

- Atypical mycobacteriosis

Fungal:

- Subcutaneous mycoses (e.g., sporotrichosis)
- Systemic mycoses (e.g., cryptococcosis)

Metabolic

Uremia/renal disease

Neoplastic

Fibrosarcoma

Lymphoma

Squamous cell carcinoma

Physical/Chemical

Drug reactions

Thermal injury (burn or frostbite)

Immune Mediated/Autoimmune

Bullous pemphigoid

Pemphigus foliaceus

Toxic epidermal necrolysis/erythema multiforme

Miscellaneous/Idiopathic

Arthropod bites

Dystrophic epidermolysis bullosa

Eosinophilic plaque

Idiopathic ulceration of dorsal neck

Indolent ulcer

Junctional epidermolysis bullosa

Skin fragility syndrome

Cutaneous asthenia (Ehlers-Danlos syndrome)

Vulvar Discharge

Modified from Willard M, Tvedten H: Small animal clinical diagnosis by laboratory methods, ed 4, St Louis, 2004, Saunders.

Hemorrhagic

- ***With Mainly Superficial (Mature)***
- ***Epithelial Cells***
- Normal proestrus, estrus, or early diestrus
- Ovarian remnant
- Ovarian pathologic condition (i.e., cystic follicles, functional ovarian tumor)
- Exogenous estrogen

Without Superficial (Mature)

- ***Epithelial Cells***
- Normal lochia
- Subinvoluted placental sites
- Vaginal laceration
- Neoplasia of vagina or uterus
- Uterine torsion
- Bleeding disorder

Mucoid

- Normal:
  - Lochia
  - Late pregnancy
  - Luteal phase (diestrus)
- Androgenic stimulation:
  - Endogenous (intersex)
  - Exogenous (mibolerone, testosterone)
- Cervicitis
- Mucometra
- Idiopathic (?)

Vomiting

Common Causes

From Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders. *NSAIDs*, Nonsteroidal antiinflammatory drugs.

Metabolic/Endocrine Disorders

- Uremia
- Hypoadrenocorticism
- Diabetes mellitus
- Hyperthyroidism
- Hepatic disease
- Endotoxemia/septicemia
- Electrolyte disorders
- Acid-base disorders

Intoxicants

- Lead
- Ethylene glycol
- Zinc
- Strychnine

Drugs

- Cardiac glycosides
- Erythromycin
- Chemotherapy agents
- Apomorphine
- Xylazine
- Medetomidine
- Penicillamine
- Tetracycline
- NSAIDs

Abdominal Disorders

- Pancreatitis
- Peritonitis
- Neoplasia

Dietary Causes

- Indiscretions
- Intolerances
- Allergy

Gastric Disorders

- Gastritis
- *Helicobacter* infection
- Parasites
- Ulceration
- Neoplasia
- Foreign bodies
- Dilatation/volvulus
- Hiatal hernia
- Obstruction

- Motility disorders

Disorders of the Small Intestine

- Inflammatory bowel disease
- Neoplasia
- Foreign body
- Intussusception
- Parasites
- Parvovirus
- Bacterial overgrowth

Disorders of the Large Intestine

- Colitis
- Obstipation
- Parasites

Vomiting, Chronic

Major Causes

Modified from Willard M, Tvedten H: Small animal clinical diagnosis by laboratory methods, ed 4, St Louis, 2004, Saunders.

Obstructive Disease

- Foreign objects (especially common)
- Intussusception
- Neoplasia (gastric or intestinal)
- Pyloric stenosis
- Gastric antral mucosal hyperplasia
- Inflammatory infiltrates (gastric or intestinal)
- Chronic partial gastric volvulus
- Idiopathic hypomotility of stomach/intestines (physiologic obstruction; rare)
- Congenital structural abnormalities (rare)

Inflammatory Disease

- Inflammatory bowel disease (common)
- Pancreatitis (common)
- Chronic gastritis
- GI ulceration/erosion
- Peritonitis (sterile or septic)
- Pharyngitis (caused by upper respiratory virus in cats)
- Parasites (e.g., *Physaloptera*)

Systemic*

- Hepatic disease/insufficiency
- Hypoadrenocorticism
- Diabetic ketoacidosis
- Uremia
- Hypercalcemia
- Cholecystitis
- Pyometra

Miscellaneous Causes

- Feline hyperthyroidism (common)
- Feline heartworm disease (variable)
- CNS disease (e.g., limbic epilepsy, tumor, encephalitis, or increased intracranial pressure; rare)
- Psychotic or behavioral changes (rare)
- Early CHF (questionable)
- *CHF,* Congestive heart failure; *CNS,* central nervous system; *GI,* gastrointestinal.

Vomiting, Acute

Major Causes

From Willard M, Tvedten H: Small animal clinical diagnosis by laboratory methods, ed 4, St Louis, 2004, Saunders.

Common

- Eating inappropriate or spoiled foods
- Motion sickness
- Postoperative nausea
- Acute gastritis-enteritis (various viral or bacterial agents or toxins):
    - Parvoviral enteritis (dogs and cats)
    - Hemorrhagic gastroenteritis
    - Parasites

GI Obstruction

- Obstructing foreign body
- Linear foreign body
- Intussusception

Dietary Indiscretion

- Overeating
- Eating inappropriate or spoiled foods

Acute Pancreatitis

-

Drug Administration

- Adriamycin
- Chloramphenicol
- Cisplatin
- Cyclophosphamide
- Digitalis
- Erythromycin
- Narcotics
- Nitrofurantoin
- Tetracycline
- Theophylline
- Xylazine

Intoxications

- Ethylene glycol
- Herbicides
- Organophosphates
- Strychnine
- *GI,* Gastrointestinal.

Vestibular Disease: Central Versus Peripheral

Modified with permission from Braund KG: Clinical syndromes in veterinary neurology, St Louis, 1994, Mosby, p 65.

	Central Vestibular Disease	Peripheral Vestibular Disease
Loss of balance	Yes	Yes
Head tilt	Yes	Yes
Falling/rolling	Yes (greater tendency to roll)	Yes
Nystagmus	Yes	Yes
Horizontal	Yes	Yes
Rotatory	Yes	Yes
Vertical	Yes	No
Positional	Yes	No
Strabismus (ventrolateral)	Yes	Yes
Cranial nerve deficits	Possible I-XII, especially V, VI, VII	Possible VII
Horner's syndrome	No	Possible
Cerebellar signs	Possible	No
Mental depression	Possible	No
Hemiparesis with ipsilateral postural reaction deficits	Possible	No

Vascular Disorders

Peripheral Vascular Diseases

From Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

Diseases of Arteries and ArteriolesOcclusive Diseases

- Arterial embolism
- Arterial thrombosis
- Angiitis, vasculitis
- Vasospasm, traumatic, toxic
- Diabetic arteriopathy

Nonocclusive Diseases

- Arteriovenous (AV) fistula
- Arterial aneurysm
- Arterial calcification
- Arteriosclerosis, hyalinosis, amyloidosis
- Atherosclerosis
- Vasculitis

Diseases of Veins

- Phlebectasia
- Varicosis
- Phlebitis and thrombophlebitis
- Venous thrombosis
- Venous malformations

Diseases of Lymphatics

- Lymphangitis
- Lymphedema
- Lymphangiectasia
- Lymphatic hypoplasia, aplasia, hyperplasia
- Lymphangioma, lymphocysts
- Lymphangiosarcoma

Tumors of Peripheral Blood Vessels

- Angioma, hemangioma, hemangiosarcoma

Vaccine Failure

Causes

From Greene C: Infectious diseases of the dog and cat, ed 2, St Louis, 1999, Saunders. γ, Uncertain.

Host Factors	Vaccine Factors	Human Error
• Primary immunodeficiencies • Maternal antibody interference • Age: very young or very old • Pregnancy • Stress, concurrent illness • Pyrexia, hypothermia • Incubating disease at time of vaccination • Drugs: cytotoxic, glucocorticoids • Anesthesia? • Hormonal fluctuations • General debilitation, malnutrition	• Rendered noninfectious during handling • Improper storage • Vaccines not protecting 100% of population (biological variation) • Disinfectant used on needles and syringes • Wrong strain • Excessive attenuation • Overwhelming exposure	• Improper mixing of products • Exposed at time of vaccination • Concurrent use of antimicrobials or immunosuppressive drugs • Simultaneous use of antisera • Too frequent administration (<2-week interval) • Disinfection of skin? • Wrong route of administration • Delay between vaccines in initial series • Omission of booster vaccination

Weight Loss

Diagnostic Considerations for Animals With Marked, Unintended Weight Loss

Modified from Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders.

Dietary History: Inadequate Diet

- Starvation
- Underfeeding
- Poor-quality food

Dietary History: Adequate Diet

- Environmental/housing factors:
  - Competition for food from other pets
  - Limited access to food
- Oral and dental disease
- Impaired use of nutrients:
  - Specific nutrient deficiency
  - Maldigestion of any cause
  - Malabsorption of any cause
  - Diabetes mellitus
  - Protein-losing disease:
    - Nephropathy
    - Gastroenteropathy
  - Cardiac disease*
- Elevated metabolism:
  - Hyperthyroidism
  - Chronic fever of any cause*
- End-stage chronic kidney disease*
- Neoplasia*
- Chronic infection*
- Chronic inflammation of any cause (e.g., immunologic disease*)

Weakness

Major Causes

Modified from Ettinger S, Feldman E: Textbook of veterinary internal medicine, ed 5, St Louis, 2000, Saunders.

- Anemia
- Abdominal effusion
- Cardiovascular
- Chronic inflammation/infections
- Chronic wasting diseases
- Drug related
- Electrolyte disorders
- Endocrine disorders
- Fever
- Metabolic dysfunction states
- Neoplasia
- Neurologic disorders
- Neuromuscular/polyneuropathies
- Nutritional disorders
- Overactivity
- Psychological disorders
- Pulmonary diseases
- Skeletal diseases

Zoonotic Diseases

Zoonoses: Diseases for Which Immunocompromised People Are at Increased Risk, and Routes of Disease Transmission

With permission from Greene C: Infectious diseases of the dog and cat, ed 2, St Louis, 1999, Saunders, p 711.

Direct Zoonoses from Pets*

- Bite, saliva: rabies, pasteurellosis, capnocytophagiosis, helicobacteriosis
- Scratch, contact: dermatophytosis, bartonellosis
- Inhaled, aerosols: plague (cat), tularemia, bordetellosis
- Feces: toxoplasmosis, cryptosporidiosis, campylobacteriosis, helicobacteriosis, salmonellosis, giardiasis, ancylostomiasis, toxocariasis
- Urine: brucellosis (dog), leptospirosis (dog)
- Transport of insect vector: bartonellosis, tularemia, plague, RMSF, dipylidiasis
- Other animal hosts: *Rhodococcus equi* infection (horse), *Mycobacterium marinum* infection (fish), psittacosis (birds), salmonellosis (reptiles and amphibians)

Environmentally Acquired Zoonoses

- Saprophytic: pneumocystosis, microsporidiosis, *Mycobacterium avium*–complex infection, cryptococcosis, coccidioidomycosis, histoplasmosis, blastomycosis, aspergillosis
- Vector acquired: ehrlichiosis, borreliosis, babesiosis, plague, RMSF, tularemia, bartonellosis

RMSF, Rocky Mountain spotted fever.

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RMSF, Rocky Mountain spotted fever.

Aspergillus spp. Serology

DEFINITION

Specific tests may detect either antibodies to *Aspergillus* spp. (by ELISA, agarose gel immunodiffusion [AGID], or counterimmunoelectrophoresis) or the presence of *Aspergillus* antigen (ELISA) in the serum.

PHYSIOLOGY

Aspergillus spp. are common environmental fungi (saprophytes) and opportunistic pathogens. Nasal aspergillosis characterized by nasal discharge, ulceration of nares, and facial pain is the most common manifestation of disease. Infection is more common in dogs than cats. Disseminated aspergillosis also occurs in dogs (most commonly German shepherd dogs, see pp. 96 and 1335).

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS:

- Antibody tests: presence of antibodies indicates exposure, but not necessarily active infection.
- Antigen: presence of serum antigen indicates systemic infection or, at the very least, colonization of skin or mucosal surfaces.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: False-positive and false-negative test results can occur with all tests for aspergillosis (including culture, Cytologie analysis, and histopathologic analysis). No single test is diagnostic. Nasal radiography or CT showing turbinate destruction and increased areas of radiolucency, and rhinoscopy for direct visualization and to obtain specimens for analysis (Cytologie, histopathologic, or microbiological) are the most informative tests.

SPECIMEN AND PROCESSING CONSIDERATIONS

IMPORTANT INTERSPECIES DIFFERENCES: Serologie tests often use species-specific antibodies. Confirm with the lab that the specific test being used is valid for the animal species in question.

SPECIMEN: Serum (red-top tube), refrigerated

RELATIVE COST: Fungal serology, $$$; fungal culture, $$; biopsy or cytology (one site), $$

PEARLS

- *Penicillium* spp. is another genus of fungus that can cause nasal disease in dogs. The organisms appear similar and can only be differentiated via culture or serologic testing, not Cytologie appearance. Serologic tests that detect antibody to either antigen are preferred.
- Both *Penicillium* spp. and *Aspergillus* spp. are ubiquitous in the environment. Positive culture results of blindly obtained specimens or nasal discharge, without cytologic/histologic evidence of inflammation and tissue invasion, may represent only contamination. Conversely, the fungal plaques are localized and blind biopsy/cytology collection often shows only nonspecific inflammation if the fungal plaques are missed. Rhinoscopy-guided collection of tissue samples is most likely to yield a positive diagnosis.

AUTHOR: LOIS ROTH-JOHNSON

1ST EDITION AUTHOR: JAMES H. MEINKOTH

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Antithrombin III (ATIII)

DEFINITION

Endogenous anticoagulant. Major plasma inhibitor of serine protease factors of the coagulation cascade (factors XII, XI, X, and IX; thrombin and plasmin).

SYNONYMS

Antithrombin, heparin cofactor

TYPICAL NORMAL RANGE

Dogs: 75%-120%. Cats: 75%-110%. Measured as a percentage of species-specific pooled samples.

PHYSIOLOGY

Synthesized in liver and endothelial cells; ATIII (with the help of heparin) binds to thrombin, preventing conversion of fibrinogen to fibrin; ATIII forms a 1:1 complex with thrombin (and other serine proteases). Heparin functions as an anticoagulant by accelerating the reaction that alters the configuration of ATIII (potentiates ATIII), increasing the rate of complex formation. Complex is cleared by hepatocytes.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Exogenous cortisol administration, inflammation (as part of positive acute-phase response)

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Increased ATIII is not clinically significant.

CAUSES OF ABNORMALLY LOW LEVELS: Decreased production (hepatopathy, portosystemic shunts), increased loss (protein-losing nephropathy, glomerulonephritis, renal amyloidosis, protein-losing enteropathy), increased hepatic clearance of ATIII enzyme complexes (disseminated intravascular coagulation [DIC])

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Assess other aspects of the coagulation cascade (activated partial thromboplastin time and prothrombin time), platelet count, fibrinogen level, d-dimers, and fibrin degradation products. A procoagulant state may exist because of low ATIII levels alone or in conjunction with other disorders (e.g., DIC).

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Exogenous cortisol administration has been associated with mild to moderate increases in ATIII in dogs (dogs with hyperadrenocorticism have decreased levels, perhaps secondary to the associated changes in the liver, which may explain the association of hyperadrenocorticism with thromboembolic disease).

LAB ARTIFACTS THAT MAY INTERFERE: Age: Lower levels of ATIII have been reported in young animals. Assay differences: ATIII may be overestimated in certain thrombin chromogenic assays (heparin cofactor II activity in addition to ATIII is detected).

SPECIMEN: Citrate (blue-top tube), separate plasma and transfer to plastic tube; freeze (store at 0°C-4°C).

RELATIVE COST: $$

PEARLS

Patients with DIC, thrombosis, or nephrotic syndrome will commonly have decreased levels. If the ATIII activity is <70% of the control, the animal likely will be unresponsive to heparin treatment; ATIII replacement therapy is required for heparin to be effective in such cases.

AUTHOR: DEBORAH G. DAVIS

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Antinuclear Antibody (ANA)

DEFINITION

Indirect immunofluorescent antibody (IFA) test to detect antibodies specific for DNA, RNA, and nucleoprotein

TYPICAL NORMAL RANGE

Reported as negative or positive; positive results will have a titer and pattern associated with it (homogeneous nuclear, speckled nuclear, nuclear rim, or nucleolar).

PHYSIOLOGY

Antinuclear antibodies are associated with autoimmune disorders, most prominently systemic lupus erythematosus (SLE).

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: SLE, some bacterial and protozoal infections

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Assess for other systemic signs consistent with SLE, rule out other infections.

SPECIMEN AND PROCESSING CONSIDERATIONS

IMPORTANT INTERSPECIES DIFFERENCES: Requires use of species-specific fluorescent antibody

DRUG EFFECTS ON LEVELS:

- Decreased or false-negative titers: cytotoxic drugs, high doses of corticosteroids
- False-positive tests: sulfonamides, tetracycline, hydralazine, procainamide, griseofulvin. False positive tests are also reported in cats treated with propylthiouracil, methimazole.

SPECIMEN: Serum (red-top tube). Store at 2°C-8°C (refrigeration).

RELATIVE COST: $$

PEARLS

- Significance of pattern in domestic animals is unclear.
- Positive ANA titers support a clinical diagnosis of SLE in dogs but are not specific.
- Low positive titers can be seen with various diseases and in older animals.
- ANA titer is much more sensitive (better screening test) for SLE than the LE prep.

AUTHOR: LOIS ROTH-JOHNSON

1ST EDITION AUTHOR: FONZIE QUANCE-FITCH

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Anion Gap

DEFINITION

Calculated value using the formula [(Na^+ + K^+) − (Cl^- + HCO^-3)]. Represents the negatively charged atoms and molecules in the bloodstream that are not measured by the analysis of these four ions.

TYPICAL NORMAL RANGE

Dogs and cats: approximately 5-15 mEq/L (mEq/L = mmol/L)

PHYSIOLOGY

The total of positive and negative charges in the blood must be equal. Routine serum biochemistry profile measures only some cations and anions. “Unmeasured anions” (e.g., lactate, charges on proteins) and “unmeasured cations” (e.g., magnesium, calcium) exist. *Unmeasured* refers to anything other than the four ions included in the anion-gap formula. Measured cations (Na^+, K^+) normally exceed measured anions (Cl^-, $HCO3^-$) by about 5-15 mEq/L. Because total positive and negative charges must be equal, unmeasured anions must outnumber unmeasured cations by that same amount. In health, excess unmeasured anions are mostly charges on proteins. An increased anion gap indicates an increase in unmeasured anions, usually resulting from organic acid (e.g., lactic acid) accumulation.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Conditions usually causing metabolic acidosis, most commonly lactic acidosis, uremia, ketoacidosis, ethylene glycol toxicosis

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Review history for ethylene glycol exposure. Evaluate serum biochemistry profile for azotemia, diabetes mellitus. Collect urine for specific gravity, ketone measurement, examination for calcium oxalate monohydrate crystals.

CAUSES OF ABNORMALLY LOW LEVELS: Decreases not usually associated with specific conditions and are not clinically relevant. May occur with hypoalbuminemia.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Potassium bromide may falsely increase serum chloride measurement, decreasing the anion gap and often producing a negative number.

LAB ARTIFACTS THAT MAY INTERFERE: Anything interfering with the measurement of the ions included in the anion-gap calculation will alter the anion-gap value (e.g., lipemia, hemolysis).

SPECIMEN: Serum (red-top tube) for routine chemistry/electrolyte profile

RELATIVE COST: $$

PEARLS

- The anion gap is commonly used for differentiating between bicarbonate loss (normal anion gap) and organic acid accumulation (high anion gap) in patients with metabolic acidosis.
- In mixed acid-base disorders, an animal may have metabolic acidosis, but the pH may be in the normal or alkaline range because of competing factors. In this situation, a high anion gap helps identify “occult” acidosis.

AUTHOR: LOIS ROTH-JOHNSON

1ST EDITION AUTHOR: JAMES H. MEINKOTH

Pricing Information

$: <$20

$$: $21-75
$$$: $76-150
$$$$: >$150

Anemia, Regenerative

DEFINITION

Anemia characterized by polychromasia or reticulocytosis; may be accompanied by basophilic stippling, Howell-Jolly bodies, and nucleated red blood cells (normoblastemia)

SYNONYM

Responsive anemia

TYPICAL NORMAL RANGE

Anemias with absolute reticulocyte count (percent reticulocyte x red blood cell count/µL) of >50,000/µL (cats) and >60,000/µL (dogs) indicate regeneration

PHYSIOLOGY

Hypoxemia induced by decreased red cell mass stimulates erythropoietin production and subsequently erythropoiesis.

CLINICAL APPLICATIONS

CAUSES: Blood loss and/or hemolysis

NEXT DIAGNOSTIC STEP TO CONSIDER IF PRESENT: Blood smear evaluation of red cell morphology for evidence of size, color, and shape changes, agglutination, and parasitic inclusions; physical examination for evidence of blood loss via gastrointestinal tract or elsewhere, ectoparasites, neoplasia; biochemical profile; fecal analysis, urinalysis; serologic testing for infectious agents, Coombs' test IMPORTANT INTERSPECIES DIFFERENCES: Dogs can mount a greater regenerative response than cats. Both aggregate and punctate reticulocytes are enumerated in cats to assess reticulocyte response.

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE: Presence of *Mycoplasma haemofelis* (formerly *Haemobartonella felis)* inclusions may falsely increase flow cytometric reticulocyte counts.

SPECIMEN: EDTA-anticoagulated blood (lavender-top tube) for CBC and reticulocyte count; fresh direct blood smear for morphologic evaluation of red cells

RELATIVE COST: $ (reticulocyte count); $$ (CBC; included in some CBC panels)

PEARLS

An absolute reticulocyte count is the most reliable means of assessing red cell regeneration. The mere presence of polychromasia on peripheral blood smears does not necessarily reflect adequacy of regenerative response. Presence of nucleated red blood cells, Howell-Jolly bodies, and basophilic stippling without polychromasia may indicate bone marrow injury, disease, or toxicosis (such as lead poisoning) interfering with red blood cell maturation.

AUTHOR: FIDELIA R. FERNANDEZ

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Anemia, Nonregenerative

DEFINITION

Anemia characterized by inadequate polychromasia or reticulocytosis

SYNONYM

Nonresponsive anemia

PHYSIOLOGY

Primary cause is decreased erythrocyte (red blood cell [RBC]) production. If decreased production is the sole cause, it may take weeks to months for anemia to be clinically evident, depending on the RBC lifespan. In anemia of chronic disease, inflammatory cytokines may decrease erythrocyte lifespan; they decrease release of erythropoietin from the kidney, resulting in decreased erythrocyte production.

CLINICAL APPLICATIONS

CAUSES: Chronic disease (renal disease, endocrinopathies, neoplasia, many others) or inflammation, primary bone marrow disease, therapeutic agents (hydroxyurea, phenylbutazone, sulfa-containing antibiotics, estrogen), long-term treatment with erythropoietin, nutritional deficiency (iron, copper, folate, or vitamin B12)

NEXT DIAGNOSTIC STEP TO CONSIDER IF PRESENT: Identification of underlying cause: serum biochemistry profile, urinalysis, diagnostic imaging if systemic illness is present and anemia of chronic disease is suspected. Advanced diagnostic testing may then include bone marrow evaluation, serologic tests for infectious disease (e.g., feline leukemia virus, ehrlichiosis), thyroid function tests, serum ferritin.

SPECIMEN AND PROCESSING CONSIDERATIONS

SPECIMEN: EDTA-anticoagulated blood (lavender-top tube) for CBC and reticulocyte count; freshly made direct blood smear for morphologic evaluation

RELATIVE COST: $$ (CBC)

PEARLS

Anemia due to early or acute hemolysis and blood loss may initially appear nonregenerative when the bone marrow has not had time to respond. It takes about 2-3 days after acute hemolysis or blood loss for reticulocytosis to be evident, and 7 days for optimum response. Thus, in cases of nonregenerative anemia where a very recent onset of the anemia is possible, serial CBC, blood smear evaluation, and reticulocyte counts are recommended to assess eventual bone marrow response. Once lack of regeneration has been determined, bone marrow assessment may be considered to help determine cause. Immune-mediated destruction of erythroid precursors could also cause a severe nonregenerative anemia.

AUTHOR: FIDELIA R. FERNANDEZ

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Amylase

DEFINITION

Enzyme principally involved in hydrolysis of complex carbohydrates (starches); concentrations measured in serum. Spectrophotometric methods are most often used; “dry reagents” are used less frequently.

TYPICAL NORMAL RANGE

Dogs: 371-1503 U/L. Cats: 530-1660 U/L.

PHYSIOLOGY

Amylase is a cytoplasmic enzyme found in high concentration in the pancreas, intestine, and liver. It is a digestive enzyme that catabolizes complex starches. Ca^{2+} is a required cofactor. Amylase is metabolized by the liver and may also be eliminated via the urinary tract. Amylase has a very short serum half-life.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Pancreatitis (may be normal to markedly increased) in dogs; vomiting; decreased glomerular filtration (increase is usually less than three times upper reference range value); gastrointestinal disease; hepatic disease; neoplasia.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Correlate with history, physical examination, CBC, and remainder of serum chemistry panel. If consistent with pancreatitis, consider abdominal ultrasonography and/or pancreas-specific lipase immunoreactivity to assess further.

IMPORTANT INTERSPECIES DIFFERENCES: Amylase is not useful for the diagnosis of pancreatitis in cats insofar as serum concentrations are usually not increased in pancreatitis in this species.

SPECIMEN AND PROCESSING CONSIDERATIONS

SPECIMEN: Serum (red-top tube), allow to clot, centrifuge, separate serum, refrigerate, and ship on ice. Amylase is fairly stable compared to other analytes measured in routine chemistry panels.

RELATIVE COST: $

PEARLS

- One-time measurement of amylase level in a dog is of very little significance with respect to pancreatitis (neither normal nor elevated levels rule out or rule in pancreatitis), likely owing to its short half-life. Trends in amylase levels over time (e.g., daily) may be more informative in terms of disease progression in patients with acute pancreatitis.
- Intestinal amylase comprises a small proportion of the total amylase in serum, but intestinal injury does not cause an increase in serum amylase concentration.
- Measurement of isoenzymes is of limited clinical value.

AUTHOR: BRUCE LEROY

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Ammonia

DEFINITION

Measurement of ammonium ($NH4^+$) concentration in plasma. $NH4^+$ is the predominant form of the analyte in blood. Routine assays require plasma, not whole blood.

SYNONYMS

Ammonia: NH3. Ammonium: $NH4^+$

TYPICAL NORMAL RANGE

Dogs: 45-120 µg/dL; cats: 30-100 µg/dL. To convert from µg/dL to µmol/L multiply by 0.5872.

PHYSIOLOGY

Ammonium is produced in the gastrointestinal tract by enteric bacterial metabolism and carried via the portal circulation to the liver. Hepatic transformation of two ammonium molecules into one urea molecule requires adequate hepatic function. Circulating ammonium concentrations are useful for assessing hepatic function. Ammonia is converted to urea in the liver, reenters the systemic circulation, and is eliminated in the urine. In patients with decreased hepatic blood flow (congenital or acquired portosystemic shunts), ammonia bypasses the liver, remains in the circulation, and results in hyperammonemia.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Decreased clearance from blood: decreased functional liver mass, decreased portal blood flow, urea cycle abnormalities, cobalamin deficiency. Increased production: postprandial, post-exertion (greyhounds, other racing dogs).

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Review history, examination, CBC, serum biochemistry panel, and abdominal imaging results to assess for signs of hepatobiliary disease and portal circulation abnormalities.

DRUG EFFECTS ON LEVELS: Decrease: antibiotics that affect gastrointestinal flora (aminoglycosides), lactulose, *Lactobacillus acidophilus* culture, enema. Increase: asparaginase, narcotics, diuretics causing hypokalemia, high protein diet.

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE: Increase: delay in harvesting plasma, specimen processing; hemolysis (if spectrophotometric assay used); prolonged tourniquet use SPECIMEN: Twelve-hour fasting specimen preferred. Collect heparinized whole blood (green-top tube), separate plasma from cells immediately, store on ice, and test within 4 hours; or freeze (—20°C) and test within 48 hours. Arterial samples are preferred but not essential.

RELATIVE COST: $$

PEARLS

Because of difficulty in proper specimen handling, measurement of preprandial and postprandial serum bile acids and urinary bile acid/creatinine ratio has replaced ammonium measurement. However, ammonia may have superior sensitivity and specificity for diagnosing portosystemic shunts. Ammonia is also superior to bile acids for assessing hepatic function if cholestasis is present.

AUTHOR: BRUCE LEROY

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Alkaline Phosphatase

DEFINITION

Alkaline phosphatase (ALP) is a membrane-associated enzyme found in liver, bone, colostrum, and many other tissues. Its physiologic function is not known.

SYNONYMS

Alk phos, ALP, sALP

TYPICAL NORMAL RANGE

Dogs: 0 to 90 U/L; cats 4 to 80 U/L

PHYSIOLOGY

Domestic mammals have two genes responsible for ALP production. I-ALP (intestinal-associated isoenzyme) is not associated with measured serum increases. Tissue nonspecific ALP is modified to two isoforms, L-ALP (liver associated) and B-ALP (bone associated). Another isoform, C-ALP, appears to be unique to dogs. Increased C-ALP is stimulated by endogenous and exogenous corticosteroids. Most routine assays measure total serum ALP, but there are tests that measure the liver and corticosteroid isoenzymes.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Cholestasis, hormone (corticosteroids) or drug (prednisone, phenobarbital) induction, osteoblast activity (normal growth in young dogs, fracture repair, osteosarcoma)

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Disregard in young animals (if no other abnormalities found); evaluate hepatobiliary structure and function; review medication history; assess for hyperadrenocorticism only if consistent history and physical examination.

IMPORTANT INTERSPECIES DIFFERENCES:

- Dogs: corticosteroid induction seems unique to dogs; laboratories can specifically measure for this form. Analysis does not differentiate source of corticosteroid, however (e.g., endogenous—stress, adrenal hyperplasia, hyperadrenocorticism —versus exogenous/iatrogenic all are measured as corticosteroid isoenzyme).
- Cats: ALP has poor sensitivity for cholestasis, except in hepatic lipidosis. Short serum half-life (8 hours in cats versus 24 hours in dogs) makes even low-magnitude ALP elevations generally more clinically significant than in the dog.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Increase: corticosteroid, phenobarbital, primidone, prednisone, thyroxine

LAB ARTIFACTS THAT MAY INTERFERE: Increase: marked hemolysis

SPECIMEN: Serum (red-top tube); allow to clot, centrifuge, collect serum, refrigerate, and ship on ice.

RELATIVE COST: $ (total serum concentration); $$ (corticosteroid isoenzyme)

PEARLS

The vast majority of dogs with increased ALP do not have hyperadrenocorticism (Cushing's disease). Therefore, an elevated serum alkaline phosphatase level warrants a detailed review of history and physical examination before determining whether testing for hyperadrenocorticism is warranted.

AUTHOR: LOIS ROTH-JOHNSON

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Aldosterone, Endogenous

DEFINITION

Mineralocorticoid steroid hormone secreted by adrenal cortex. Endogenous aldosterone measurement determines circulating aldosterone concentration.

TYPICAL NORMAL RANGE

Dog: 2-96 pg/mL. To convert pg/mL to ng/dL, divide pg/mL result by 10. To convert pg/mL to pmol/L, multiply pg/mL result by 2.775.

PHYSIOLOGY

Synthesized by adrenal cortex in response to angiotensin II. Acts on receptors throughout the body, but primarily in distal renal tubules, to enhance retention of sodium and water and promote excretion of potassium, effectively maintaining or increasing blood pressure.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Adrenal neoplasia or hyperplasia, low sodium intake, wide variety of nonadrenal diseases leading to hypovolemia

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Evaluate for decreased blood volume. If patient is euvolemic or hypertensive and there is hypokalemia/hyperkaluria, hypernatremia with decreased urine excretion, and/or hypertension, evaluate for adrenal hyperplasia/neoplasia.

CAUSES OF ABNORMALLY LOW LEVELS: Hypoadrenocorticism/adrenal atrophy (idiopathic, secondary to medication, pituitary disease), high sodium intake

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Review treatment/medication history; ACTH stimulation test to evaluate hypothalamic, pituitary, adrenal axis.

DRUG EFFECTS ON LEVELS:

- Decrease: angiotensin converting enzyme inhibitors, nonsteroidal antiinflammatory drugs, propranolol
- Increase: lithium, spironolactone

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE: Artifactual decrease: storage at 22○C for =3 days or at 37○C for 1 day SPECIMEN: Plasma collected in EDTA (lavender-top tube) or heparin (green-top tube). Centrifuge, collect plasma as soon as possible. Freeze, ship on ice.

RELATIVE COST: $$

PEARLS

Test is rarely indicated. A working diagnosis of hyperaldosteronism may be obtained by simpler means (e.g., adrenal mass in persistently severely hypokalemic patient). Evaluating aldosterone concentration in light of the plasma renin concentration (aldosterone/renin ratios) may aid determination of an appropriate or inappropriate response.

AUTHOR: BRUCE LEROY

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Albuminuria and Proteinuria

DEFINITION

The presence of excess protein, and/or albumin specifically, in urine

TYPICAL NORMAL RANGE

Wet chemistry instrument methods: 4-95 mg/dL protein. Urine dipstick: negative, trace, +1 (with no evidence of urinary tract disease). Urine concentration (specific gravity) should be taken into consideration; urine that is more concentrated may have greater protein concentrations (e.g., +1 rather than negative or trace) irrespective of health or disease.

PHYSIOLOGY

- Proteins <68,000 daltons readily pass the glomerular filter, but most are resorbed in the proximal tubules. Although it is a relatively small protein, albumin is too large to filter through the normal glomerulus and thus stays in the circulation of healthy animals.
- Tamm-Horsfall protein—a mucoprotein secreted by tubular and collecting duct cells—and albumin make up most of the protein found in the urine of healthy animals.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS:

- Overflow proteinuria: caused by increased plasma levels of protein (e.g., hemoglobinuria, hyperglobulinemia, myoglobinuria)
- Tubular proteinuria: caused by decreased protein resorption
- Glomerular proteinuria: caused by increased glomerular permeability
- Hemorrhage in urinary system
- Inflammation in urinary system, causing increased vascular permeability

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH:

- Examine urine sediment for evidence of inflammation or hemorrhage.
- Examine serum for evidence of hemolysis.
- Measure serum protein (hyperproteinemia, hyperglobulinemia, or hypoalbuminemia).
- Urine protein/creatinine ratio

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE:

- False increase (with dipstick method): prolonged contact with alkaline urine
- False decrease (with dipstick method): if protein is other than albumin (e.g., Bence Jones proteinuria does not react with dipstick reagent)
- False decrease (acid precipitation method): if urine is highly alkaline
- False increase (sulfosalicylic acid method): after administration of iodine-based contrast media, sulfisoxazole, very large doses of penicillin, and precipitation of crystals due to low pH

SPECIMEN: Urine in clean container

RELATIVE COST: $ (reported as part of urinalysis)

AUTHOR: ELIZABETH G. WELLES

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150

$$$$: >$150

Albumin

DEFINITION

Albumin is the predominant protein in peripheral blood. Serum albumin concentration is measured, but different dye binding assays may also include some nonalbumin proteins.

TYPICAL NORMAL RANGE

Dogs and cats: 2.5-4.0 g/dL (25 to 40 mg/mL); neonates and young animals often have slightly lower concentrations.

PHYSIOLOGY

Albumin is synthesized by the liver. It is the major contributor to plasma oncotic pressure and also functions as a transport protein for ions, bilirubin, thyroxine, numerous drugs, and other compounds. Spectrophotometric method is usually used for measuring serum albumin.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Dehydration, laboratory error. Glucocorticoid administration may cause mild increases in albumin concentration. In dogs, hyperalbuminemia has been associated with hepatocellular carcinoma. NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Assess hydration status; if normal, recheck results.

Review history/medical record for glucocorticoid usage.

CAUSES OF ABNORMALLY LOW LEVELS:

- Loss: nephropathy/glomerular disease; enteropathy, severe exudative skin lesions/burns, massive hemorrhage (total protein and globulin are also low).
- Decreased production: severe chronic liver disease; acute inflammation (negative acute-phase protein); protein malnutrition secondary to starvation or severe gastrointestinal diseases
- Dilutional effects: IV fluid overload, fluid accumulation disorders (e.g., congestive heart failure, syndrome of inappropriate antidiuretic hormone secretion; total protein and albumin are also low)

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Review history and physical exam with respect to intestinal, renal, and liver function. Assess in conjunction with hematocrit, total protein, serum globulin, liver enzymes, and renal function. Calculation of the albumin/globulin (A:G) ratio may allow detection of subtle protein abnormalities. If a cause is not determined, additional testing to be considered includes preprandial and postprandial bile acids, serum protein electrophoresis, urine protein/creatinine ratio, fecal flotation, fecal occult blood, and fecal alpha-1-protease inhibitor. Additional tests (radiographs, ultrasound, biopsy) should be dictated by history, physical examination, and previous test results.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Long-term therapy with hepatotoxic drugs (e.g., anticonvulsants) may cause low levels secondary to liver injury. LAB ARTIFACTS THAT MAY INTERFERE:

- Decrease: use of reagents for human testing (bromocresol purple dye binding reaction)
- Increase: bromocresol green dye may bind to globulin.

SPECIMEN: Serum (red-top tube); allow specimen to clot, then centrifuge, collect serum, refrigerate, and ship on ice.

RELATIVE COST: $

PEARLS

Concentration may be slightly lower in very young and very old patients.

AUTHOR: BRUCE LEROY

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Alanine Aminotransferase (ALT)

DEFINITION

Enzyme located in hepatocyte cytoplasm

SYNONYM(S)

Serum glutamic pyruvate transaminase (SGPT)

TYPICAL NORMAL RANGE

Dogs: 0 to 30 U/L; cats: 10 to 25 U/L

PHYSIOLOGY

ALT is released from the cytoplasm following injury to the hepatocyte cell membrane. Low concentrations in erythrocytes or skeletal muscle may cause minor (usually clinically insignificant) increases in hemolytic diseases or with muscle injury, respectively.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Hepatocellular injury from any cause. Liver injury may be primary (e.g., hepatitis, neoplasia, blunt trauma) or secondary (e.g., translocation of enteric bacteria due to intestinal disease). Dystrophin-deficient muscular dystrophy causes slight to moderate increases in dogs and slight to marked increases in cats.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: If elevations >2 times the upper limit of reference range persist, assess history for exposure to hepatotoxins (including medications). If none, assess hepatic structure (e.g., abdominal radiographs, ultrasound) and function (preprandial and postprandial serum bile acids; alkaline phosphatase, bilirubin). Consider biopsy if values remain elevated or increase or if aforementioned tests reveal abnormalities.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Many drugs induce hepatocellular injury. Drugs commonly implicated include glucocorticoids and phenobarbital.

LAB ARTIFACTS THAT MAY INTERFERE: Increase: lipemia, hemolysis (in vivo or artifactual)

SPECIMEN: Serum (red-top tube); allow to clot, centrifuge, separate serum from clot. RELATIVE COST: $

PEARLS

ALT elevation indicates hepatocyte damage but is not a test of hepatic function. ALT does not provide information on the reversibility of hepatic injury. Mild elevations in ALT may indicate serious disease processes or relatively benign conditions; correlating the finding to the remainder of the case and monitoring trends if necessary are essential for properly interpreting high ALT values.

AUTHOR: BRUCE LEROY

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Activated Partial Thromboplastin Time (APTT)

DEFINITION

Screening test for disorders of the intrinsic and common coagulation pathways

SYNONYM

Partial thromboplastin time (PTT)

TYPICAL NORMAL RANGE

Reported in seconds. Approximate ranges for normal animals are 8.6-12.9 seconds (canine) and 13.7-30.2 seconds (feline), but laboratory-, instrument-, and species-specific reference ranges must be used. Prolonged when at least one coagulation factor is <70% of normal.

PHYSIOLOGY

Citrated plasma is incubated at 37°C with excess procoagulant phospholipid. Contact activator is added to activate the intrinsic pathway via factors XII and XI. Citrate in the specimen chelates Ca^{2+}, limiting activation beyond factor Xla. After additional incubation, CaCl2 is added to saturate the citrate and allow the reaction to continue to clot formation. The APTT is the time from addition of CaCl2 to clot formation.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Liver disease (decreased factor production), vitamin K inactivation (anticoagulant rodenticides, coumarin therapy), decreased vitamin K absorption (biliary obstruction), increased factor inactivation or consumption (disseminated intravascular coagulation [DIC]), factor dilution (massive blood loss, with colloid or crystalloid fluid replacement), hereditary factor defects, heparin therapy NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Assess history for exposure to toxic substances or treatment. Measurement of individual factors if hereditary disease is suspected.

IMPORTANT INTERSPECIES DIFFERENCES: Prolonged APTT is reported in cats without evidence of clinical hemostatic disease, leading to increased false-positive results in this species.

DRUG EFFECTS ON LEVELS: Increased: heparin, aspirin. Polymerized bovine hemoglobin (Oxyglobin) administration interferes with ability to detect clot.

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE:

- Decrease: contamination with tissue factor when specimen obtained; overfilling citrate tube
- Increase: underfilling of citrate tube; old/improperly stored samples

SPECIMEN:

- Citrated whole blood (blue-top tube). Fill completely. Refrigerate and submit to reference lab. If time interval between sampling and testing is >6 hours, mix thoroughly, centrifuge, collect plasma, freeze. Samples stored at −20°C may show significant false increases in APTT.
- Minimally traumatic phlebotomy is required to prevent tissue factor from falsely shortening the result. Ideally, collect a sufficient volume of blood to place first aliquot in red-top tube and discard (or use for serologic tests). Acceptable samples for APTT may be collected from an indwelling venous catheter.

RELATIVE COST: $$

PEARLS

APTT values generally increase before PT values with heparin therapy, but not with warfarin/anticoagulant rodenticide toxicosis or

coagulopathy of liver disease.

AUTHOR: BRUCE LEROY

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Activated Coagulation Time (ACT)

DEFINITION

The time interval from contact of blood with diatomaceous earth pellets to formation of a visible clot. ACT evaluates the intrinsic and common pathways but is less sensitive than activated partial thromboplastin time (APTT).

TYPICAL NORMAL RANGE

Dogs: <120 seconds. Cats: <165 seconds.

PHYSIOLOGY

Contact activation occurs when whole blood is drawn into a warmed (37°C) tube containing diatomaceous earth pellets. After multiple inversions for mixing, the tube is kept in a heating block or tucked in the clinician's axilla and checked for clot formation every 5-10 seconds.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Decreased concentration of any of coagulation factors of the intrinsic or common coagulation pathways (all factors except VII) to less than 5% of normal; severe thrombocytopenia (< 10,000 platelets/μL); uremia. In the absence of coagulopathy, critically ill dogs may have prolongation of ACT due to inflammatory disease.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Confirm with tests that are more sensitive (activated partial thromboplastin time); platelet count.

DRUG EFFECTS ON LEVELS: Prolonged by heparin or aspirin therapy, some antibiotics (newer lipoglycopeptide antibiotics may interfere with factor Xa), and barbiturates (contribute to splenic sequestration of platelets).

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE: Considered an in-office test. Any variation in test protocol may alter results. Endpoint (visual clot detection) is subject to observer variability. Difficult venipuncture causing platelet activation may falsely shorten ACT.

SPECIMEN: Whole blood into siliceous (gray top, with large granules) tube, prewarmed to 37°C. Mix by inversion, incubate at 37°C (purpose-made heating block, water bath, or human axilla), and check for clot formation every 5-10 seconds. Do not incubate in a closed palm, as it does not provide a consistent 37°C environment.

PEARLS

Considered an insensitive test but may be useful for suspected warfarin-intoxicated dogs if APTT unavailable. Carriers of hemophilia (coagulation factors are 40%-60% of normal) and beagles with hereditary factor VII deficiency will not be detected by the ACT.

AUTHOR: BRUCE LEROY

ACTH (Adrenocorticotropic Hormone), Endogenous/Baseline

DEFINITION

Peptide hormone secreted by anterior pituitary in response to corticotrophin releasing hormone (CRH) secreted by hypothalamus

SYNONYM

Corticotropin

TYPICAL NORMAL RANGE

Dogs: 10 to 110 pg/mL; cats: 0 to 110 pg/ml. To convert pg/mL to pmol/L, multiply pg/mL by 0.22.

PHYSIOLOGY

Stress causes hypothalamic release of CRH. CRH stimulates anterior pituitary release of a large precursor hormone, proopiomelanocortin (POMC), which undergoes proteolytic cleavage to yield ACTH, β-endorphin, melanocyte-stimulating hormone, and other hormones. ACTH stimulates cortisol and aldosterone release from the adrenal cortex. High circulating levels of cortisol inhibit release of CRH (feedback inhibition). High baseline ACTH concentrations help differentiate pituitary-dependent hyperadrenocorticism from functional adrenal cortical tumors, in which serum ACTH is subnormal.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Hypocortisolism, either natural (primary Addison's disease) or iatrogenic (after sudden cessation of chronic glucocorticoid administration); pituitary-dependent hyperadrenocorticism due to pituitary neoplasia. Additionally, there are rare instances of nonendocrine neoplasms producing high concentrations of ACTH (ectopic ACTH syndrome).

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH:

- Determine treatment (glucocorticoid, including topical medications) history.
- ACTH stimulation test if no history of glucocorticoid administration
- Evaluation for occult nonendocrine neoplasm (rare)

CAUSES OF ABNORMALLY LOW LEVELS: High endogenous cortisol levels, either spontaneously (hyperadrenocorticism/Cushing's disease) or iatrogenic (during administration of glucocorticoids); panhypopituitarism

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Rule out sampling error (see below). Evaluate for hyperadrenocorticism. If history, physical examination, and diagnostic tests support hyperadrenocorticism, and ACTH level is below the normal range, a diagnosis of adrenal cortical neoplasia is suspected, and further testing (e.g., abdominal ultrasonography) is warranted.

IMPORTANT INTERSPECIES DIFFERENCES: Adrenal disease is uncommon in cats; test is infrequently done in this species.

DRUG EFFECTS ON LEVELS:

- Increase: insulin
- Decrease: glucocorticoid administration

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE: Decrease: thawing of specimen; collection or storage in glass tubes SPECIMEN: Morning sample preferred. Collect in cold, heparinized plastic syringe; centrifuge; collect plasma immediately; freeze in plastic tubes. Samples must be shipped frozen and remain frozen until analysis to avoid degradation of ACTH. Aprotinin-containing tubes may help prevent degradation in unfrozen samples.

RELATIVE COST: $$

PEARLS

Useful for differentiating pituitary-dependent Cushing's disease from adrenal cortical tumor. The hormone is very labile, however; inappropriate specimen handling yields false-negative results.

AUTHOR: BRUCE LEROY

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Acetylcholinesterase Level

DEFINITION

Blood level of the enzyme that catabolizes acetylcholine

SYNONYM

Cholinesterase level

TYPICAL NORMAL RANGE

500 to 1500 U/L for dogs. A positive diagnosis of low level means the patient's level is at least 25% less than the lower limit of normal range.

PHYSIOLOGY

Acetylcholine is the main neurotransmitter at the neuromuscular junction, and the enzyme responsible for catabolism of acetylcholine is acetylcholinesterase. When acetylcholinesterase levels are low, there is decreased catabolism of acetylcholine, resulting in poorly controlled or uncontrolled neuromuscular activation. Muscle tremors and smooth-muscle activation (gastrointestinal and other autonomic signs) occur. Organophosphates antagonize acetylcholinesterase, leading to these clinical signs. Organophosphate intoxication is the most common cause of low blood levels of this enzyme. Measurement of red blood cell acetylcholinesterase concentration helps diagnose intoxication with organophosphate-containing insecticides.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY LOW LEVELS: Organophosphate intoxication, carbamate intoxication

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Response to treatment

IMPORTANT INTERSPECIES DIFFERENCES: Cats naturally have lower cholinesterase levels, making the test less reliable in this species (false-positive results).

SPECIMEN AND PROCESSING CONSIDERATIONS

SPECIMEN: Whole blood in EDTA (lavender-top tube) or heparin (green top); 20 grams of brain tissue may be used for postmortem diagnosis.

RELATIVE COST: $$

PEARLS

Turnaround time is usually longer than clinical condition allows, so the test is often confirmatory (retrospective). Treatment decisions must be based on physical exam findings +/− known history of intoxication before results are available. See Organophosphate Intoxication, p. 792.

AUTHOR: LOIS ROTH-JOHNSON

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Acetylcholine Receptor Antibody Test

DEFINITION

Test for detection of antiacetylcholinereceptor (AChR) antibodies, which cause acquired myasthenia gravis

SYNONYMS

ARAT, myasthenia gravis titer

TYPICAL NORMAL RANGE

0 to 0.6 nmol/L (dogs), 0 to 0.3 nmol/L (cats)

PHYSIOLOGY

Acetylcholine is released from a neuron's presynaptic membrane at the neuromuscular junction. In myasthenia gravis patients, the acetylcholine fails to adequately bind to muscle-based receptors in the postsynaptic membrane (sarcolemma) because the receptors are inactivated by autoantibodies. This test detects the autoantibodies in the serum.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Myasthenia gravis

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: The ARAT is the confirmatory diagnostic test for myasthenia gravis; assessment of the response to immunosuppressive and/or oral pyridostigmine treatment may further support the diagnosis but is variable (some cases may be refractory to treatment). Intravenous edrophonium (Tensilon) is occasionally used for immediate relief of signs, but response rate is low even in confirmed cases.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: False negative: corticosteroid or other immunosuppressive therapy. If clinically feasible, treatment should be stopped at least 4 weeks prior to testing.

LAB ARTIFACTS THAT MAY INTERFERE: False negative: failure to keep specimen chilled

SPECIMEN: Serum (red-top tube), 2 mL minimum; separate from clot as soon as possible. Should be frozen and sent on dry ice (preferable) or cold pack to reference lab immediately (courier/overnight express delivery). RELATIVE COST: $$$

PEARLS

Some dogs with myasthenia gravis are negative for AChR antibodies but have immune complexes associated with other antigens at the neuromuscular junction that interfere with neurotransmission. Nerve stimulation studies may be needed in these patients (see p. 1255).

AUTHOR: LOIS ROTH-JOHNSON

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Acanthocyte

DEFINITION

Erythrocyte morphologic abnormality characterized by irregular, usually blunt projections from the normally smooth round cell membrane (from the Greek *akantha,* meaning “thorn”).

SYNONYMS

Burr cell, spur cell, echinoacanthocyte

TYPICAL NORMAL RANGE

Not reported unless seen on blood film. Healthy dogs and cats should not have appreciable numbers of circulating acanthocytes on properly prepared, fresh blood films.

PHYSIOLOGY

Mechanism for membrane shape abnormality is not known. Associated with abnormalities in red blood cell membrane lipids.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Hemangiosarcoma; liver, splenic or renal disease; artifact of blood film preparation

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Repeat CBC to confirm; if consistent finding, evaluate for liver, splenic, or renal disease and metabolic abnormalities as suggested by clinical signs.

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE: Specimen age artifact (delay in preparing blood film, sample not refrigerated); artifact of blood film preparation SPECIMEN: Whole blood in EDTA (lavender-top tube) or heparin (green-top tube); include a blood film prepared when specimen was collected to help rule out specimen age artifact.

RELATIVE COST: Reported if present on blood film; $/$$ (depending on reflex testing included in CBC panel)

PEARLS

Considered nonspecific and a common artifact; should be evaluated in a second, fresh specimen prior to drawing diagnostic conclusions

AUTHOR: LOIS ROTH-JOHNSON

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Buffy Coat

DEFINITION

The thin white layer of packed leukocytes and platelets found atop the packed erythrocytes following high-speed centrifugation of anticoagulated blood

TYPICAL NORMAL RANGE

Typically not measured. The height of this layer in a spun blood specimen was previously used as a crude index of the total leukocyte count.

PHYSIOLOGY

Leukocytes and platelets are less dense than erythrocytes, so they deposit above the packed erythrocytes following centrifugation. A specific hematology analyzer (IDEXX VetAutoread) can expand and differentiate the layers of buffy coat to generate hemograms.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Any condition causing leukocytosis or thrombocytosis will increase thickness of buffy coat layer.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: CBC with blood smear examination CAUSES OF ABNORMALLY LOW LEVELS: Leukopenia

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: CBC with blood smear examination

SPECIMEN AND PROCESSING CONSIDERATIONS

SPECIMEN: EDTA whole blood (lavender-top tube)

RELATIVE COST: $$

PEARLS

- Smears of buffy coat cells can be an important tool for concentrating abnormal leukocytes that occur in very low number. Examples: detection of mastocytemia as a staging tool in dogs with mast cell neoplasm, detection of infectious agents in neutrophils or monocytes (e.g., *Histoplasma* in cats, *Hepatozoon* in dogs).
- Low numbers of circulating mast cells occur more often as an incidental finding in dogs (and rarely in cats) with various inflammatory diseases, compared to dogs with systemic mast cell neoplasms. Therefore, buffy coat detection of mast cells is more helpful as a staging tool for dogs and cats with confirmed mast cell neoplasms, rather than a means to screen for mast cell neoplasms.

AUTHOR: STEPHEN D. GAUNT

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Bruceila Slide Agglutination

DEFINITION

ELISA test for detection of *Brucella canis* antibody in serum

SYNONYM

Rapid slide agglutination test (RSAT)

TYPICAL NORMAL RANGE

Agglutination indicates positive test; serum from noninfected dogs fails to agglutinate.

PHYSIOLOGY

Highly sensitive screening test used for detecting active *B. canis* infection. Patient serum is mixed with heat-killed *B. ovis* on slide. Specimens from patients with antibodies to *B. canis* have positive agglutination.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: *B. canis* infection; false-positive test may occur in patients with antibodies to *Bordetella bronchiseptica, Pseudomonas* spp., *Moraxella* spp., or other gram-negative bacteria. Overall, approximately 40% of positive tests are associated with true *B. canis* infection.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Confirm positive test results with 2-mercaptoethanol tube agglutination, agar gel immunodiffusion (AGID), or culture. Appropriate culture samples (vaginal exudate, aborted pups, semen) depend on clinical signs and associated available tissues or specimens.

CAUSES OF ABNORMALLY LOW LEVELS: For the first 3-4 weeks after infection, serologic tests may be negative even if bacteremia is present.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Retesting after 30 days is suggested before admission to breeding kennels. Low or intermediate titers may indicate previous disease or recent exposure. Follow-up blood culture may be helpful in these animals.

SPECIMEN AND PROCESSING CONSIDERATIONS

SPECIMEN: Serum (red-top tube); separate serum from clot, refrigerate sample.

RELATIVE COST: **$$**

PEARLS

- Humans are susceptible (zoonosis), but infections are rare.
- Post-bacteremia, organisms may concentrate in prostate and epididymis. Agglutination titers decline.
- Chronically infected female dogs typically have recurrent bacteremia and highest titers during proestrus, estrus, pregnancy, or abortion. Testing is suggested at these times.
- The test has a high sensitivity and thus is a reasonable screening test.

AUTHOR: LOIS ROTH-JOHNSON

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Bromide

DEFINITION

Active ingredient in potassium (KBr) or sodium bromide (NaBr), drugs used for treating seizure disorders

TYPICAL NORMAL RANGE

Serum level target therapeutic range: 0.5-2.3 mg/mL

PHYSIOLOGY

- As a seizure-controlling drug, bromide competes with chloride transport across cell membranes, resulting in neuronal hyperpolarization and increased seizure threshold. Neuron excitability is depressed.
- The standard method for measuring serum concentration is spectrophotometrically using the gold chloride method. Measurement by ion-selective electrode is considered inaccurate.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Excessive therapeutic dose NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Lower dose IMPORTANT INTERSPECIES DIFFERENCES: Used primarily in dogs; cats are more prone to exhibiting toxic side effects (lethargy, vomiting, polydipsia, polyuria, constipation, pancreatitis).

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: High-chloride diets and diuretics enhance bromide elimination, increasing the bromide dose required for therapeutic effect. Conversely, low-chloride diets and concurrent use of central nervous system depressants can enhance bromide effects/toxicity.

LAB ARTIFACTS THAT MAY INTERFERE: Increase: ion-selective electrode method of measurement (chloride interference)

SPECIMEN: Serum (red-top tube), refrigerate. First sample should be submitted within 1 week of loading dose; second specimen at 1 month; monitor every 3-6 months. RELATIVE COST: $$

PEARLS

- Higher incidence of adverse reactions in older patients and patients with renal dysfunction.
- Bromides are not approved by the U.S. Food and Drug Administration for use in animals.
- Serum bromide concentration at which toxic signs manifest is known to be variable in humans; variability in sensitivity to toxicity is likely in animal species as well.

AUTHOR: SHERRY J. MORGAN

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Borreliosis (Lyme Disease) Serology

DEFINITION

Lyme borreliosis is a tickborne disease of dogs, cats, and humans that is caused by the spirochete *Borrelia burgdorferi*

TYPICAL NORMAL RANGE

- In-house SNAP qualitative ELISA for antibody to the C6 peptide of *B. burgdorferi* antigen: positive or negative result
- Quantitative C6 antibody test negative result (reference laboratory): <30 units/mL
- Immunofluorescent antibody (IFA; reference laboratory) negative result: <1:64
- Consult laboratory conducting the test for exact reference values for C6 antibody and IFA tests.

PHYSIOLOGY

Borrelia spp. organisms are inoculated into the skin via an *Ixodes* tick bite, where they proliferate and spread to many tissues, including joints and the central nervous system. Persistent infections are common; they may produce no clinical signs or may result in chronic debilitating disease such as arthritis, meningitis, or protein-losing nephropathy. Host's own inflammatory response likely plays a role in development of disease.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: In-house SNAP qualitative or quantitative C6 ELISA assay: positive test indicates natural exposure to *B. burgdorferi.* Whole-cell ELISA or IFA: seropositivity indicates natural exposure to pathogenic or nonpathogenic *Borrelia* organisms or vaccination with borreliosis vaccine.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: If the in-house SNAP qualitative C6 ELISA test is positive, consider the quantitative C6 antibody test to establish a baseline titer for monitoring effect of treatment in dogs. If IFA is positive, consider Western blot, ELISA testing for specific outer surface proteins, or C6 ELISA assay. PCR and blood culture have been used for confirming a diagnosis, but these tests have low sensitivity (difficult to detect organisms).

CAUSES OF NEGATIVE TEST/TITER: Early infection or noninfected

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Consider repeating C6 antibody test or IFA in 3-5 weeks if clinically appropriate (if early infection caused undetectable titer initially).

IMPORTANT INTERSPECIES DIFFERENCES: Despite evidence of seropositivity for *Borrelia* in cats, natural disease has not been described as a distinct clinical entity in this species. Cats may be more resistant than dogs to developing clinical signs of Lyme borreliosis. Polyarthritis and meningitis have been observed in some experimentally infected cats. The C6 ELISA assay may be used in cats.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: C6 titer may decrease within 4-5 months following successful treatment with doxycycline or amoxicillin.

SPECIMEN: The in-house SNAP C6 qualitative ELISA test requires 1 mL of serum or plasma (red-top or lavender-top tube). IFA and Western blot: 1 mL of serum (red-top tube). Samples are stable for up to 4 days at refrigerator temperature.

RELATIVE COST: $$ (Quantitative C6, ELISA); $$$ (Western blot)

PEARLS

A large proportion of dogs exposed to *Borrelia* (and therefore, having a positive test result) do not develop clinical signs of Lyme disease; the decision to treat should always be based on clinical characteristics in addition to serologic test results.

AUTHOR: PATTY J. EWING

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Bone Marrow Cytology

DEFINITION

Cytologic evaluation allowing assessment of blood precursor cell production and morphology

TYPICAL NORMAL RANGE

Marrow particles should contain 25%-75% hematopoietic cells, with all cell lines exhibiting orderly, complete maturation and normal shape, size, and features (morphology). The normal myeloid/erythroid (M:E) ratio is approximately 1:1, but can range from 0.6:1 to 4:1.

PHYSIOLOGY

Bone marrow contains trabecular bone with marrow spaces containing capillaries, hematopoietic cells, and adipocytes. Hematopoietic activity occurs in response to peripheral demand. Bone marrow aspiration is indicated when there are unexplained cytopenias (nonregenerative anemia, neutropenia, and/or thrombocytopenia), hyperglobulinemia, suspicion of neoplasia, or as part of staging of confirmed lymphoma and systemic mastocytosis cases.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Hyperplasia of one or more cell lines may occur secondary to increased peripheral demand for cells due to cell destruction, increased utilization, or loss. Neoplasia such as acute or chronic leukemia (with or without maturation and morphologic abnormalities) results in high marrow cellularity and effacement of normal marrow tissue. Lymphocytes and plasma cells may be increased in marrow because of antigenic stimulation or neoplasia. Iron stores may be increased with anemia of chronic disease and hemolytic anemia. Inflammation, infiltrating neoplasia, or hemophagocytic disease also results in increased cellularity of the marrow.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Dependent on differential diagnosis based on history, physical exam findings, and results of CBC, serum biochemistry profile, and other diagnostic tests.

CAUSES OF ABNORMALLY LOW LEVELS

- Marrow hypoplasia indicates decreased cell production. Causes include anemia of chronic disease, chronic kidney disease, ehrlichiosis (dogs), drug-induced or immune-mediated destruction of precursor cells in the marrow, toxic insult (e.g., sulfa antibiotics, albendazole, phenylbutazone), viral infection (i.e., feline leukemia virus, parvovirus, canine distemper), myelofibrosis.
- Maturation arrest and dysplastic changes of red blood cells occur with viral infection, iron deficiency, myelodysplastic syndrome, or toxic insult.
- Iron stores are decreased with blood loss and iron deficiency.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Dependent on differential diagnosis based on history, physical exam findings, and results of CBC, serum biochemistry profile, and other diagnostic tests. Bone marrow aspiration often is the final diagnostic step for confirming hematopoietic disorders.

IMPORTANT INTERSPECIES DIFFERENCES: Iron stores are not usually visible in cat bone marrow and cannot be evaluated cytologically.

SPECIMEN AND PROCESSING CONSIDERATIONS

SPECIMEN: Aspirated marrow should immediately be made into fresh smears and also placed in an EDTA (lavender-top) tube. Proper collection and preparation of slides are essential for accurate interpretation. Hematopoietic cells degenerate rapidly after collection. Slides must be prepared immediately (before a clot forms) or within 30 minutes after collection if anticoagulant is used. A good bone marrow aspirate has several marrow particles for evaluation, with spreading of the cells in a monolayer for evaluation of morphology.

RELATIVE COST: $$, plus cost of aspiration procedure

PEARLS

- Bone marrow aspirates must be interpreted concurrently with CBC results.
- An accompanying bone marrow core biopsy may help in the interpretation of overall cellularity of the bone marrow, which complements the evaluation of morphology and maturation sequence from the marrow aspirate.
- A fresh smear of the marrow aspirate should be stained and examined for the presence of marrow spicules/cells while the animal is still sedated/anesthetized; if spicules are not adequate, the procedure may be repeated immediately.

AUTHOR: RUANNA GOSSETT

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Blood Urea Nitrogen (BUN)

DEFINITION

Concentration of urea in serum, plasma, or whole blood (usually measured in serum)

SYNONYM

Serum urea nitrogen (SUN)

TYPICAL NORMAL RANGE

- Dogs: 10-25 mg/dL
- Cats: 5-30 mg/dL
- Conversion: mg/dL × 0.36 = mmol

PHYSIOLOGY

Most of serum urea is synthesized via hepatic urea cycle, which converts ammonium derived from bacterial metabolism of dietary protein to urea. A small amount of ammonium is derived from deamination of amino acids. The kidneys excrete urea. Urea is freely filtered by glomeruli: some is resorbed by tubular epithelial cells to establish (with sodium) the medullary concentration gradient. Serum urea concentration often parallels creatinine concentration.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS

- Mild to moderate increases can result from prerenal causes such as dehydration, decreased cardiac output, or shock (increased concentration of BUN often exceeds creatinine).
- Renal disease with decreased GFR (glomerular filtration rate) of virtually any etiology (inflammatory, degenerative, neoplastic, congenital, toxic, or other) can cause azotemia (concentrations of BUN and creatinine often parallel).
- Urinary outflow obstruction results in postrenal azotemia (increased BUN and creatinine).
- Gastrointestinal hemorrhage results in increased urea production (less effect on creatinine concentration).

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Urine specific gravity, measurement of volume of urine production, evaluation of any disorder that may cause renal tubular cells to have decreased response to actions of ADH and therefore have lower than expected urine concentrating ability.

CAUSES OF ABNORMALLY LOW LEVELS

- Lack of hepatic urea production owing to decreased dietary protein (low-protein diet, anorexia), hepatic failure, decreased functional hepatic mass, portosystemic shunt, congenital deficiency of urea cycle enzymes (rare).
- Increased urea excretion is due to crystalloid or osmotic diuresis or marked polydipsia/polyuria, such as iatrogenic water drinkers (rare) or nephrogenic or central diabetes insipidus.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Assess urine specific gravity, urine output, water intake, serum concentrations of electrolytes and calcium.

SPECIMEN AND PROCESSING CONSIDERATIONS

SPECIMEN: Serum (red-top tube) preferred. Heparinized plasma (green-top tube) acceptable. Some methods can use EDTA plasma (lavender-top tube) or whole blood.

RELATIVE COST: $$ (part of most serum biochemistry profiles); $ (as a single test)

PEARLS

- High doses of gastroduodenal ulcerogenic drugs (corticosteroids, nonsteroidal antiinflammatories) may cause intestinal

hemorrhage, increasing BUN, but with little effect on creatinine

- Elevated BUN with concurrent isosthenuria (urine specific gravity approximating 1.008-1.012) signifies compromised renal function, with three exceptions: hypoadrenocorticism, diabetes insipidus, and diuretics may cause these laboratory changes without necessarily indicating that renal function is decreased.

AUTHOR: ELIZABETH G. WELLES

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Blood Typing

DEFINITION

Identification of specific inherited characteristic cell surface antigens on erythrocyte membrane

TYPICAL NORMAL RANGE

- Canine: dog erythrocyte antigen (DEA) 1.1, 1.2, 1.3 (the “A” system). Other classification systems exist, but the “A” system is most important for transfusion purposes. Any DEA can elicit an antibody response in dogs that lack it.
- Feline: type A (most common), type B (less common), type AB (rare)

PHYSIOLOGY

- Canine: The recognized canine antigens are DEA 1.1, 1.2, 1.3, 3, 4, 5, 6, and 7. DEA 1.1 antigen in particular can induce acute hemolytic reactions in sensitized dogs; identified by monoclonal antibodies on blood typing cards (see p. 1234).
- Feline: type A (>95%), type B (<5%); defined by preexisting, naturally occurring isoantibodies against the antigen they lack; type AB lacks antibodies: isoantibodies responsible for transfusion reactions and neonatal isoerythrolysis (see p. 1234).

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Reported result is individual animal's blood type.

IMPORTANT INTERSPECIES DIFFERENCES

- Dogs do not have naturally occurring antierythrocyte surface antigen antibodies; a first transfusion will not cause hemolytic reaction (cross-matching is unnecessary for first transfusion, but typing is still recommended to provide transfused blood of a type that is least likely to elicit a long-term antibody response).
- All type B cats >3 months of age have high titers of naturally occurring type A antibodies that act as strong hemagglutinins and hemolysins. Type A or AB kittens born to type B queens are at risk of developing neonatal isoerythrolysis. Generally higher incidence of type B blood: British shorthair, Devon Rex, Cornish Rex breeds, DSH and DLH on U.S. west coast, Europe, Japan, and Australia (see p. 1379).

SPECIMEN AND PROCESSING CONSIDERATIONS

SPECIMEN

- EDTA whole blood (lavender-top tube)
- Typing cards are species specific. Dog blood typing cards can be used for determining DEA 1.1 antigen status, and cards for cats can be used for determining type A, B, or AB.
- Marked anemia, marked hemolysis, or autoagglutination can interfere with results.

RELATIVE COST: $$$

PEARLS

- Dogs: blood groups that have the most clinical relevance are DEA 1.1 and DEA 1.2, also called *A1* and *A2*. Because DEA 1.1 is the most antigenic, DEA 1.1-negative dogs are recommended as donors for patients with unknown blood types.
- Cats: because of the widespread prevalence of naturally occurring erythrocyte antigens, blood from blood donor cats and the recipient cat should be typed, and a cross-match performed (see p. 1234) prior to any blood transfusion. Blood types should be compatible (acceptable: A into A; B into B; A, B, or AB into AB) and the cross-match should not show incompatibility.

AUTHOR: DEBORAH G. DAVIS

Pricing Information

$: <$20

$$: $21-75
$$$: $76-150
$$$$: >$150

Blood pH

DEFINITION

Measure of the hydrogen ion (H^+) concentration (acidity) of the blood

TYPICAL NORMAL RANGE

Dogs, 7.31-7.42; cats, 7.24-7.40

PHYSIOLOGY

Blood pH is inversely related to H^+ concentration; increased [H^+] = decreased pH. Hydrogen ions are continuously produced by metabolic processes and excreted via the kidneys or bound to buffers.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Increased pH indicates alkalosis, either respiratory (decreased Pco2) or metabolic (increased bicarbonate). Metabolic causes: vomiting, diuretics, overadministration of bicarbonate. Respiratory alkalosis is caused by hyperventilation due to pulmonary disease, direct stimulation of central nervous system (pain, anxiety), septicemia.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Respiratory: thoracic radiography/ultrasound, evaluate mentation and respiratory rate and depth, blood cultures. Metabolic: evaluate for vomiting, review treatment history.

CAUSES OF ABNORMALLY LOW LEVELS: Decreased pH indicates acidosis, either metabolic (low bicarbonate) or respiratory (increased Pco2). Metabolic causes: bicarbonate loss (and/or production of endogenous acids) due to diarrhea, lactic acidosis, ketoacidosis, uremia, ingestion of exogenous toxins (ethylene glycol). Respiratory causes: pulmonary parenchymal disease, pulmonary restrictive disease (pleural effusion, pneumothorax, diaphragmatic hernia), central nervous system depression (anesthesia, narcotics, brainstem disease), airway obstruction.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Consider serial blood lactate measurements to monitor progression if clinically indicated. Metabolic: calculate anion gap to determine if due to loss of bicarbonate (anion gap normal) or accumulation of organic acid (high anion gap). Evaluate serum biochemistry profile and urinalysis for renal disease, diabetes mellitus, and other systemic causes. Respiratory: ensure patent airway, thoracic radiography/ultrasound, evaluate mentation.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Decrease: sedative, narcotic, general anesthetics causing respiratory depression. Increase: bicarbonate or diuretic administration.

LAB ARTIFACTS THAT MAY INTERFERE: Decrease: delayed analysis of sample, excessive heparin in syringe. Increase: sample exposure to room air.

SPECIMEN: Whole blood collected and maintained in heparinized syringe, 0.05-0.1 mL of heparin/mL blood. Cap syringe end to limit exposure to room air. Specimens analyzed within 15 minutes of collections are preferred. Storage in a capped syringe on ice at 4°C for up to 2 hours is acceptable.

RELATIVE COST: $$ (reported as part of blood gas analysis)

PEARLS

Disturbances of pH can be life threatening. Periodic monitoring during prolonged anesthesia and in patients with severe metabolic illness (vomiting, diarrhea, shock) is critical.

AUTHOR: LOIS ROTH-JOHNSON

1ST EDITION AUTHOR: JAMES H. MEINKOTH

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Blood Gas Analysis

DEFINITION

Evaluation of blood pH, Pco2, Po2, and bicarbonate. Other calculated parameters may be included. A blood pH lower than normal indicates acidosis, whereas a blood pH higher than normal indicates alkalosis. The acidosis is considered metabolic if a low $Hco^{-}3$ is a predominant coabnormality; conversely, is considered respiratory if high Pco2 is a predominant coabnormality.

SYNONYM

Acid-base analysis

TYPICAL NORMAL RANGE

- Arterial pH: dog, 7.35-7.45; cat, 7.30-7.42
- Pco2 (mm Hg): dog, 31-42; cat, 25-37
- Po2 (arterial, breathing room air; mm Hg): dog, 90-100; cat, 90-100
- $Hco^{-}3$ (mEq/L): dog, 19-26; cat, 14-21

PHYSIOLOGY

- Blood pH is maintained within narrow limits by a variety of buffers acting in concert. Pco2 and bicarbonate (Hco3) are the main parameters used for detecting respiratory and metabolic derangements (respectively) altering pH. Arterial Po2 is used for evaluating pulmonary function. Normal respiration maintains high Po2 and relatively low Pco2 concentration.
- General interpretive steps are to determine whether the pH has changed significantly and then evaluate the $Hco^{-}3$ and Pco2 to determine whether the change is due to metabolic or respiratory abnormalities, respectively.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: See individual tests, particularly pH.

CAUSES OF ABNORMALLY LOW LEVELS: See individual tests, particularly pH.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Diuretics such as furosemide can cause metabolic alkalosis.

LAB ARTIFACTS THAT MAY INTERFERE: Exposure to room air will result in falsely increased Po2 and decreased Pco2. Failure to analyze samples promptly can result in decreases in pH and Po2.

SPECIMEN: Whole blood collected and maintained in heparinized syringe (0.05-0.1 mL of heparin [1000 units/mL] per mL blood). Cap end of syringe to limit exposure to room air. Specimens analyzed within 15 minutes of collection are preferred. Storage in a capped syringe on ice at 4○C for up to 2 hours is acceptable.

RELATIVE COST: $$

PEARLS

- Alterations in pH can be life threatening. Handheld point-of-care analyzers are available for use in clinics.
- Venous blood samples are sufficient for routine evaluation of pH, Pco2, and $Hco^{-}3$. Arterial samples are more difficult to obtain but are needed for meaningful interpretation of Po2 levels.
- Submission of specimens to a reference lab may not be practical because of specimen sensitivity to environmental influence.

AUTHOR: LOIS ROTH-JOHNSON

1ST EDITION AUTHOR: JAMES H. MEINKOTH

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Blastomyces Testing

DEFINITION

Blastomycosis is a systemic fungal infection caused by the dimorphic fungus *Blastomyces dermatitidis.*

SYNONYMS

Agar-gel irnmunodiffusion (AGID) test for antibody, enzyme immunoassay (EIA) test for antigen

PHYSIOLOGY

Following inhalation of *Blastomyces* spores, a primary lung infection develops, with subsequent dissemination via blood and lymphatics to multiple tissues, most notably skin, eye, bone, lymph nodes, and brain.

TYPICAL NORMAL RANGE

- Consult the laboratory conducting the test for information regarding reference range for AGID.
- Reference range for EIA antigen test is <0.1 EIA units (EU); 1-2 EU is considered a weak positive and should be verified by repeat testing (sensitivity and specificity reported as 90% and 80%-93%, respectively).

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: A positive AGID test indicates exposure to *Blastomyces.* A positive EIA indicates possible *Blastomyces* infection. NEXT DIAGNOSTIC STEP TO CONSIDER IF TEST IS POSITIVE: If EIA positive, consider AGID, culture (only in laboratory with special handling capabilities), and cytology or biopsy. Correlate serology results with clinical signs and radiographic findings. Demonstration of the organism in Cytologie or tissue biopsy samples is required for definitive diagnosis. DNA probe testing is also available.

CAUSES OF NEGATIVE RESULT: Negative test result indicates lack of exposure, or early infection, or inadequate immune response to exposure.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: If high clinical suspicion of *Blastomyces* spp. exists, but antibody and antigen tests are negative, consider collection of relevant Cytologie samples or biopsy samples to demonstrate organisms. PCR testing may detect early infections.

IMPORTANT INTERSPECIES DIFFERENCES: Blastomycosis is more common in dogs than cats.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Effective antifungal treatment may decrease antigen levels in the EIA test. LAB ARTIFACTS THAT MAY INTERFERE: Interfering substances for the EIA test include sputolysin, sodium hydroxide, EDTA, rheumatoid factor, and heterophile antibodies.

SPECIMEN: Submit 1 mL of serum (red-top tube) for AGID serology test. Submit 2 mL of urine (preferred sample), heparinized plasma (green-top tube), BAL, CSF, or sterile body cavity fluid for EIA test. Sample for EIA is stable for 1 week at room temperature, for 1 month with refrigeration, and indefinitely if frozen.

RELATIVE COST: $$ (AGID); $$$ (EIA)

PEARLS

EIA antigen test has higher sensitivity than AGID for diagnosing canine blastomycosis. Specificity of EIA may be lower because of possible cross-reactions with histoplasmosis and other endemic mycoses. EIA antigen test may be used for monitoring response to therapy and for early detection of relapse.

AUTHOR: PATTY J. EWING

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Bilirubinuria

DEFINITION

The presence of bilirubin in urine. Most common is conjugated bilirubin, which is water soluble; some unconjugated bilirubin is bound to albumin if albuminuria or proteinuria present.

TYPICAL NORMAL RANGE

- Negative in healthy cats; rarely trace or +1 in normal cats with extremely concentrated urine (>1.055 specific gravity).
- Negative in healthy dogs, trace or +1 in normal dogs with moderately or highly concentrated urine.

PHYSIOLOGY

Bilirubin is a byproduct of erythrocyte hemoglobin metabolism. Increased bilirubin production/release is caused by hemolytic states and abnormalities in hepatobiliary excretion of bilirubin. Water-soluble conjugated bilirubin is readily filtered through the glomerulus; dogs have especially low renal thresholds, with minimal tubular resorption of bilirubin such that bilirubinuria precedes hyperbilirubinemia (icterus). Also, canine renal tubular epithelial cells are capable of bilirubin production from hemoglobin resorbed from urine. Cats have higher thresholds and greater tubular resorption of conjugated bilirubin; therefore, bilirubinuria is more clinically significant than in dogs and usually indicates hepatobiliary disease. Albumin-bound unconjugated bilirubin does not pass the glomerulus readily, but animals with albuminuria/proteinuria may have enough albumin/protein in urine to get measurable amounts of unconjugated bilirubin in urine.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Hemolytic diseases and decreased hepatobiliary excretion of bilirubin

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Assess urine specific gravity, hematocrit (if very low, likely bilirubinuria secondary to hemolytic crisis), liver enzymes (alanine aminotransferase, alkaline phosphatase, ± γ-glutamyl transferase; if significantly increased, bilirubinuria likely caused by decreased hepatobiliary excretion), and serum total bilirubin concentration.

IMPORTANT INTERSPECIES DIFFERENCES: In health, only dogs are expected to have bilirubinuria; however, cats with extremely concentrated urine may have trace or +1 reaction on dipstick.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS

- Indican (a substance that may occur in the urine of normal animals) and etodolac metabolites may cause spurious increase.
- Ascorbic acid may cause spurious decrease.

LAB ARTIFACTS THAT MAY INTERFERE: Ultraviolet light causes bilirubin degradation. It is best if the urine sample has less than 30 minutes of direct ultraviolet light exposure prior to analysis.

SPECIMEN: Urine (minimum 5 mL) in clean/sterile container collected by free catch, catheterization, or cystocentesis

RELATIVE COST: $ (reported as part of urinalysis)

AUTHOR: ELIZABETH G. WELLES

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Bilirubin

DEFINITION

A pigment produced by the degradation of the heme portion of hemoglobin (and to a lesser extent, other porphyrin-containing compounds)

TYPICAL NORMAL RANGE

- Dogs: approximately 0-0.3 mg/dL
- Cats: approximately 0-0.1 mg/dL.
- Specific values vary among laboratories.
- For mmol/L, multiply mg/dL × 17.1.

PHYSIOLOGY

During the breakdown of red blood cells (either senescent or pathologic hemolysis), heme is split to iron and protoporphyrin; protoporphyrin is converted to biliverdin then to unconjugated bilirubin predominately in macrophages of the spleen, bone marrow, and liver. Unconjugated bilirubin is released into the circulation, where it is bound to carrier proteins (albumin, globulins) and transported to the liver for uptake, conjugation, and secretion into bile. Conjugation renders bilirubin water soluble. Laboratory assays include total serum bilirubin, direct (conjugated) bilirubin, and indirect (unconjugated) bilirubin, which is a calculated value.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Hemolysis, decreased hepatic uptake, decreased functional liver mass, decreased bile excretion (intrahepatic or extrahepatic)

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Assess for hemolytic disease (CBC, saline prep for autoagglutination, Coombs' test), bile obstruction (alkaline phosphatase [ALP], imaging), hepatic disease (alanine aminotransferase, ALP, liver biopsy).

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE

- Hemolysis interferes with (either increases or decreases, depending on the method) measurement.
- Lipemia falsely increases bilirubin.
- Light degrades bilirubin (up to 50% in 1 hour in direct sunlight or fluorescent light).

SPECIMEN: Nonhemolyzed serum (red top tube). Separate serum from red blood cells as soon as possible. Store at 2°C-8°C (refrigeration). Protect from light.

RELATIVE COST: $$ (Typically part of chemistry profile); $ (as an individual test)

PEARLS

Determination of conjugated and unconjugated forms of bilirubin is not usually useful in differentiating hemolytic from hepatic/biliary causes of icterus in dogs and cats.

AUTHOR: LOIS ROTH-JOHNSON

1ST EDITION AUTHOR: FONZIE QUANCE-FITCH

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Bile Acids (Blood, Urinary)

DEFINITION

Family of detergent-like compounds (predominately cholic acid and chenodeoxycholic acid) synthesized in the liver from cholesterol and secreted in bile to aid in digestion and absorption of fat and fat-soluble vitamins.

TYPICAL NORMAL RANGE

- Fasting bile acids normally <5 mmol/L
- Fasting bile acids >20 mmol/L, postprandial samples >25 mmol/L, and/or urine bile acid/creatinine ratio >7.1 indicate liver disease.
- Urine: urine sulfated bile acids (USBA)/creatinine (crt) and total BA: crt are considered diagnostically useful.
- Dogs: USBA:crt > 1.0 and total BA:crt > 7 suggest liver disease
- Cats: USBA: crt > 2.0 and total BA:crt > 4 suggest liver disease

PHYSIOLOGY

Bile acids are stored in the gallbladder; released as a bolus into the small intestines upon feeding. In health, an efficient enterohepatic circulation exists, and up to 95% of bile acids are recycled via this cycle. Serum bile acids are evaluated in paired samples (fasting, postprandial). When portal blood clearance or biliary excretion is impaired, urinary excretion of BA increases. Urinary bile acid/creatinine ratios reflect an average serum bile acid concentration. Only a single urine sample is required.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Decreased clearance from blood (decreased functional liver mass, compromised portal circulation [congenital or acquired portosystemic shunt]). Cholestasis due to obstruction, cirrhosis, inflammation. Specific causes are many.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Assess for cholestasis (bilirubin, alkaline phosphatase), portosystemic shunt (imaging), other liver diseases (alanine aminotransferase, imaging, liver biopsy).

CAUSES OF ABNORMALLY LOW LEVELS: Low bile acid values are not clinically significant.

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE

- Decrease: hemolysis, lipemia (spectrophotometric method), no effect on radioimmunoassay
- Increase: hypertriglyceridemia (spectrophotometric method), no effect on radioimmunoassay

SPECIMEN

- Serum (red-top tube): 12-hour fasting sample and 2-hour postprandial sample recommended separate serum from red blood cells as soon as possible. Store at 2°C-8°C (refrigeration).
- Urine: fresh urine, avoid blood contamination.

RELATIVE COST: Serum (single), $$ serum (paired), $$; urine bile acid/crt, $$

PEARLS

- If cholestasis is present (e.g., patient is icteric without evidence of hemolysis), bile acids do not provide any additional information on hepatic function. Bile acids are a good indicator of hepatobiliary function but are not specific for the type of underlying disease.
- Extrahepatic disorders (e.g., gastrointestinal disease) can elevate bile acid concentrations.
- Urine bile acids are more specific for canine liver dysfunction than serum bile acids.
- Occasional preprandial values that exceed postprandial values are attributed to spontaneous gallbladder contraction.
- Urine test has low diagnostic sensitivity (false negatives common) but good specificity (few false positives).

AUTHOR: LOIS ROTH-JOHNSON

1ST EDITION AUTHOR: FONZIE QUANCE-FITCH

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Bicarbonate

DEFINITION

An anion that is the major extracellular buffer in blood

TYPICAL NORMAL RANGE

Dogs and cats: 17-24 mEq/L (mEq/L = mmol/L).

PHYSIOLOGY

Bicarbonate is formed from the conversion of carbon dioxide and water to carbonic acid by carbonic anhydrase. Carbonic acid dissociates into bicarbonate and hydrogen ion. During metabolic acidosis, bicarbonate minimizes pH changes by binding to excess H^+. Binding excess H^+ decreases measurable Hco^-3.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Metabolic alkalosis (causes: vomiting, diuretics, overadministration of bicarbonate) or respiratory acidosis (causes: pulmonary parenchymal disease [pneumonia, pulmonary edema], pulmonary restrictive disease [pleural effusion, pneumothorax, diaphragmatic hernia], hypoventilation/central nervous system depression [anesthesia, narcotics, brain stem disease], airway obstruction)

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Evaluate arterial blood gas profile (particularly pH and Pco2) to differentiate between metabolic alkalosis (high pH, high Hco^-3, high Pco2) and metabolic compensation for respiratory acidosis (low pH, high Pco2, high Hco^-3). Evaluate for underlying causes listed above.

CAUSES OF ABNORMALLY LOW LEVELS: Metabolic acidosis (causes: bicarbonate loss due to diarrhea, lactic acidosis, ketoacidosis, uremia, and ingestion of ethylene glycol) or compensation for respiratory alkalosis (causes: pulmonary disease [pneumonia, pulmonary edema], direct stimulation of central nervous system [pain, anxiety], septicemia)

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Evaluate arterial blood gas profile to differentiate between metabolic acidosis (low pH, low Hco^-3, low Pco2) and metabolic compensation for respiratory alkalosis (high pH, low Pco2, low Hco^-3). Evaluate for underlying causes listed above.

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE: Decrease: processing delay. Specimens analyzed within 15 minutes of collections are preferred. Storage in a capped syringe on ice at 4°C for up to 2 hours is acceptable.

SPECIMEN: Bicarbonate is a calculated value provided as part of a blood gas analysis. Whole blood in a heparinized syringe, avoiding exposure to room air, is used as described for blood gas analysis.

RELATIVE COST: $$ (part of blood gas analysis, not available as a separate test)

PEARLS

- Total carbon dioxide (Tco2) estimates plasma bicarbonate, which is part of most serum biochemistry profiles. Tco2 is the total amount of co2 gas that can be released from serum.
- At physiologic pH (7.4), about 95% of the potential gas is co2 and 5% is Hco^-3. Therefore, although Tco2 is usually slightly higher (1-2 mEq/L) than bicarbonate on a blood gas profile, it is considered a clinically accurate assessment of bicarbonate.
- May not be practical to submit to a reference laboratory, owing to sensitivity of specimen to environmental influences and time constraints for accurate test results

AUTHOR: LOIS ROTH-JOHNSON

1ST EDITION AUTHOR: JAMES H. MEINKOTH

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Bence Jones Urinary Proteins

DEFINITION

Unassociated immunoglobulin light chains produced in excess by abnormal plasma cells, typically with malignant plasma cell neoplasia (multiple myeloma).

SYNONYMS

Free immunoglobulin light chains, M-proteins, myeloma proteins, paraproteinuria

TYPICAL NORMAL RANGE

Reported as negative or positive

PHYSIOLOGY

Light chains are a component of immunoglobulins. Increased production occurs with increased immunoglobulin production or catabolism, as with multiple myeloma or (rarely) plasma cell tumors, the benign counterpart. Bence Jones proteins precipitate when heated, followed by redissolving when boiled and precipitation again when cooled.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Multiple myeloma; less often associated with extramedullary plasmacytoma or chronic lymphocytic leukemia; rarely associated with chronic infectious diseases

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Confirm monoclonal gammopathy with plasma immunoelectrophoresis. Assess for osteolytic bone lesions (radiographs); bone marrow plasmacytosis or plasma cell neoplasia (cytologic analysis of aspirate, or biopsy); urine protein electrophoresis (monoclonal spike in β or d regions).

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE: False positives can occur with marked proteinuria.

SPECIMEN: Urine: Store at 2°C-8°C (refrigeration).

RELATIVE COST: $$

PEARLS

Heat precipitation method is not highly sensitive. Urine protein dipstick tests do not detect Bence Jones protein. The presence of Bence Jones proteins in the urine does not indicate glomerular disease (the molecules are sufficiently small to pass through normal glomerular fenestrations).

AUTHOR: LOIS ROTH-JOHNSON

1ST EDITION AUTHOR: FONZIE QUANCE-FITCH

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Basophils

DEFINITION

White blood cell (granulocytic leukocyte) that has a segmented nucleus and metachromatic (purple) granules in cytoplasm. Basophils are rarely encountered in the blood of healthy animals.

TYPICAL NORMAL RANGE

Dogs and cats: 0-0.1 × 10^3 basophils/µL.

PHYSIOLOGY

Basophilic precursors undergo differentiation in the bone marrow, enter peripheral blood circulation for a few hours, and then enter tissue. Basophils produce leukotrienes and release histamine, heparin, and other mediators from their granules. Basophils participate in immunoglobulin E-mediated hypersensitivity reactions. They are similar in morphology to mast cells, but mast cells have a nonsegmented nucleus and primarily reside in tissue.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Allergic reactions (e.g., food, insect sting); parasitism (e.g., dirofilariasis/heartworm disease, flea infestation): mast-cell neoplasm; basophilic leukemia; myeloproliferative neoplasms (e.g., essential thrombocythemia, polycythemia vera)

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Additional tests directed by history, physical exam findings, and results of ancillary diagnostic tests to rule out causes of high values listed above

IMPORTANT INTERSPECIES DIFFERENCES: The granules in feline basophils stain lavender or light violet. The metachromatic staining of granules in feline basophilic myelocytes diminishes as the basophilic precursors undergo maturation in the marrow. Because canine basophils have comparatively low numbers of metachromatic granules, a grey basophilic cytoplasm, and are large, they can be misidentifled as monocytes on blood smear.

SPECIMEN AND PROCESSING CONSIDERATIONS

SPECIMEN: EDTA whole blood (lavender-top tube) and freshly prepared blood smear

RELATIVE COST: $$ (reported as part of CBC)

PEARLS

Basophilia often accompanies eosinophilia, a further indication of allergic or parasitic disease. Careful examination is necessary to identify basophils; when stained with the rapid Romanowsky stains (e.g., Diff-Quik), the cytoplasmic granules of canine basophils may be even less apparent.

AUTHOR: STEPHEN D. GAUNT

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Bartonellosis Testing

DEFINITION

Bartonella spp. are a group of vector-transmitted, intraerythrocytic bacterial organisms that can induce persistent infections in dogs, cats, and humans.

TYPICAL NORMAL RANGE

Consult laboratory for information regarding reference ranges. Some general guidelines include:

- Immunofluorescence antibody (IFA) test for *B. vinsonii* and *B. henselae*. Negative titer is <1:64.
- Western immunoblot (FeBart) for multiple *Bartonella* spp. in dogs and cats. Results available as negative or +1 to +4, with +3 and +4 considered positive and +2 considered to be possibly affected.

PHYSIOLOGY

Following vector transmission, chronic intravascular infections may produce no clinical signs or cause acute, life-threatening disease or chronic debilitating illness. Cats may exhibit fever, lymphadenopathy, or central nervous system (CNS) signs. Seropositive dogs may exhibit polyarthritis, endocarditis, myocarditis, CNS signs, idiopathic pleural effusion, granulomatous disease, cutaneous vasculitis, uveitis, immune-mediated hemolytic anemia, or immune-mediated thrombocytopenia.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Seropositivity indicates exposure to *Bartonella* spp.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: If seropositive, consider: (1) submitting whole blood for preenrichment culture (with BAPGM) followed by PCR and subculture onto agar plates; (2) tissue biopsy for histopathologic analysis, Warthin-Starry stain; or (3) submit whole blood or 25-50 mg of fresh or frozen tissue for PCR. Speciation for *B. henselae, B. clarridgeiae, B. quintana,* and *B. vinsonii* is possible with PCR testing. Diagnosis may be difficult to confirm.

IMPORTANT INTERSPECIES DIFFERENCES: Culture may be a less sensitive method for diagnosis in dogs than in cats, but the newly introduced preenrichment culture method has greatly improved sensitivity.

CAUSES OF ABNORMALLY LOW LEVELS: In both species, cyclic bacteremia can result in false negatives for both blood culture and PCR.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Pursue additional testing techniques, repeat testing, or empirical treatment.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Effective antibiotic treatment may decrease serology titers. Use of effective antibiotics prior to sample collection may result in a false-negative culture or PCR test.

LAB ARTIFACTS THAT MAY INTERFERE: PCR: false-positive results via contamination of samples; false-negative results due to degradation of nucleic acids via improper sample handling and storage. SPECIMEN: Contact laboratory for specific instructions. IFA: submit 1 mL serum (red-top tube). Western immunoblot (FeBart): submit whole blood, serum (red-top tube), or plasma (green-top or lavender-top tube). PCR: submit whole blood collected in EDTA (lavender-top tube). Preenrichment culture with PCR: submit 2 mL whole blood collected in EDTA (lavender-top tube).

RELATIVE COST: $$ (IFA, Western blot, PCR)

AUTHOR: PATTY J. EWING

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150

$$$$: >$150

Baermann Fecal Examination

DEFINITION

A method used for microscopic evaluation of fecal specimens for parasite larvae. Rather than being drawn to the surface, as with a fecal flotation, parasites are detected after being drawn to the bottom of the Baermann apparatus. The Baermann apparatus is a funnel with a rubber tube attached to the stem, usually supported by a ring stand. Feces are put on cheesecloth in a strainer, which is placed in the funnel. Water is added to cover the specimen, which is then macerated. An aliquot of fluid collected after a few hours is examined microscopically for parasitic larvae.

TYPICAL NORMAL RANGE

Reported as negative or positive with species identification

PHYSIOLOGY

The Baermann apparatus uses the larvae's tendency to migrate from fecal matter to warm water.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Filarid parasite *(Filaroides osleri, F. milksi, F. hirthi, Crenosoma vulpis,* and *Aelurostrongylus abstrusus)* infections are most likely to be detected by this method of fecal examination.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Positive fecal with parasite identification is considered diagnostic.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Anthelmintics may decrease larval shedding. LAB ARTIFACTS THAT MAY INTERFERE: Test is not sensitive. A negative test does not rule out infection because fecal shedding of larvae is intermittent.

SPECIMEN: Fresh (less than 24 hours old) fecal specimen submitted in dry container.

RELATIVE COST: $$

PEARLS

Bronchoscopy is preferred for detection of *F. osleri,* but the procedure is time consuming, more costly, and requires general anesthesia. Baermann fecal flotation is considered to have a slight advantage over usual fecal flotation for detection of larvae in feces; no advantage for detection of ova.

AUTHOR: LOIS ROTH-JOHNSON

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Cyclosporine Serum Levels

DEFINITION

Cyclosporine is an immunosuppressant drug that has a selective inhibitory effect on T lymphocytes, suppressing the early cellular response to antigenic and regulatory stimuli.

TYPICAL NORMAL RANGE

400-600 ng/mL (FPIA Assay) at 6-8 hours post administration

PHYSIOLOGY

Peak plasma levels usually occur 1.3-4 hours after oral administration. Ingestion of a fatty meal significantly delays absorption of cyclosporine in the gelatin capsule formulation (Sandimmune) but not in the more commonly used microemulsion formulation (Neoral, Atopica). In whole blood, 50%-60% of cyclosporine accumulates within erythrocytes, 10%-20% accumulates within leukocytes, and the remainder of the drug in circulation is associated with plasma lipoproteins. Half-life is approximately 6 hours. Extensive metabolism in the liver to >30 metabolites. Elimination primarily via bile. In the presence of hepatic dysfunction, dosage adjustments may be necessary. Major toxic effect is renal, but other potential toxicities include systemic hypertension, hepatotoxicity, neurotoxicity, gingival hyperplasia, gastrointestinal toxicity.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Overdosage, hepatic impairment, interaction with drugs (see below) CAUSES OF ABNORMALLY LOW LEVELS: Interaction with drugs (see below), insufficient dosage

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Interacts with a variety of commonly used drugs. Clearance is accelerated with coadministration of phenobarbital, phenytoin, trimethoprim-sulfamethoxazole, and rifampin (induction of hepatic P450). Clearance is decreased when coadministered with amphotericin B, erythromycin, or ketoconazole.

SPECIMEN: A blood cyclosporine level is typically checked 1-2 days after initiating therapy and then at 2- to 4-week intervals. Trough levels (24-hour): either whole blood or plasma is satisfactory but because of binding to red/white blood cells, values will vary depending upon sample submitted; check with laboratory prior to submission.

RELATIVE COST: $$$$ (peak and trough)

PEARLS

The decrease in cyclosporine excretion caused by ketoconazole can be used advantageously. Cyclosporine is a costly medication, whereas ketoconazole is inexpensive. Therefore ketoconazole, 5 mg/kg PO q 24 h may be coadministered with cyclosporine microemulsion (e.g., Neoral), 5 mg/kg PO q 24 h, which halves the required cyclosporine dose (from q 12 h to q 24 h) while maintaining the same serum cyclosporine concentration. To ensure avoidance of potentially toxic levels, monitoring plasma/blood levels is recommended. Metabolites may be active, so monitor response to therapy, not only blood levels of parent compound, to reduce risk of toxicosis.

AUTHOR: SHERRY J. MORGAN

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Culture and Sensitivity, Bacterial

DEFINITION

Submission of infected tissue or fluid for enhanced growth and isolation of bacteria and evaluation of the antibiotics (antibacterials) that could kill or inactivate them

TYPICAL NORMAL RANGE

- Bacterial isolates are reported by genus and species.
- Antibiotic sensitivity, which is determined either by disk diffusion method

(Kirby-Bauer) or determination of minimum inhibitory concentration (MIC) method, is reported as sensitive, intermediate (or indeterminate), or resistant.

PHYSIOLOGY

Small quantities of suspect tissues are aseptically plated on media that enhance the growth of bacteria. Individual colonies are isolated and identified by morphologic features (texture, color) and specific chemical reactions. Isolated colonies are exposed to known concentrations of antibiotics and evaluated for growth inhibition.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Bacterial infection or contamination

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Select an appropriate antibiotic based on sensitivity, appropriate method of delivery (e.g., injection, oral, topical), and site of infection.

IMPORTANT INTERSPECIES DIFFERENCES

- Some organisms are normal flora in some species but pathogens in others.
- Some antibiotics are appropriate for one species of patient but toxic in another.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Previous or concurrent antibiotic therapy, even if not the drug of choice, may inhibit culture growth.

LAB ARTIFACTS THAT MAY INTERFERE

- Contamination (during collection by use of nonsterile containers, prolonged storage at room temperature, or delays in shipment) may result in overgrowth.
- Contaminant organisms may inhibit growth of more fastidious organisms.

SPECIMEN: Fresh tissue or fluid in sterile container; culture swab is acceptable for both aerobic and anaerobic culture. Blood specimens should be collected in blood specimen vials. Serum (red-top tubes) with serum-separator plug should not be used for blood culture specimen.

RELATIVE COST: $$

PEARLS

Monitor potential antibiotic toxicosis by appropriate clinical monitoring and laboratory tests. MIC is the lowest concentration (greatest dilution) of an antibiotic that inhibits bacterial growth in culture media. Serial dilutions of antibiotic are made, and the highest effective dilution is reported as the MIC. Therefore, the higher the reported MIC, the more effective an antibiotic is for inhibiting the growth of a particular organism; an MIC result of 1:256 indicates an antibiotic that inhibits bacterial growth much more effectively than an antibiotic with MIC of 1:8, for example.

AUTHOR: LOIS ROTH-JOHNSON

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Crystals in Urine Sediment

DEFINITION

Precipitation of salts of metabolic products, forming crystals observed in urine sediment

SYNONYM

Crystalluria

TYPICAL NORMAL RANGE

- Reported as negative or number of crystals per microscopic high-power field, with specific identification
- Normal dogs and cats may have low numbers of crystals.

PHYSIOLOGY

Metabolic products that are normal, abnormal, or related to medication may precipitate, forming crystals that may be seen in urine sediment. Crystal formation depends on urine pH, temperature, and compound concentration.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Abnormal or increased metabolic products, changes in urine pH, enhancing formation of specific crystals NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH

- Assess diet, medication history, or evaluate for metabolic abnormalities suggested by specific crystals.
- Urine culture and sensitivity in all dogs with struvite crystalluria, because infection with urease-producing bacteria is the most common cause.

IMPORTANT INTERSPECIES DIFFERENCES: Dalmatian dogs normally can have ammonium urate crystals; in other breeds, this may indicate hepatic dysfunction.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Sulfonamides, radiopaque injectable contrast are associated with crystalluria.

LAB ARTIFACTS THAT MAY INTERFERE: Crystals may dissolve over time as urine pH changes following voiding. Conversely, refrigeration of specimens may result in in vitro formation of both struvite (ammonium magnesium phosphate, triple phosphate) and oxalate crystals over time, which remain when specimens are returned to room temperature. Therefore, immediate processing is recommended, and retesting of fresh specimens is suggested if numbers of crystals are high and the possibility of clinical significance exists.

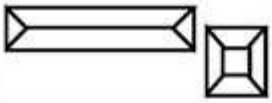
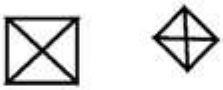
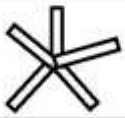
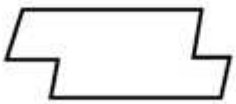
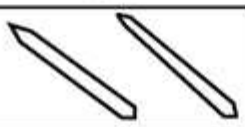
SPECIMEN: Fresh urine in sterile container for urinalysis; at least 5 mL; 10 mL is preferred by most laboratories.

RELATIVE COST: $ (reported as part of urinalysis)

PEARLS

Crystalluria may be indicative of urolithiasis. Absence of crystals does not rule out disease. If clinically significant (calcium oxalate) crystalluria is suspected, a fresh specimen should be analyzed.

AUTHOR: LOIS ROTH-JOHNSON

Cell Name	Appearance	Clinical Relevance
Ammonium magnesium phosphate (triple phosphate, struvite)		Common in dogs (infection) and cats (nutrition), especially with alkaline urine or as artifact
Ammonium biurate		Infrequent in healthy patients except Dalmatians and English bulldogs; if numerous, suggests liver dysfunction or shunt in dogs and cats
Bilirubin		Associated with bilirubinuria
Calcium oxalate monohydrate		Suggests ethylene glycol toxicity
Calcium oxalate dihydrate		Seen in healthy patients; suggests ethylene glycol toxicity
Calcium phosphate		Seen in healthy dogs
Cyst(e)ine		Rare; suggests liver disease or primary cyst(e)inuria (e.g., breed-related)
Cholesterol		Uncommon in healthy dogs; may occur with hypercholesterolemia or renal disease
Drug crystals		Sulfa, contrast media; renal elimination of material
Hippuric acid		Rare; should be distinguished from calcium oxalate monohydrate (history, physical exam)

CRYSTALS IN URINE SEDIMENT

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Cryptococcus Antigen Test

DEFINITION

Cryptococcus is a saprophytic dimorphic fungus with a worldwide distribution. *C. neoformans* is the most common species to cause disease in animals. *C. gattii* is an emerging pathogen in the Pacific Northwest, affecting immunocompetent animals and people. The antigen test detects capsular antigen (for both *C. neoformans* and *C. gatti)* present in the patient's serum.

PHYSIOLOGY

- Pigeon droppings are considered the main reservoir for *C. neoformans.* Inhalation is the presumed mode of infection. Nasal or pulmonary infection occurs; potential dissemination to central nervous system, eyes, skin, bones, lymph nodes.
- Colonization of nasal passages can occur without producing overt clinical signs.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Methods include latex agglutination and ELISA. Positive titer confirms active infection. Ability to detect antigen is high (sensitivity ~97%), but false-negative results do occur, possibly due to localized disease or a prozone effect (excessively high concentrations that paradoxically inhibit reaction). False-positive results are very uncommon (specificity approaches 100%). Higher titers are seen with disseminated disease. Monitoring titers is useful to evaluate therapeutic success; declining titers are considered a good prognostic sign.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Cytologie evaluation, histopathologic evaluation, and culture of specimens may be useful to confirm but generally are unnecessary when a positive antigen test result occurs in a patient with compatible clinical signs.

SPECIMEN AND PROCESSING CONSIDERATIONS

SPECIMEN

- Serum (most common), urine, or cerebrospinal fluid (CSF); check with individual laboratory
- CSF is preferred if central nervous system signs are present; may be more sensitive.

RELATIVE COST: $$

PEARLS

Titers from different laboratories using different methods can vary considerably; use the same method if performing repeated titers to monitor treatment.

AUTHOR: ROBIN W. ALLISON

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Cross-Matching

DEFINITION

Laboratory procedure to detect antibodies between an animal and potential blood donor. Major cross-match involves patient's serum and donor blood cells; the minor uses donor serum and patient's blood cells.

TYPICAL NORMAL RANGE

Lack of agglutination

PHYSIOLOGY

Major cross-match determines if there are agglutinating and/or hemolytic antibodies against the donor antigens in the patient. Incompatible reactions occur when blood is transfused to a patient having antibodies (whether naturally occurring antibodies, as occurs in all cats, or antibodies induced by a previous mismatched transfusion, which can occur in any species) or isosensitization from transplacental immunization. The placenta is impermeable to immunoglobulins such that a developing fetus's blood type may be different from its dam's, even if the dam has circulating antibodies against the fetal erythrocytes; ingestion of immunoglobulin rich colostrum by the neonate in the first day postpartum allows maternal antibodies to lyse neonatal erythrocytes because of neonatal gastrointestinal permeability (see p. 757). Incompatible minor cross-match is not associated with severe transfusion reactions.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Agglutination (either macroscopic or microscopic) or significant hemolysis in the cross-match tubes but not in control indicates an incompatible donor.

IMPORTANT INTERSPECIES DIFFERENCES: Cross-matching should always be performed prior to transfusion in cats, regardless of previous transfusion history, owing to the presence of naturally occurring antibodies. Transfusion of type A blood into type B cats causes rapid hemolysis (in minutes to 2 days instead of the typical 29- to 39-day transfused erythrocyte lifespan in cats) and severe anaphylaxis.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Glucocorticoids and other immunosuppressants may reduce the incidence of incompatibility (reduce negative cross-matches).

LAB ARTIFACTS THAT MAY INTERFERE: Agglutination in the control tubes (patient serum added to patient red blood cells [RBCs] or donor serum added to donor RBCs) indicates reagent contamination or autoagglutination. SPECIMEN: Two tubes are preferred, one EDTA (lavender-top tube) and one tube without anticoagulant (red-top tube or serum-separator tube).

RELATIVE COST: $$

PEARLS

A compatible cross-match does not indicate that the animal and the donor have the same blood type; it merely means that erythrocyte antibodies were not detected. Therefore blood typing remains essential in all donors and recipients.

AUTHOR: DEBORAH G. DAVIS

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Creatinine

DEFINITION

Creatinine is a waste product that results from degradation of muscle creatine or creatine phosphate.

TYPICAL NORMAL RANGE

Dogs and cats: approximately 0-1.5 mg/dL (0-133 µmol/L)

PHYSIOLOGY

Creatinine is continuously produced from slow, daily degradation of muscle creatine and is excreted in urine. It is freely filtered by the glomerulus and is not resorbed by renal tubular epithelial cells.

CAUSES OF ABNORMALLY HIGH LEVELS

- Decreased glomerular filtration rate (GFR) causes increased creatinine concentration.
- Animals with greater muscle mass, such as greyhounds, have higher creatinine concentrations than less well-muscled animals. Healthy greyhounds often have a creatinine concentration of 1.5-2.5 mg/dL.

CLINICAL APPLICATIONS

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Check serum urea (BUN) concentration and urine specific gravity. Urea and creatinine concentrations increase in parallel in many urinary tract disorders of dogs and cats.

CAUSES OF ABNORMALLY LOW LEVELS: Thin body condition/muscle loss may result in low creatinine concentration.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Evaluate for causes of muscle loss/pathologic weight loss if present on physical exam.

SPECIMEN: Serum (red-top tube) or heparinized plasma (green-top tube)

RELATIVE COST: $$ (part of most serum biochemistry profiles); $ (as a single test)

AUTHOR: ELIZABETH G. WELLES

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Creatine Kinase (CK)

DEFINITION

Cytosolic enzyme that has the highest activity in skeletal muscle, cardiac muscle, smooth muscle, brain, and nerves. Skeletal muscle injury is responsible for clinically significant elevations in dogs and cats.

SYNONYM

Creatine phosphokinase (CPK)

TYPICAL NORMAL RANGE

Dogs: 10-200 U/L. Cats: 64-440 U/L.

PHYSIOLOGY

- CK is critical for energy production to cause muscle contraction.
- CK catalyzes the formation of adenosine triphosphate (ATP) by transfer of high-energy phosphate from creatine phosphate to adenosine diphosphate (ADP). It also catalyses the reverse reaction when muscles are at rest.
- Serum CK activity is primarily of muscle origin. It is a sensitive indicator of skeletal muscle damage.
- CK is released into the interstitium when muscle membrane becomes permeable or is damaged. The plasma concentration increases 4-6 hours after injury and peaks at approximately 12 hours. Values return to normal within 24-48 hours.
- The half-life in blood is approximately 2-4 hours. Persisting elevation of CK indicates ongoing muscle damage.
- CK isoenzymes may be measured to more specifically localize muscle damage to cardiac or skeletal muscle. CK isoenzyme measurements are not routinely used in veterinary medicine. In human cardiology, other biomarkers have superseded CK (see p. 1505).

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Trauma, exertion, seizures, malignant hyperthermia, intramuscular injections, degenerative muscle disease, infectious and noninfectious myopathies, ischemia, necrosis, metabolic myopathies, toxic, drug-induced and nutritional myopathies, arterial thromboembolism, anorexia in cats resulting in muscle catabolism

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Evaluate for muscle disease or injury or muscle catabolism. In dogs, as in people, serum cardiac troponin-I levels are probably more sensitive and specific for myocardial damage than CK myocardial isoenzyme.

IMPORTANT INTERSPECIES DIFFERENCES: CK elevation commonly occurs in anorexic cats.

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE

- Increase: hemolysis, lipemia, hyperbilirubinemia, contamination of blood with muscle fluid during difficult venipuncture; dilution of samples (attributed to dilution of CK inhibitors in serum)
- Decrease: collection in citrate (blue-top tube) or sodium fluoride (grey-top tubes)

SPECIMEN: Serum (red-top tube), heparinized plasma (green-top tube), or EDTA plasma (lavender-top tube). Refrigerated samples are stable for 8-12 hours; samples stored at −20°C are stable for 2-3 days.

RELATIVE COST: $

PEARLS

Persistent exceedingly high CK levels (e.g., >200,000 U/L) are strongly suggestive of muscular dystrophy.

AUTHOR: RUANNA GOSSETT

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Cortisol

DEFINITION

Cortisol is a glucocorticoid hormone produced by the adrenal gland cortex. It initiates synthesis of proteins and receptors for hormones and cytokines involved in gluconeogenesis, protein catabolism, lipolysis, immune responses, and water balance.

TYPICAL NORMAL RANGE

Baseline cortisol concentration in health is 0.4-6 µg/dL or 10-160 nmol/L in dogs and 0.4-4 µg/dL or 10-110 nmol/L in cats.

PHYSIOLOGY

Identification of a naturally occurring, abnormally high concentration of cortisol is helpful towards making a diagnosis, because concentrations fluctuate numerous times daily. Increased concentrations may need to be provoked or suppressed for diagnostic purposes.

ACTH released from pituitary adenomas/adenocarcinomas stimulates adrenal cortical release of cortisol. Adrenocortical adenoma/adenocarcinoma in dogs and most cats overproduce cortisol. In ferrets and some cats, adrenocortical tumors produce other steroid hormones such as estrogen or progesterone and may result in clinical signs of hyperadrenocorticism. Ovarian/Sertoli cell tumors in dogs can produce cortisol-like compounds. Stress of systemic disease causes increased release of ACTH from the pituitary gland, with subsequent increased release of cortisol from adrenal glands. Administration of exogenous ACTH for use in the diagnosis of hyperadrenocorticism causes increased adrenal gland production and release of cortisol. Administration of exogenous corticosteroids (specifically dexamethasone) is used for suppressing production/release of ACTH, with subsequent decrease in adrenal release of cortisol. Dexamethasone is used for this test because it cross-reacts with cortisol minimally [<0.1%], which is considerably less than most other available corticosteroids.

With lack of appropriate ACTH secretion from pituitary gland or atrophy or destruction/necrosis of adrenal cortex, cortisol concentration can be low: hypoadrenocorticism (Addison's disease). Sudden withdrawal of administration of exogenous glucocorticoids that had caused adrenal gland atrophy can precipitate iatrogenic hypoadrenocorticism.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS

- Pituitary tumor production of excess ACTH: pituitary-dependent hyperadrenocorticism (Cushing's disease)
- Adrenal tumor production of excess cortisol: functional adrenal adenoma or adenocarcinoma
- Stress of systemic disease (endogenous production of increased ACTH)
- Ovarian/Sertoli tumor production of cortisol-like compounds
- Administration of exogenous **ACTH NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH:** Low-dose dexamethasone suppression test, imaging of adrenal glands, ACTH stimulation test **CAUSES OF ABNORMALLY LOW LEVELS**
- Primary hypoadrenocorticism (Addison's disease) caused by immune-mediated atrophy or destruction of the adrenal cortex can result in low concentrations of cortisol, cortisol and aldosterone, or only aldosterone.
- Secondary hypoadrenocorticism (ACTH deficiency) is caused by destruction, necrosis, or removal of the pituitary gland.
- Iatrogenic hypoadrenocorticism occurs secondary to sudden withdrawal of exogenously administered corticosteroids that have caused adrenal gland atrophy.
- Ketoconazole inhibits steroid biosynthesis, which can cause low concentrations of cortisol.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: ACTH stimulation test

IMPORTANT INTERSPECIES DIFFERENCES

- Cat adrenal tumors may produce hormones (progesterone) other than cortisol.
- Ferret adrenal tumors usually produce hormones (estrogen and progesterone) other than cortisol.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Immunoassays for cortisol measurement have significant cross-reactivity with other glucocorticoids:

cortisol (100%), prednisolone (69%), prednisone (6.4%), 11-deoxycortisol (7.5%), cortisone (4.2%), corticosterone (3.5%), spironolactone (<0.2%), and dexamethasone (<0.1%).

SPECIMEN

- Serum (red-top tube) or EDTA plasma (lavender-top tube)
- Cortisol in EDTA plasma is more stable than in serum and more stable in cooled samples compared with warm samples.
- Cortisol is equally distributed between red cells and plasma; therefore, rapid separation of plasma from cells (previously reported) is of no added benefit.
- EDTA interferes with some methods of testing; check with reference laboratory if submitting EDTA plasma.

AUTHOR: ELIZABETH G. WELLES

Coombs' Test

DEFINITION

Demonstrates the presence of immunoglobulin (Ig) or complement bound to the surfaces of erythrocytes

SYNONYM

Direct antiglobulin test (DAT)

TYPICAL NORMAL RANGE

Reported as negative or positive

PHYSIOLOGY

Coombs' reagent (polyvalent, species-specific anti-IgG, anti-IgM, and anti-complement antibodies) is added to patient's washed red blood cells. If Ig or complement is present on the patient's red blood cells, cross-linking will occur, resulting in agglutination (positive result).

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Immune-mediated hemolytic anemia (IMHA)

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Examine blood smear for spherocytes, assess for anemia, rule out infectious or neoplastic conditions that may cause positive test.

IMPORTANT INTERSPECIES DIFFERENCES: Species-specific Coombs' reagent is required.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Treatment with glucocorticoids may cause false-negative results.

LAB ARTIFACTS THAT MAY INTERFERE

- Positive result not associated with IMHA may be seen if: post transfusion (>3 to 7 days after transfusion) with nonspecific coating of erythrocytes, or with in vitro complement binding during storage.
- False-negative result may be seen if: antibody is present in too low a titer to be detected by test, weakly bound antibody elutes during washing, or antibody or complement detaches from RBCs due to sample aging.

SPECIMEN: Whole blood collected in EDTA (lavender-top tube), store at 8°C; test as soon as possible.

RELATIVE COST: $$

PEARLS

- Test is supportive of but not specific for IMHA. Positive results can occur in patients with infectious or neoplastic disease. Coombs' test is unnecessary (already "positive") in patients with spontaneous autoagglutination.
- A Coombs' test is neither sensitive nor specific. Physical exam, erythrocyte indices, and examination of a blood smear may be sufficient for determining the diagnosis of IMHA.

AUTHOR: LOIS ROTH-JOHNSON

1ST EDITION AUTHOR: FONZIE QUANCE-FITCH

Pricing Information

$: <$20

$$: $21-75
$$$: $76-150
$$$$: >$150

Complete Blood Count

DEFINITION

A group of routine hematologic tests for measuring several parameters of erythrocytes, leukocytes, and platelets. Tests include blood cell concentrations, measurement of cell sizes and hemoglobin concentration, differential leukocyte count, and evaluation of morphology of blood cells on a stained blood smear. A refractometric plasma protein concentration is also included by many labs.

SYNONYMS

CBC, hemogram

TYPICAL NORMAL RANGE

See Hematocrit, Leukocytes, and other Section-IV entries for specific information, including reference intervals.

PHYSIOLOGY

See Hematocrit, Leukocytes, and other Section-IV entries for specific information.

SPECIMEN AND PROCESSING CONSIDERATIONS

SPECIMEN: EDTA (lavender-top tube) blood sample and freshly prepared blood smear for lab to stain

RELATIVE COST: $$

PEARLS

Although automated hematology analyzers provide 3- or 5-part differential leukocyte counts as part of a CBC, the differential counts obtained from stained blood smears remain the most accurate method for differentiating leukocytes and detecting left shifts in dogs and cats.

AUTHOR: STEPHEN D. GAUNT

Cell Name	Appearance	Clinical Relevance
Acanthocyte (burr cell)		Associated with vascular, liver, or renal disease
Codocyte (target cell)		Regenerative anemia; liver or renal disease; abnormal lipid metabolism
Eccentrocyte (burr cell)		Oxidative injury
Keratocyte		Vascular disease, including hemangiosarcoma and disseminated intravascular coagulation
Heinz body		Oxidative injury
Leptocyte		Iron deficiency
Schistocyte		Vascular disease including hemangiosarcoma, disseminated intravascular coagulation
Spherocyte		Immune-mediated hemolysis or partial phagocytosis. Unlike small red blood cells (microcytosis), spherocytes have no central pallor

COMPLETE BLOOD COUNT Red cell abnormalities. See also for discussion of various red blood cell morphologic abnormalities (i.e., poikilocytosis).

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Colloid Osmotic Pressure

DEFINITION

The portion of serum osmotic pressure generated by colloids (typically proteins) and other molecules too large to freely cross the vascular endothelium

SYNONYM

Oncotic pressure

TYPICAL NORMAL RANGE

- Dogs: 14-27 mm Hg
- Cats: 21-34 mm Hg

PHYSIOLOGY

Colloid osmotic pressure (COP) and hydrostatic pressure control fluid movement between the intravascular and interstitial spaces. In health, COP is generated largely by albumin (~80%), with the remainder being mostly fibrinogen and globulins. Therapeutic administration of colloidal solutions (plasma, polymerized bovine hemoglobin [Oxyglobin], hetastarch) can be used for compensating for pathologic decreases in COP.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Marked hyperglobulinemia (e.g., plasma cell myeloma, feline infectious peritonitis), overadministration of therapeutic colloids (i.e., Oxyglobin)

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Evaluate serum proteins; protein electrophoresis; review drug history for administration of colloids.

CAUSES OF ABNORMALLY LOW LEVELS: As for hypoalbuminemia (hemorrhage, gastrointestinal or renal protein loss, hepatic failure). Acidosis lowers COP independently of protein concentration. NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Evaluate serum proteins, screen for blood/plasma loss, urine protein, liver function.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Increase: therapeutic administration of colloids (intended effect)

LAB ARTIFACTS THAT MAY INTERFERE: Marked hemolysis may increase COP.

SPECIMEN: Plasma collected in heparin (green-top tube) or EDTA (lavender-top tube), spun, and separated from cells. A specific instrument (colloid osmometer) is required for measurement; COP is not reported routinely on small-animal blood profiles.

RELATIVE COST: NA; not offered by most reference laboratories

PEARLS

- COP is superior to albumin measurement (and therefore is most useful) when evaluating and monitoring the oncotic pressure of an animal receiving treatment with nonalbumin-type colloids such as synthetic colloids (hetastarch, pentastarch).
- COP must be interpreted in context of clinical situation.
- Decreased COP due to acute changes in protein concentration (hemorrhage) is more likely to result in clinical abnormalities than the same low COP due to chronic hypoalbuminemia.
- Trends in COP change may be more significant than a single value.
- COP may be useful in differentiating causes of edema (decreased COP versus increased hydrostatic pressure versus vasculitis [COP normal for the latter two]).
- Equations to estimate COP using serum/plasma protein concentration are unreliable in critically ill animals. Direct measurement using a colloid osmometer is needed.
- For clinical use, the terms *colloid osmotic* and *oncotic* pressure can be used interchangeably.

AUTHOR: LOIS ROTH-JOHNSON

1ST EDITION AUTHOR: JAMES H. MEINKOTH

Coccidioides immitis Serology

DEFINITION

Coccidioides immitis is a soil-borne dimorphic fungus restricted to certain geographic regions, specifically the Lower Sonoran life zone within the southwestern United States, Mexico, and Central and South America. Serologie testing measures the anti-*Coccidioides* antibodies that may be present in serum by one of several methods.

PHYSIOLOGY

Infection is typically acquired by inhalation, initially causing pulmonary infection that may disseminate to lymph nodes, bones, eyes, heart, testicles, brain, spinal cord, and other visceral organs.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Interpretation of positive titers varies substantially depending upon the type of test performed. Consult with individual laboratory.

- Tube precipitin (TP) antibody: detects immunoglobulin (Ig)M; positive early in infection only
- Complement fixation (CF) antibody: detects IgG; positive with past exposure or active infection; titers =1:64 usually indicate severe or disseminated disease
- Latex agglutination: detects IgM; positive early; some false-positive results in dogs
- Agar gel immunodiffusion (AGID) with TP antigen: more sensitive than TP antibody in early infection
- AGID with CF antigen: detects IgG; more sensitive than CF antibody
- ELISA for IgM: ~15% false positives; may cross react with blastomycosis
- ELISA for IgG: similar to CF and AGID/CF; may cross-react with blastomycosis

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Confirm diagnosis with Cytologie or histopathologic analysis of specimens if appropriate samples can be obtained.

IMPORTANT INTERSPECIES DIFFERENCES: Both CF and TP antibodies may persist in cats for long periods of time (years), even with therapy.

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE

- False-negative CF antibody test in dogs may be due to interference from anti-complement factors in 15%-25% of normal dog sera.
- Cross-reactivity with blastomycosis possible in ELISA tests

SPECIMEN: Serum, single sample or paired samples obtained 4-6 weeks apart. Refrigerate.

RELATIVE COST: $$

PEARLS

Specimens from patients thought to have coccidioidomycosis should not be cultured without biosafety precautions; mycelial phase is highly infectious to humans by inhalation.

AUTHOR: ROBIN W. ALLISON

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Cobalamin

DEFINITION

Water-soluble vitamin with a porphyrin ring; side chains bound to cobalt

SYNONYMS

Cyanocobalamin, vitamin B^{12}

TYPICAL NORMAL RANGE

- Dog serum: 238-733 ng/L
- Cat serum: 290-1500 ng/L
- Conversion: 1 pg/mL = 0.1 ng/dL; 1 pg/mL × 0.7378 = pmol/L

PHYSIOLOGY

Source is dietary. Released from food during gastric digestion and bound to R-proteins (nonspecific binding proteins) found in salivary and gastric secretions. Transferred to intrinsic factor (IF) in alkaline intestinal pH. IF enhances ileal cobalamin absorption. Cobalamin is stored in the liver. It is a required cofactor in metabolic pathways involving folate and formation of neuronal lipids.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Uncommon; dietary supplementation and hepatocellular necrosis (theoretical)

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Review oral or parenteral supplements, sampling and testing protocol.

CAUSES OF ABNORMALLY LOW LEVELS: Decreased ileal absorption due to inflammation, villous atrophy or other mucosal disease; decreased IF production due to gastric disease in dogs and exocrine pancreatic insufficiency in dogs and cats; congenital insufficiency of IF in giant Schnauzers, border collies; malabsorption; bacterial overgrowth in proximal small intestine (enteric bacteria bind cobalamin).

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Assess for inflammatory bowel disease (IBD): history, physical exam, serial fecal flotations, and possibly empirical parasiticide treatment and/or abdominal ultrasonography to rule out other causes; biopsy of small intestine ultimately needed for histologic demonstration of IBD). Assess for pancreatic exocrine insufficiency (serum trypsin like immunoreactivity).

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Oral or parenteral supplements increase concentration.

LAB ARTIFACTS THAT MAY INTERFERE

- Falsely increased by hemolysis or heparin
- Falsely decreased by excessive light exposure

SPECIMEN: Serum; separate from clot as soon as possible; store at 8°C.

RELATIVE COST: $$

PEARLS

- Assays for human specimens are unreliable in dogs and cats because of species-specific carrier.
- Assessment of cobalamin (and folate) levels is no longer considered reliable for the diagnosis of antibiotic-responsive enteritis/small-intestinal bacterial overgrowth.

AUTHOR: LOIS ROTH-JOHNSON

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Coagulation Profile

DEFINITION

Series of tests designed to assess the coagulation pathway and localize specific hemostatic defects causing coagulopathies. Consists of partial thromboplastin time (PT), activated partial thromboplastin time (APTT), and activated clotting time (ACT).

TYPICAL NORMAL RANGE

- ACT: 60-100 seconds (dogs) and <65 seconds (cats)
- APTT: 8.6-12.9 seconds (dogs) and 13.7-30.2 seconds (cats)
- PT: 5.1-7.9 seconds (dogs) and 8.4-10.8 seconds (cats)
- Reference values are laboratory-and instrument-specific; the ranges listed above are approximate.
- Neonates (<24 hours old) may normally have greater values than adults.

PHYSIOLOGY

Coagulation factors are a cascade of enzymes that require sequential activation. They stabilize the platelet plug through the conversion of fibrinogen to fibrin, forming a fibrin platelet plug that resists plasmin degradation. The coagulation cascade is divided into intrinsic, extrinsic, and common pathways. Pathways of activation are through tissue thromboplastin (extrinsic; released from cell surface membranes of injured tissues) and by contact activation of basement membranes and negatively charged surfaces of collagen or platelets (intrinsic; e.g., contact with a vessel denuded of endothelium). The division is imperfect because the tissue factor/factor Vlla complex is a potent activator of both factors IX and X.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS

- Prolonged PT: extrinsic (factor Vll) or common coagulation (X, V, ll, thrombin, and fibrinogen) pathway defect; most sensitive test of warfarin-type toxicity; increased with a decrease/absence of factors of extrinsic or common pathway, disseminated intravascular coagulation (DIC), FDPs, antiphospholipid antibodies, antibodies to coagulation factors, acquired vitamin K deficiency, biliary obstruction, liver failure
- Prolonged APTT: defects in intrinsic pathway (factors Xll, Xl, IX, Vlll); hemophilia, von Willebrand disease, DIC, vitamin K antagonism or absence, bile insufficiency or liver failure
- Prolonged ACT: any disorder that sufficiently increases PT, aPTT, or both (common pathway) can increase ACT.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Platelet count, buccal mucosal bleeding time, fibrin degradation products, specific factor analysis

CAUSES OF ABNORMALLY LOW LEVELS: Coagulation times shorter than reference range are uncommon and unlikely associated with clinical disease.

DRUG EFFECTS ON LEVELS: Increased: warfarin, heparin therapy

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE: Increase: inadequately filled tubes, causing specimen dilution by anticoagulant

SPECIMEN: Citrated plasma (blue-top tube) for most tests. Diatomaceous earth (gray-top tube) for ACT. Fill tubes completely. Refrigerate, send to lab on ice.

RELATIVE COST: $$

PEARLS

- ACT is insensitive except in cases of severe coagulopathy (e.g., severe warfarin intoxication); it is an immediate point-of-care test that should always be followed up with PT and APTT assessments.
- Low PT, APTT, ACT values do not indicate a procoagulant or thrombogenic state.

AUTHOR: DEBORAH G. DAVIS

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Cholesterol

DEFINITION

A lipid that is found only in animal tissues. The test measures circulating blood (serum) levels.

Hyperlipidemia is a term that groups hypercholesterolemia and hypertriglyceridemia.

TYPICAL NORMAL RANGE

Dogs: 112-328 mg/dL. Cats: 82-218 mg/dL.

PHYSIOLOGY

Synthesized by the liver or absorbed in intestines from dietary sources. Cholesterol is essential to life as a major component of cell membranes and precursor for synthesis of steroid hormones and bile acids. The liver is the major site of cholesterol synthesis, excretion, and catabolism. Cholesterol and other lipids are insoluble in water. They are transported in the blood attached to apoproteins. Lipid-apoprotein complexes are called *lipoproteins.* They contain variable proportions of triglycerides, cholesterol, cholesterol esters, and phospholipid. In laboratory analysis, lipoproteins can be separated by ultracentrifugation into chylomicra, high-density lipoproteins (HDL), intermediate-density lipoproteins, low-density lipoproteins (LDL), and very low-density lipoproteins (VLDL), but the clinical importance of lipoprotein profiling in small-animal medicine is minimal compared to human medicine.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS

- Primary hyperlipidemia: idiopathic in schnauzer dogs and rarely in other breeds; hypercholesterolemia of Briard dogs, Doberman pinschers, and rottweilers; familial hyperchylomicronemia of cats
- Secondary hyperlipidemia: postprandial (most common), hypothyroidism, diabetes mellitus, liver disease, hyperadrenocorticism, pancreatitis in dogs and cats, nephrotic syndrome, high fat diet

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH

- Ensure that blood sample was drawn after >= 12-hour fast.
- Assess for causes of secondary hyperlipidemia (endocrine or metabolic disease). If no cause is identified, consider primary hyperlipidemia.

CAUSES OF ABNORMALLY LOW LEVELS: Chronic liver disease, starvation NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Evaluate for chronic liver disease. Rule out starvation. IMPORTANT INTERSPECIES DIFFERENCES: Dogs and cats are resistant to atherosclerosis, partly owing to the low concentration of very low-density lipoproteins in these species. High-density lipoproteins are the major lipoproteins in dogs and cats.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS

- Increase: exogenous corticosteroids, phenytoin, methimazole
- Decrease: lipid-lowering diets, bile acid sequestrants, hepatic hydroxymethylglutaryl coenzyme A reductase inhibitors (statins), and dirlotapide lower cholesterol levels.

LAB ARTIFACTS THAT MAY INTERFERE: Increase: hemolysis

SPECIMEN

- A 10- to 12-hour fast is required. Postprandial hypercholesterolemia is mild, (usually associated with less than a twofold elevation).
- Serum (red-top tube), heparinized plasma (green-top tube), or EDTA plasma (lavender-top tube). Stable for 1 week at 2°C-8°C and 4 weeks at −20°C.

RELATIVE COST: $

PEARLS

The most common cause for hypercholesterolemia and no other CBC/serum biochemistry abnormalities in an adult fasted dog is hypothyroidism.

AUTHOR: RUANNA GOSSETT

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Chloride

DEFINITION

Major extracellular fluid (ECF) anion. Serum [Cl^-] essentially equals ECF [Cl^-]. Na^+, Hco^-3 influence CT concentrations.

TYPICAL NORMAL RANGE

Dogs: 105-115 mEq/L. Cats: 115-125 mEq/L; mEq/L = mmol/L.

PHYSIOLOGY

Major component of gastric juices; intestinal resorption coupled to Na^+ resorption, Hco^-3 secretion. Kidneys play major regulatory role: filtered by glomeruli, reabsorbed in renal tubules following Na^+ and water. Acid-base balance helps regulate serum levels: inverse relationship between serum [CT] and [Hco^-3]. Serum [Na^+] and [Cl^-] usually change proportionally, but if [Na^+] remains the same, increased [Cl^-] causes hyperchloremic acidosis; decrease causes hypochloremic alkalosis.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS

- With proportional [Na^+] increase: same as hypernatremia (see pp. 1517 and 559)
- Without proportional increase in [Na^+]: hyperchloremic acidosis caused by gastrointestinal (GI) or renal loss of Hco^-3, compensation for chronic respiratory alkalosis

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH

- Evaluate in relation to serum [Na^+], acid-base balance.
- Calculate corrected serum [Cl^-] to determine if proportional change relative to [Na^+]: [Cl^-] (corrected) = [Cl^-] (measured) × ([Na^+] (mean normal)/[Na^+] (measured). Reference interval for conected [Cl^-] is the same as for [Cl^-].

CAUSES OF ABNORMALLY LOW LEVELS

- With proportional decrease in serum [Na^+]: same as hyponatremia (see pp. 1517 and 559)
- Without proportional decrease in [Na^+]: hypochloremic alkalosis caused by loss/sequestration of HC1 (gastric vomiting, upper GI obstruction), compensation for chronic respiratory acidosis

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW

- Evaluate in relation to [Na^+], acid-base balance.
- Calculate corrected serum [Cl^-] to determine if proportional change.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS

- Decreased: thiazide or loop diuretics, $NaHco^-3$, Na penicillin (high doses)
- Increased: NH4Cl, KCl, parenteral saline administration, acetazolamide, spironolactone

LAB ARTIFACTS THAT MAY INTERFERE

- Marked hyperlipidemia/hypercholesterolemia or hyperproteinemia may decrease measured [Cl^-] by electrolyte exclusion effect (method dependent). Serum osmolality is normal.

- False increase: halides (bromide, iodide) are measured as Cl^-.

SPECIMEN: Serum (red-top tube) preferred; heparinized plasma (green-top tube) may be used.

RELATIVE COST: **$**

PEARLS

Changes independent of [Na^+] should be interpreted in conjunction with the anion gap. Mixed acid-base disorder is suggested by selective hypochloremia with high anion gap. Most reference laboratory methods are subject to electrolyte exclusion effect artifacts.

AUTHOR: ROBIN W. ALLISON

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Cerebrospinal Fluid (CSF) Analysis

DEFINITION

Cerebrospinal fluid (CSF) is the aqueous fluid that surrounds the brain and spinal cord. *Pleocytosis* refers to an increased cellularity of the CSF sample. *Xanthochromia* refers to a yellow discoloration of the sample, typically from blood that has been present in the CSF for days or longer. *Albuminocytologic dissociation* refers to a disproportionate elevation of CSF protein compared to minimally elevated or normal CSF cell count.

TYPICAL NORMAL RANGE

Dogs: red blood cell (RBC), <30/µL; white blood cell (WBC), 0-4/µL; protein, <35 mg/dL. Cats: RBC, <30/µL; WBC, 0-4/µL; protein, <36 mg/dL.

PHYSIOLOGY

CSF provides support and protection for neural structures, serves as a transport medium for metabolic products to and from the brain, and provides a barrier to control the microenvironment of the nervous system. It is normally colorless, clear, and almost acellular. Cytocentrifugation is required for cytologic evaluation of cells to assess for inflammation, hemonhage, and infectious agents. Protein (primarily albumin) concentration is normally very low and requires microprotein assays for accurate assessment.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS

- Increased protein: hemorrhage, increased permeability of the blood-CSF barrier, or localized production of immunoglobulins
- Increased protein with normal cellularity: trauma, degenerative disease, intervertebral disc disease, fibrocartilaginous embolism, cervical spondylomyelopathy, neoplasia, and viral infections
- Increased protein and cell counts: inflammation, infection (viral, fungal, protozoal, bacterial, rickettsial, parasitic), granulomatous meningoencephalitis, steroid responsive meningitis, neoplasia, immune mediated disease, vasculitis, and necrotizing meningoencephalitis. Neoplastic cells are rare in CSF; lymphoma is the most commonly identified neoplasm.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Correlate CSF findings with history, general physical, neurologic, and radiographic findings.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Glucocorticoids may reduce inflammatory cell counts after 24 hours of initiation of treatment, but glucocorticoid treatment may be initiated for patient stabilization if a high degree of steroid-responsive disease exists. Provided CSF tap occurs within 24 hours, accurate CSF cell counts are expected.

SAMPLE FOR COLLECTION AND ANY SPECIAL SPECIMEN HANDLING NOTES: Fluid in EDTA (lavender-top tube) or plain red-top tube; refrigerate. Analysis should be performed as soon as possible; cells deteriorate and lyse rapidly because of the low protein concentration. Addition of autologous serum to CSF (1:1) helps preserve cells for cytologic evaluation. However, a separate aliquot of CSF must be submitted for protein determination and cell counts.

RELATIVE COST: $$

AUTHOR: RUANNA GOSSETT

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Casts in Urine Sediment

DEFINITION

Coagulum of protein, cells, and/or cell debris forming in renal tubules and observed during microscopic examination of urine sediment

SYNONYM

Cylindruria

TYPICAL NORMAL RANGE

- Reported as negative or average number of casts per low-power microscope field with cast identification
- Up to two hyaline casts in moderately concentrated urine (e.g., specific gravity >1.020) is considered normal.

PHYSIOLOGY

Tamm Horsfall mucoprotein, secreted by renal tubular epithelium, combines with cells in renal tubules, forming cylindrical structures (casts) that are passed in urine. This type of cast is occasionally referred to as a *hyaline cast.* Some casts (granular, cellular, fatty) are composed of renal tubular epithelial cells or material that reflects their degeneration. Waxy casts are uncommon and indicative of chronic kidney disease. They form from granular casts that have degenerated. Others are composed of leukocytes or red blood cells, indicating inflammation or hemorrhage, respectively.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Toxic renal tubular injury, pyelonephritis

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Evaluate history for exposure to renal toxins; kidney biopsy if otherwise clinically indicated.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Gentamicin, amikacin, or other renal tubular toxins may cause granular, cellular, or fatty casts.

LAB ARTIFACTS THAT MAY INTERFERE: Delay in examination, excessive specimen mixing, and alkaline urine promote disintegration of casts and false-negative results.

SPECIMEN: Fresh urine (at least 10 ml) in clean, sterile container for urinalysis

RELATIVE COST: $ (reported as part of urinalysis)

PEARLS

Failure to see casts does not rule out renal tubular disease.

AUTHOR: LOIS ROTH-JOHNSON

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Canine Parvovirus Tests

DEFINITION

Canine parvoviral enteritis is a highly infectious, often fatal disease of Canidae caused by a small, nonenveloped DNA virus, CPV-2, that requires rapidly dividing cells for replication.

SYNONYM

Parvo

TYPICAL NORMAL RANGE

Negative or positive with titer. Available tests: serum immunoglobulin (Ig)M and IgG immunofluorescent antibody (IFA), serum antibody by hemagglutination inhibition (HI), fecal antigen ELISA, and electron microscopy for identification of parvovirus particles.

PHYSIOLOGY

Following oronasal exposure to contaminated feces, CPV-2 replicates in oropharyngeal lymphoid tissue, mesenteric lymph nodes, and thymus. Viremia develops 1-5 days post exposure, without enteric shedding. Virus infects intestinal crypt epithelium, causing necrosis and clinical signs that may include lethargy, anorexia, vomiting, and bloody diarrhea. Virus spreads to lymphoid tissue and bone marrow, causing necrosis, subsequent leukopenia, and immunosuppression. Without treatment, secondary infection, gram-negative sepsis, and death may ensue.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS:

- Positive fecal ELISA test indicates viral antigen shedding due to natural infection or recent (5-12 days) vaccination with modified live vaccine.
- Positive serum IgM by IFA indicates recent exposure (natural or vaccination); usually positive by the time clinical signs are present.
- Positive IgG titer by IFA indicates exposure (natural or vaccination); can demonstrate rising titer in acute and 10- to 14-day convalescent serum samples, although urgency of initial diagnosis and treatment usually minimizes utility of this approach.
- Serum antibody titer by HI of >=1:64 indicates previous exposure (natural or vaccination) and protective antibody.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Positive fecal ELISA with appropriate clinical signs is generally diagnostic.

CAUSES OF ABNORMALLY LOW LEVELS

- Negative fecal ELISA indicates uninfected, very early postexposure, or end of viral shedding (virus seldom detectable 10-12 days after natural infection; 5-7 days of clinical signs).
- False-negative fecal ELISA may occur if the sample is obtained ex vivo (e.g., defecated stool) rather than being swabbed from the rectum.
- Negative serologic result indicates lack of exposure to virus and inadequate vaccine protection.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: If clinical signs and laboratory findings are consistent, but ELISA and IFA are negative, electron microscopic exam of feces can be performed. Additional tests—such as histopathologic evaluation of necropsy or biopsy tissue, or tissue culture—are possible but are invasive and potentially hazardous to the patient.

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE: Severe hemolysis and lipemia interferes with IFA.

SPECIMEN: ELISA: fresh fecal swab stored for =48 hours (2°C-8°C). HI, IFA: serum (red-top tube), can be stored at 2°C-8°C up to 4 days.

RELATIVE COST: $$ (ELISA, IFA)

PEARLS

Some (but not all) ELISA tests for canine parvovirus will also detect feline parvovirus (panleukopenia) in the feces of cats that are shedding virus. False-negative results occur in early stages (prior to fecal shedding) or late stages (virus has become bound to specific antibody). Positive results due to vaccination may occur in cats for up to 2 weeks post inoculation.

AUTHOR: PATTY J. EWING

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Canine Distemper Testing

DEFINITION

Canine distemper is a multisystemic disease caused by canine distemper virus (CDV), a *Morbillivirus.*

TYPICAL NORMAL RANGE

Refer to laboratory conducting the tests. Available tests include serum immunofluorescent antibody test (IFA) titer, direct IFA, and viral neutralization assay.

PHYSIOLOGY

Distemper is spread via inhalation. Virus attaches to upper respiratory tract epithelium and replicates in macrophages. It spreads to regional lymph nodes and subsequently to bone marrow, thymus, spleen, mesenteric lymph nodes, and gastrointestinal tract. Then 8-14 days later, it spreads to epithelial tissue and the central nervous system, at which time it becomes most easily detected with clinical diagnostic tests. Young dogs may develop fever, leukopenia, respiratory signs, and demyelinating encephalomyelitis. Viral persistence is associated with chronic encephalitis.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS:

- Positive IFA immunoglobulin (Ig) M titer indicates recent exposure to vaccine or acute natural infection. IgM is detectable from 1-4 weeks post exposure. Positive IFA IgG titer indicates exposure to vaccine, presence of maternal antibody, or chronic natural infection. Serum viral neutralization assay is preferred for determining protective antibody response to vaccination.
- Positive direct IFA on Cytologie or histopathologic sample is diagnostic of infection.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Direct immunofluorescence is used for detecting antigen in Cytologie smears of conjunctival, tonsillar, genital, or urinary bladder epithelium, or in white blood cells (buffy coat or bone marrow). Cerebrospinal fluid (CSF): increased protein and lymphocytic pleocytosis are common. Increased anti-CDV antibody in CSF not contaminated with serum is a sensitive and specific indicator of distemper encephalitis. PCR testing can be performed on CSF, ocular or nasal swab, whole blood, or tissue. Routine Cytologie evaluation of conjunctival smears for inclusions (routine staining, with or without IFA) is generally unrewarding.

CAUSES OF ABNORMALLY LOW LEVELS: Lack of protective vaccine antibody titer. Early infection with natural exposure.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: If clinically indicated, evaluate IgM titer or repeat IgG titer in 2-3 weeks (expect increase if original low/absent level was due to early infection).

SPECIMEN AND PROCESSING CONSIDERATIONS

SPECIMEN: Serologie test: 1 mL of serum (red-top tube). May store 4 days refrigerated or up to months frozen. IFA: conjunctival, urinary sediment, buffy coat smears air dried and preferably fixed in acetone for 5 minutes. Whole blood in EDTA (lavender-top tube) stored for no more than 48 hours refrigerated may be used in place of buffy coat smear. PCR: Minimum 0.5 mL of CSF or whole blood in EDTA (lavender-top tube).

RELATIVE COST: $$ (IFA, PCR)

PEARLS

- Serologie testing is the most sensitive and specific test in the live patient: IgM titers rise early in infection and, barring a recent history of vaccination, are specific to infection.
- Although studies suggest that currently available commercial vaccinations offer protection from disease for 3 years, determination of protective serum titer values has not been done. Immunologically competent dogs that have been vaccinated should be able to mount an anamnestic response that would prevent viral exposure leading to disease.

AUTHOR: PATTY J. EWING

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Calcium, Serum

DEFINITION

Essential mineral with important regulatory functions (cell signaling). Serum total calcium includes protein-bound (35%), anioncomplexed (10%), and ionized (55%) fractions.

TYPICAL NORMAL RANGE

- Total Ca^{2+}: 8-11.5 mg/dL (2-3.8 mmol/L)
- Ionized Ca^{2+}: 4.5-6 mg/dL (1.1-1.5 mmol/L)
- Unit conversion: mg/dL × 0.2495 = mmol/L; mEq/L × 0.5 = mmol/L

PHYSIOLOGY

Serum levels are regulated by parathyroid hormone (PTH) and calcitriol (vitamin D metabolite) affecting intestine, kidney, and bone. Dietary absorption depends on calcitriol. Glomeruli filter nonproteinbound Ca^{2+}; 98% reabsorbed by tubules. Low ionized Ca^{2+} stimulates PTH production, mobilizing Ca^{2+} from bone, increasing renal tubular resorption, stimulating calcitriol synthesis.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Hypercalcemia of malignancy, hypoadrenocorticism, primary hyperparathyroidism, osteolysis, granulomatous conditions, hypervitaminosis D, renal failure, excess supplementation (rare from oral supplementation alone) NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Measure ionized Ca^{2+}. If ionized hypercalcemia, evaluate for neoplasia (including rectal palpation for anal sac neoplasm in adult dogs), exposure to oral vitamin D (rodenticides, supplements, ointments). Measure serum phosphorus, parathormonerelated peptide, PTH.

CAUSES OF ABNORMALLY LOW LEVELS: Hypoalbuminemia, renal failure, pancreatitis, puerperal tetany, hypoparathyroidism, severe tissue trauma, ethylene glycol intoxication, exocrine pancreatic insufficiency, malabsorption syndromes, hypomagnesemia, phosphate enema, acute tumor lysis syndrome

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Measure ionized Ca^{2+}, serum albumin levels. Evaluate for renal failure, gastrointestinal diseases. Measure serum PTH, magnesium levels.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS

- Increase: thiazide diuretics, supplements containing vitamin D, rodenticides, excess oral phosphate binders
- Decrease: furosemide, glucocorticoids, phosphate enemas, Ca^{2+}-binding anticoagulants

LAB ARTIFACTS THAT MAY INTERFERE

- Decreased: Ca^{2+}-binding anticoagulants (EDTA, citrate, oxalate; artifactual/in vitro decrease)
- Increased: lipemia, hemolysis
- Decreased ionized Ca^{2+}: aerobic sample handling, overheparinization. Increased ionized Ca^{2+}: prolonged exposure to erythrocytes, serum separator tubes.

SPECIMEN

- Serum (red-top tube) preferred; heparinized plasma (green-top tube) may be used.
- Ionized Ca^{2+}: anaerobic handling necessary. Harvest serum or plasma within 1 hour. Stable in heparinized blood for 9 hours (4○C), serum or plasma for 1 week (4○C). Do not use serum separator tubes. Heparin concentration should not exceed 15 U/mL of blood.

RELATIVE COST: $ (serum calcium, single test); $$ (as part of serum electrolyte profile); $$ (ionized calcium)

PEARLS

- Use of correction formula in hypoalbuminemic dogs no longer recommended because of inaccuracy; measure ionized Ca^{2+} instead.
- Acidosis increases ionized serum Ca^{2+} concentration; alkalosis decreases it. Acid-base status affects signs associated with hypocalcemia.

AUTHOR: ROBIN W. ALLISON

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Digoxin, Serum Level

DEFINITION

Digoxin, a drug in the cardiac glycoside class, has complex cardiovascular actions. It is used in the management of supra-ventricular arrhythmias (e.g., atrial fibrillation) and certain cases of congestive heart failure.

SYNONYM

Digitalis

TYPICAL RANGE

In humans, serum level >2 ng/mL is suggestive of toxicosis; therapeutic levels range from 0.5-1.5 ng/dL or 0.8-2 ng/mL (see below). In veterinary medicine, the same values are used, but no clinical trial has ever proven that “therapeutic levels” are beneficial over empirical dosing.

PHYSIOLOGY

Digoxin is rapidly absorbed as an oral elixir (serum levels detectable in 45 minutes; bioavailability 100%) and slightly less so in tablet form (hours; bioavailability 80%). Intravenous administration is no longer recommended. Regardless of administration route, excretion is renal. The linear dose/response curve of digoxin suggests that serum levels previously considered “subtherapeutic,” which are associated with fewer side effects, may provide beneficial effects. Revised therapeutic serum levels of 0.5-1.5 ng/mL have been suggested in human cardiology. The primary mechanism of action of cardiac glycosides is interference with Na/K-ATPase, with resultant increase in intracellular calcium. Adverse effects, including severe lethargy, anorexia, and arrhythmias such as atrioventricular block due to progressive interference with electrical conduction and increase in vagal tone, may occur.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Large body size, obesity (digoxin is not distributed in fat), and renal failure warrant lowering digoxin dose; otherwise, high serum levels and toxicity may occur. Dosing based on body surface area has been recommended. The half-life of cardiac glycosides is highly variable among patients.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Adjust dose, depending on suspected cause.

CAUSES OF ABNORMALLY LOW LEVELS: A rninimum serum concentration for clinical effect has not been established for dogs and cats. Hypokalemia potentiates digitalis-induced anhythmias. If toxicosis is evident but the serum concentration is not excessive, serum potassium should be evaluated.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Measure serum potassium.

IMPORTANT INTERSPECIES DIFFERENCES: Enterohepatic recycling of cardiac glycosides is very important in humans, less so in dogs.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVEL: Drugs inducing hepatic metabolism (e.g., phenytoin, rifampin) accelerate digitoxin metabolism, resulting in higher than expected digoxin serum levels. Quinidine elevates serum concentrations by decreasing clearance and volume of distribution. Other drugs that may increase serum digoxin concentrations include verapamil, diltiazem, amiodarone, flecainide, and spironolactone.

SAMPLE FOR COLLECTION AND ANY SPECIAL SPECIMEN HANDLING NOTES: Serum (red-top tube); store at 2°C-8°C.

RELATIVE COST: $$

PEARLS

Serum digoxin levels may be used for confirming ingestion of plants (milkweed, foxglove, oleander, dogbane) that contain cardiac glycosides.

AUTHOR: SHERRY J. MORGAN

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

D-Dimer

DEFINITION

Protein fragments that are formed from the degradation of cross-linked fibrin. They are specific for fibrin degradation products (fibrinolysis). This is a specific method of detecting active coagulation and fibrinolysis.

TYPICAL NORMAL RANGE

0.02-0.28 mg/mL

PHYSIOLOGY

D-dimers form when plasmin digests cross-linked fibrin; the test is more specific than fibrinogen degradation products (FDPs) and indicates both thrombin and plasmin generation.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Increased fibrinolysis or decreased clearance of fibrin degradation products by the liver or mononuclear phagocytic system; specific causes include local and disseminated intravascular coagulation, internal hemorrhage, liver disease, chronic renal failure.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Evaluation of the coagulation system: platelet count, antithrombin III, activated coagulation time (ACT) or activated partial thromboplastin time (APTT), prothrombin time (PT), thrombin time (TT), fibrinogen. If clinical suspicion of pulmonary thromboembolism exists, further evaluation (ultrasound, thoracic radiography and arterial blood gas measurement; possibly angiography) may be indicated.

SPECIMEN AND PROCESSING CONSIDERATIONS

SPECIMEN: Citrate (blue top) tubes are used; it is important that traumatic venipuncture be avoided to prevent activation of platelets and the coagulation systems; blood and anticoagulant should be mixed thoroughly immediately after collection. Tubes should be completely filled.

RELATIVE COST: $$

PEARLS

Assays for D-dimers are still being evaluated for their usefulness in veterinary medicine. Quantitive assays are replacing semiquantitative assays, allowing precise monitoring and early detection of thrombosis.

AUTHOR: DEBORAH G. DAVIS

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Ethylene Glycol Bench Test

DEFINITION

Test kit for diagnosing ethylene glycol (antifreeze) poisoning

SYNONYM

EGT kit (manufactured by PRN Pharmacal)

TYPICAL NORMAL RANGE

Qualitative test reported as positive or negative

PHYSIOLOGY

Intoxication occurs from consumption of antifreeze or “snow globe” liquid. Following ingestion, ethylene glycol is metabolized to toxic metabolites via the action of alcohol dehydrogenase. The glycolic acid metabolite causes severe high-anion-gap metabolic acidosis. The oxalic acid metabolite combines with serum calcium, forming calcium oxalate crystals that deposit in renal tubules. Severe renal tubular damage can lead to anuric or oliguric renal failure. The test kit detects only ethylene glycol, not the metabolites.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Positive result indicates recent consumption (usually within 12 hours) of ethylene glycol.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Determination of anion and osmolal gap (increased in ethylene glycol poisoning). Electrolyte panel and blood gas determination to evaluate for metabolic acidosis and electrolyte abnormalities (hypochloremia/hyperkalemia). Renal profile and urinalysis to evaluate for renal failure and presence of calcium oxalate monohydrate crystals. When crystalluria and/or systemic abnormalities (azotemia, hyperkalemia) is/are present, extensive and irreversible renal damage has usually occurred. Therefore, a positive EGT test result with normal urinalysis and serum biochemistry panel are the most promising for successful treatment and prognosis.

CAUSES OF ABNORMALLY LOW LEVELS: Ethylene glycol is rapidly metabolized and excreted. Test results are negative if >12-18 hours since consumption.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: If historic evidence suggests toxicosis is suspected, evaluate renal function, electrolyte status. Determine serum levels of metabolite (glycolic acid).

IMPORTANT INTERSPECIES DIFFERENCES: The bench test is approved for use in dogs only.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Positive: propylene glycol or glycerol

SPECIMEN: 1 mL EDTA-anticoagulated whole blood (lavender-top tube). Sample is stable for 48 hours at 0○C-4○C, but it should be brought to laboratory and run as a stat test because of clinical urgency.

RELATIVE COST: $$$

PEARLS

- If antifreeze toxicity is suspected but it has been >48 hours since ingestion, blood urea nitrogen and creatinine are increased, and patients are acidotic with an increased anion gap.
- Local human hospitals may also be able to perform the test. Because the test evaluates only the concentration of ethylene glycol, a human assay can be used for animals.

AUTHOR: SHERRY J. MORGAN

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Estradiol/Estrogen, Serum Levels

DEFINITION

Hormone synthesized and secreted by developing ovarian follicles

TYPICAL NORMAL RANGE

Baseline estradiol/estrogen in canine anestrus is 5-15 pg/mL.

PHYSIOLOGY

- Dogs: Proestrus is under the influence of progressively increasing circulating concentrations of estradiol, which is produced by the developing ovarian follicles. A rising estradiol level correlates with development of marked changes in the vaginal mucosa, vulva, and uterus. Serum estradiol concentrations start to increase just before proestrus becomes clinically detectable. Estradiol concentrations above 25 pg/mL are typical of early proestrus, and concentrations greater than 60-70 pg/dL are typical of late proestrus. Peak estradiol serum concentrations are reached 24-48 hours prior to the end of proestrus before standing heat (estrus). Male dogs with Sertoli cell tumors and male feminization syndrome have increased production of estrogens by testicular tumor cells, or increased androgenous hormone conversion to estrogens by metabolic tissues (liver, neural tissue, etc.) or testicular cells, or normal estrogen levels are concurrent with decreased androgen levels. In male dogs with Sertoli cell tumors, estrogens are typically not measured. Typically, the feminizing syndrome is recognized through overt clinical signs, and the underlying tumor is surgically removed without serologic testing. • Cats: Anestrus and interestrus periods typically are associated with estradiol serum concentrations <12-15 pg/mL. Estradiol concentrations >20 pg/mL typically accompany follicular activity (follicular phase of the feline cycle averages 7.0-7.7 days, depending on whether coitus is experienced and whether ovulation is induced). Day 1 of the follicular phase of estrus typically is associated with an estradiol concentration ≈25 pg/mL; at day 3 it is ≈45 pg/mL, at day 5 it is ≈50 pg/mL or above, at day 7 it is ≈20-25 pg/mL, and by day 8 it has returned to ≈10 pg/mL.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: In intact female dogs, high levels indicate mid- to late proestrus. In intact female cats, high levels indicate the mid-follicular phase of the cycle. In ovariectomized female cats, high levels (above baseline) suggest incomplete excision of ovarian tissue.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: In ovariectomized cats: administer hCG to cause luteolysis of follicles, check for increasing progesterone. If progesterone increases above 2.5 ng/mL 5-7 days later, exploratory surgery is recommended (persistent ovarian tissue). This test is not used in dogs.

CAUSES OF ABNORMALLY LOW LEVELS

- Ovariectomy
- Basal (low) concentrations of estradiol occur in anestrus and diestrus.
- Important interspecies differences: cats are induced ovulators and are seasonally polyestrous; dogs are spontaneous ovulators and have a typical interestrus interval of 7-12 months.

SPECIMEN

LAB ARTIFACTS THAT MAY INTERFERE: Increased: hemolyzed or lipemic specimens

SAMPLE FOR COLLECTION AND SPECIAL SPECIMEN HANDLING NOTES: Serum (red-top tube), 2 mL minimum. Do not use serum-separator tubes.

RELATIVE COST: $$

PEARLS

Measurement of luteinizing hormone is the preferred test for assessing for ovarian remnants and evaluating spay status.

AUTHOR: ELIZABETH G. WELLES

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Erythropoietin

DEFINITION

Renal hormone that stimulates erythropoiesis in the bone marrow in response to tissue hypoxia

SYNONYM

EPO

TYPICAL NORMAL RANGE

Radioimmunoassay method: dogs, 8.4-28 mU/mL; cats, 10-30 mU/mL

PHYSIOLOGY

EPO is produced primarily by the kidney (sole source in dogs), with small amounts produced by the liver in some species. Tissue hypoxia stimulates EPO production. EPO induces differentiation of erythroid progenitor cells to rubriblasts, stimulates mitosis of erythroid cells, reduces maturation time, and accelerates release of reticulocytes from the bone marrow into circulation.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: hypoxemia-inducing cardiovascular or pulmonary disease; hypoxemia due to high altitude; inappropriate EPO production due to EPO-producing neoplasia, renal cyst, pyelonephritis, or hydronephrosis; hyperthyroidism; EPO therapy. Regardless of cause, secondary polycythemia is the result.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH

- Confirm polycythemia. If polycythemia is absent, EPO result may be spurious or represent early disease. Serial monitoring of hematocrit is warranted in these cases.
- Identify cause of any hypoxemia-inducing condition: thoracic radiographs, arterial blood gas measurement, possibly echocardiography.
- Evaluate for neoplasia, renal disease, and endocrinopathy.

CAUSES OF ABNORMALLY LOW LEVELS: Decreased EPO in the presence of polycythemia and normal Po2 suggests polycythemia vera; chronic renal failure (anemia concurrent).

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Assess renal structure and function.

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE: Increased: hemolyzed or lipemic specimens

SPECIMEN: Serum (red-top tube) or heparinized plasma (green-top tube); separate serum or plasma from erythrocytes, freeze, and transport frozen. Do not use serum-separator tubes.

RELATIVE COST: $$$

PEARLS

Measurement of serum EPO levels is an appropriate test in patients with repeat-able absolute polycythemia without hypoxemia.

AUTHOR: FIDELIA R. FERNANDEZ

Pricing Information

$: <$20
$$: $21-75

$$$: $76-150
$$$$: >$150

Eosinophils

DEFINITION

Granulocytic leukocyte with eosinophilic granules in cytoplasm and a segmented nucleus

TYPICAL NORMAL RANGE

Dogs: 0.1-1.3 × 10^3 eosinophils/µL. Cats: 0-1.5 × 10^3 eosinophils/µL.

PHYSIOLOGY

Eosinophilic precursors develop in the marrow under influence of interleukin 5 (IL-5). Mature eosinophils are released into blood to circulate for a few hours and then enter tissue. Eosinophils contain major basic protein, which is important in attacking helminthic parasites. Eosinophils can both promote and inhibit hypersensitivity reactions. Eosinophilic inflammation occurs more often in cutaneous, respiratory, and intestinal tissues.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Parasitism (e.g., dirofilariasis, larval migration in tissues); allergic reactions (e.g., flea bite hypersensitivity); idiopathic eosinophilic inflammation (e.g., hypereosinophilic syndrome in cats, eosinophilic bronchopneumopathy in dogs); hypoadrenocorticism ("relaxed" leukogram, which is the unexpected absence of stress leukogram with eosinopenia in an ill patient); mast cell neoplasm; eosinophilic leukemia (rare)

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Use history and physical exam findings to assess for causes listed.

CAUSES OF ABNORMALLY LOW LEVELS: Stress leukogram, from endogenous or exogenous glucocorticoids; acute inflammation

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Low values are rarely of clinical significance.

IMPORTANT INTERSPECIES DIFFERENCES

- In canine eosinophils, the granules are round and can vary considerably in size and number. In some dogs (especially greyhounds), clear vacuoles appear instead of eosinophilic granules.
- Feline eosinophils have distinctive rod-shaped granules.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Glucocorticoids cause increased sequestration of eosinophils in tissues, with development of eosinopenia.

SPECIMEN: EDTA whole blood (lavender-top tube) and freshly prepared blood smear for lab to stain

RELATIVE COST: $$ (reported as part of CBC)

AUTHOR: STEPHEN D. GAUNT

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Ehrlichia Serology

DEFINITION

Detection of serum antibodies directed against *Ehrlichia* spp. (most commonly *E. canis)*

TYPICAL NORMAL RANGE

Reporting differs among reference laboratories. Consult with laboratories for proper interpretation of values.

PHYSIOLOGY

Ehrlichia spp. are rickettsial agents that infect a wide range of host species. Numerous species of *Ehrlichia* have been shown to infect dogs. *E. canis* produces an acute disease (canine monocytic ehrlichiosis) from which animals recover, but which typically remains subclinical and may later produce more severe disease. Early (7 days post infection) titers are due to immunoglobulin (Ig)A and IgM; 3 weeks postinfection titers are mostly due to IgG. Most laboratories measure IgG.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS

- The presence of antibodies directed against *E. canis* indicates exposure to *E. canis* or related organisms. Some antigens of *E. canis, E. ewingii,* and *E. chaffeensis* are cross-reactive, whereas others are not.
- A positive titer indicates only exposure and does not prove that current clinical signs are due to active infection.
- *E. canis* can cause a persistent subclinical infection, so a dog with a positive titer is likely to still be infected unless treated with appropriate antimicrobial therapy.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Evaluate whether the patient's current signs are consistent with ehrlichiosis, and consider treatment with appropriate antimicrobial therapy. A positive test for ehrlichial DNA via PCR supports active infection and can determine the specific species of *Ehrlichia* involved.

CAUSES OF ABNORMALLY LOW LEVELS: Infection with different *Ehrlichia* spp.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: If a clinical suspicion for ehrlichiosis persists despite a negative titer to *E. canis,* titers to other ehrlichial species (e.g., *Anaplasma phagocytophilum,* formerly *E. equi)* should be performed, because cross-reactivity does not occur reliably.

SPECIMEN AND PROCESSING CONSIDERATIONS

IMPORTANT INTERSPECIES DIFFERENCES: Serologic tests often use species-specific reagents, and *Ehrlichia* serologic testing is most often performed on dogs. Check with lab as to appropriateness if testing cats.

SPECIMEN: Serum (red-top)

RELATIVE COST: $$

PEARLS

- Some dogs maintain persistent titers for years despite appropriate therapy and apparent resolution of disease.
- An in-clinic, ELISA-based serology test (SNAP4Dx, IDEXX Labs) for detecting *E. canis* antibody appears to have high specificity when compared with immunofluorescent assay, but it may not detect low titers.
- Dogs may have negative titers if early in infection or if infected with other ehrlichial species other than those being evaluated.
- *Ehrlichia* serologic testing is much more sensitive (i.e., better screening test) than evaluating a blood smear for the presence of ehrlichial inclusions in leukocytes.

AUTHOR: LOIS ROTH-JOHNSON

1ST EDITION AUTHOR: JAMES H. MEINKOTH

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Eccentrocyte

DEFINITION

Erythrocyte damaged by oxidants. Characterized by focal area of fused membranes with eccentric displacement of hemoglobinized cytosol and loss of any central pallor. The collapsed area with fused membranes appears as a clear area at periphery of erythrocyte which is outlined by a barely visible cell membrane.

SYNONYMS

Bite cell, hemighost

TYPICAL NORMAL RANGE

Absent in health

PHYSIOLOGY

During oxidative damage, hemichromes (oxidized forms of hemoglobin) bind to the band 3 protein of the membrane cytoskeleton. This creates cross-linking and fusion of the erythrocyte cytoskeleton and alters the membrane, with externalizing of antigenic proteins and attachment of autoantibodies. Hemichromes can also precipitate to form Heinz bodies.

CLINICAL APPLICATION

CAUSES OF ABNORMALLY HIGH LEVELS

- Oxidative damage to erythrocyte from toxins such as acetaminophen, onions, and benzocaine in dogs and cats, zinc and garlic in dogs. Heinz bodies may also be seen in conjunction with eccentrocytes.
- Also reported in dogs with vitamin K antagonist intoxication, T-cell lymphoma, and diabetic ketoacidosis
- Decreased antioxidant activity of erythrocytes (rare): congenital deficiency of glucose-6-phosphate dehydrogenase, with decreased production of reduced nicotinamide adenine dinucleotide phosphate (NADPH) in erythrocytes NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Evaluate history for source of oxidative damage to erythrocytes.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS: Associated with propofol anesthesia in dogs

SPECIMEN: EDTA whole blood and freshly prepared blood smear for lab to stain

RELATIVE COST: $$ (reported as part of CBC)

AUTHOR: STEPHEN D. GAUNT

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Fungal Culture

DEFINITION

Analysis of tissue or exudate for fungal organisms

TYPICAL NORMAL RANGE

Reported as negative or degree (slight, moderate, heavy) of growth of specific pathogens

PHYSIOLOGY

Laboratory conditions enhance growth of pathogens and allow isolation of fungal colonies and their identification by morphologic features and chemical tests.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Fungal infection. Common fungal infections include dermatophytosis, aspergillosis, cryptococcosis, blastomycosis, histoplasmosis, and coccidioidomycosis. Saprophytes may cause skin lesions or systemic disease in immunocompromised patients.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Culture is definitive. Used as a confirmatory test for dermatophytes. *Aspergillus* spp. may be cultured for specific identification if organisms are seen in cytologic or histologic specimens. Dimorphic fungi are typically not cultured owing to health risk for laboratory personnel; instead, serologic tests and/or cytologic demonstration of organisms are confirmatory.

IMPORTANT INTERSPECIES DIFFERENCES: Dermatophytes may cause pseudomycetoma (deep granulomatous or pyogranulomatous lesions) in cats, especially Persian cats.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Corticosteroids and other immunosuppressive therapies may decrease patient resistance, enhancing organism growth.

LAB ARTIFACTS THAT MAY INTERFERE: False negative: improper media or growth conditions

SPECIMEN

- Dermatophytes: hair plucked from affected areas should be submitted in dermatophyte test media or sterile dry containers.
- Tissue or exudate: sterile, dry container

RELATIVE COST: $$

PEARLS

Do not submit specimens for culture if cryptococcosis, blastomycosis, histoplasmosis, or coccidiomycosis is suspected. In culture, these organisms are health hazards to laboratory personnel (zoonosis via inhalation or accidental inoculation), and serologic tests coupled with cytologic or histologic lesions are appropriate for diagnosis instead.

AUTHOR: LOIS ROTH-JOHNSON

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Fructosamine

DEFINITION

Fructosamine is an amino sugar formed by the reduction of osazone glucosamine. It is dependent on the concentration of glucose-bound serum proteins. The test is used for assessing the average serum glucose concentration over the preceding 2-3 weeks.

TYPICAL NORMAL RANGE

Range varies with instrument. Heska SpotChem: roughly <200 mmol/L in healthy dogs and cats.

PHYSIOLOGY

Persistent hyperglycemia results in irreversible binding of glucose to reactive molecules such as serum proteins, erythrocyte membranes, and other cell membranes. Transient hyperglycemia may result in noncovalent reversible binding of glucose to reactive molecules. Therefore, this test may help differentiate transient stress-induced hyperglycemia from diabetes mellitus in cats.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Persistent hyperglycemia.

- With Heska SpotChem: Values of 200-450 mmol/L in diabetic dogs and 165-350 mmol/L in diabetic cats are considered indicators of reasonably good glycemic control. If patients are near the upper end of these intervals or have signs of poor regulation (polyuria, glucosuria, polyphagia, weight loss), management should be reevaluated.
- Patients with values >450 mmol/L (dogs) and >350 (cats) have suboptimal to poor glycemic control.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Review history and physical exam for findings indicative of diabetes mellitus. Check serum glucose level and urine for the presence of glucose +/− ketones.

CAUSES OF ABNORMALLY LOW LEVELS

- Animals with hypoproteinemia and hypoalbuminemia may have lowered fructosamine. If hypoalbuminemia is concurrent with diabetes mellitus, the fructosamine level may appear falsely low.
- Hyperthyroid cats have lower fructosamine than healthy cats because of accelerated protein (albumin) turnover.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Check serum albumin and globulin concentrations.

In cats >6 years old, test for hyperthyroidism.

IMPORTANT INTERSPECIES DIFFERENCES: Glucose has a higher affinity for albumin in dogs and globulins in cats, and conection methods are used by reference laboratories.

SPECIMEN AND PROCESSING CONSIDERATIONS SPECIMEN: Serum (red-top tube) or heparinized plasma (green-top tube)

RELATIVE COST: $$

PEARLS

Fructosamine is not typically used for assessing persistent hypoglycemia, as would occur in patients with insulinoma.

AUTHOR: ELIZABETH G. WELLES

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Folate

DEFINITION

The anionic form of folic acid. Part of B-vitamin complex.

SYNONYM

Folic acid

TYPICAL NORMAL RANGE

Dogs: 6.5-11.5 mg/L. Cats: 9.7-21.6 mg/L.

PHYSIOLOGY

Primary source is diet; also produced by enteric bacteria. Ingested folate is released from food and hydrolyzed in proximal small intestine. Dietary and bacterial-origin folate is taken up by intestinal epithelium, metabolized, and systemically absorbed (blood).

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Intestinal bacterial overgrowth, exocrine pancreatic insufficiency (EPI), excessive gastric acid production, over-supplementation

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Test for bacterial overgrowth, EPI. Evaluate diet.

CAUSES OF ABNORMALLY LOW LEVELS: Small-intestinal mucosal disease, dietary deficiency, medication (sulfasalazine, phenytoin, antibiotics that deplete gastrointestinal flora, causing decreased folate production), extensive intestinal neoplasia

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Evaluate diet, medication history. Assess for intestinal mucosal disease (endoscopy or surgery). IMPORTANT INTERSPECIES DIFFERENCES: Different reference ranges for dogs and cats. High serum concentration in cats is of no known clinical significance. Cobalamin deficiency has been associated with decreased folate utilization and resultant increased folate values in cats. Increased serum folate (due to bacterial overgrowth) associated with low immunoglobulin A in German shepherd dogs.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Decrease: associated with sulfasalazine, phenytoin, and antibiotics that disturb intestinal flora.

LAB ARTIFACTS THAT MAY INTERFERE: False increase: hemolyzed specimens (released from red blood cells). SPECIMEN: Nonhemolyzed serum (red-top tube; separate serum from clot immediately, and place in fresh red-top tube for submission). Stable at 4°C for 1 day, −20°C for 6-8 weeks. Avoid repeated freezing, thawing.

RELATIVE COST: $$

PEARLS

- Folate should be evaluated in conjunction with cobalamin and trypsinlike immunoreactivity for best interpretation. Low cobalamin concentration may result in a functional folate deficiency, with measured folate concentration within the reference interval.
- Maternal folate deficiency is associated with congenital malformations (neural tube and conotruncal cardiac defects) in humans, but there is no evidence of a similar problem in dogs and cats.

AUTHOR: LOIS ROTH-JOHNSON

Pricing Information

$: <$20

$$: $21-75
$$$: $76-150
$$$$: >$150

Fluid Analysis

DEFINITION

Biochemical and Cytologie analysis of fluid aspirated from body cavities (abdominal, pleural, pericardial) or joints (see p. 1519). Typically includes assessment of color, turbidity, viscosity, protein concentration, total cell counts (may include differential), and Cytologie description.

TYPICAL NORMAL RANGE

Body cavity effusions are classified as: *Conversion: for mg/mL, multiply g/dL by 10.

	Protein (g/dL)*	Cell Count (Cells/µL)
Transudate	<2.5	<1500
Modified transudate	2.5-7.5	1000-7000
Exudate	>7.5	>7000

PHYSIOLOGY

- Transudates: decreased plasma osmotic pressure, usually due to hypoalbuminemia, results in fluid movement from vasculature to body cavities. Causes include protein-losing enteropathy and nephropathy, severe chronic liver disease with decreased protein production.
- Modified transudate: results from increased hydrostatic pressure or increased vascular permeability; causes are numerous, including congestive heart failure, inflammation, and neoplasia.
- Exudate: due to inflammation with increased vascular permeability

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Altered plasma protein osmotic pressure, hypoproteinemia, vascular obstruction, inflammation, neoplasia

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Assessment of history and physical examination findings in combination with serum biochemical changes and Cytologie appearance of fluid help determine if fluid accumulation is the result of metabolic, inflammatory, orneoplastic disease.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Peritoneal lavage, IV or subcutaneous fluid administration may alter protein concentration and cell counts. Corticosteroid administration may have adverse affect on cell morphology.

SPECIMEN

- Obtain specimens using sterile technique. Fill EDTA (lavender-top) tube to prevent clotting. A sterile tube (red top) or other container should be used for specimens to be cultured.
- Submission of direct or sediment smears prepared when the specimen is obtained is suggested to allow evaluation of cells before autolytic changes occur.

RELATIVE COST: $$

PEARLS

- Clear, colorless fluids are usually transudates; increasing turbidity is associated with increased protein concentration and/or cell counts and classified as modified transudates or exudates.
- Sediment smears should be prepared if low cellularity is suspected.
- Fluid analysis from cysts or abscesses is not diagnostically useful. Fluid from these sources should be submitted only for Cytologie analysis.

AUTHOR: LOIS ROTH-JOHNSON

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Fibrinogen

DEFINITION

A glycoprotein important in hemostasis; a positive acute-phase protein that increases due to inflammation or tissue injury; important in tissue repair

TYPICAL NORMAL RANGE

Dogs: 150-300 mg/dL; cats: 150-300 mg/dL

PHYSIOLOGY

Made in the liver; production is upregulated with inflammation or tissue damage (due to cytokines interleukin [IL]-1, IL-6, and tumor necrosis factor [TNF]). It is a nonenzymatic coagulation factor (factor I), cleaved (activated) by thrombin to form fibrin and promote stable clot formation.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Two major causes include dehydration (hemoconcentration) and increased production by the liver (positive acute-phase protein) in response to cytokines IL-1, IL-6, and TNF due to inflammation or tissue damage. Can also increase with physiologic stress (pregnancy).

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Look for source of inflammation/tissue injury: review history and physical exam; CBC (determine if inflammatory leukogram is present), serum biochemistry profile; if hyperglobulinemia, serum protein electrophoresis is warranted to document a polyclonal gammopathy supportive of an inflammatory process.

CAUSES OF ABNORMALLY LOW LEVELS: Increased consumption in disseminated intravascular coagulation or increased fibrinogenolysis, decreased hepatic fibrinogen synthesis, inherited/congenital disorders (documented in bichon frise, Bernese mountain dogs, Lhasa apso, vizsla, and collie).

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Full coagulation profile (activated partial thromboplastin time, prothrombin time, thrombin time, platelet count, and fibrinogen degradation products) to assess for disseminated intravascular coagulation. Serum biochemistry profile to evaluate hepatic parameters. Serum bile acids to evaluate hepatobiliary function.

SPECIMEN AND PROCESSING CONSIDERATIONS

SPECIMEN: Citrated plasma (blue-top tube). Centrifuge and remove plasma within 1 hour of collection and transfer to plain red-top tube. Label as plasma. Test as soon as possible. Stable at 2-8°C for 24 hours; freeze if there is a longer time interval before testing.

RELATIVE COST: $$

AUTHOR: DEBORAH G. DAVIS

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Fibrin or Fibrinogen Degradation Products

DEFINITION

Fibrin or fibrinogen degradation products (FDPs) are protein fragments of fibrin or fibrinogen that have been cleaved by plasmin as part of fibrinolysis. Assays to detect FDPs are used for identifying increased fibrin or fibrinogen breakdown that is seen with excessive coagulation (disseminated intravascular coagulation [DIC]). Plasmin can act on both fibrinogen and fibrin, and assays for FDPs do not differentiate between fibrinolysis and fibrinogenolysis.

TYPICAL NORMAL RANGE

Semiquantitative normal values: dogs, 0-10 mg/mL; cats, 0-8 mg/mL. Abnormal values are reported as moderately increased or markedly increased. Exact values are laboratory dependent.

PHYSIOLOGY

- Formed by plasmin breakdown of non-cross-linked fibrin and fibrinogen. FDPs are potent inhibitors of coagulation; they compete with fibrinogen for the active sites on thrombin and interfere with the conversion of fibrinogen to fibrin.
- Interfere with platelet aggregation; they bind to the fibrinogen-binding site on platelets.
- Eliminated by the liver and kidney, so patients with hepatic or renal disease can have elevated FDPs in the absence of significantly elevated levels of fibrin(ogen) breakdown.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS

- Increased fibrinolysis: internal hemorrhage, local or disseminated intravascular coagulation, sepsis or other severe inflammation
- Decreased FDP clearance: hepatic disease, renal failure

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH

- CBC with platelet count/serum chemistry profile/urinalysis
- Coagulation profile: activated partial thromboplastin time, prothrombin time, thrombin time, angiotensin lll and D-dimer levels

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE: False increases can occur when FDP generation occurs during collection (traumatic venipuncture).

SPECIMEN: Serum assay: use tubes filled with thrombin, or reptilase (snake venom) with soybean trypsin inhibitor or aprotinin (light blue-top tubes with yellow label). Plasma assays: citrated (light blue top-tube). Tubes should be completely filled.

RELATIVE COST: $$

PEARLS

- Serum (plain red-top tube) specimens cannot be used because clot formation consumes FDPs, lowering measurement. A clot in the citrate tube will interfere with accuracy of the plasma assay.
- D-dimer assays continue to be evaluated in small-animal medicine and may prove to be more sensitive and/or specific than FDP assays for detecting coagulation and clot lysis.

AUTHOR: DEBORAH G. DAVIS

Pricing Information

$: <$20
$$: $21-75

$$$: $76-150
$$$$: >$150

Feline Leukemia Virus Immunofluorescent Antibody (IFA)

DEFINITION

Feline leukemia virus (FeLV) is a retrovirus of cats that causes hematopoietic neoplasia, immunosuppression, and/or anemia.

TYPICAL NORMAL RANGE

Reported as positive or negative

PHYSIOLOGY

Following exposure to FeLV via the oronasal route, the virus replicates in oropharyngeal lymphoid tissue. The virus may be cleared with an effective immune response. An ineffective immune response results in viremia and replication in bone marrow and lymphoid cells. Affected cats may be transiently viremic with latent virus residing in the marrow, may become persistently viremic, or may be overtly healthy carriers. Persistent viremia may result in immunosuppression, myelosuppression, hematopoietic neoplasia, immune complex diseases, or reproductive disorders.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: IFA detects the cell-associated FeLV core antigen, p27, in cells; therefore, a positive IFA indicates infection with FeLV and probable bone marrow infection. A positive IFA with a negative ELISA is always a false result, and both tests should be repeated.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Correlate with history, clinical findings, and laboratory data.

CAUSES OF ABNORMALLY LOW LEVELS: A negative IFA with a positive ELISA indicates either uninfected (false-positive ELISA) or early infection.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: If positive ELISA and negative IFA, repeat both tests in 6-8 weeks to determine effective clearance of virus versus persistent infection.

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE: Marked thrombocytopenia, marked leukopenia, eosinophilia, or poor-quality buffy coat or bone marrow smear may cause false-negative or false-positive results.

SPECIMEN

- 1 mL EDTA-anticoagulated whole blood (lavender-top tube); stable at 4°C for 4 days.
- Air-dried buffy coat smears or bone marrow smears: store at room temperature.

RELATIVE COST: $$

PEARLS

- Vaccination for FeLV involves a different component of the virus (gp70 protein) than the one detected by IFA. Therefore, prior vaccination does not affect test results.
- The FeLV IFA test is less sensitive (does not catch all FeLV-positive cases) but more specific (positive result is reliably positive) compared to the FeLV ELISA. Therefore, FeLV IFA is not a good initial screening test but is an excellent confirmatory test.

AUTHOR: PATTY J. EWING

Pricing Information

$: <$20
$$: $21-75

$$$: $76-150
$$$$: >$150

Feline Leukemia Virus (ELISA)

DEFINITION

Feline leukemia virus (FeLV) is a retrovirus of cats that causes hematopoietic neoplasia, immunosuppression, and/or anemia.

SYNONYMS

FeLV enzyme-linked immunosorbent assay

TYPICAL NORMAL RANGE

Reported as positive or negative

PHYSIOLOGY

Following exposure to FeLV via the oronasal route, the virus replicates in oropharyngeal lymphoid tissue. The virus may be cleared with an effective immune response. An ineffective immune response results in viremia and replication in marrow and lymphoid cells. Affected cats may be transiently viremic with latent virus residing in the marrow, may become persistently viremic, or may be overtly healthy carriers. Persistent viremia may result in immunosuppression, myelosuppression, hematopoietic neoplasia, immune complex diseases, or reproductive disorders.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: ELISA detects the free soluble FeLV core antigen, p27; therefore, a positive ELISA indicates that the cat is viremic (infected with FeLV). False-positive results due to technical error can occur, but this occurs infrequently (sensitivity and specificity are reported to be 99.9%).

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Confirm with FeLV IFA test.

CAUSES OF ABNORMALLY LOW LEVELS: A negative ELISA indicates that either the cat is not infected or has an early infection.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: If the cat was recently exposed to an FeLV positive cat but the ELISA is negative, early infection is possible and retesting in 30-90 days is recommended.

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE: Hemolysis may cause a false-positive or false-negative result.

SPECIMEN: 1 mL serum (red-top tube) or EDTA plasma (lavender-top tube)

RELATIVE COST: $

PEARLS

- Vaccination for FeLV involves a different component of the virus (gp70 protein) than the one detected by ELISA. Therefore, prior vaccination does not affect test results.
- The FeLV ELISA test is more sensitive (more likely to catch all FeLV-positive cases) but less specific (may also erroneously identify a few FeLV-negative cases as positive) compared to the FeLV IFA. Therefore, FeLV ELISA is a good initial screening test, but positive results may or may not be true positives and need to be confirmed with IFA.

AUTHOR: PATTY J. EWING

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Feline Immunodeficiency Virus Testing

DEFINITION

Feline immunodeficiency virus (FIV) is a retrovirus (lentivirus) that attacks the immune system of cats and results in progressive immunosuppressive disease.

TYPICAL NORMAL RANGE

Reported as positive or negative

PHYSIOLOGY

FIV is inoculated via saliva or blood from bite wounds. There are three stages of infection. *Acute phase:* FIV initially infects T lymphocytes and salivary glands, with subsequent spread to other mononuclear cells; cats may have fever, leukopenia, and lymphadenopathy. *Subclinical phase:* cats may be without clinical signs for years. *Chronic phase:* progressive immunosuppression with development of a wide variety of clinical disorders, including stomatitis/gingivitis, anemia and leukopenia, neurologic signs, enteritis, weight loss, and opportunistic infections. A cat may have no clinical signs for years, owing to a prolonged subclinical phase that follows acute infection. Available tests measure circulating FIV antibody levels, not viral antigen. The extended natural course of lentivirus infections makes the presence of antibody essentially equivalent to infection (exceptions: maternal antibody, vaccination).

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Screening test: ELISA (SNAP) or rapid immunomigration assay—positive indicates possible exposure to FIV or FIV vaccine; positive or equivocal result requires confirmatory testing. Due to maternally transferred antibody, FIV testing of kittens <6 months of age is unreliable (false positives) and is not recommended.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Confirmatory tests: Western blot or IFA. Positive Western blot or IFA indicates maternal antibody (kittens <6 months old) or exposure to FIV or the vaccine. PCR test may be a useful test in the future for differentiating vaccine exposure from true infection; however, currently available tests vary markedly in their diagnostic accuracy and should be interpreted with caution.

CAUSES OF ABNORMALLY LOW LEVELS: Negative ELISA indicates lack of exposure or acute infection.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: If clinical signs suggest FIV infection, retest in 4-12 weeks.

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE: PCR: false-positive results due to contamination of samples; false-negative results due to degradation of nucleic acids via improper sample handling and storage. Up to 50% false-negative results due in part to insufficient primer and probe sequences (many strain variations of FIV present). SPECIMEN

- ELISA: 1 mL serum (red-top tube) or plasma (lavender- or green-top tube)
- Western blot or IFA: 1 mL of serum (red-top tube)

RELATIVE COST: $$ (IFA, ELISA); $$$ (Western blot)

AUTHOR: PATTY J. EWING

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Feline Coronavirus Testing

DEFINITION

Feline coronavirus (FCV) infection refers to two distinct entities: feline infectious peritonitis (FIP) and feline enteric corona-viral (FECV) enteritis. FIP is a systemic viral disease of high mortality characterized by insidious onset, fever, disseminated pyogranulomatous inflammation, and in some cases, proteinaceous exudative effusions in body cavities ("wet form"). FECV causes mild transient diarrhea and/or vomiting and, less commonly, chronic or severe diarrhea. A positive titer does not distinguish between these two entities.

TYPICAL NORMAL RANGE

Consult with laboratory conducting the test.

PHYSIOLOGY

In FIP FCV is ingested and then replicates in intestinal epithelial cells and probably tonsils and oropharynx. The virus infects macrophages, with subsequent extension to multiple tissues. Antiviral antibodies are produced such that immune complexes form and are deposited in blood vessels of serosal surfaces, uvea, kidney, liver, and other tissues. A pyogranulomatous response ensues. Proteinaceous abdominal or thoracic effusion results from increased vascular permeability. FIP-type coronavirus is thought to represent a spontaneous mutation of FCV that occurs in vivo in certain individual cats.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Positive FCV titer indicates nonspecific exposure to any of the following: FIP coronavirus, feline enteric coronavirus, other coronaviruses, or FIP vaccine. Serology is therefore nonspecific.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Correlate with history, physical exam findings, and other laboratory data. Consider cytologic evaluation, A: G ratio, PCR, or IFA on effusion fluid, all of which are supportive but not definitive (none of these tests differentiates between FIP coronavirus and enteric coronavirus). Quantitative mRNA PCR Multi-Test on blood, feces, and effusion or tissue aspirate may differentiate FIP-coronavirus from enteric coronavirus. Histopathologic analysis of biopsy or necropsy tissue is generally required for definitive diagnosis.

CAUSES OF ABNORMALLY LOW LEVELS: False-negative serologic test results may arise from peracute infection, low antibody level, lack of antibody production, or antibody bound within immune complexes.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: If FIP is still suspected, consider same diagnostic steps as if test is positive.

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE: PCR: false-positive results due to specimen contamination; false-negative results due to degradation of nucleic acids via improper sample handling and storage

SPECIMEN: One mL serum (red-top tube) for serology. Samples for serologic analysis can be stored up to 4 days at refrigerator temperature or for longer periods at −20°C without loss of antibody. For mRNA PCR Multi-Test, submit (at room temperature) up to 700 µL of EDTA blood (lavender-top tube) and/or sample fluid (body cavity fluid, CSF, joint fluid), tissue or fecal swab, or piece of tissue not larger than 5 mm in diameter in special sample buffer (obtained from Auburn University, http://www.vetmed.auburn.edu/molecular-diagnostics/faq).

RELATIVE COST: $$ (IFA serum antibody, PCR), $$$ (IFA tissue)

PEARLS

A negative titer alone does not rule out FIP, nor does a positive titer alone indicate FIP. Multiple sampling and evaluation via the FIP mRNA PCR test increases sensitivity over single sampling, and detection of FIP mRNA via PCR in any extraintestinal sample confirms FIP with nearly 100% specificity.

AUTHOR: PATTY J. EWING

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Fecal Flotation

DEFINITION

Screening test for detection of parasitic ova and larvae in feces

TYPICAL NORMAL RANGE

Reported as negative or positive with species identification

PHYSIOLOGY

Flotation of parasitic ova and cysts is promoted in solutions with a greater osmolarity than water. Fecal specimens are mixed with saturated sugar or zinc sulfate solution in a small cylinder topped with a coverslip. After allowing time for ova or cysts to rise to the surface, the coverslip is examined microscopically.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Gastrointestinal or, less commonly, respiratory parasitic infection. Ova of ascarids, hookworms, and flukes. Coccidia, tapeworm segments, and protozoa may be identified.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Positive test result is definitive.

CAUSES OF ABNORMALLY LOW LEVELS: Intermittent shedding of ova

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Serial fecal analyses, empirical anthelmintic treatment, further diagnostic testing of gastrointestinal or respiratory system

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Anthelmintic treatment may decrease parasite burden.

LAB ARTIFACTS THAT MAY INTERFERE: Freezing or delayed specimen processing distorts or destroys ova. decreasing detection.

SPECIMEN: Fresh feces (<24 hours, room temperature or refrigerated) in dry container. If a delay in processing is anticipated, a solution of feces (one part) and sodium acetate/acetic acid formalin (three parts) may be submitted. To prepare solution, combine 1.5 g sodium acetate, 2 mL glacial acetic acid, 4 mL 40% formaldehyde, and 92.5 mL water. Indicate that specimen has been diluted.
RELATIVE COST: $

PEARLS

- Diarrhea may decrease ova concentration.
- Ova shedding is intermittent, so a single negative test does not rule out infection. Serial testing (at least three) should be done if parasitic disease is suspected.

AUTHOR: LOIS ROTH-JOHNSON

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Fecal Culture

DEFINITION

Analysis of feces for enteric bacterial pathogens

TYPICAL NORMAL RANGE

Reported as negative or degree (slight, moderate, heavy) of growth of specific pathogens

PHYSIOLOGY

Chronic diarrhea, especially in patients with signs of systemic disease (intermittent or persistent fever, leukocytosis or leukopenia) or melena, may be due to enteric bacterial infection. Laboratory conditions enhance growth of pathogens, allowing isolation of bacterial colonies and their identification by morphologic features and chemical tests.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Enteric infection. Common enteric pathogens include *Salmonella* spp., *Clostridium* spp., *Shigella* spp., *Yersinia* spp., *Escherichia coli,* and *Campylobacter* spp. Culture results that include only normal enteric organisms are not helpful in identifying enteric diseases resulting from their overgrowth. In such cases, underlying causes for clinical disease including immune deficiencies, and primary viral infections should be considered.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Request specific antibiotic sensitivity.

IMPORTANT INTERSPECIES DIFFERENCES: Bacterial enteritis is an uncommon but serious disease in dogs and very rare in cats.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Low-level antibiotic therapy may inhibit culture growth.

LAB ARTIFACTS THAT MAY INTERFERE: False-negative results: delay in setting up culture, contamination or overgrowth of normal flora, failure to notify lab of suspected fastidious pathogens requiring special handling, exposure of anaerobes to oxygen

SPECIMEN: Fresh feces in sterile container. If shigellosis, campylobacteriosis, or clostridial infection is suspected, special transport media may be needed, depending on transport time to reference laboratory. Contact laboratory to obtain appropriate transport media.

RELATIVE COST: $$

PEARLS

- Most enteric pathogens cause disease in humans; specimen-handling precautions are necessary to reduce risk of zoonosis.
- Much overlap exists between bacterial flora of dogs with enteritis and normal dogs. Identification of certain fecal bacteria does not necessarily indicate a cause-and-effect relationship.

AUTHOR: LOIS ROTH-JOHNSON

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Glycated Hemoglobin

DEFINITION

The concentration of glucose bound to hemoglobin. The test is used for assessing the average serum glucose concentration over the preceding 2-3 months.

SYNONYMS

Glycosylated hemoglobin, hemoglobin

TYPICAL NORMAL RANGE

Reference interval is laboratory-specific.

PHYSIOLOGY

Persistent hyperglycemia results in irreversible binding of glucose to reactive molecules such as hemoglobin. The time frame over which glycated hemoglobin indicates glucose levels (2-3 months) is a reflection of the average blood glucose concentration and red blood cell lifespan.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Persistent hyperglycemia, typically due to uncontrolled or poorly controlled diabetes mellitus

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Review history and physical exam for findings indicative of diabetes mellitus. Assess for hyperglycemia and the presence of urine glucose and ketones. If the patient is diabetic and being treated with insulin, check insulin expiration date and owner's technique for storing, preparing, and administering the insulin; reassess the dosage (may be too low or too high [Somogyi]); and investigate insulin-antagonistic disorders (e.g., hyperadrenocorticism or hyperprogesteronism) if relevant.

SPECIMEN AND PROCESSING CONSIDERATIONS

SPECIMEN: Anticoagulated whole blood (EDTA [lavender-top tube] or heparin [green-top tube]); keep refrigerated, submit on ice.

RELATIVE COST: $$$

PEARLS

Glycated hemoglobin is used less often than fructosamine values to assess hyper-glycemic conditions. Increased glycated hemoglobin values take longer to develop and are dependent on hematocrit and red blood cell life span.

AUTHOR: ELIZABETH G. WELLES

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Glucosuria

DEFINITION

Glucose in urine

SYNONYM

Glycosuria

TYPICAL NORMAL RANGE

Negative in healthy dogs and cats, rarely positive in healthy cats with “stress hyperglycemia”

PHYSIOLOGY

Glucose is a small molecule that is freely filtered by glomeruli. Renal tubular epithelium normally resorbs all glucose. Serum glucose concentrations above which tubular cells are unable to fully resorb glucose from urine filtrate (renal threshold) are 180-220 mg/dL (10-12.2 mmol/L) in dogs and 250-300 mg/dL (13.9-16.7 mmol/L) in cats.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS

- Persistent (several hours to days) hyperglycemia caused by diabetes mellitus or administration of glucose-containing fluids
- Transient hyperglycemia if the renal threshold is exceeded for a sufficient time and bladder has minimal glucose-free urine for dilution (e.g., stress hyperglycemia in cats)
- Defective renal tubular resorption due to acute tubular disease, acute renal failure, or Fanconi syndrome

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Measure serum glucose concentration. May need to measure serum fructosamine to differentiate diabetes mellitus from transient stress-induced hyperglycemia, especially in cats.

IMPORTANT INTERSPECIES DIFFERENCES: Compared with dogs, cats have a higher renal threshold for hyperglycemia before glucosuria occurs but are also prone to much greater levels of hyperglycemia caused by stress.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: With most urine dipsticks (glucose oxidase method), vitamin C/ascorbic acid causes a falsely decreased reaction. With the Clinitest (copper reduction method), ascorbic acid and cephalosporin antibiotics can cause false-positive reactions.

LAB ARTIFACTS THAT MAY INTERFERE: False-positive/increase: hydrogen peroxide and sodium hypochlorite (bleach). False-negative/decrease: ketones, very concentrated samples, and cold urine.

SPECIMEN: Clean urine collected as free catch, catheterization, or cystocentesis and of sufficient quantity into which to dip the urine dipstick. Alternatively, a large drop can be placed on the specific reagent pad on the dipstick.

RELATIVE COST: $ (reported as part of urinalysis)

PEARLS

Urine should be at least room temperature or warmer (>20°C or 70°F) for enzymes in reagent pad of dipstick to have appropriate activity. Dipstick +1 and +2 readings lack accuracy; repeated analysis at later date or measurement of urine glucose by clinical chemistry analyzer may provide a more accurate assessment.

AUTHOR: ELIZABETH G. WELLES

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Glucose, Blood

DEFINITION

Blood concentration of the sugar utilized for energy production

SYNONYM

Blood sugar

TYPICAL NORMAL RANGE

Dogs: 60-125 mg/dL (33-6.9 mmol/L). Cats: 70-150 mg/dL (3.9-8.3 mmol/L).

PHYSIOLOGY

Carbohydrates in the diet are catabolized to glucose for absorption and transport to the liver and other tissues. The liver produces glucose via gluconeogenesis and glycogenolysis, and stores glucose in the form of glycogen or converts glucose to amino acids and lipids. Blood glucose levels are regulated by dietary intake and such hormones as insulin and glucagon that regulate its hepatic storage and release and tissue utilization. Glucose metabolism and blood glucose concentration are affected by many disorders.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Diabetes mellitus, glucose-containing fluids, hyperadrenocorticism, stress, hyperthyroidism, acromegaly/hyperpituitarism, acute pancreatitis, excitement-induced epinephrine release (primarily cats), postprandial (minor elevations)

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Assess for persistent hyperglycemia, glucosuria and ketonuria, serum fructosamine.

CAUSES OF ABNORMALLY LOW LEVELS: Paraneoplastic (insulinoma, leiomyosarcoma, other tumors), insulin overdose, neonatal or juvenile hypoglycemia (infrequent feedings, parasitism, other), advanced chronic liver disease, congenital portosystemic shunt, extreme exertion, sepsis, hypoadrenocorticism, hypopituitarism, long-term starvation (rare cause of hypoglycemia in adults) or malabsorption, glycogen storage diseases, artifact (delay in processing, or centrifuging and separating red blood cells from whole blood sample)

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Resample to verify persistent hypoglycemia. Correlate with other clinical and laboratory findings. Serum insulin levels to assess for hyperinsulinism due to insulinoma.

IMPORTANT INTERSPECIES DIFFERENCES: Hyperglycemia due to excitement-induced epinephrine release is common in cats.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS

- Increase: glucocorticoids; adrenocorticotropic hormone; intravenous fluids containing dextrose, growth hormone, megestrol acetate, thiazide diuretics, xylazine, ketamine in cats, morphine, and phenothiazine tranquilizers
- Decrease: insulin injection, ethanol, salicylates, sulfonylurea, and o, p'-DDD

LAB ARTIFACTS THAT MAY INTERFERE

- Decrease: delayed separation of serum or plasma from red blood cells results in artificial depression due to utilization of glucose by blood cells.
- Increase: lipemia

SPECIMEN: Serum (red-top tube) or heparinized plasma (green-top tube). Separate from cells within 30 minutes after sample collection. Use fluoride oxalate anticoagulant (grey-top tube) if plasma separation is not possible: stable at 2°C-8°C for 4 days.

RELATIVE COST: $

AUTHOR: RUANNA GOSSETT

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Globulins

DEFINITION

In routine serum chemistry profiles, globulin concentration is calculated from subtraction of measured albumin from measured total serum protein. Globulins can be classified as α, β, or γ via protein electrophoresis (see p. 1511).

TYPICAL NORMAL RANGE

Dogs: 2-4 g/dL. Cats: 2.5-5 g/dL. Conversion: g/dL × 10 = g/L.

PHYSIOLOGY

Globulins are a heterogeneous group of large serum proteins including immunoglobulins, coagulation factors, complement, and many acute-phase proteins and lipoproteins, with a wide variety of physiologic functions.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS

- Polyclonal gammopathy: chronic inflammation, hepatic disease, feline infectious peritonitis, immune-mediated disease, rarely neoplasia
- Monoclonal gammopathy: multiple myeloma, lymphosarcoma, canine ehrlichiosis, leishmaniasis
- If concurrent hyperalbuminemia: dehydration

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH

- Evaluate albumin/globulin (A: G) ratio. Decreased A: G ratio when albumin within reference interval and globulin level is high indicates increased globulin production. If the A:G ratio ≈1, consider dehydration as a cause for a relative increase in globulin.
- Protein electrophoresis and/or immunoelectrophoresis to identify mono-versus polyclonal.

CAUSES OF ABNORMALLY LOW LEVELS

- If concurrent with normal albumin level: failure of passive transfer (neonates), immunodeficiencies, hepatic insufficiency
- If concurrent with hypoalbuminemia: hemorrhage, gastrointestinal (rarely renal) protein loss, severely inadequate nutrient intake/maldigestion/malabsorption, hepatic insufficiency

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW

- Evaluate A: G ratio.
- Evaluate for possible hemorrhage.
- Assess for gastrointestinal protein loss, hepatic failure, poor dietary history, maldigestion, or malabsorption.

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE: As a calculated value, anything affecting accuracy of total protein or albumin measurements will be reflected in globulin concentration.

SPECIMEN: serum in red-top tube

RELATIVE COST: $$ (part of serum biochemistry profile; serum protein electrophoresis)

PEARLS

Magnitude of increase of a and β globulins are usually insufficient to cause an increase in globulin values. An electrophoresis is needed to identify increased peaks (see p. 1511).

AUTHOR: LOIS ROTH-JOHNSON

1ST EDITION AUTHOR: FONZIE QUANCE-FITCH

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Giardiasis Testing

DEFINITION

Giardia lamblia is a protozoan causing chronic severe diarrhea in pets and humans. Contaminated water is the usual source of infection. Fecal flotation using zinc sulfate detects trophozoites. Fecal ELISA detects antigen. Real-time PCR detects organism DNA.

SYNONYMS

Lamblia intestinalis, “beaver fever”

TYPICAL NORMAL RANGE

Reported as negative or positive for trophozoites (fecal flotation), fecal antigen (ELISA), or DNA (real time PCR).

PHYSIOLOGY

- Zinc sulfate fecal flotation depends on accurate identification of trophozoites in fecal specimens combined with zinc sulfate solution. Trophozoites float to the surface, and an aliquot of fluid is examined microscopically.
- ELISA test detects specific antigens in feces.
- Real-time PCR detects *Giardia* sp. DNA by amplification of specific genetic material.
- A true positive result with any of these tests indicates shedding, which is likely—but not certain—to indicate causality in a patient with diarrhea.

For example, a prevalence of *Giardia* infection of up to 40% in puppies has been documented, mostly as subclinical infections.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Intestinal infection

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Identification of organisms or positive detection of antigen or DNA is considered diagnostic of organism shedding, and most clinicians advocate anti-*Giardia* treatment based on a positive result.

CAUSES OF ABNORMALLY LOW LEVELS: Intermittent shedding, previous antiprotozoal therapy

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Repeat testing as clinically indicated.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Anthelmintic drug treatment may lower fecal shedding of organisms.

LAB ARTIFACTS THAT MAY INTERFERE: Feces for flotation must be fresh (analyzed =24 hours since passed). Even with skilled microscopists and optimal technique, fecal flotation has low sensitivity (50%) and specificity (76%). Specimens should be examined within 15 minutes of flotation setup to minimize cyst rupture or distortion. At least three negative results should be obtained before giardiasis is ruled out. ELISA test is more sensitive (92%) and specific (99%). In-office testing devices are available. Real-time PCR is highly specific. Single tests may not detect low levels of DNA.

SPECIMEN: Fresh (=24 hours) fecal specimen in clean dry container, store at 2°C-8°C. Freeze or preserve in formalin for longer storage. ELISA test kits are available for in-office testing.

RELATIVE COST: $$ (ELISA, PCR)

PEARLS

- Affects humans, though recent work indicates a less severe risk of zoonosis than previously suspected (more common-source infections). The disease is especially severe in immunocompromised humans, dogs, and cats, and thorough washing of hands with soap remains important following cleaning up pet waste. Babies should be kept away from pets with diarrhea.
- Animals that test positive may be asymptomatic but be a source of environmental contamination and zoonotic infection.

AUTHOR: LOIS ROTH-JOHNSON

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Gastrin

DEFINITION

Group of peptide hormones secreted by G cells of gastric antrum and duodenum in response to protein meal. Functions to stimulate parietal-cell secretion of gastric acid and histamine release by enterochromaffin cells. Also stimulates pancreatic acinar cells when bound to cholecystokinin.

SYNONYM(S)

G-34 (big gastrin), G-17, g-14 (mini gastrin)

TYPICAL NORMAL RANGE

0-27.8 ng/L (most normal dogs have undetectable levels)

PHYSIOLOGY

Ingestion of protein meal stimulates release. Binds to receptors (parietal, enterochromaffin cells), regulating gastric acid release for protein digestion. Enhances digestion by stimulating gastric blood flow, antral motility, and pancreatic secretion. Stimulates DNA, RNA production, and proliferation of parietal cells and gastric mucosa.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Excess secretion (gastrinoma/Zollinger-Ellison syndrome) associated with gastric mucosa hypertrophy, gastric and duodenal ulceration. The underlying cause is typically a neoplasm of pancreatic islet d cells (gastrinoma); when these cells undergo neoplastic transformation, they regain the ability to produce gastrin (normally only occurs in the fetus).

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Evaluate gastric mucosa (endoscopy) for hypertrophy, ulceration; assess for pancreatic islet (8-cell) tumor (abdominal ultrasound and, if a pancreatic mass or liver lesions suggestive of metastases, laparotomy).

SPECIMEN AND PROCESSING CONSIDERATIONS

SPECIMEN: Frozen serum (red-top tube); fasting specimen suggested

RELATIVE COST: $$

PEARLS

- Send out test to specialized gastrointestinal laboratories for most commercial reference labs.
- Recommended cutoff value for diagnosis of gastrinoma is 10 times upper limit of reference interval (278 ng/L).

AUTHOR: LOIS ROTH-JOHNSON

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Gamma-Glutamyltransferase

DEFINITION

Serum enzyme used as marker for liver disease associated with cholestasis

SYNONYMS

GGT, γ-glutamyltransferase

TYPICAL NORMAL RANGE

Dogs: −0-6 U/L. Cats: −0-4 U/L.

PHYSIOLOGY

Membrane-bound enzyme present in many cells, with biliary epithelium, renal tubular epithelial cells, pancreatic cells, and mammary epithelial cells (especially during lactation) having the greatest activity. Significant increases in serum activity associated primarily with liver disease. Renal urinary GGT may be measured as evidence for renal tubular damage. Colostrum of some species contains high levels of GGT.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Cholestasis, biliary hyperplasia, ingestion of colostrum in neonates; may be induced by corticosteroid administration in dogs

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH

- Evaluate recent drug administration.
- Measure alkaline phosphatase (ALP), bilirubin, bile acids; liver biopsy.

CAUSES OF ABNORMALLY LOW LEVELS: Low end of reference intervals are usually very low, and low serum levels are not clinically significant.

IMPORTANT INTERSPECIES DIFFERENCES: Colostrum in most species contains high GGT concentrations. Increase in serum GGT occurs within 24 hours of suckling: sensitive indicator of passive transfer. In pups, levels fall to within reference intervals by 10 days of age.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Increases secondary to therapeutic drugs causing cholestasis. Increases also seen with anticonvulsant and corticosteroid therapy.

LAB ARTIFACTS THAT MAY INTERFERE: Increase: heparin (therapy or use as anticoagulant for collection) in samples measured by transmission photometry.

SPECIMEN: Serum; separate as soon as possible, store at 8°C.

RELATIVE COST: $ (as individual test); may be included in some chemistry/hepatic chemistry profiles

PEARLS

GGT is more sensitive but less specific than ALP in the cat (for all diseases except hepatic lipidosis) and more specific but less sensitive in the dog.

AUTHOR: LOIS ROTH-JOHNSON

1ST EDITION AUTHOR: FONZIE QUANCE-FITCH

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Howell-Jolly Bodies

DEFINITION

Retained nuclear fragments. They are spherical, 0.5- to l-µm diameter, magenta structures in the cytoplasm of red blood cells.

TYPICAL NORMAL RANGE

Howell-Jolly bodies are occasionally found in the erythrocytes of clinically normal animals. Up to 1% of normal feline red blood cells may contain Howell-Jolly bodies. They are only reported as part of the CBC if they are excessive.

PHYSIOLOGY

During development in the bone marrow, mammalian erythroid progenitor cells contain nuclei. Howell-Jolly bodies are composed of nucleic acids and represent tiny nuclear fragments that have separated from the nucleus of the developing erythrocyte. They are removed from erythrocytes by the splenic mononuclear phagocyte system. In health, red cells usually do not contain more than a single Howell-Jolly body.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Increased numbers of Howell-Jolly bodies have been associated with hyposplenism or splenectomized animals, regenerative anemias, macrocytosis of poodles, and megaloblastic anemias.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Review history for prior splenectomy. If patient is a toy or miniature poodle, consider macrocytosis of poodles (MCV may range from 90-100). If a strongly regenerative anemia is present, no further investigation of the Howell-Jolly bodies is necessary. Mega-loblastic anemias are rare in veterinary medicine but have been associated with anticonvulsant therapy.

IMPORTANT INTERSPECIES DIFFERENCES: As above for cats

SPECIMEN AND PROCESSING CONSIDERATIONS

SPECIMEN: Anticoagulated blood sample collected in EDTA (lavender-top tube), citrate (blue-top tube), or heparin (green-top tube)

RELATIVE COST: $$ (reported as part of CBC, and only if excessive)

PEARLS

If numerous inclusions suspected to be Howell-Jolly bodies are found, the smear should be reviewed by a clinical pathologist for confirmation.

AUTHOR: BRUCE E. LEROY

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

High-Dose Dexamethasone Suppression Test

DEFINITION

Administration of dexamethasone suppresses production/release of hypothalamic corticosteroid releasing hormone (CRH) and pituitary adrenocorticotrophic hormone (ACTH), with subsequent reduction in production/release of cortisol from adrenal glands.

SYNONYMS

HDDST, high-dose dex

TYPICAL NORMAL RANGE

Baseline cortisol: 0.4-6 µg/dL (10-160 nmol/L) in dogs; 0.4-4 µg/dL (10-110 nmol/L) in cats. Postdexamethasone cortisol concentration at 4 or 8 hours: <1 or <1.4 mg/dL (<30 or 40 nmol/L) in dogs; variable lab reference intervals. In cats: <1.4 µg/dL (<35 nmol/L). A 50% reduction in cortisol concentration from baseline to either 4 or 8 hours post dexamethasone administration (or both) is also interpreted as adequate suppression.

PHYSIOLOGY

- The HDDST is used for helping to differentiate pituitary-dependent hyperadrenocorticism from functional adrenal adenoma/adenocarcinoma. Dexamethasone sodium phosphate is administered IV at 0.1 mg/kg in dogs and 1 mg/kg in cats. Serum cortisol level is measured predexamethasone administration and at 4 and 8 hours postadministration.
- HDDST results in adequately decreased cortisol concentration in 75% of cases of hyperadrenocorticism caused by pituitary tumors, whereas hyperadrenocorticism caused by adrenal tumors does not result in adequately decreased cortisol concentration with HDDST. Dogs with nonadrenal illness and healthy dogs should have adequately decreased cortisol concentration (same response as dogs with pituitary dependent hyperadrenocorticism).

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Adrenal neoplasia and 25% of patients with pituitary dependent hyperadrenocorticism

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Imaging for assessment of adrenal size: abdominal ultrasound most commonly, or by more sophisticated modalities such as nuclear scan, MRI, or CT.

CAUSES OF ABNORMALLY LOW LEVELS: If cortisol concentration is adequately decreased after HDDST, a glucocorticoid-producing adrenal neoplasm is very unlikely to be present.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: As clinically indicated, consider evaluating for nonadrenal disease and/or performing an MRI scan of brain to assess for pituitary lesion.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS

- Immunoassays for cortisol measurement have significant cross-reactivity with other glucocorticoids: prednisolone (69%), prednisone (6.4%), 11-deoxycortisol (7.5%), cortisone (4.2%), corticosterone (3.5%), spironolactone (<0.2%), and dexamethasone (<0.1%).
- Ketoconazole inhibits steroid biosynthesis, causing low cortisol concentration.

SPECIMEN

- Serum (red-top tube) or EDTA plasma (lavender-top tube)
- Cortisol in EDTA plasma is more stable than in serum and more stable in cooled samples compared with warm samples. Cortisol is equally distributed between red cells and plasma; therefore, rapid separation of plasma from cells (previously reported) is of no added benefit.

RELATIVE COST: $$ (equilibrium dialysis method); $$$ (radioimmunoassay)

PEARLS

- Careful measurement of dexamethasone dose is important for accuracy. For small dogs, an insulin syringe may be used (no dead space in hub of needle and syringe); if dilution is needed for accuracy, dexamethasone should be added to diluent and not vice versa.
- When a highly skilled ultrasonographer and high-resolution ultrasound machine are available, imaging often supersedes HDDST testing.

AUTHOR: ELIZABETH G. WELLES

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Hemolysis

DEFINITION

Hemolysis is rupture of erythrocytes, releasing hemoglobin. It results in red discoloration of serum or plasma.

PHYSIOLOGY

Hemolysis is most commonly an in vitro artifact from traumatic venipuncture or improper sample handling. It may also occur in vivo secondary to pathologic intravascular or extra vascular hemolysis. Hemolysis may interfere with certain laboratory assays by discoloration of sample, altering spectrophotometric assay results; dilution of normal substances in serum; or leakage of analytes from red blood cells (RBCs), resulting in false increase in these substances in the serum or plasma. The degree of hemolysis of a sample may affect some analytes more than others (see individual test entries in this section of the textbook). The analytes affected and degree of interference depend on the method and type of analyzer. Many laboratories report the presence and degree of hemolysis as well as the expected severity of interference and analytes affected.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: As listed above

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE

- Hemolysis causes artifactual increase in hemoglobin, mean corpuscular hemoglobin concentration, calcium, potassium, alanine aminotransferase, aspartate aminotransferase, creatine kinase, lactate dehydrogenase, triglycerides, and total protein.
- Hemolysis causes artifactual decrease in RBC count, hematocrit, glucose, creatinine, total bilirubin, bile acids, alkaline phosphatase, gammaglutamyltransferase, amylase, and lipase.
- Ways to prevent in vitro hemolysis include: avoid traumatic venipuncture, avoid using a needle with an inappropriately small diameter, avoid excess negative pressure when drawing blood into syringe and excessive agitation of the sample in the tube, ensure prompt separation of serum from the clot and proper storage of sample (refrigeration; avoid freezing), and avoid delay in sample analysis or delayed transport of samples to the laboratory for analysis.

AUTHOR: RUANNA GOSSETT

Hemoglobinuria and Hematuria

DEFINITION

Hemoglobinuria is the presence of hemoglobin in urine and is associated with red to brown urine that persists in the specimen even with centrifugation. Hematuria is the presence of red cells in urine and is associated with red, cloudy urine that clears with centrifugation. Either one may cause a positive reaction on the blood reagent square of a urine dipstick.

TYPICAL NORMAL RANGE

Hemoglobin is not found in normal urine. Finding fewer than 5 red blood cells (RBCs) per high-power microscope field is considered normal in urine sediment.

PHYSIOLOGY

Free hemoglobin in the plasma binds haptoglobin. Complex is cleared in the liver. When haptoglobin becomes saturated, the free hemoglobin splits into dimers which are excreted by the kidneys. Hemoglobin in glomerular filtrate is absorbed by proximal tubules and metabolized to bilirubin, iron, and globin. Unabsorbed hemoglobin appears in urine (hemoglobinuria).

Erythrocytes may appear in the urine from upper urinary (renal, rarely ureteral), lower urinary (bladder, urethra), urogenital (prostate, testes, prepuce, uterus, vagina, vulva), or artifactual (traumatic sampling) sources.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS

- Hemoglobinuria: severe intravascular hemolysis. Free hemoglobin may appear in urine in cases of hematuria where large numbers of red cells lyse in very dilute (specific gravity =1.008) or alkaline urine.
- Hematuria may be associated with hemorrhage, trauma, inflammation, necrosis, or neoplasia in the urinary tract.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH

- Hemoglobinuria: identify cause of hemolysis by blood smear evaluation for hemic parasites, Heinz bodies, spherocytes, and RBC membrane defect. Systemic evaluation (CBC, serum biochemistry profile, abdominal and thoracic imaging) may be indicated for identifying triggers of hemolytic anemia.
- Hematuria: determine when hematuria occurs during micturition. Hematuria at the beginning of urination suggests lower urinary or genital origin; at the end of urination, bladder origin (calculi, polyps); throughout urination, renal disease, diffuse bladder disease, prostatic disease. Radiographic and ultrasonographic evaluations are helpful in localizing the lesion.

DRUG EFFECTS ON LEVELS: Drugs causing intravascular hemolysis can also result in hemoglobinuria.

PEARLS

Cystocentesis and catheterization are frequently associated with microscopic hematuria. These collection methods are not recommended for monitoring remission or progression of hematuria. Free-catch urine from bitches in heat (proestrus) may also be contaminated with blood. A urine reagent strip that is positive for blood in the absence of red cells on urine sediment warrants evaluation for hemoglobinuria or myoglobinuria.

AUTHOR: FIDELIA R. FERNANDEZ

Hematocrit

DEFINITION

The percentage of blood composed of red cells. Electronic cell counters calculate hematocrit using the formula: (MCV × RBC/10 = HCT, where HCT is hematocrit, MCV is mean corpuscular volume (in femtoliters [fL]), and RBC is erythrocyte count ($\times 10^6$/fL). Provided Hb (hemoglobin) reading is accurate (i.e., no interference from hemolysis, lipemia, Heinz bodies, etc), HCT = Hb × 3.

SYNONYMS

Centrifugal microhematocrit, HCT, packed cell volume, PCV

TYPICAL NORMAL RANGE

Dogs: 36%-60%. Cats: 29%-48%.

PHYSIOLOGY

HCT values are slightly less than packed cell volume (PCV) because there is no trapped plasma in an automated hematocrit calculation, as can occur with spun packed cell volumes. Sources of variation:

- Due to the variable MCV of domestic animals, values for HCT may be erroneous if the instrument is not calibrated for specific species.
- Abnormal plasma osmolality and electrolyte balance may also result in a difference between HCT and PCV that is generally not clinically significant.
- Although PCV measures change in red cell volume as they occur in vivo, dilution of red cells with normal saline and standing in hematology instruments may cause red cells to return to their normal volume.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Polycythemia due to breed (sight hounds), dehydration, or splenic contraction ("relative polycythemia"), or due to hypoxemia, independent erythropoietin production (renal lesions), or polycythemia vera (myeloproliferative disease of erythrocytes or primary absolute polycythemia)

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Assess hydration status, review clinical history, evaluate for causes of polycythemia.

CAUSES OF ABNORMALLY LOW LEVELS: Anemia, overhydration

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Blood smear evaluation for type of anemia and evidence of regeneration (e.g., polychromasia), absolute reticulocyte count, then further testing as indicated.

IMPORTANT INTERSPECIES DIFFERENCES: Greyhounds and whippets have slightly higher normal values (up to 65% is considered normal, with some individuals exceeding even this level).

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Erythropoietin injections increase HCT; drugs toxic to bone marrow (hydroxyurea, methimazole, many others) and drugs that cause hemolysis (e.g., zinc, methylene blue, benzocaine) can decrease HCT.

LAB ARTIFACTS THAT MAY INTERFERE

- Hemolysis, lipemia, and specimen clotting prevent accurate reading.
- Decrease: insufficient filling of EDTA (lavender-top) tube dilutes specimen; tubes should be filled to capacity for accurate results.

SPECIMEN: EDTA anticoagulated blood (lavender-top tube); two capillary tubes for PCV; Vacutainer tubes must be completely filled. Transport at room temperature or refrigerate.

RELATIVE COST: $

PEARLS

The differences between HCT and PCV values are not clinically significant except at very high values (PCV/HCT > 65%), where plasma trapping becomes substantial.

AUTHOR: FIDELIA R. FERNANDEZ

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Heinz Bodies

DEFINITION

Single or multiple precipitated denatured hemoglobin particles on the red cell (erythrocyte) membrane, often associated with oxidative damage

SYNONYMS

Erythrocyte refractile body or ER body, HB, Schmauch body

TYPICAL NORMAL RANGE

Low proportion seen in red blood cells (RBCs) of normal cats (see below)

PHYSIOLOGY

Oxidants may cause irreversible denaturation of hemoglobin molecule, causing Heinz body (HB) formation. HBs have affinity for membrane protein band 3, forming a complex with it, resulting in clustering of membrane protein band 3 on both the internal and external RBC membrane. External clustering of protein band 3 creates a recognition site for autoantibodies. HBs also make RBCs rigid and less deformable (via cross-linking of spectrin and hemoglobin). These mechanisms make affected RBCs prone to lysis (intravascular hemolysis) or phagocytosis by macrophages in the spleen (extravascular hemolysis).

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Drugs (see drug effects) and chemicals from food (onions, garlic, chives) or other substances (zinc); deficiency of enzymes that protect against oxidants

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH:

- Review patient history (diet, drug or toxin exposure).
- Check CBC, urinalysis, chemistry profile for anemia, hemolysis.

IMPORTANT INTERSPECIES DIFFERENCES: Normal in feline RBCs (5%-96% may have HBs) because of innately unstable hemoglobin structure, predisposition to form methemoglobin (low methemoglobin reductase activity), and inefficient removal by spleen. Normally occurring HBs are not associated with anemia or hemolysis. Increased HB formation may also occur without significant anemia in diabetes mellitus, hyperthyroidism, and lymphoma. In other species, increased numbers of HBs may be seen post splenectomy.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Acetaminophen, benzocaine-containing products, dl-methionine, methylene blue, phenacetin, phenazopyridine, phenothiazine, and vitamin K^3 cause HB formation and hemolytic anemia.

SPECIMEN: EDTA whole blood (lavender-top tube) for CBC and new methylene blue stained smears

RELATIVE COST: $$ (reported as part of CBC)

PEARLS

Free HBs may falsely increase instrument platelet counts and hemoglobin measurement. HBs may occur concurrently with eccentrocytes (also a result of oxidative injury) and spherocytes (due to removal of HBs from cell membranes in the spleen).

AUTHOR: FIDELIA R. FERNANDEZ

Pricing Information

$: <$20

$$: $21-75
$$$: $76-150
$$$$: >$150

Heartworm Filter Test

DEFINITION

Concentration method for the detection of circulating microfilariae of *Dirofilaria immitis.*

SYNONYMS

Difil test, filaria filter test, Knott's test

TYPICAL NORMAL RANGE

Reported as negative or positive

PHYSIOLOGY

Circulating microfilariae are the larval (L1) stage of adult heartworms *(D. immitis).* Must be distinguished from circulating larval form of Acanthocheilonema (formerly *Dipetalonema) reconditum.*

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Circulating microfilariae of *D. immitis* or *A. reconditum*

NEXT STEP TO CONSIDER IF LEVELS HIGH: Rule out *A. reconditum* larva is larger than a red blood cell; (diameter of *D. immitis* is smaller than a red blood cell); confirm with heartworm antigen test; thoracic radiographs (+/− CBC, serum biochemistry profile, urinalysis, echocardiography) may be useful to stage the disease.

CAUSES OF ABNORMALLY LOW LEVELS: Occult infections (adult heartworms are present but circulating microfilariae are absent) may be present due to single-sex infection, immature worms, immune-mediated destruction of microfilariae, prophylactic administration without initial testing.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Heartworm antigen test to rule out occult infection

IMPORTANT INTERSPECIES DIFFERENCES: Cats with heartworm disease are frequently microfilaria negative.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Animals receiving monthly heartworm prophylaxis may be microfilaremia negative despite having heartworm disease.

SPECIMEN: Anticoagulated whole blood in EDTA (lavender-top tube), citrate (blue-top tube) or heparin (green-top tube)

RELATIVE COST: $

PEARLS

As a screening test, the heartworm microfilaria test is less sensitive than the heartworm antigen test. It has been replaced almost entirely by antigen testing, except in large colony environments where the lower material cost of microfilaria testing makes it the only feasible choice (e.g., certain shelter contexts).

AUTHOR: LOIS ROTH-JOHNSON

1ST EDITION AUTHOR: FONZIE QUANCE-FITCH

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150

$$$$: >$150

Heartworm Antigen and Antibody Tests

DEFINITION

Antigen test kits detect adult heartworm *(Dirofilaria immitis)* antigen. Antibody tests detect circulating antibody to either microfilarial cuticular antigen or to adult heartworm antigen.

SYNONYM

Occult heartworm test

TYPICAL NORMAL RANGE

Results are reported as negative or positive. Some tests are semiquantitative, reported as weakly positive. This is not necessarily indicative of worm burden (see causes of abnormally low levels).

PHYSIOLOGY

- Antigen tests detect an antigen primarily derived from adult female heartworm reproductive tract in the circulating blood of the host.
- Antibody tests detect host species-specific circulating antibodies against either adult heartworms or larvae.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS

- Antigen: infection with adult heartworms
- Antibody: indicates exposure to *D. immitis,* but not all infected animals will develop adult heartworms or heartworm disease.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Thoracic radiographs, CBC, serum biochemistry panel, urinalysis, +/–echocardiogram (if significant changes in aforementioned tests)

CAUSES OF ABNORMALLY LOW LEVELS

- Antigen test: falsely low levels may be seen with very low worm burden (one or two female worms), single-sex (male) infection, immature worms (<5 months old).
- Antibody test: false negatives may occur <30 days postinfection or if animal fails to produce detectable antibodies.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Retest in 1-2 months, assess for clinical signs of heartworm disease.

IMPORTANT INTERSPECIES DIFFERENCES: Antigen tests are less sensitive in the cat (low worm burden, single-sex infections). Antibody tests can be useful in cats with clinical signs, but even these may only become positive 2-3 months postinfection and return to negative within 3 months thereafter. Therefore, a combination of an antigen and antibody test, and possibly echocardiography, may improve overall sensitivity in cats compared to the use of individual antibody tests alone.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Antigen test may remain positive up to 16 weeks post adulticide treatment.

LAB ARTIFACTS THAT MAY INTERFERE: Severe hemolysis or lipemia may interfere with test (false positives, some false negatives). Antigen may degrade if sample not properly handled or stored.

SPECIMEN: Serum (red-top tube). Store at 2°C-8°C. Some assays may also allow whole blood or plasma.

RELATIVE COST: $

PEARLS

Echocardiography (cardiac ultrasound) rivals or surpasses the heartworm antibody test for sensitivity of detection of adult heartworms in cats.

AUTHOR: LOIS ROTH-JOHNSON

1ST EDITION AUTHOR: FONZIE QUANCE-FITCH

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Iron Profile

DEFINITION

A group of tests that typically includes serum iron, total iron-binding capacity (TIBC), and serum ferritin. Some profiles include unbound iron-binding capacity (UIBC) and percent transferring saturation, values calculated from other parameters in the profile.

SYNONYMS

Iron panel, Fe profile or panel. Individual tests: serum Fe, SI, TIBC, UIBC, % transferring saturation.

TYPICAL NORMAL RANGE

Dog: serum iron 125-225 µg/dL; TIBC 225-325 µg/dL; ferritin 525-1100 µg/L

PHYSIOLOGY

Body stores of iron are regulated by absorption. Iron is absorbed from the gut lumen into enterocytes where it is bound to the protein ceruloplasmin. Ceruloplasmin is needed to transfer iron from intestinal epithelium to transferrin, an iron-binding molecule in serum. Iron is stored in macrophages bound to ferritin or as hemosiderin. It is incorporated into erythrocytes during heme synthesis.

- Profile is helpful in evaluating patients with nonregenerative anemia due to iron deficiency or chronic disease, and patients with iron overload.
- In serum, iron is bound to the protein transferrin. Measurement of serum iron by itself is not a good assessment of total body stores.
- TIBC is a measurement of the maximum amount of iron plasma proteins (primarily transferrin) will carry.
- Ferritin is the protein responsible for binding iron within cells. In the bound state, iron is kept soluble and non-toxic. Assays for ferritin are species specific.
- UIBC is the difference between TIBC and serum iron.
- % transferrin saturation equals (serum Fe concentration × 100) divided by TIBC.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS

- Serum iron: excess intake via dietary supplements or injection, release from damaged tissues, excess endogenous or exogenous glucocorticoids in dogs
- TIBC: increased production during iron deficiency
- Ferritin: increased serum iron, inflammation, release from damaged tissue

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Evaluate history for supplementation or accidental ingestion. Assess liver function.

CAUSES OF ABNORMALLY LOW LEVELS:

- Serum iron: chronic blood loss, decreased intake, inflammation (acute and chronic)
- TIBC: inflammation, liver disease (decreased production of transferrin), protein-losing disorders (enteritis or renal disease)
- Ferritin: decreased iron stores

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Evaluate for blood loss, including parasitism (fleas, hookworms, ticks); assess for chronic inflammatory disease, enteric disease, liver dysfunction, or protein-losing nephropathy or enteropathy. Bone marrow evaluation may be useful for assessing iron stores.

IMPORTANT INTERSPECIES DIFFERENCES: Cats: bone marrow iron does not stain in cytologic or histologic specimens.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Glucocorticoids increase serum iron levels in dogs (unknown mechanism).

LAB ARTIFACTS THAT MAY INTERFERE: Hemolysis falsely increases serum iron

SPECIMEN: Fast patient overnight. Collect in serum (red-top) tube; spin and separate cells from serum within 2 hours; transfer serum to plastic tube. Freeze and ship to lab on ice. Specimen must be free of hemolysis.

RELATIVE COST: $$$

PEARLS

- Kittens (especially) and puppies often have low serum iron, TIBC, and ferritin.
- Patients with iron deficiency typically have low serum iron and ferritin and normal to high TIBC.
- Patients with anemia of chronic disease typically have normal to low serum iron, TIBC, and normal to high serum ferritin.
- Ferritin is a good indicator of total body stores of iron in cats and dogs.

AUTHOR: LOIS ROTH-JOHNSON

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Insulin and Insulin/Glucose Ratio

DEFINITION

Insulin is a hormone produced and secreted by the β cells of the pancreatic islets of Langerhans. It promotes cellular uptake of glucose, notably by fat, skeletal muscle, and liver, but not neurons, red blood cells (RBCs), renal tubular epithelial cells, enterocytes, or ocular lens. It promotes anabolic metabolism of carbohydrates, proteins, lipids, and nucleic acids.

The amended insulin/glucose ratio is calculated according to the following formula: serum insulin (μU/mL) × 100/ serum glucose (mg/dL) − 30; if the denominator is negative, substitute 1.

This formula compares the insulin concentration in relationship with serum glucose concentration; however, it is generally considered inaccurate and should not be used. Rather, the absolute serum insulin concentration during hypoglycemic episodes should be evaluated along with history, physical examination findings, and laboratory test results.

TYPICAL NORMAL RANGE

Serum insulin reference interval varies with laboratory and should be established for each laboratory. Insulin/glucose ratio <30 is considered normal, ratio >30 is suggestive of hyperinsulinism but is nonspecific for neoplasia (other causes of hypoglycemia also elevate this ratio in dogs).

PHYSIOLOGY

Under normal conditions, high blood glucose levels trigger insulin release, and high insulin levels decrease blood glucose levels. This feedback mechanism ensures glucose homeostasis and is the reason the insulin/glucose ratio is low (<30) in health. Persistent and/or excessive (e.g., paraneoplastic) hyperinsulinism may cause rapid, excessive cellular uptake of glucose, which results in hypoglycemia and associated clinical signs. Decreased concentrations of insulin are absolute with type I diabetes mellitus and often relative with type II and type III diabetes mellitus.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Pancreatic β-cell neoplasia (insulinoma), leiomyosarcoma, insulin therapy, artifact (see below)

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Measure serum glucose concentration simultaneously. Assess pancreas and small intestine by ultrasonographic examination.

CAUSES OF ABNORMALLY LOW LEVELS: Diabetes mellitus, although serum insulin levels are not usually measured as part of diagnosis or management of diabetic patients

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Check serum glucose concentration, urine glucose, and urine ketones. In diabetes mellitus, the serum glucose is increased; if untreated, there is often glucosuria ± ketonuria.

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE: Antiinsulin antibodies (contributors to diabetes mellitus) interfere with insulin assays and cause false, markedly increased insulin concentration results.

SPECIMEN: Serum (red-top tube)

RELATIVE COST: $$

PEARLS

- Insulin should always be assessed concurrently with serum glucose.
- Insulin levels are almost always measured when investigating hypoglycemia and are virtually never indicated for assessment of hyperglycemia.
- Several noninsulinoma diseases may cause ratio results >30; this ratio is often inaccurate and should not be used as the sole test to diagnose insulinoma. Absolute insulin concentration in hypoglycemic patients, together with signalment, history, physical examination findings, and other laboratory results, should be evaluated.

AUTHOR: ELIZABETH G. WELLES

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Ketonuria

DEFINITION

Ketones (acetoacetate, β-hydroxybutyrate, acetone) in urine

TYPICAL NORMAL RANGE

Reported as negative or slight (1+), moderate (2+), marked (+3)

PHYSIOLOGY

Urine is normally negative for ketones. Their presence in urine is the result of increased fat/lipid metabolism and decreased utilization of carbohydrates as an energy source. The standard laboratory (dipstick) test only detects acetoacetate and acetone.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Diabetes mellitus, hypoglycemia, starvation

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Assess nutritional condition, evaluate for diabetes mellitus (serum glucose, ± fructosamine concentration), evaluate for disorders of glucose metabolism (especially in young patients).

DRUG EFFECTS ON LEVELS: False increases: streptozotocin, aspirin

LAB ARTIFACTS THAT MAY INTERFERE: Standard test does not detect β-hydroxybutyrate, considered the ketone excreted in the earliest stages of diabetes mellitus. Acetate tablet method (Bayer) is considered a more sensitive method and is recommended if ketonuria is suspected.

SPECIMEN AND PROCESSING CONSIDERATIONS

SPECIMEN: Fresh urine specimen in sterile container for standard urinalysis

RELATIVE COST: $ (reported as part of urinalysis)

PEARLS

If ketonuria coexists with glucosuria and hyperglycemia, diabetes mellitus ± diabetic ketoacidosis is likely. Serum Na, K, P, and blood gas determinations are recommended. Ketonuria without glucosuria is suggestive of starvation, fasting.

AUTHOR: LOIS ROTH-JOHNSON

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Lymphocytes (Lymphocytosis, Lymphopenia)

DEFINITION

The mononuclear leukocytes that mediate immune responses. Most lymphocytes are small with scant basophilic cytoplasm, although very low numbers have fine magenta granules clustered near nucleus (granular lymphocytes).

TYPICAL NORMAL RANGE

Dogs: 1.0-5.0 × 10^3 lymphocytes/µL. Cats: 1.5-7.0 × 10^3 lymphocytes/µL.

PHYSIOLOGY

Most lymphocytes are produced in lymphoid tissues such as lymph nodes, spleen, and thymus. Lymphocytes are long-lived cells. They emigrate from blood into lymphoid tissues but then circulate in the lymphatic system to reenter venous circulation via the thoracic duct. Using surface receptors as markers, lymphocytes can be classified as T lymphocytes (e.g., CD3 positive) that mediate cell-mediated responses, B lymphocytes (e.g., CD79a positive) that mediate humoral responses, or null cells that mediate cytotoxicity. Most of the circulating lymphocytes in blood are T lymphocytes.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS

- Inflammatory diseases (especially infectious causes) with antigenic stimulation
- Excitement with epinephrine release (especially young cats)
- Lymphoid neoplasms (e.g., leukemia, lymphoma)
- Hypoadrenocorticism (“relaxed” leukogram: lymphocytosis without neutrophilia in an obviously stressed animal; conspicuous absence of a stress leukogram)

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Evaluate for causes listed, depending on clinical signs.

CAUSES OF ABNORMALLY LOW LEVELS

- Endogenous or exogenous glucocorticoids (stress leukogram)
- Acute inflammation (especially viral infections)
- Disruption of lymphatic flow (e.g., chylothorax, lymphadenopathy, lymphangiectasia)
- Immunodeficiency (e.g., severe combined immunodeficiency)

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Evaluate for causes listed, depending on clinical signs.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Glucocorticoids cause lymphopenia by causing sequestration of lymphocytes in lymphoid tissue and lympholysis.

SPECIMEN: EDTA whole blood (lavender-top tube) and freshly prepared blood smear for laboratory to stain

RELATIVE COST: $$ (reported as part of CBC)

PEARLS

In evaluating lymphocytosis, cell morphology is important. Markedly increased numbers of large or atypical lymphocytes indicate lymphoblastic leukemia, whereas a marked increase in small, well-differentiated lymphocytes occurs with chronic lymphocytic leukemia.

AUTHOR: STEPHEN D. GAUNT

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Luteinizing Hormone (LH)

DEFINITION

A glycoprotein gonadotrophin produced by the anterior pituitary

TYPICAL NORMAL RANGE

2-29 ng/mL; considerable variability during anestrus

PHYSIOLOGY

LH synergizes with follicle-stimulating hormone (FSH) to initiate ovulation as well as secretion of progesterone. LH is essential for corpus luteum formation. In males, LH is important for normal growth and function of testicular interstitial (Leydig) cells, which secrete testosterone.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Preovulation, cystic ovary disease

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: A marked increase in LH concentration occurs approximately 48 hours prior to ovulation. Monitor progesterone concentrations subsequently to determine if pregnancy has occurred. Evaluation for cystic ovaries with abdominal ultrasound.

CAUSES OF ABNORMALLY LOW LEVELS: Low values are associated with anestrus.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Evaluate for anestrus.

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE: Hemolyzed samples should not be used for LH ELISA. Hemolysis does not interfere with radioimmunoassay.

SPECIMEN: Serum should be used for LH ELISA. Collect blood in red-top tube, spin, and collect serum. Sample should be free of hemolysis and lipemia. Ship frozen or on ice.

RELATIVE COST: $$

PEARLS

To facilitate ovulation timing, once visible signs of estrus have begun and vaginal cytology reveals >70% cornified cells, serum LH levels should be measured daily to ensure detection of the preovulatory LH surge and optimal timing of breeding/insemination.

AUTHOR: BRUCE LEROY

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Lupus Erythematosus Preparation (LE Prep)

DEFINITION

Preparation of incubated clotted blood crushed through a wire sieve. Fluid is collected and centrifuged; buffy coat is mixed with equal amounts of serum, smeared, and stained with Wright stain or new methylene blue. Preparations positive for lupus erythematosus (LE) show rosetting of neutrophils around nuclear material and LE cells (neutrophils with phagocytized smooth, homogeneous nuclear material).

SYNONYMS

LE clot test, LE preparation/prep

TYPICAL NORMAL RANGE

Reported as negative or positive. Positive test indicates active disease (systemic lupus erythematosus [SLE]).

PHYSIOLOGY

LE cell formation occurs in the presence of sufficient immunoglobulin G antibody to deoxyribonucleoprotein along with complement. This antinuclear antibody binds the nuclei of traumatized or nonviable leukocytes. Viable neutrophils then phagocytize the opsonized nuclear material, forming the LE cell.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Active systemic lupus erythematosus

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Assess presence of antinuclear antibodies by indirect immunofluorescence (ANA test).

LAB ARTIFACTS THAT MAY INTERFERE: Mere phagocytosis of nuclear material with intact chromatin pattern (tart cell) does not constitute an LE cell.

SPECIMEN AND PROCESSING CONSIDERATIONS

SPECIMEN: 5-10 mL of blood in a glass test tube. Heparinized blood (green-top tube) may also be used.

RELATIVE COST: $$

PEARLS

- LE cells may occur in skin lesions and joint fluid of patients with active SLE.
- Absence of LE cells does not rule out SLE: the test is specific (positive is true positive) but is a very poor screening test (low sensitivity; positives are seen very uncommonly in patients with SLE).
- ANA testing and correlation with clinical signs are needed for diagnosis of SLE.

AUTHOR: FIDELIA R. FERNANDEZ

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Low-Dose Dexamethasone Suppression Test

DEFINITION

Administration of dexamethasone to suppress production/release of hypothalamic corticosteroid releasing hormone (CRH) and pituitary adrenocorticotrophic hormone (ACTH), with subsequent reduction in production/release of cortisol from adrenal glands. It is most often used as a "screening" test for hyperadrenocorticism in dogs and cats (8-hour sample result), but can be used as a "discriminating" test between pituitary-dependent hyperadrenocorticism and adrenal tumor hyperadrenocorticism (4-hour sample result) in dogs (not cats).

SYNONYMS

LDDST, Low-dose dex

TYPICAL NORMAL RANGE

Baseline cortisol: 0.4-6 µg/dL or 10-160 nmol/L (dogs); 0.4-4 µg/dL or 10-110 nmol/L (cats). After dexamethasone administration: expect cortisol concentration <30 or 40 nmol/L or <1-1.4 µg/dL (depends on lab reference intervals, healthy dogs); <1.4 µg/dL or <35 nmol/L (healthy cats). Reduction in cortisol concentration of 50% or more from baseline (at 4 or 8 hours post dexamethasone injection) can also be interpreted as adequate suppression. Failure to suppress is strongly suggestive of hyperadrenocorticism (either pituitary based or primary adrenal based).

PHYSIOLOGY

LDDST is a screening test for hyperadrenocorticism. Serum or plasma cortisol concentration is determined before administration (0.01 mg/kg IV in dogs, 0.1 mg/kg IV in cats) of dexamethasone. In health, hypothalamic CRH and pituitary ACTH production/release are suppressed for several hours (up to 24-48 hours in dogs), with subsequent reduction in adrenal cortisol production/release. Cortisol half-life is 2 hours; at 4 and 8 hours post dexamethasone administration, cortisol concentration in healthy dogs and cats should be markedly decreased. LDDST can cause adequately decreased cortisol in dogs with pituitary-dependent hyperadrenocorticism (up to 80% of patients in some studies) but almost never in adrenal tumor-dependent cases of hyperadrenocorticism. However, nonadrenal illness also may cause failure of LDDST to suppress cortisol levels (false positive). To use LDDST as a discriminating test able to distinguish pituitary-dependent hyperadrenocorticism from adrenal tumor-dependent hyperadrenocorticism, one or more of three criteria must be met: (1) 4-h plasma cortisol <1.4 µg/dL, (2) 4-h plasma cortisol <50% of basal concentration, or (3) 8-h plasma cortisol <50% of basal concentration. If cortisol adequately suppresses, then pituitary-dependent hyperadrenocorticism is likely.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS (FAILURE TO SUPPRESS)

- Hyperadrenocorticism: pituitary dependent or adrenal neoplasia
- Nonadrenal illness. If the patient is ill (owing to adrenal or nonadrenal disease), LDDST should not be performed. Stabilize the patient prior to testing.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH

- Imaging of abdomen by ultrasound, MRI, or CT to evaluate size (enlargement) of adrenal glands
- Review history, physical examination findings, and laboratory data.
- Repeat LDDST when other (nonadrenal) problems are controlled.

CAUSES OF ABNORMALLY LOW LEVELS (ADEQUATE SUPPRESSION): Patients with adequate cortisol suppression are either healthy (vast majority) or have pituitary-dependent hyperadrenocorticism (some dogs, not in cats).

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Reassess history, physical exam, CBC, serum chemistry profile, urinalysis, blood pressure measurement, and diagnostic imaging results for other causes of clinical signs. If hyperadrenocorticism remains a possible differential diagnosis, LDDST may be repeated 1-3 months later, or abdominal imaging can define adrenal size by a more sophisticated modality such as nuclear scan, MRI, or CT.

IMPORTANT INTERSPECIES DIFFERENCES: Hyperadrenocorticism is rare in cats. Cats require administration of 0.1 mg/kg

dexamethasone IV because 15%-20% of healthy cats fail to suppress with 0.01 mg/kg dose (dose used in dogs).

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS

- Immunoassays for cortisol measurement have significant cross reactivity with other glucocorticoids and drugs: prednisolone (69%), prednisone (6.4%), 11-deoxycortisol (7.5%), cortisone (4.2%), corticosterone (3.5%), spironolactone (<0.2%), and dexamethasone (<0.1%).
- Ketoconazole inhibits steroid biosynthesis, causing low cortisol concentration.

SPECIMEN

- Serum (red-top tube) or EDTA plasma (lavender-top tube)
- Cortisol in EDTA plasma is more stable than in serum. Cool specimens are more stable than warm samples. Cortisol is equally distributed between red cells and plasma; therefore, rapid separation of plasma from cells (previously reported) is of no benefit.

RELATIVE COST: $$ (equilibrium dialysis method); $$$ (radioimmunoassay)

PEARLS

Very small volumes of dexamethasone are used (0.01 mg/kg using dexamethasone 4 mg/mL equals 0.01 mL for a 4-kg [9-lb] dog, for example). Therefore, dead space in a regular syringe and needle hub should be considered. Either dilution (add dexamethasone to diluent, not the other way around) or use of an insulin syringe (no dead space in hub) should be considered.

AUTHOR: ELIZABETH G. WELLES

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Lipemia

DEFINITION

Lipemia is the increased concentration of triglyceride-rich lipoproteins (chylomicra and very low density lipoproteins) in blood, resulting in the cloudy/turbid appearance of serum or plasma.

TYPICAL NORMAL RANGE

Normally absent from a fasting blood sample

PHYSIOLOGY

Lipemia may interfere with certain laboratory assays by causing dilution of substances in serum, or turbidity of the sample which affects the results of spectrophotometric assays. Lipemia causes hemolysis that further contributes to interference with laboratory assays.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Postprandial specimens, primary hyperlipidemia, secondary hyperlipidemia

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH

- Determine whether specimen is postprandial. Normally, lipemia may be avoided by fasting for 12-24 hours prior to sample collection. Ultracentrifugation may clear lipemic serum. If lipemia in dogs persists with fasting, it may be cleared (for purposes of eliminating lipemia related artifacts) by injection of 100 U/kg of sodium heparin intravenously and collection of the blood sample 15 minutes later. Triglycerides should be measured in an aliquot of the fasting lipemia serum prior to clearing.
- Evaluation for causes of secondary hyperlipidemia (hypothyroidism, diabetes mellitus, acute pancreatitis, hyperadrenocorticism, nephrotic syndrome, and high-fat diet) is indicated if lipemia is present in a fasted blood sample. If no evidence of these conditions is found, consider primary hyperlipidemia.

PEARLS

- Examples of analytes that can be artifactually increased by lipemia include hemoglobin, mean corpuscular hemoglobin concentration, triglycerides, plasma protein measured by refractometer, and spectrophotometric assays for glucose, calcium, phosphorus, alanine aminotransferase (ALT), creatine kinase (CK) and total bilirubin.
- Examples of analytes that can be artifactually decreased by lipemia include lipase, amylase, bile acids and albumin.
- Hypercholesterolemia does not cause lipemia.

AUTHOR: RUANNA GOSSETT

Lipase

DEFINITION

Enzyme that hydrolyzes triglycerides to fatty acids and glycerol

TYPICAL NORMAL RANGE

Serum lipase activity based on enzymatic activity:

- Dogs: 100-750 IU/L
- Cats: 10-195 IU/L

Pancreas-specific lipase immunoreactivity (spec cPLI for canine and fPLI for feline: species-specific immunoassay utilizing antipancreatic lipase antibodies):

- Dogs: normal ≤200 µg/L (pancreatitis is unlikely); questionable range is 201-399 µg/L (evaluate other possible diagnoses; recheck cPLI in 2-3 weeks); >400 µg/L is consistent with pancreatitis.
- Cats: normal ≤3.5 µg/L (pancreatitis is unlikely); questionable range is 3.6-5.3 µg/L (evaluate other possible diagnoses; recheck fPLI in 2-3 weeks); =5.4 µg/L is consistent with pancreatitis.

PHYSIOLOGY

Lipase is present in pancreas, adipose tissue, gastric mucosa, and duodenal mucosa. Pancreatic lipase catabolizes triglycerides into fatty acids and glycerol, monoglycerides, and diglycerides in the proximal small intestine. Bile salts and colipase enhance the efficiency of lipase activity. The pancreas is considered the primary source of serum lipase concentration, although other tissues may contribute. Pancreas-specific lipase immunoreactivity is a sensitive and specific test for pancreatic lipase levels in the serum of dogs and cats.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Pancreatitis, renal failure, azotemia, hepatic disease, gastrointestinal disease (gastroenteritis, duodenal obstruction, peritonitis, inflammatory bowel disease), neoplasia

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: If clinical signs consistent with pancreatitis (dogs and cats), with or without increase in serum amylase (dogs only), assess pancreatic lipase immunoreactivity (spec cPLI, fPLI) and/or abdominal ultrasound. Evaluate for concurrent disease such as IBD, gastroenteritis, proximal intestinal foreign body, hepatic disease, neoplasia, and especially in cats, cholangiohepatitis and hepatic lipidosis.

CAUSES OF ABNORMALLY LOW LEVELS: Exocrine pancreatic insufficiency

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Serum trypsinlike immunoreactivity, cobalamin, folate

IMPORTANT INTERSPECIES DIFFERENCES: Total serum lipase levels are not a reliable indicator of pancreatitis in cats. Pancreatic-specific lipase immunoreactivity is a much more sensitive and specific test for diagnosis of pancreatitis in both dogs and cats.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Dexamethasone and prednisone therapy increase lipase activity, without concurrent increase in amylase.

LAB ARTIFACTS THAT MAY INTERFERE: Decrease: lipemia, hemolysis, icterus

SPECIMEN: Serum (red-top tube) or serum separator tube (red-top SST). Fasted sample preferred. Stable at 2°C-8°C for 3 weeks. Avoid freeze/thaw.

RELATIVE COST: $ (serum lipase); $$ (spec cPL, spec fPL)

PEARLS:

- Degree of elevation of lipase in serum does not correlate with severity of pancreatitis. Rather than using individual values, continued elevations, decreases, or plateau of levels are likely to provide more diagnostic information.
- Pancreas-specific lipase may be measured serially in a confirmed pancreatitis patient (dog or cat) to assess disease progression.

AUTHOR: RUANNA GOSSETT

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Leukocytes (Leukocytosis/Leukopenia)

DEFINITION

Leukocyte is the term for blood cells that can be categorized as either granulocytic (neutrophils, eosinophils, and basophils) or mononuclear (lymphocytes and monocytes). *Leukocytosis* indicates an increase above the normal range; *leukopenia* indicates a decrease below the normal range.

SYNONYM

White blood cells (WBCs)

TYPICAL NORMAL RANGE

Dogs: 6-17 × 10^3 leukocytes/µL. Cats: 6-19 × 10^3 leukocytes/µL.

PHYSIOLOGY

Encompasses several different types of cells with different functions and kinetics. More specific analysis of neutrophils, lymphocytes, monocytes, eosinophils, and basophils is indicated (see respective topics). Changes in the number and morphology of each different leukocyte should be investigated.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Increased numbers of neutrophils (neutrophilia) and lymphocytes (lymphocytosis) are the most common contributors to leukocytosis. Leukocytosis does not automatically equal inflammation. A variety of disorders can induce leukocytosis, and stress leukograms (due to epinephrine release) are common in dogs and less so in cats. Leukocytosis caused by inflammation can be accompanied by band neutrophils/left shift, toxic neutrophilic changes, or both. Leukocytosis should be interpreted with physical exam findings and other laboratory test results.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Evaluate the absolute concentrations of each leukocyte type to determine the specific cause of leukocytosis.

CAUSES OF ABNORMALLY LOW LEVELS: Leukopenia is most often attributed to neutropenia or lymphopenia.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW:

- Evaluate the absolute concentration of each leukocyte type to determine the specific cause of leukopenia.
- The most common next diagnostic step indicated in patients with persistent leukopenia attributed to neutropenia without an identifiable systemic cause is bone marrow aspiration for cytology, although in cats, retroviral testing (feline leukemia virus, feline immunodeficiency virus) should be performed first.

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE: Nucleated erythrocytes (NRBCs) cannot be accurately differentiated from leukocytes by leukocyte counting instruments, so any NRBC present would add to the total leukocyte concentration. A correction formula is used for calculating the concentration of total leukocytes when RBCs are present: correct WBC/µL = counted WBC/µL × 100/100 + number of NRBCs. Be aware that not all laboratories necessarily make this correction on the final CBC report, and “leukocytosis” in the presence of NRBC should prompt investigation of this possible artifact.

SPECIMEN: EDTA whole blood (lavender-top tube) and freshly prepared blood smear for laboratory to stain

RELATIVE COST: $$ (reported as part of CBC)

PEARLS

- Rather than total leukocyte count (especially if it is within the reference interval), the absolute concentrations of individual leukocytes should be evaluated: neutrophil, lymphocyte, monocyte, eosinophil, and basophil.
- Severe leukocytosis (>50,000), regardless of cause, is generally associated with a guarded to poor prognosis.

AUTHOR: STEPHEN D. GAUNT

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Leukocyte Function Tests

DEFINITION

Tests of the in vitro ability of leukocytes to perform specific functions unique to that cell type (e.g., neutrophils, lymphocytes). These tests are not routine; the specific leukocyte may have to be isolated from blood, and tests are only available at research laboratories.

PHYSIOLOGY

Neutrophil function tests include measuring response to chemotactic stimuli, respiratory burst and release of oxidative metabolites, phagocytosis and killing of bacteria, and expression of activation cell markers (e.g., CD18). Monocytes are tested for ability to phagocytose particles. Lymphocyte tests include proliferative response to specific mitogens (e.g., concanavalin A, pokeweed mitogen), expression of Band T-cell receptors and other markers, using flow cytometry or PCR and immunoelectrophoresis and quantitation of serum antibodies.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY LOW LEVELS: Abnormal function of neutrophils: congenital disorders such as canine leukocyte adhesion defect, cyclic hematopoiesis of grey collies. Abnormal function of lymphocytes: congenital disorders such as severe combined immunodeficiency.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Tests are diagnostic of cell function abnormalities.

SPECIMEN AND PROCESSING CONSIDERATIONS

SPECIMEN: The laboratory performing tests should be contacted for specific sample collection and shipment handling, although heparinized blood (green-top tube) is typically used for leukocyte isolation and function testing.

AUTHOR: STEPHEN D. GAUNT

Leptospira Serology, Canine

DEFINITION

Leptospirosis is a zoonotic disease caused by pathogenic serovars of *Leptospira interrogans,* a motile, spiral-shaped bacterium (spirochete). Serovars of importance include canicola, icterohaemorrhagiae, grippotyphosa, pomona, hardjo, bratislava, and autumnalis.

TYPICAL NORMAL RANGE

Reported as titer values; panel of serovars varies among laboratories.

PHYSIOLOGY

Organisms penetrate abraded skin and/or mucous membranes, replicate within bloodstream; rapid dissemination to multiple organs, most importantly liver and kidney (allows shedding in urine). Organisms replicate in the renal tubular epithelium, causing chronic tubulointerstitial nephritis and persistent carrier state if untreated.

Vaccines elicit immunity against canicola and icterohaemorrhagiae serovars; newer vaccine (Fort Dodge Duramune) elicits immunity against these plus grippotyphosa and pomona.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Microscopic agglutination test (MAT): a titer of =1:800 or fourfold rise in titer (paired serum 3 weeks apart) to a serovar against which the dog has not previously been vaccinated suggests active disease. Vaccine-induced titers are generally low (<1:800) but may be as high as 1:3200; these higher titers generally do not persist longer than 3 months.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: PCR using urine, blood, cerebrospinal fluid, aqueous humor, or tissue is possible, as is direct fluorescent antibody testing on tissue (kidney, liver). Darkfield microscopy or culture (blood, urine) prior to antibiotic therapy can be performed but is technically difficult and not widely available.

CAUSES OF ABNORMALLY LOW LEVELS: Early infection, antibiotic treatment

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: ELISA for immunoglobulin (Ig) G and IgM antileptospiral antibodies. IgM may be detected 1 week after infection. May be useful in detecting acute leptospirosis prior to IgG increase.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Antibiotic therapy may cause a decreased MAT titer, prevent a rising titer in paired sample, and cause negative PCR results and negative culture results.

SPECIMEN: Collect 2 mL of serum (red-top tube). Stable for 4 days at 4°C or longer at 0°C.

RELATIVE COST: $$

PEARLS

The diagnosis can be missed if relevant serovars are excluded from serologic testing, because there is no consistent serologic cross-reactivity from one serovar to another. Serovars currently recommended for testing: canicola, pomona, grippotyphosa, bratislava, icterohaemorrhagiae, hardjo, and autumnalis. It may be useful to evaluate urine PCR and serology concurrently.

AUTHOR: PATTY J. EWING

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150

$$$$: >$150

Left Shift

DEFINITION

The presence of band neutrophils (or earlier neutrophilic precursors such as metamyelocytes or myelocytes) in peripheral blood. This finding nearly always indicates active inflammation. It is clinically useful to define the type of left shift present in leukograms. When segmented neutrophils are also increased, the left shift can be described as "regenerative," suggesting appropriate marrow response to increased tissue demands for neutrophils. Alternately, when the segmented neutrophil count is unchanged or decreased, the left shift is described as "degenerative," suggesting the granulopoietic response of marrow is outweighed by tissue demand.

TYPICAL NORMAL RANGE

Dogs: 0-0.3 × 10^3 band neutrophils/µL. Cats: 0-0.2 × 10^3 band neutrophils/µL.

PHYSIOLOGY

Band neutrophils, metamyelocytes, and myelocytes are late neutrophilic precursors that normally remain in the marrow storage pool to differentiate into segmented neutrophils. If intense tissue demand for neutrophils during inflammation depletes the segmented neutrophils from the marrow storage pool, band neutrophils (and earlier precursors) can be prematurely released from the marrow into blood.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Acute inflammation, granulocytic leukemia

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Identify source of inflammation; if none is found despite comprehensive evaluation and repeated assessments, a bone marrow aspirate and core biopsy could be indicated to assess for granulocytic leukemia (rare).

SPECIMEN AND PROCESSING CONSIDERATIONS

SPECIMEN: EDTA whole blood (lavender-top tube) and freshly prepared blood smear for laboratory to stain

PEARLS

- Always examine a stained blood smear for band neutrophils, because the neutrophil counts generated by automated hematology analyzers do not distinguish between segmented and band neutrophils. The presence of toxic changes in neutrophils is another indicator of intense inflammation.
- The hyposegmentation of neutrophils in Pelger Huët syndrome is not considered a left shift.

AUTHOR: STEPHEN D. GAUNT

Lead, Blood Level

DEFINITION

Lead intoxication is relatively common, and whole-blood lead levels are the diagnostic test of choice. Exposure is usually by ingestion. Inhalation, dermal, subcutaneous/intramuscular exposure occur uncommonly.

TYPICAL TOXIC RANGE

- 0.6 ppm or greater is diagnostic of lead toxicosis.
- 0.35 ppm or greater with signs and confirmatory tests (d-aminolevulinic acid [ALA] or fecal lead) is also diagnostic.

PHYSIOLOGY

Although lead is poorly absorbed from the digestive tract, once absorbed it is retained by tissues (kidney, bone). Blood levels decline slowly; they may be elevated for 1-2 months after a single exposure. Blood concentration indicates exposure but does not reflect exposure duration or total body concentration. Lead crosses the placental barrier and is also excreted in milk. Young animals are more susceptible to toxicosis.

Lead exposure results in increased urinary excretion of ALA and inhibits conversion of coproporphyrinogen III to protoporphyrin and heme synthetase. Interference with hemoglobin synthesis, hemogram abnormalities such as basophilic stippling, and increased number of nucleated red blood cells in nonanemic patients are suggestive but not diagnostic of lead toxicosis.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Exposure to lead

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Serum ALA dehydratase inhibition and erythrocyte protoporphyrin assays are highly sensitive tests for exposure and an indication of possible effect of lead. They are not a substitute for blood lead assay, which confirms the presence of lead. Fecal lead analysis may be of benefit; a value of =35 ppm is suspect.

IMPORTANT INTERSPECIES DIFFERENCES: Lead toxicosis is less common in cats than dogs.

SPECIMEN AND PROCESSING CONSIDERATIONS

SPECIMEN: Heparinized (green-top tube) or EDTA (lavender-top tube) whole blood. Because 90% of circulating lead is bound to erythrocytes, serum lead is not routinely used and not readily interpretable.

RELATIVE COST: $$

PEARLS

- Kidney and liver tissue may be submitted if blood is not available. Kidney is considered preferable (=10 ppm is diagnostic). Formalin-fixed samples may be used for retrospective analyses.
- Chronic exposure is more common than acute exposure.
- Blood levels and clinical signs do not always correlate. Blood levels are the best indicator of lead exposure but may not indicate duration or dose of exposure.
- Ingested items containing lead may be seen radiographically.

AUTHOR: SHERRY J. MORGAN

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Lactate

DEFINITION

Metabolic end product of anaerobic glycolysis

SYNONYM

Lactic acid

TYPICAL NORMAL RANGE

Range: 1.8-22.5 mg/dL; <2 mEq/L (experimental studies, primarily in dogs at rest). Unit conversion: mg/dL × 0.112 = mEq/L; 1 mmol/L = 1 mEq/L.

PHYSIOLOGY

Normally produced in small quantities in skin, erythrocytes, brain, skeletal muscle, GI tract. Increased production occurs when tissues (primarily skeletal muscle and GI tract) must maintain energy production under anaerobic conditions (tissue hypoxia). Abnormal carbohydrate metabolism associated with some diseases may also increase production. Liver and kidney are the primary consumers of lactate. Lactic acidosis occurs when production exceeds utilization.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS

- Hypoxemic: strenuous exercise, seizures, any cause of decreased oxygen availability (shock, hypovolemia, cardiac disease, pulmonary edema)
- Nonhypoxemic: gastric dilatation/volvulus, diabetes mellitus, liver failure, neoplasia, sepsis, renal failure, hypoglycemia, babesiosis, rare hereditary defects (mitochondrial myopathy, pyruvate dehydrogenase deficiency)

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH

- Not measured as part of routine biochemical profile, but cageside use is increasingly common in emergency/critical care setting.
- Lactic acidosis should be suspected when there is an unexplained increase in the anion gap. Evaluate patient for underlying causes.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Increases associated with salicylates, ethylene glycol, epinephrine, and phenobarbital

LAB ARTIFACTS THAT MAY INTERFERE: Increased: delayed plasma harvest, venous stasis (prolonged holding off of the vein), struggling during venipuncture. Decreased: free hemoglobin, bromide (method dependent).

SPECIMEN: Plasma collected in lithium heparin (green-top tube) or sodium fluoride (grey-top tube); must be centrifuged immediately and plasma removed from erythrocytes. Refrigerate immediately or freeze. Some blood gas analyzers use whole blood.

RELATIVE COST: $$$ (at reference laboratory)

PEARLS

Markedly elevated lactate concentrations have been associated with a poor prognosis in critical care settings. For example, dogs with gastric dilatation/volvulus have a 99% survival rate if plasma lactate <6 mmol/L but a 58% survival rate if plasma lactate >6 mmol/L.

AUTHOR: ROBIN W. ALLISON

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Lactate Dehydrogenase

DEFINITION

Cytosolic enzyme found in most cells in the body

TYPICAL NORMAL RANGE

Dogs: 50-380 U/L. Cats: 46-350 U/L.

PHYSIOLOGY

Lactate dehydrogenase (LDH) catalyzes the oxidation of L-lactate to pyruvate and the reverse reaction. LDH is nonspecific because it is present in many tissues. It is concentrated in heart, skeletal muscle, liver, kidney, and erythrocytes. Leakage of this enzyme into the blood and extracellular space occurs with injury to most tissues. It also increases with only slight sample hemolysis. There are five LDH isoenzymes that can be separated electrophoretically. These isoenzymes are present in certain tissues and are therefore more specific: one primarily in myocardium, another primarily in skeletal muscle, and the remaining isoenzymes are present in several different tissues. Therefore LDH isoenzyme determination may be used to identify cardiac or skeletal muscle injury. Yet LDH isoenzyme measurement is usually restricted to research applications in veterinary medicine. LDH isoenzyme determination is not practical, readily available, or cost effective in the clinical setting, since there are other more sensitive and specific markers of muscle and hepatic injury.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Cardiac disease, skeletal muscle disease, renal injury, liver disease, and hemolysis

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Evaluate for muscle injury, hepatic disease, or hemolytic anemia.

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE: Hemolysis results in false elevation, because red blood cells contain LDH.

SPECIMEN: Serum (red-top tube). Store at 4°C.

RELATIVE COST: $

AUTHOR: RUANNA GOSSETT

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Myoglobinemia, Myoglobinuria

DEFINITION

Myoglobin is a low-molecular-weight heme protein found in muscle tissue.

TYPICAL NORMAL RANGE

Serum myoglobin in dogs: <10.0-13.6 ng/mL. Cats: <10.0-13.8 ng/mL. Not present in urine of healthy animals.

PHYSIOLOGY

Myoglobin stores and transports oxygen in muscle fibers. It is released from muscle when there is severe disruption of the muscle membrane or necrosis. Myoglobin is detected in the serum within 2-4 hours after injury. Myoglobin does not significantly bind serum proteins. It passes quickly through the glomerulus and is excreted in urine. Red to brown urine discoloration due to myoglobinuria occurs before the plasma appears discolored. Myoglobin causes a positive occult blood test on urine dipstick.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Trauma, ischemia, toxic injury, or necrosis of muscle tissue

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Evaluate for muscle injury or necrosis (e.g., serum creatine kinase level) versus laboratory evidence of hemolysis.

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE: Must distinguish myoglobinuria from other causes of positive reaction for blood on urine dipstick such as hematuria, hemoglobinuria, and substances that cause a false-positive reaction (high bilirubin concentration, contamination of urine with oxidizing agents in disinfectants, leukocytes, bacteria, peroxidase, or iodine)

SPECIMEN

- Myoglobinemia: serum (red-top tube), heparinized plasma (green-top tube), or EDTA plasma (lavender-top tube). Refrigerate at 2°C-8°C.
- Myoglobinuria: 1 mL urine (clean container without additives)

RELATIVE COST: $$$

PEARLS

Myoglobinuria may be distinguished from hemoglobinuria and hematuria by checking the urine sediment for the presence (hematuria) or absence of red blood cells and evaluating the color of the plasma or serum for a pink discoloration (hemoglobinemia). Hemoglobin in plasma binds haptoglobin and is not readily cleared by the glomerulus. Pink discoloration of the serum indicates hemolysis and suggests hemoglobinuria as cause for positive urine blood result. Myoglobin is readily excreted in the urine, so the serum is usually clear to yellow. If there is no hematuria in urine sediment and no evidence of hemoglobinemia, positive blood result on urine dipstick suggests myoglobinuria by process of elimination. Myoglobinuria may be confirmed with an ammonium sulfate precipitation test on urine as well as checking for other clinical and laboratory evidence of muscle damage such as elevation of serum creatine kinase. Addition of ammonium sulfate to urine to 80% concentration will cause hemoglobin to precipitate. Myoglobin does not precipitate and will continue to give a positive occult blood result on urine dipstick.

AUTHOR: RUANNA GOSSETT

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Mycoplasma spp. Culture

DEFINITION

Laboratory growth of infectious *Mycoplasma* spp. agents to allow isolation and identification

TYPICAL NORMAL RANGE

Reported as no growth or growth with identification of pathogens

PHYSIOLOGY

Mycoplasma spp. are the smallest, simplest self-replicating bacteria. Hemotropic *Mycoplasma* spp. (previously called *Haemobartonella* spp.) are associated with hemolytic anemia. This type of organism is fastidious and grows slowly in culture.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Infection is associated with arthritis, respiratory disease, hemolytic disease, and conjunctivitis.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Assess immune function; clinical disease is more likely in immunocompromised patients.

IMPORTANT INTERSPECIES DIFFERENCES: Diseases caused solely by *Mycoplasma* spp. other than hemotropic *Mycoplasma* are uncommon in cats and dogs. Coinfection with *Mycoplasma* and other species of bacteria may occur in more than 60% of dogs with pneumonia, however. Mycoplasmal conjunctivitis and respiratory disease are more likely to occur in cats; arthritis is more likely to occur in dogs. Hemotropic *Mycoplasma*most often infects male cats allowed outdoors.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Glucocorticoid or other immunosuppressive therapies may enhance growth.

LAB ARTIFACTS THAT MAY INTERFERE: Contamination with commensals may mask growth. Organism takes a long time to grow in culture, and cultures may be discarded inadvertently if laboratory personnel are not informed that *Mycoplasma* spp. infection is suspected.

SPECIMEN: Swabs, exudate, or tissue should be submitted in specific transport media to enhance growth. Laboratory should be contacted to obtain media for sample submission.

RELATIVE COST: $$

PEARLS

Growth in culture may take up to 2 weeks: serologic tests or PCR should be used for confirming infection.

AUTHOR: LOIS ROTH-JOHNSON

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Mycobacterial Culture

DEFINITION

Laboratory growth, isolation, and identification of *Mycobacterium* spp.

TYPICAL NORMAL RANGE

Reported as growth or no growth, with identification of organisms

PHYSIOLOGY

When an infection is present, organisms may be shed intermittently in respiratory specimens (tracheal exudate) but should be present constantly in solid tissue specimens (skin, lymph node). The organism must be isolated from other flora and grown in media specific for *Mycobacterium* spp. Growth and identification of these fastidious organisms may take 2-4 months.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Infection with *Mycobacterium* spp. Common sites of infection include skin and respiratory tract. Infections may become systemic, involving lymphatics system and bone marrow.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH:

Determine appropriate antibiotic for treatment.

IMPORTANT INTERSPECIES DIFFERENCES

- Feline leprosy *(M. lepraemurium)* and atypical mycobacteriosis *(M. avium. M. fortuitum, M. thermoresistibile, M. xenopi, M. phlei,* and *M. smegmatis)* are considered unique to the cat.
- Dogs, especially basset hounds, are susceptible to systemic disease caused by *M. avium.*
- Humans can transmit *M. bovis* to dogs.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Concurrent or recent antibiotic therapy may inhibit growth.

LAB ARTIFACTS THAT MAY INTERFERE: Contamination or overgrowth by commensal organisms may mask growth.

SPECIMEN: Tissue or exudate from lesion in a sterile container. If zoonotic *Mycobacterium* spp. are suspected, the container should have a screw top and a double outer container should be used; label as biohazard. Submit to laboratory as soon as possible.

RELATIVE COST: $$

PEARLS

- Cutaneous or localized infections are more likely to become systemic in immunocompromised hosts. Immunocompromised owners may be more susceptible to zoonotic infection.
- Fine-needle aspirates of solid tissue lesions are characterized by macrophages containing rod-shaped organisms that appear as negative images with Wright-Giemsa or Diff-Quik stains.
- Organisms will stain with acid-fast stains.
- PCR testing for detection of DNA is available for some of the zoonotic strains of *Mycobacterium* spp.

AUTHOR: LOIS ROTH-JOHNSON

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150

$$$$: >$150

Monocytes (Monocytosis, Monocytopenia)

DEFINITION

Largest leukocyte on blood smear. It has an oval to lobulated nucleus and gray basophilic cytoplasm with fine azurophilic granules and occasionally clear vacuoles. Monocytes become macrophages upon entering tissues and fluids.

TYPICAL NORMAL RANGE

Dogs: 0.1-1.5 × 10^3 monocytes/µL. Cats: 0-1 × 10^3 monocytes/µL.

PHYSIOLOGY

Monocytes are produced in the marrow, with a short transit time from monoblast to monocyte, which quickly enters blood. Monocytes and macrophages are involved in several different functions that include killing bacteria and fungi, presenting antigens to lymphocytes, removal of necrotic and apoptotic cell debris, and destruction of senescent or abnormal erythrocytes.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS

- Inflammation, acute or chronic
- Stress leukogram, from endogenous or exogenous glucocorticoids
- Monocytic leukemia, myelomonocytic leukemia

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Evaluate for given causes, depending on history and physical exam.

CAUSES OF ABNORMALLY LOW LEVELS: Monocytopenia is not considered a clinically significant abnormality, because monocytes often occur in very low numbers naturally.

SPECIMEN AND PROCESSING CONSIDERATIONS

SPECIMEN: EDTA whole blood (lavender-top tube) and freshly prepared blood smear for laboratory to stain

RELATIVE COST: $$ (reported as part of CBC)

PEARLS

After acute onset of neutropenia caused by transient suppression of hematopoiesis (e.g., chemotherapy), monocytes return to high levels in blood sooner than neutrophils. Therefore, in neutropenic patients, monocytosis can signal hematopoietic recovery and impending resolution of neutropenia.

AUTHOR: STEPHEN D. GAUNT

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Methemoglobinemia, Methemoglobinuria

DEFINITION

Methemoglobinemia: accumulation of methemoglobin in blood. Methemoglobinuria: presence of methemoglobin in urine. Methemoglobin has an iron moiety that has been oxidized to the ferric (Fe^{3+}) state from the normal ferrous (Fe^{2+}) state in hemoglobin.

SYNONYM

MetHb

TYPICAL NORMAL RANGE

- Methemoglobin spot test: drop of venous blood on a white paper towel normally is bright red; if methemoglobin concentration is >10%, spot remains dark with a brown tinge.
- Blood/urine levels: methemoglobin normally represents <1% of total hemoglobin.

PHYSIOLOGY

Increased production of methemoglobin results from exposure to oxidant chemicals, drugs, plants, or decreased reduction of methemoglobin due to a hereditary deficiency of erythrocyte methemoglobin reductase. Methemoglobin cannot bind and carry oxygen to tissue. If sufficient amounts of methemoglobin are present, low blood oxygen tension (hypoxemia) results.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Hereditary deficiency of methemoglobin reductase or exposure to oxidant chemicals (nitrite, copper), drugs (e.g., acetaminophen, benzocaine, phenazopyridine, zinc), or plants

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH

- If spot test is positive, consider arterial blood gas, pulse oximetry, and if available, cooximetry analysis. Cooximetry measures concentrations of methemoglobin as a percentage of the total hemoglobin concentration in the blood sample.
- CBC to determine if hemolytic anemia is present, because it is a common sequela to oxidant injury of erythrocytes
- Evaluation of red blood cell morphology for Heinz bodies and eccentrocytes (hallmarks of oxidant injury)
- Methemoglobin reductase level determination if hereditary deficiency is suspected

SPECIMEN AND PROCESSING CONSIDERATIONS

SPECIMEN

- Anticoagulated whole blood collected in EDTA (lavender-top tube) for spot test; 0.5 mL minimum
- Methemoglobin reductase level determination: prior arrangements must be made with a laboratory before submitting samples. Whole blood (1 mL in EDTA [lavender-top tube]) should be refrigerated and sent chilled (not frozen) to a laboratory allowing assay to be done the same day the specimen is collected. One or more samples collected from normal animals should be submitted with the patient samples for use as controls. Not offered by most veterinary reference labs; may be run in human lab if erythrocyte lysing agent does not cause methemoglobin formation.

PEARLS

- Severe methemoglobinemia produces chocolate brown discoloration of the blood.
- Most chemicals producing methemoglobinemia also produce Heinz body hemolytic anemia.
- Spot testing (see above) is rapid, inexpensive, and may be done in-house.

AUTHOR: SHERRY J. MORGAN

Magnesium

DEFINITION

Essential nutrient and major divalent cation. Serum total magnesium includes protein-bound (30%), anioncomplexed (15%), and ionized (55%) fractions.

SYNONYMS

Mg, Mg^{2+}

TYPICAL NORMAL RANGE

Range: 1.5-2.7 mg/dL. Unit conversion: mg/dL × 0.4114 = mmol/L; mEq/L × 0.5 = mmol/L.

PHYSIOLOGY

Sources: dietary; commercial foods are fortified. Absorbed in small intestine; vitamin D may enhance absorption. Excreted in urine, feces, milk. Extracellular fluids contain <2% of total, bone contains 50%-60%, remainder is intracellular. Shifts from extracellular to intracellular compartments. Ionized Mg^{2+} is the biologically active form.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Decreased urinary excretion (decreased glomerular filtration rate, renal failure). Uncommon: excess oral administration (antacids, laxatives), intravenous Mg.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Evaluate renal function, review oral and parenteral supplements.

CAUSES OF ABNORMALLY LOW LEVELS

- Hypoproteinemia: decreases protein-bound Mg; no effect on ionized Mg
- Excess urinary excretion: fluid diuresis; diuretic drugs; renal tubular disease
- Inadequate gastrointestinal absorption: chronic diarrhea, malabsorption syndromes, binding to other nutrients (excess fatty acids, oxalate, phosphate, fiber)
- Shifts from extracellular to intracellular compartments: treatment for diabetic ketoacidosis (insulin, bicarbonate infusions)
- Diabetes mellitus, hyperparathyroidism, hyperthyroidism, pancreatitis, trauma, sepsis may predispose

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW

- Measure serum albumin; measure serum ionized magnesium.
- Evaluate for renal, gastrointestinal disease as a primary or contributing cause.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS

- Renal excretion increased by loop and osmotic diuretics, and drug-induced renal tubular injury (e.g., aminoglycosides, cisplatin, amphotericin B)
- Insulin, glucose, or bicarbonate infusions promote intracellular shifting, decreasing serum Mg.
- Administration of Mg-containing laxatives, antacids causes increases.

LAB ARTIFACTS THAT MAY INTERFERE

- Falsely increased by hemolysis or delayed removal of serum from clot
- Falsely decreased if anticoagulants that bind Mg are used (EDTA [lavender-top tube], citrate [blue-top tube], oxalate)

SPECIMEN: Serum preferred (red-top tube); heparinized plasma (green-top tube) may be used. Remove serum from erythrocytes

promptly after centrifugation.

RELATIVE COST: $

PEARLS

Concurrent hypocalcemia, hypokalemia may be refractory to therapy until hypo-magnesemia is corrected.

AUTHOR: ROBIN W. ALLISON

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

N-Terminal Pro-B-Type Natriuretic Peptide (NT-proBNP)

DEFINITION

Circulating biomarker for cardiac disease in dogs and cats

TYPICAL NORMAL RANGE

Dog:

- <900 pmol/L within reference interval
- 900-1800 pmol/L slight increase; cardiac workup suggested if clinical signs present
- >1800 pmol/L consistent with heart disease

Cat:

- <100 pmol/L within reference interval
- 100-270 pmol/L slight increase; cardiac workup suggested if clinical signs present
- >270 pmol/L consistent with heart disease

PHYSIOLOGY

When intracardiac hydrostatic pressure is increased, BNP is released from cardio-myocytes. In circulation it is enzymatically separated into two products. Serum increases of the biologically active moiety, C-terminal BNP, reflect acute changes in cardiac volume but are diagnostically limited because of its short half-life (minutes). NT-proBNP has a longer half-life, and elevations in serum levels can be interpreted as indicative of cardiac lesions of longer duration. Daily variations in concentrations are reported.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Increased intracardiac hydrostatic pressure. Azotemia (renal, prerenal) and dehydration may cause mild elevations. Lung disease has been reported to cause elevations, presumably by causing cor pulmonale and not from the lungs directly. Serum NT-proBNP levels accurately differentiate between dyspneic patients with cardiogenic pulmonary edema (high NT-proBNP) and dyspneic patients with noncardiac disease (normal NT-proBNP) in both dogs and cats.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Cardiac workup including ultrasound

IMPORTANT INTERSPECIES DIFFERENCES: The test is a species-specific ELISA test, because the NT-proBNP molecule is different between species.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Drugs used for treating cardiac disease (diuretics, angiotensin-converting enzyme inhibitors, β-adrenergic receptor Mockers, vasodilators, antiarrhythmics) may decrease values.

LAB ARTIFACTS THAT MAY INTERFERE: Prolonged contact with glass, delayed separation of cells from plasma, and improper or prolonged storage will decrease values.

SPECIMEN

- Collect blood in EDTA (lavender-top) tube, spin, and separate immediately, transferring to special transport tube. 1 mL plasma minimum. May be stored 2°C-8°C in transport tube for up to 48 hours. Freeze at 0°C if there will be a longer testing interval.
- Call testing laboratory to obtain transport tubes prior to obtaining specimen.

RELATIVE COST: $$

PEARLS

- Patients with pulmonary hypertension or renal disease may have elevated NT-proBNP values.
- Daily variation may occur secondary to physical exertion, fluid intake, and suspected circadian rhythm.

- NT-proBNP does not consistently distinguish between normal patients and patients with compensated (“asymptomatic”) heart disease, so this test cannot be used as a screening test for heart disease in patients with no clinical signs.

AUTHOR: LOIS ROTH-JOHNSON

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Neutrophils (Neutrophilia, Neutropenia)

DEFINITION

Blood leukocyte with segmented nucleus and inconspicuous cytoplasmic granules. Its primary functions during inflammation are phagocytosis and killing bacteria.

SYNONYMS

Polymorphonuclear neutrophil (PMN), segmented neutrophil

TYPICAL NORMAL RANGE

Dogs: 3-11.5 × 10^3 neutrophils/µL. Cats: 2.5-12.5 × 10^3 neutrophils/µL.

PHYSIOLOGY

Precursors in bone marrow respond to colony-stimulating factors produced during inflammatory and immune responses. Mature neutrophils are initially retained in marrow as part of storage pool. In blood, neutrophils occur either in the circulating pool or are associated with endothelial cells as marginal pool and then migrate into tissue. Neutrophils circulate for only a few hours. In blood samples collected for CBC, only neutrophils in the circulating pool are counted.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS (NEUTROPHILIA)

- Inflammation, whether acute or chronic, infectious or noninfectious. If acute inflammation, left shift and/or toxic changes may be present.
- Stress leukogram (glucocorticoids shift neutrophils from marrow storage pool and from marginal pool into circulating pool).
- Excitement leukocytosis (increased blood flow shifts neutrophils from marginal to circulating pool).
- Paraneoplastic production of colony-stimulating factor
- Granulocytic leukemia
- Canine leukocyte adhesion deficiency

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Assess for cause depending on clinical signs.

CAUSES OF ABNORMALLY LOW LEVELS (NEUTROPENIA)

- Intense inflammation, especially if bacterial cause (increased tissue demand)
- Endotoxemia (shift from circulating to marginal pool)
- Acute parvoviral infection (decreased marrow production and endotoxemia)
- Decreased granulopoiesis (e.g., feline leukemia virus [FeLV] infection, feline immunodeficiency virus [FIV] infection, drugs [see below], myelophthisis)
- Destruction of mature neutrophils (e.g., immune-mediated neutropenia)
- Previous use of recombinant human colony-stimulating factor

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Bone marrow aspirate or core biopsy

IMPORTANT INTERSPECIES DIFFERENCES

- Neutrophilia from excitement is more likely in young cats, whereas neutrophilia from glucocorticoids (stress leukogram) is more likely in dogs.
- Dogs typically have higher degrees of neutrophilia than cats.
- Cats may have benign idiopathic neutropenia (diagnosis of exclusion).

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS

- Increase: glucocorticoids
- Decrease: albendazole, methimazole, trimethoprim-sulfa, many chemotherapeutic anticancer agents, many others

SPECIMEN: EDTA whole blood (lavender-top tube) and freshly prepared blood smear for laboratory to stain

RELATIVE COST: $$ (reported as part of CBC)

PEARLS

Inflammation is not the only cause of neutrophilia; other causes are stress leukogram and excitement leukocytosis. Extreme neutrophilia (>50,000 neutrophils/µL) is more often reported in dogs with pyometra, hepatozoonosis, immunemediated hemolytic anemias, paraneoplastic production of colony-stimulating factor, or chronic granulocytic leukemia.

AUTHOR: STEPHEN D. GAUNT

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Neospora caninum Serology

DEFINITION

Detection of serum antibody to *Neospora caninum* by IFA or ELISA

PHYSIOLOGY

N. caninum is a coccidian parasite whose morphology is identical to *Toxoplasma gondii* under light microscopy. Clinical manifestations of *N. caninum* in dogs are primarily neurologic and musculoskeletal. Transplacental transmission occurs.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS

- Infection with or prior exposure to *N. caninum.* Rising titer (>fourfold) confirms active infection. Positive cerebrospinal fluid titers are considered suggestive of disease.
- IFA tests have little cross-reactivity with other parasites, including *T. gondii*. However, cross-reactivity depends on the antigen source used for the assay (among other laboratory-based factors) and may vary.
- Most dogs with confirmed neosporosis have titers =1:200. High titers have been found in clinically normal dogs, suggesting subclinical disease.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Treatment for neosporosis if clinical signs are compatible with this disease.

IMPORTANT INTERSPECIES DIFFERENCES: Serologic tests use species-specific reagents and must be adapted for the species of interest. Cats have been experimentally infected, but clinically, neosporosis in cats is unknown; natural disease in small animals is mainly seen in dogs. *N. caninum* is an important cause of abortion in ruminants.

SPECIMEN AND PROCESSING CONSIDERATIONS

SPECIMEN: Serum (red-top tube), refrigerated

RELATIVE COST: $$$

PEARLS

- Diagnosis is sometimes made via observation of tachyzoites of *N. caninum* in biopsy/necropsy tissue or in Cytologic preparations. The morphology of the tachyzoites of *N. caninum* and *T. gondii* is identical, but differentiation can be made via direct fluorescent antibody or immunohistochemistry of tissue samples using species specific antibodies. Alternatively, molecular techniques (PCR) have been used for differentiating the two organisms.
- Almost all commercially available laboratory tests for antibody are for immunoglobulin G.
- Transplacental transmission may occur in dogs.

AUTHOR: LOIS ROTH-JOHNSON

1ST EDITION AUTHOR: JAMES H. MEINKOTH

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Pyuria

DEFINITION

The presence of increased numbers of leukocytes in urine sediment

TYPICAL NORMAL RANGE

Fewer than 5 leukocytes/high power field (HPF = 40x objective)

PHYSIOLOGY

In health, a few leukocytes from the kidneys, urinary bladder, reproductive tract, or urethra enter the urine (free catch or catheterization).

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Inflammation of genital or urinary tract

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH

- Assess method of urine collection: free catch, catheterization, cystocentesis.
- If free catch, obtain fresh sample (for further evaluation) via cystocentesis if possible or via urethral catheter or midstream catch if not possible.
- Similarly, if catheter sample, obtain fresh sample by cystocentesis if possible.
- Assess other findings in urinalysis, such as pH, numbers of red cells, and presence of bacteria.
- Bacterial culture and antibiotic susceptibility testing of urine.

CAUSES OF ABNORMALLY LOW LEVELS

- Diseases that hamper neutrophil function (e.g., diabetes mellitus, hyperadrenocorticism) may falsely reduce the number of leukocytes observed in a patient with urinary tract infection.
- Diseases that cause urine to be dilute (endocrinopathies, liver disease, renal failure, others) may give the misleading appearance of a low concentration of leukocytes (or their absence) in the urine of patients with urinary tract infections.
- Samples that are not analyzed in a timely fashion, dilute urine, or alkaline urine may have decreased numbers of leukocytes due to lysis of cells.

SPECIMEN AND PROCESSING CONSIDERATIONS

SPECIMEN: Urine in clean/sterile container. Sediment examination of urine should be done within a few of hours of collection, because leukocytes deteriorate, falsely decreasing their numbers.

RELATIVE COST: $ (reported as part of urinalysis)

PEARLS

- Should be detected during sediment examination, a part of urinalysis
- For negative bacterial urine culture with concurrent pyuria, consider antibiotic effect, fungal or algal urinary tract infection.
- A urine culture with antibiotic susceptibility testing is indicated even when pyuria is absent if the differential diagnosis includes diseases that reduce neutrophil function and/or cause dilute urine.
- Patients with chronic kidney disease, in particular, may not show pyuria despite having low-grade pyelonephritis. Identifying such an infection through culture and susceptibility is important because it offers the possibility of reversing renal tubular damage with appropriate antibiotic treatment.

AUTHOR: ELIZABETH G. WELLES

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Prothrombin Time

DEFINITION

Screening coagulation test of the extrinsic and common coagulation pathways

SYNONYMS

One-stage prothrombin time (OSPT); PT

TYPICAL NORMAL RANGE

Values are approximate (normals are laboratory and instrument specific). Dogs: 7-11 seconds. Cats: 5-8 seconds.

PHYSIOLOGY

Plasma to be tested and the reagent (Ca^{2+}-thromboplastin reagent) are warmed and mixed together to allow tissue factor in the reagent to activate factor VII in the plasma, initiating the extrinsic pathway and then the common pathway. A fibrin clot is formed that is detected by the instrument. The prothrombin time (PT) is the time from the plasma and reagent mixing to the formation of the clot.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Prolonged PT: hepatic disease, vitamin K deficiency, disseminated intravascular coagulation (DIC), anticoagulant intoxication, hereditary defects in extrinsic or common pathway (factors VII, X, V, II, and I), heparin, presence of fibrin degradation products (FDPs), antibodies to phospholipids or coagulation factors.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Rule out acquired causes and DIC; specific coagulation factor assays (rare).

CAUSES OF ABNORMALLY LOW LEVELS: Shortened PT is not a reliable measure of hypercoagulability.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG **EFFECTS ON** LEVELS: Warfarin can cause a prolonged PT. PT is often the first coagulation test affected by warfarin administration.

LAB ARTIFACTS THAT MAY INTERFERE: Different thromboplastin reagents can produce different results; improper blood/citrate ratios falsify results (too little blood can prolong results, and too much blood can shorten coagulation times).

SPECIMEN: Citrated plasma (blue-top tube). Care should be taken to avoid traumatic venipuncture, which can cause in vitro activation of tissue factor, artifactually shortening the PT. Immediately mix the blood and anticoagulant.

RELATIVE COST: $

PEARLS:

- Antagonism or absence of vitamin K-dependent coagulation factors, as occurs in anticoagulant rodenticide intoxication or liver disease, tends to increase PT before activated partial thromboplastin time (APTT). This is due to the short half-life of factor VII.
- Citrate (blue-top) tube must be filled to capacity generated by its vacuum to avoid artifactual alteration of result.
- A patient with overt clinical signs of hemorrhage due to anticoagulant rodenticide intoxication will invariably have an elevated PT (usually markedly elevated).
- Decreased PT does not indicate hypercoagulability; rather, it is usually a result of suboptimal phlebotomy (sample collection artifact).

AUTHOR: DEBORAH G. DAVIS

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Proteins Induced by Vitamin K Absence or Antagonism (PIVKA)

DEFINITION

Proteins induced by vitamin K absence or antagonism (PIVKA) are inactive precursor coagulation proteins that accumulate in the peripheral blood when vitamin K is absent or inhibited.

SYNONYMS

PIVKA, Thrombotest

TYPICAL NORMAL RANGE

Dogs: 12-20 seconds. Cats: 20-30 seconds.

PHYSIOLOGY

Factors II, VII, IX, and X, factor C, and factor S are all vitamin K-dependent proteins involved in coagulation homeostasis. They are synthesized in inactive precursor form in the liver and require carboxylation of their glutamyl residues by vitamin K for activation. The enzyme, vitamin K epoxide reductase, is critical for this carboxylation. In the absence of vitamin K or if vitamin K epoxide reductase is inhibited (e.g., by anticoagulant rodenticides), a bottleneck phenomenon occurs whereby the inactive coagulation precursors (PIVKAs) and vitamin K epoxide accumulate in the blood, where they can be measured. Thus, the PIVKA test is a sensitive indicator of anticoagulant intoxication.

CLINCIAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Decreased vitamin K: neonate born to malnourished mother, sterilization of gastrointestinal tract (due to antibiotic therapy), prolonged anorexia/abnormal diet, malabsorption of vitamin K (cholestasis, exocrine pancreatic in-sufficiency, infiltrative bowel disease). Vitamin K antagonism: anticoagulant rodenticides, cephalosporins, and sulfonamides.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: CBC/profile, urinalysis, coagulation profile, determine if recent exposure to drugs or anticoagulant rodenticides. Urinalysis should not be obtained by cystocentesis, and blood sampling should be drawn from a compressible vein (e.g., limb, not jugular) in patients with elevated PIVKA concentrations and therefore with a bleeding tendency.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Numerous drugs can worsen the effects of anticoagulant rodenticide toxicity through platelet inhibition (nonsteroidal antiinflammatory drugs, corticosteroids), decreased protein binding (phenylbutazone, corticosteroids, sulfonamides), and increased hepatic metabolism (antibiotics including rifampin, chloramphenicol; barbiturates).

SPECIMEN: Plasma collected in citrate (blue-top tube). Tube must be filled to capacity generated by its vacuum to avoid artifactual alteration of result. Spin and separate plasma. Refrigerate specimens that will be analyzed within 3 hours; freeze >3 hours.

RELATIVE COST: $$

PEARLS

Although helpful in confirming a diagnosis of rodenticide toxicity, in most cases treatment decisions must be made before test results are available.

AUTHOR: DEBORAH G. DAVIS

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150

$$$$: >$150

Protein Electrophoresis

DEFINITION

Qualitative and quantitative determination of proteins, typically measured in serum but may also be performed on cerebrospinal fluid and urine. Proteins separate into groups (fractions) based on their rate of migration in an electric field. Protein charge and size determine migration rate.

TYPICAL NORMAL RANGE

Conversion: for mg/mL: multiply g/dL by 10.

	Dogs	Cats
α1	0.2-0.5 g/dL	0.2-1.1 g/dL
α2	0.3-1.1 g/dL	0.4-0.9 g/dL
β1	0.6-1.2 g/dL	0.3-0.9 g/dL
β2	0.6-1.4 g/dL	0.6-1.0 g/dL
γ1	0.5-1.3 g/dL	0.6-1.0 g/dL
γ2	0.4-0.9 g/dL	1.4-1.9 g/dL

PHYSIOLOGY

The five major fractions of soluble body proteins are albumin and the four globulin fractions: a1, a2, β, and γ; β and γ globulins each has two fractions. Albumin is the largest fraction in healthy animals. The a1 globulin fraction primarily contains acute-phase proteins. The a2 globulin and β globulin fractions contain acute phase proteins, lipoproteins, and some immunoglobulins. The γ globulin fraction contains immunoglobulin (Ig) A, IgG, and IgM. Elevation of γ globulins may be seen on the electrophoresis tracing as a broad-based peak (polyclonal) or a single narrow peak (monoclonal).

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS

- Increased a globulin: acute inflammation, nephrotic syndrome, corticosteroid administration
- Increased β globulin: acute inflammation, nephrotic syndrome, liver disease, immune responses, neoplasia
- Increased γ globulins: immune stimulation, neoplasia

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH

- Polyclonal gammopathy: assess for inflammation, infection, immune-mediated disease, liver disease, neoplasia (neoplasia less commonly polyclonal).
- Monoclonal gammopathy: assess for plasma cell myeloma, B-cell lymphoma, lymphocytic leukemia; inflammatory or infectious disease (ehrlichiosis, feline infectious peritonitis, leishmaniasis, plasmacytic stomatitis, lymphoplasmacytic enterocolitis [infection less commonly monoclonal]).

CAUSES OF ABNORMALLY LOW LEVELS

- Albumin: acute phase response, glomerular disease, liver disease, starvation, cachexia
- Albumin and globulins: gastrointestinal disease (protein losing enteropathy), blood loss, sequestration in body cavity effusion, severe exudative skin disease, excess fluid therapy or water intake
- Globulins: failure of passive transfer (FPT), inherited or acquired immunodeficiency

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Based on which fraction(s) is/are low, investigate for albumin loss or decreased albumin synthesis, globulin loss, FPT, acquired or inherited immunodeficiency

SPECIMEN AND PROCESSING CONSIDERATIONS

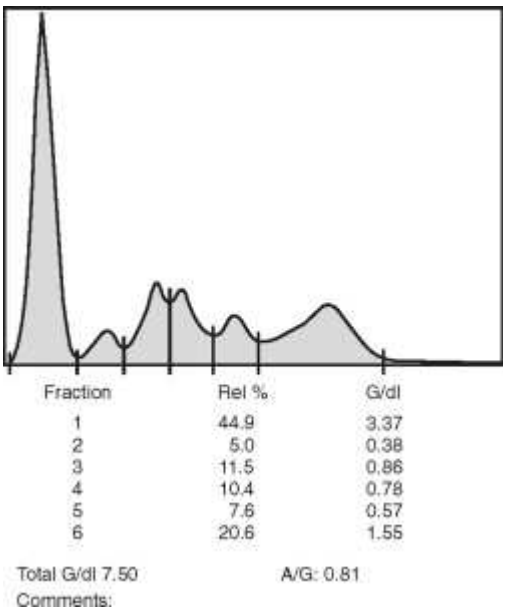
LAB ARTIFACTS THAT MAY INTERFERE: Hemolysis artificially elevates β globulins, because hemoglobin migrates in this region on electrophoresis; lipemia promotes hemolysis.

SPECIMEN: Serum (red-top tube), refrigerate. Heparinized plasma (green-top tube) is acceptable.

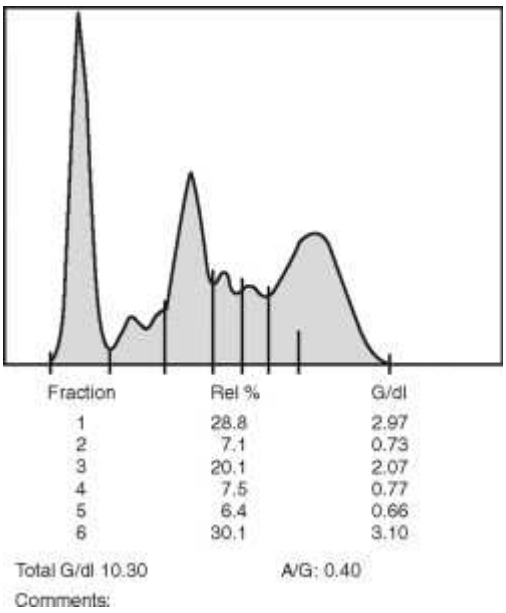
RELATIVE COST: $$

PEARLS

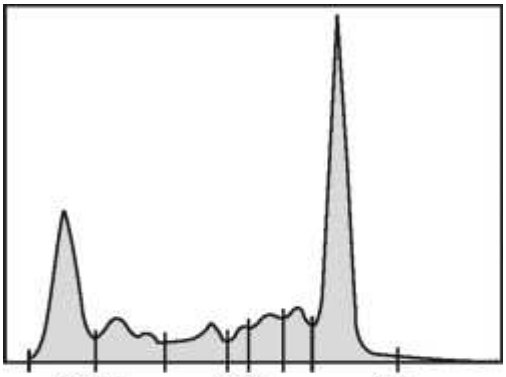
The numerical values obtained from protein electrophoresis must be assessed in conjunction with the tracing. The values alone do not differentiate between monoclonal and polyclonal gammopathies.



PROTEIN ELECTROPHORESIS, NORMAL Serum protein electrophoresis tracing demonstrating a normal distribution of serum proteins.



PROTEIN ELECTROPHORESIS, POLYCLONAL Serum protein electrophoresis tracing demonstrating hyperglobulinemia that is polyclonal in distribution, as is typical of inflammation.



Fraction	Rel %	G/dl
1	23.4	2.41
2	10.4	1.07
3	7.7	0.79
4	3.2	0.33
5	7.0	0.72
6	6.7	0.69
7	41.7	4.30

Total G/dl 10.30 A/G: 0.31
Comments:

PROTEIN ELECTROPHORESIS, MONOCLONAL Serum protein electrophoresis tracing demonstrating hyperglobulinemia that is monoclonal in distribution (single peak). This patient had multiple myeloma.

AUTHOR: RUANNA GOSSETT

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Progesterone

DEFINITION

Steroid hormone secreted by corpora lutea of the ovaries and by the placenta

TYPICAL NORMAL RANGE

Depends on stage of estrous cycle; concentrations exceeding 2 ng/mL indicate luteal function.

PHYSIOLOGY

Progesterone is secreted by the cells of developing corpus luteum, the presence of which indicates pregnancy, diestrus, or an ovarian lesion (e.g., cyst or neoplasm). Concentrations greater than those of anestrus (i.e., >2 ng/mL) are used for predicting time of ovulation in bitches. Proestrus is characterized by increased estrogen concentration, vulvar swelling, and vaginal discharge. Decreasing estrogen concentration and increasing progesterone concentration, resulting from increased luteinizing hormone (LH), indicates estrus. Behavioral changes (receptivity to breeding) are also important features to be observed. Ovulation occurs approximately 48 hours after the LH surge. Progesterone is needed to maintain pregnancy and is secreted by the placenta. Decreasing progesterone concentrations (<2 ng/mL) indicate the onset of parturition within 24 hours in most bitches.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Developing corpora lutea followed by pregnancy; residual ovarian tissue in a patient thought to have been spayed; luteal cysts; granulosa cell tumor

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Confirm the presence of ovarian abnormalities (e.g., with abdominal ultrasound) if not evaluating a breeding bitch.

CAUSES OF ABNORMALLY LOW LEVELS: Depends on stage of cycle; may indicate normal anestrus or failure to ovulate, become pregnant, or maintain pregnancy; parturition

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Evaluate for infertility if repeated failure to maintain pregnancy.

IMPORTANT INTERSPECIES DIFFERENCES: Test used primarily in dogs; not used in cats because they are induced ovulators.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Minimal interference by deoxycortisol, deoxycortisone, and dihydroprogesterone

LAB ARTIFACTS THAT MAY INTERFERE: Falsely decreased with storage at room temperature or delay in separation of serum or plasma from red blood cells (separation should be performed immediately); lipemia interference if measured by chemiluminescence; use of serum separator tubes falsely decreases values.

SPECIMEN: Depends on the laboratory; serum (red-top tube) or heparinized (green-top tube) or EDTA plasma (lavender-top tube) may be used. Do not use serum separator tubes. Separate serum or plasma from red blood cells as soon as possible. Store at 2°C-8°C.

RELATIVE COST: $$

AUTHOR: LOIS ROTH-JOHNSON

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Potassium

DEFINITION

Major intracellular cation continually pumped into cell by energy-dependent sodium/potassium-ATPase pump at cell membrane; important in cardiac and neuromuscular membrane potentials/excitability

SYNONYM

K^+

TYPICAL NORMAL RANGE

Typically 3.5-5.5 mEq/L (= mmol/L)

PHYSIOLOGY

Influenced by acid-base status. Metabolic acidosis (e.g., with renal failure) causes extracellular shift and hyperkalemia. Under normal conditions, excess plasma K^+ is excreted in the urine. Hyperkalemia is uncommon if renal function is normal (exceptions: postrenal lesions, hypoadrenocorticism, iatrogenic). Potassium is released during normal platelet coagulation, potentially causing artifactual hyperkalemia.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Decreased renal excretion (oliguric/anuric renal failure, urinary tract obstruction or rupture), hypoadrenocorticism, artifact (due to normal platelet clumping or in Asian dog breeds [e.g., Akita]), gastrointestinal disease (salmonellosis, trichuriasis), chylothorax with repeated drainage, diabetic ketoacidosis, metabolic acidosis (due to inorganic acids), rhabdomyolysis (see p. 556)

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Repeat measurement using green-top tube (heparin) to collect blood sample if sample was collected in a red-top tube; CBC, serum biochemistry profile, and urinalysis; evaluate for drugs that can cause hyperkalemia; abdominal ultrasound/radiographs (check integrity of urinary tract), ACTH stimulation test to rule out hypoadrenocorticism if clinically compatible; blood gas determination to assess acid-base status.

CAUSES OF ABNORMALLY LOW LEVELS: Increased loss (vomiting, diarrhea), chronic kidney disease (cats), postobstructive diuresis, inappropriate fluid therapy (dilutional hypokalemia), diuresis associated with diabetes mellitus, ketoacidosis, hyperaldosteronism, alkalemia, and hypokalemic periodic paralysis of Burmese cats (see p. 556)

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: CBC/serum biochemistry profile/urinalysis/blood gas

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS

- Hyperkalemia: angiotensin-converting enzyme inhibitors, potassium-sparing diuretics (e.g., spironolactone), K^+ penicillin G, oversupplementation of fluids with K^+, o,p'-DDD (iatrogenic hypoadrenocorticism)
- Hypokalemia: loop diuretics (furosemide), thiazide diuretics, amphotericin B, penicillin, administration of K^+-free fluids

LAB ARTIFACTS THAT MAY INTERFERE: Serum K^+ is higher than plasma K^+, especially if thrombocytosis is present; marked hemolysis in dogs (Akitas, English springer spaniels) with high K^+ red blood cell concentration, marked leukocytosis. Avoid by prompt separation of plasma from cells. Drawing blood through an intravenous catheter may dilute sample, resulting in false decrease.

SPECIMEN: Serum (red-top tube); K^+ will remain stable for extended periods of time, but platelet activation-induced K^+ release makes sampling into heparin (green-top) tubes and separation of plasma from red cells preferable. K^+ EDTA (lavender-top tube) should not be used as an anticoagulant.

RELATIVE COST: $

PEARLS

- It is important to measure the acid-base status of hypokalemic/hyperkalemic animals.
- Normal K^+ levels in the presence of metabolic acidemia suggest low K^+ stores. Normal K^+ in an alkalotic animal suggests the total body K^+ is high.
- Hemolysis alone rarely causes artifactual hyperkalemia, and when it does, the patient is generally of a breed that has unusually high intra-RBC K^+ stores [e.g., Asian dog breeds].

AUTHOR: DEBORAH G. DAVIS

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Polycythemia

DEFINITION

Increased circulating erythrocyte mass, with increased hematocrit (or packed cell volume [PCV]), hemoglobin concentration, and/or erythrocyte count of blood. Occurs from increase in the circulating erythrocytes only (relative polycythemia) or an increase in both circulating erythrocytes and erythropoietic cells (absolute polycythemia).

SYNONYM

Erythrocytosis; some consider this to be the accurate term and reserve *polycythemia* for states in which all circulating blood cell lines are elevated.

PHYSIOLOGY

Relative polycythemia occurs most commonly, with the increase in circulating erythrocytes from decreased plasma volume (e.g., dehydration) or the release of sequestered erythrocytes following epinephrine-induced splenic contraction. Absolute polycythemia indicates an increase in circulating and erythropoietic cells, the result of increased erythropoietin concentration or heightened response to erythropoietin. Appropriate increase in erythropoietin occurs secondary to hypoxemia. Inappropriate production of erythropoietin occurs uncommonly from hypoxia restricted to kidneys (e.g., right-to-left shunting patent ductus arteriosus [PDA]) or paraneoplastic expression of erythropoietin from neoplasm (usually renal). Polycythemia vera is a myeloproliferative disease resulting from clonal proliferation of well-differentiated erythrocytes without any increase in basal levels of erythropoietin. The resultant erythrocytosis, especially in cases of absolute polycythemia, can cause increased viscosity of blood, sludging of blood flow, and resultant tissue hypoxia and thrombosis. See .

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Dehydration (relative polycythemia); splenic contraction (relative polycythemia); high altitude, most right-to-left cardiac shunts, or chronic pulmonary diseases (appropriate absolute polycythemia); renal hypoxia (due to right-to-left shunting PDA), renal carcinoma with erythropoietin secretion (inappropriate absolute polycythemia); polycythemia vera.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Verify instrument PCV with manual test (spun hematocrit). After ruling out the more common causes of relative polycythemia (e.g., physical exam and evaluation of serum albumin concentration for dehydration), urinalysis and abdominal ultrasound (evaluate kidneys), chest radiographs, echocardiography, arterial Po2 measurement, +/– erythropoietin assay should be considered.

IMPORTANT INTERSPECIES DIFFERENCES

- Polycythemia caused by epinephrine-induced splenic contraction is more likely in cats, although it may be appreciated in breeds of dogs (e.g., dachshunds, greyhounds) with normally higher hematocrits.
- Sight hounds (e.g., greyhounds, deer-hounds, wolfhounds, Afghan hounds) have a higher normal hematocrit/PCV (may exceed 65%).

SPECIMEN AND PROCESSING CONSIDERATIONS

SPECIMEN: EDTA whole blood (lavender-top tube)

PEARLS

Hypovolemia/dehydration is the most common cause of polycythemia in dogs and cats.

AUTHOR: STEPHEN D. GAUNT

Poikilocytes

DEFINITION

General term for presence of abnormally shaped mature erythrocytes in blood. This shape change can be artifactual (e.g., crenation) or pathologic (e.g., spherocytes, schistocytes).

TYPICAL NORMAL RANGE

Only low numbers of artifactually induced poikilocytes (e.g., crenation) should be observed in the blood of healthy animals.

PHYSIOLOGY

Normal shape of mature erythrocyte is discocyte (biconcave disk). With damage to cell membrane (e.g., antibodies, toxins, or lipid accumulation) or damage to hemoglobin (e.g., oxidation), the plasma membrane and/or protein cytoskeleton of the erythrocyte is/are altered and an abnormal erythrocyte shape results.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Immune-mediated hemolytic anemias (spherocytes), erythrocyte fragmentation (schistocytes, acanthocytes), oxidative damage (Heinz bodies, eccentrocytes), hepatic diseases (acanthocytes), venomous snake bite (echinocytes, spherocytes), bee sting (spherocytes), congenital defect in erythrocyte membrane proteins (elliptocytes, spherocytes).

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Repeat blood smear for definitive determination of the specific type of poikilocytes present.

IMPORTANT INTERSPECIES DIFFERENCES: Crenation (artifact) occurs more commonly in feline erythrocytes. Spherocytosis is more easily detected in the erythrocytes of dogs, because normal canine erythrocytes have a prominent central pallor which is lacking in spherocytes.

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE

- Poorly prepared blood smears will distort canine erythrocytes so that central pallor is lost and cells may resemble spherocytes.
- Erythrocytes on blood smears allowed to slowly air dry during preparation could have refractile markings and distortion; best to rapidly dry smears by waving or use heat block.
- Lipemia will cause lysis and distortion of erythrocyte morphology.
- Crenation often occurs from effects of smear preparation on erythrocytes.

SPECIMEN: EDTA whole blood (lavender-top tube) and freshly prepared blood smear for laboratory to stain.

PEARLS

See for a differential diagnosis diagram of various poikilocytes.

AUTHOR: STEPHEN D. GAUNT

Platelets

DEFINITION

- Thrombocytopenia: decreased platelet count
- Thrombocytosis: increased platelet count
- Thrombopathia: abnormal platelet function

TYPICAL NORMAL RANGE

- Dogs: 150,000-500,000/mcL
- Cats: 150,000-400,000/mcL
- 7-15 platelets per 100× field (blood film) associated with adequate platelet numbers

PHYSIOLOGY

Platelets form from megakaryocytes in bone marrow, spleen, and lung. Platelets are discoid, anucleate, 5- to 7-mcm cytoplasmic fragments important in primary hemostasis. They adhere to subendothelium by the binding of von Willebrand factor (vWF) to platelet glycoprotein Ib (GPIb). Aggregation occurs through binding of platelet membrane $a^{IIb}\beta^{3}$ with fibrinogen or vWF. Activated platelets release granule contents (fibrinogen, factor V, ADP, ATP, plasminogen), thromboxane A2, and arachidonic acid. Mediator release and reactions with leukocytes are important in inflammation and wound healing.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Redistribution (exercise, epinephrine release), neoplasia (essential thrombocythemia, acute megakaryocytic leukemia), increased production (inflammation, iron deficiency, rebound from thrombocytopenia). Associated with hyperadrenocorticism and administration of glucocorticoid, although the mechanism is not known.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Examine blood film to confirm increase; serum iron profile, CBC/serum biochemistry profile for evidence of inflammation (neutrophilia with left shift, elevated globulins); bone marrow aspirate.

CAUSES OF ABNORMALLY LOW LEVELS: Thrombocytopenia: acute, severe blood loss; drugs (myelotoxic); immune-mediated destruction; bone marrow replacement (myelofibrosis, neoplasia); megakaryocytic neoplasia; localized or disseminated intravascular coagulation (DIC); infectious diseases (canine distemper, canine parvovirus, cytauxzoonosis, endotoxemia, feline leukemia virus [FeLV], feline infectious peritonitis [FIP], ehrlichiosis, babesiosis, histoplasmosis, leptospirosis, Rocky Mountain spotted fever, leishmaniasis).

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Review history and physical exam for signs of underlying disorder/trigger; evaluation of blood film for hemotropic infectious agents, clumping; coagulation profile to rule out bleeding, DIC; bone marrow aspirate; serologic titers for infectious diseases.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS

- Thrombocytosis: vincristine, vinblastine, exogenous corticosteroids
- Thrombocytopenia: chemotherapeutic agents, estrogens, phenylbutazone, certain diuretics, certain antibiotics/antimicrobials

LAB ARTIFACTS THAT MAY INTERFERE: Clumping, large platelets (macroplatelets) falsely decrease analyzer count. Heparinized samples often have excessive platelet clumping; macroplatelets (and resultant undercounting by automated analyzers [pseudothrombocytopenia]) are an incidental finding in Cavalier King Charles spaniels.

SPECIMEN: EDTA whole blood (lavender-top tube) preferred; citrated whole blood (blue-top tube) can be used.

RELATIVE COST: $ (manual platelet count); automated platelet counts and estimates are reported with CBC ($$)

PEARLS

In a patient with a bleeding disorder, suspect thrombopathia if platelet count, hematocrit, coagulation parameters (prothrombin time,

activated partial thromboplastin time), and vWF are normal but buccal mucosal bleeding time is prolonged. Causes include hereditary, drug associated (barbiturate anesthetics, nonsteroidal antiinflammatory drugs, antihistamines, penicillin), fibrin degradation products, hepatic disease, hyperglobulinemia (with multiple myeloma, ehrlichiosis), FeLV, uremia. Document with specific platelet function tests.

AUTHOR: DEBORAH G. DAVIS

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Phosphorus

DEFINITION

Inorganic form of phosphate; the major intracellular anion; primarily located in bone (as hydroxyapatite), with the remainder in soft tissues and in circulation

SYNONYMS

Phosphate, $Po4^{2-}$

TYPICAL NORMAL RANGE

Dogs: 3.2-8.1 mg/dL (1.03-2.61 mmol/L). Cats: 3.2-6.5 mg/dL (1.03-2.09 mmol/L).

PHYSIOLOGY

Clinical assays measure only the total inorganic phosphorus, although both organic and inorganic phosphorus are present (depending on pH). Blood levels are affected by intestinal absorption, shifting between intracellular and extracellular compartments, renal clearance, and animal age. Parathyroid hormone (PTH) triggers phosphaturia.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Decreased glomerular filtration rate (decreased renal excretion due to renal failure, prerenal or postrenal azotemia), hypoparathyroidism, acromegaly, increased intestinal absorption (phosphate enema, increased vitamin D, ischemic intestinal lesions), myopathies, hyperthyroidism in cats, osteolytic bone lesions, normal bone growth.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH

- Rule out artifact (repeat test).
- Evaluate kidney function, rule out urinary obstruction or rupture; determine PTH levels, thyroid hormone level (cats), ionized calcium; survey skeletal radiographs.

CAUSES OF ABNORMALLY LOW LEVELS: Increased renal excretion (Fanconi syndrome in dogs, prolonged fluid diuresis), prolonged anorexia, intestinal malabsorption, hypovitaminosis D, humoral hypercalcemia of malignancy, primary hyperparathyroidism, hyperinsulinism (endogenous or treatment for diabetic ketoacidosis)

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: CBC/chemistry profile/urinalysis; repeat to rule out artifact, ionized calcium.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS

- Decrease: phosphate-binding antacids, anesthetics, diuretics, insulin, anticonvulsants, bicarbonate, mithramycin, salicylates
- Increase: phosphate enemas, intravenous supplementation, furosemide, vitamin D, hydrochlorothiazide, minocycline

LAB ARTIFACTS THAT MAY INTERFERE

- Increase: hemolysis (in vivo or in vitro), delayed separation of serum from clot, hyperlipidemia, hyperproteinemia, thrombocytosis
- Decrease: postprandial carbohydrates (mild), hyperbilirubinemia (with certain assays)

SPECIMEN: Serum (red-top tube) preferred; can also be measured in heparinized plasma (green-top tube) and urine.

RELATIVE COST: $

PEARLS

- Healthy animals <1 year of age may normally have elevated serum phosphorus levels.
- Acute hypophosphatemia (e.g., during initial management of diabetic ketoacidosis) carries the risk of causing severe hemolytic anemia.

AUTHOR: DEBORAH G. DAVIS

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Phenobarbital Serum Level

DEFINITION

Used for monitoring patients receiving phenobarbital for treating seizures and for determining whether therapeutic or potentially toxic levels have been reached

SYNONYMS

PB, PhB, Pheno

TYPICAL NORMAL RANGE

Therapeutic range: 15-40 mg/mL

PHYSIOLOGY

The elimination half-life of orally administered phenobarbital in dogs ranges widely, from 12-125 hours (average approximately 48 hours). Peak levels occur 4-8 hours after administration. Pharmacokinetics can be altered by chronic administration, concurrent disease (especially liver disease), age, and concurrent administration of other drugs. For this reason, monitoring of serum drug levels at steady state (14-16 days after starting treatment) is recommended. Peak and trough levels, which were previously recommended, are not considered necessary for making therapeutic decisions.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: >45 mg/mL considered toxic

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Correlate levels with clinical signs (i.e., presence or absence of seizures). Consider effect of concurrently administered drugs or concurrent disease on pharmacokinetics. Evaluate a liver profile. Whether liver disease, other disease, or drugs are present, high levels should prompt the consideration of dose reduction, with institution of a second antiseizure drug if needed.

CAUSES OF ABNORMALLY LOW LEVELS: Serum levels <10 mg/mL are subtherapeutic.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Correlate drug levels with clinical signs (seizures) to decide whether to increase dose, replace with other antiseizure drug, or discontinue.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Concurrent administration of many other drugs, such as certain antibiotics (e.g., doxycycline, chloramphenicol, metronidazole), anticoagulants (warfarin), cardiopulmonary drugs (e.g., aminophylline/theophylline, certain β-blockers, quinidine), glucocorticoids (prednisone, others) and many others, may increase or decrease levels of phenobarbital. Consult a pharmacology textbook or pharmacist for information regarding specific drug interactions.

LAB ARTIFACTS THAT MAY INTERFERE: Collection of blood in a serum separator tube can falsely decrease levels. Moderate to marked lipemia or icterus may artifactually increase reported drug levels.

SPECIMEN: 1 mL of serum (red-top tube; do not use serum separator tube)

RELATIVE COST: $$

PEARLS

Phenobarbital is involved in many drug interactions; consult a pharmacology textbook or pharmacist if multiple medications.

AUTHOR: SHERRY J. MORGAN

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Pelger Huët

DEFINITION

A congenital defect in nuclear lobulation of leukocytes that is rarely reported in dogs and cats. The characteristic appearance of a hyposegmented nucleus is most evident in neutrophils but also occurs in eosinophils, basophils, monocytes, and megakaryocytes. The nuclear shape of affected neutrophils can be bilobed ("pince nez" cell), band, round, or oval, similar to neutrophilic precursors, but the nuclear chromatin of affected neutrophils is coarsely condensed, similar to mature neutrophils.

SYNONYMS

Pelger Huët anomaly or syndrome, pseudo-Pelger Huët

PHYSIOLOGY

Segmented neutrophils in dogs and cats typically have 3-5 nuclear lobes. In the congenital form of Pelger-Huët, hetero-zygotes are most common, and they exhibit hyposegmented neutrophils, many of which resemble band neutrophils. The heterozygous condition is considered benign because affected animals have no ill effects, and neutrophil function tests are not significantly altered. The low incidence of homozygotes is attributed to embryonic death. Rarely, during the course of severe inflammatory disease in unaffected animals, hyposegmentation of neutrophils will occur as a transient reversible condition ("pseudo" Pelger Huët).

SPECIMEN AND PROCESSING CONSIDERATIONS

SPECIMEN: EDTA whole blood (lavender-top tube) and freshly prepared blood smear for laboratory to stain

PEARLS

- When an otherwise unremarkable CBC report has a substantial left shift in an apparently healthy dog or cat, consider the likelihood of Pelger Huët anomaly.
- Pelger Huët is essentially an incidental finding in dogs, with no clinical adverse effect.

AUTHOR: STEPHEN D. GAUNT

Parathyroid Hormone-Related Protein

DEFINITION

Humoral factor with a molecular structure similar to parathyroid hormone (PTH); can bind to PTH receptors. It plays an important role in humoral hypercalcemia of malignancy.

SYNONYM

PTHrP

TYPICAL NORMAL RANGE

Not normally found circulating in the blood. Dogs: <2 pmol/L.

PHYSIOLOGY

Important endocrine and paracrine hormone in the fetus. Produced in minimal amounts in tissues of normal adults and functions in a paracrine manner. In humoral hypercalcemia of malignancy, neoplastic cells secrete excess amounts of PTHrP and other cytokines. PTHrP binds to the PTH receptors in bone and kidney and mimics the effects of PTH. It results in osteoclastic bone resorption, increased renal resorption of calcium, and decreased renal resorption of phosphate. Malignancies associated with increased levels of PTHrP are T-cell lymphoma, thymoma, and apocrine gland adenocarcinoma of the anal sac. Sporadic cases of humoral hypercalcemia of malignancy have been seen with other carcinomas as well.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Humoral hypercalcemia of malignancy.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Review physical exam, including rectal palpation in all dogs (apocrine gland adenocarcinoma, sublumbar lymphadenopathy). Measure serum ionized calcium, serum phosphorus, serum PTH. Humoral hypercalcemia of malignancy usually causes elevated ionized calcium level, low-normal or low PTH level, and low phosphorus level. CBC, serum biochemistry profile, urinalysis, and diagnostic imaging to identify and define extent of neoplastic disease.

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE: Repeated thawing causes degradation of the protein and interferes with validity of results (either falsely increasing or decreasing). Proteases in serum can degrade PTHrP and cause false-negative results.

SPECIMEN: Contact laboratory for specifics. If serum is sent, immediately spin the sample after it clots, separate serum, transfer to plastic tube, and freeze. Ship frozen. If plasma is used, EDTA (lavender-top tube) with a protease inhibitor (apoprotinin or leupeptin) should be added. Plasma should be separated from the erythrocytes, transferred to a plastic tube, and shipped frozen.

RELATIVE COST: $$$

PEARLS

Three mechanisms can cause cancer-associated hypercalcemia: humoral hypercalcemia of malignancy, local bone resorption induced by hematologic neoplasms growing into the bone marrow (e.g., multiple myeloma), and local bone resorption induced by metastatic bone lesions.

AUTHOR: DEBORAH G. DAVIS

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Parathyroid Hormone

DEFINITION

Hormone produced by parathyroid glands in response to low blood calcium levels; important in the rapid and precise regulation of calcium

SYNONYMS

Parathormone, PTH

TYPICAL NORMAL RANGE

Dogs and cats: 2-13 pmol/L. Results may vary among laboratories; established reference ranges for the laboratory should be used for exact interpretation of results.

PHYSIOLOGY

Parathyroid hormone (PTH) acts directly on bone and kidney and indirectly on the gastrointestinal (GI) tract to increase serum calcium levels. PTH acts on the kidney to increase renal excretion of phosphate, increase tubular resorption of calcium, and convert vitamin D precursors to active vitamin D (which along with PTH increases calcium absorption from the GI tract). PTH acts on bone to mobilize calcium and phosphate. Ultimately, these actions result in elevation of blood calcium and hypophosphatemia.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Hyperparathyroidism: primary hyperparathyroidism (parathyroid adenoma/hyperplasia), multiple endocrine neoplasia, chronic kidney disease (renal secondary hyperparathyroidism), pseudohyperparathyroidism (decreased PTH-receptor receptiveness). Rare: nutritional secondary hyperparathyroidism.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Serum ionized calcium, CBC, serum chemistry profile, urinalysis, high-resolution cervical ultrasound (radiologist), thoracic and abdominal imaging of other endocrine organs

CAUSES OF ABNORMALLY LOW LEVELS: Parathyroid inflammation and degeneration (lymphocytic parathyroiditis), inadvertent surgical removal of parathyroid (thyroidectomy in cats), decreased PTH production due to inhibition (hypervitaminosis D, hypercalcemic disorders except primary hyperparathyroidism)

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Same as for elevated PTH

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE: Prolonged storage (>2 months) or thawing of sample may cause artificial results, either increased or decreased. Lipemia and hemolysis falsely decrease measurement. EDTA plasma samples have higher values.

SPECIMEN: Serum (red-top tube without additive; do not use serum separator tube) is used for the assay. Samples should be centrifuged immediately after clotting, frozen, and shipped frozen for analysis as soon as possible.

RELATIVE COST: $$

PEARLS:

- It is important to know both serum ionized calcium and PTH levels to correctly correlate laboratory results. Ionized hypercalcemia should cause PTH levels to be low or undetectable.
- Renal disease and secondary hyperparathyroidism will typically produce increased ionized calcium and normal to decreased PTH.
- PTH levels in the mid- or high-normal range (or higher) with concurrently elevated ionized calcium suggest primary hyperparathyroidism. With normal parathyroid gland function, ionized hypercalcemia should cause feedback inhibition and very low PTH levels.

AUTHOR: DEBORAH G. DAVIS

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Rocky Mountain Spotted Fever Serology

DEFINITION

Rocky Mountain spotted fever (RMSF) is a tickborne acute systemic disease caused by *Rickettsia rickettsii*. It is characterized by fever, anorexia, thrombocytopenia, uveitis, and necrotizing vasculitis in dogs.

TYPICAL NORMAL RANGE

Consult the laboratory conducting the test for information regarding reference ranges. General guideline: IFA-negative titer is <1:64.

PHYSIOLOGY

R. rickettsii is inoculated via a tick bite *(Dermacentor* spp.; possibly *Amblyomma* sp. or *Rhipicephalus* sp.), enters the circulatory system, and infects and replicates within endothelial cells of small blood vessels, where it induces vasculitis. Vasculitis leads to increased vascular permeability, microvascular hemorrhage, thrombocytopenia, disseminated intravascular coagulation (DIC), edema, and ultimately hypotensive shock with multiple-organ damage.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: A positive titer indicates exposure to the RMSF organism. A very high single immunoglobulin (Ig) G titer (≥1: 1024), fourfold increase in paired IgG titers (2-4 weeks apart), or a positive IgM titer with characteristic signs is consistent with active infection.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: A PCR test, direct FA staining of infected tissues, and tissue culture are available but may not be necessary if clinical signs are compatible with RMSF and the titer(s) are positive.

CAUSES OF ABNORMALLY LOW LEVELS: A negative titer indicates lack of exposure or early/acute infection.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: If clinical signs of RMSF are present and initial titer is negative, submit a convalescent titer in 2-4 weeks.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Effective antibiotic treatment may decrease serologic titers. Use of effective antibiotics prior to sample collection may result in a false-negative culture or PCR test.

SPECIMEN: Serum (red-top tube), 1 mL minimum. Can store for 4 days at 4°C or at 0°C for several weeks. Paired IgG titers should be submitted to the same laboratory for testing at the same time.

RELATIVE COST: $$

PEARLS

Because of the rapid progression of clinical RMSF, the diagnosis often is made on suggestive physical and general clinicopathologic findings in order to institute treatment rapidly. The turnaround time of RMSF serology may make the result confirmatory in retrospect (i.e., the decision to treat cannot always wait for the test result).

AUTHOR: PATTY J. EWING

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Rheumatoid Factor

DEFINITION

Autoantibodies to the Fc portion of autologous immunoglobulin (Ig) G

TYPICAL NORMAL RANGE

Reported as negative or positive; positive results will have an associated titer with interpretation specific for each reference laboratory.

PHYSIOLOGY

Predominantly IgM antibodies form immune complexes in sera, synovial fluid, and synovial membranes. Immune complexes localized within inflamed cartilage activate complement and contribute to synovial inflammation.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Rheumatoid arthritis. False-positive results are common and seen in healthy dogs or animals with other causes of polyarthritis, heartworm disease, pyometra, leishmaniasis, and systemic lupus erythematosus.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Synovial fluid analysis, synovial biopsy, serologic testing for infectious diseases (fungal, rickettsial, parasitic [heartworm] diseases; borreliosis), radiography of affected joint(s)

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE

- Decrease/false negative: freezing of specimen destroys antibodies.
- Increase/false positive: animals with antibodies to sheep red blood cells

SPECIMEN: Serum (red-top tube)

RELATIVE COST: $$

PEARLS

Not a reliable test in dogs; neither sensitive nor specific for routine diagnostic use. Rheumatoid factors are only present in about one-fourth of dogs with rheumatoid arthritis. Also can be present in animals with polyarthritis due to other etiologies (e.g., heartworm disease, pyometra, leishmaniasis, systemic lupus erythematosus).

AUTHOR: LOIS ROTH-JOHNSON

1ST EDITION AUTHOR: FONZIE QUANCE-FITCH

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Reticulocytes

DEFINITION

Erythroid precursors that have expelled their nuclei and have larger volume, more ribosomes and RNA, and less hemoglobin than mature erythrocytes. Name derived from reticulum that forms after RNA is precipitated by supravital dyes (e.g., new methylene blue).

SYNONYM

Polychromatophilic erythrocyte

TYPICAL NORMAL RANGE

Dogs: (nonanemic): <80 × 10^3 reticulocytes/µL (or × 10^9/L). Cats: (nonanemic): <60 × 10^3 reticulocytes/µL (or × 10^9/L).

PHYSIOLOGY

With increased erythropoietin and proliferation of erythroid precursors, increased numbers of reticulocytes are released into blood. Two forms of maturating reticulocytes are identified in cats. Aggregate reticulocytes have increased RNA that forms a prominent reticulum with supravital staining and appear as polychromatophilic erythrocytes on Romanowsky-stained smears. Punctate reticulocytes have less RNA that forms pinpoint inclusions on supravital stain. They are not apparent on Romanowsky-stained smears. This distinction has species-related implications (see below).

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Regenerative anemias from blood loss or hemolysis (e.g., immune-mediated hemolytic anemia, mycoplasmosis, oxidative anemias, fragmentation anemia)

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Determine specific cause of blood loss or hemolysis.

CAUSES OF ABNORMALLY LOW LEVELS: Decreased erythropoietin (e.g., chronic renal failure), inflammation-induced suppression of erythropoiesis, iron deficiency, decreased erythroid precursors in marrow (e.g., immune-mediated attack on erythroid precursors, feline leukemia virus or feline immunodeficiency virus infection, myelophthisis)

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Bone marrow aspirate or core biopsy

IMPORTANT INTERSPECIES DIFFERENCES

- In cats, punctate reticulocytes circulate for 10-14 days, so they occur after erythropoietic response and increase in aggregate reticulocytes have abated. Only aggregate reticulocytes should be counted in cats.
- In dogs, punctate reticulocytes do not persist significantly longer than aggregate reticulocytes.
- Dogs mount a higher reticulocyte response than cats during regenerative anemias.

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE: Autoagglutination decreases the number of detectable reticulocytes. Presence of intraerythrocytic inclusions (e.g., basophilic stippling, Pappenheimer bodies, Heinz bodies) could falsely increase the reticulocyte concentration.

SPECIMEN: EDTA whole blood (lavender-top tube) for flow-cytometric counting by analyzers (preferred) or manual counting of supravital stained smears.

RELATIVE COST: $ (reflex reticulocyte counts part of some CBC profiles)

PEARLS

- An increase in absolute concentration (rather than percentage) of reticulocytes is the gold standard for determining whether anemia is regenerative or nonregenerative.

- Reticulocyte counts may not be included in routine CBC; be sure it is included for anemic patients.
- Following acute blood loss or hemolysis of significant degree, increased numbers of reticulocytes are not expected to occur in peripheral blood until at least 3 days afterward.

AUTHOR: STEPHEN D. GAUNT

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Relaxin

DEFINITION

Peptide hormone produced by the reproductive tract of many species during pregnancy

TYPICAL NORMAL RANGE

Relaxin is measured by a commercially available assay (Witness Relaxin, Synbiotics). Positive/negative result; negative (undetectable) in nonpregnant (diestral) bitches.

PHYSIOLOGY

The tissue source of relaxin varies with species and stage of the reproductive cycle. It may be produced by the corpus luteum (CL), placenta, or uterus. In pregnant dogs, relaxin is initially produced by the CL, followed by the placenta. The primary effects of relaxin occur during implantation and later during parturition. Relaxin promotes uterine, cervical, and vaginal growth during pregnancy. It may also play an important role in mammary development in some species. Additionally, relaxin is involved in nonreproductive processes such as fibrosis, wound healing, and protection against myocardial ischemia.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Pregnancy. High concentration may persist following abortion. Nonpregnant cats with ovarian cysts have been reported to have high serum concentrations of relaxin.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Evaluate for pregnancy (abdominal radiographs, ultrasound).

IMPORTANT INTERSPECIES DIFFERENCES: Relaxin is of value for diagnosing pregnancy in both wild and domestic canids. Small studies have shown it to accurately detect pregnancy in cats.

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE: Hemolysis must be avoided; hemolyzed samples should not be used, as they may cause a false negative.

SPECIMEN: Plasma or serum. Collect blood in EDTA (lavender-top tube), citrate (blue-top tube), or heparin (green-top tube) or serum (red-top tube). Spin down, collect plasma or serum, and transfer to a clean tube without additives.

Do not use whole blood or hemolyzed samples.

RELATIVE COST: $$$

PEARLS

Relaxin is the only protein found to be associated specifically with pregnancy in dogs. It is also useful for ruling out pseudopregnancy, as these dogs do not have detectable relaxin concentrations.

AUTHOR: BRUCE E. LEROY

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Rabies Diagnostic Testing

DEFINITION

Evaluation of presence or absence of rabies virus infection

TYPICAL NORMAL RANGE

Results are reported as positive or negative.

PHYSIOLOGY

Rabies is an acute encephalitis caused by an RNA virus of the rhabdovirus family. Virus localizes to central nervous system. Direct IFA testing of brain tissue is the method used for definitive diagnosis. Submission of appropriate specimens requires necropsy examination. The test detects viral antigen in the neural tissue of infected animals.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Viral infection

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Exposed personnel should consult their physicians immediately. Exposed animals should be quarantined and observed for development of clinical signs (see p. 961).

SPECIMEN AND PROCESSING CONSIDERATIONS

SPECIMEN: Fresh brain tissue. Note: Aerosolization of rabies virus is possible during craniotomy portion of necropsy or during removal of head (exposure of spinal cord). Therefore, removal of head or brain should be reserved for qualified personnel (e.g., pathologist or state veterinarian). Body of rabies suspect should be chilled (refrigerated), not frozen. Cut brain in sagittal (longitudinal) section. Submit half in clean, dry double bag for IFA test. Clearly label as rabies suspect.

RELATIVE COST: $$—$$$$ (charges vary widely among state labs)

PEARLS

- Most testing is done at state diagnostic laboratories.
- Half the brain should be submitted in formalin to assess for other diseases if rabies testing is negative.
- Brain tissue is the only suitable specimen; other tissue such as whiskers or peripheral nerve are not.
- Dogs and cats that have an implanted microchip, are currently vaccinated for rabies, and have a protective titer certified by the FVNA Laboratory at Kansas State University or the Veterinary Command Food and Diagnostic Laboratory, Fort Sam Houston, Texas may avoid quarantine when traveling from the continental United States to Hawaii or the United Kingdom if they meet other criteria. For more details regarding pet travel, refer to http://www.aphis.usda.gov/animal_welfare/pet_travel/pet_travel.shtml.

AUTHOR: LOIS ROTH-JOHNSON

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Synovial Fluid Analysis

DEFINITION

Analysis of the viscous fluid secreted by synoviocytes that lubricates joints and transports nutrients to articular cartilage.

SYNONYM

Joint fluid analysis.

TYPICAL NORMAL RANGE

Normal synovial fluid is colorless to pale yellow, viscous, has high mucin (hyaluronic acid) content, and does not clot. Red blood cells are absent. Nucleated cell counts vary among species and the joint sampled but are usually 500/µL (up to 3000 cells/µL occasionally reported in normal joints). Synoviocytes and macrophages predominate. Protein concentration ranges from 1.8-4.8 g/dL (refractometer).

PHYSIOLOGY

Analysis includes assessment of viscosity, mucin clot test, cell counts, protein concentration, and Cytologic evaluation. Microscopic examination assesses cell population distribution and may detect infectious agents.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS

- Increased erythrocytes indicate iatrogenic blood contamination or hemarthrosis.
- Increased nucleated cells occur with degenerative and inflammatory arthropathies, and may also occur with neoplasia.
- Mononuclear cells predominate in degenerative arthropathy or joint instability. Causes include trauma, osteoarthrosis, osteochondritis dissecans, or aseptic necrosis of the femoral head.
- Neutrophils predominate in inflammatory arthropathies (infectious, non-infectious such as crystal-induced, immune-mediated). Bacterial infection is usually monoarticular and due to penetrating trauma. Polyarticular infection may be due to systemic bacterial infection, tickborne disease, fungal infection, and (rarely) mycoplasma infection. Noninfectious inflammatory arthropathies are polyarticular or have shifting leg lameness (immune-mediated diseases; chronic progressive polyarthritis in cats).

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH

- Hemorrhage: distinguish iatrogenic versus pathologic. Erythrophagocytosis suggests hemarthrosis. If hemarthrosis, evaluate for trauma versus bleeding disorder.
- Degenerative arthropathy: joint radiographs, assess for joint instability or ligament tear.
- Inflammatory arthropathy: culture synovial fluid, *Borrelia* spp. and *Ehrlichia* spp. serology, serum antinuclear antibody test, assess for systemic disease, and joint radiographs to assess for erosive lesions.

SPECIMEN AND PROCESSING CONSIDERATIONS

SPECIMEN: Fluid in EDTA (lavender-top tube) for cell counts, Cytologic evaluation; red-top tube (culture); refrigerate. Include clinical history.

RELATIVE COST: $$ (Most labs apply lower prices for specimens from multiple joints submitted at the same time.)

PEARLS

Some samples are very viscous, and the addition of a drop of crystalline hyaluronidase allows for a more accurate assessment of cell counts. Addition of hyaluronidase should be done at the reference laboratory after viscosity and protein concentration are measured and after the mucin clot test is done and slides for Cytologic evaluation are prepared.

AUTHOR: RUANNA GOSSETT

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Spherocytes

DEFINITION

Small, dense-staining red blood cells with no central pallor, considered the hallmark of immune-mediated hemolytic anemia (IMHA) or a normal finding post blood transfusion.

PHYSIOLOGY

Partial phagocytosis of antibody-coated red cells by macrophages results in loss of surface membrane without loss of volume, resulting in spherocyte formation. Pitting (excision) of Heinz bodies in the spleen also leads to spherocyte formation. May also be seen in cases of canine babesiosis and hemotropic mycoplasmosis (previously hemobartonellosis) in cats and dogs.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Immune-mediated hemolysis or erythrocyte fragmentation associated with snake bite, bee sting, hemoparasitism, zinc toxicosis, neoplasia, or idiopathic; normal phenomenon beginning 2-3 days after transfusion of red cells (even if properly cross-matched).

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Evaluate history for causes of anemia; Coombs' test and slide autoagglutination test if IMHA suspected.

IMPORTANT INTERSPECIES DIFFERENCES: Spherocytes are easily detected in dogs because of normally prominent central pallor; difficult to identify in other domestic animals (cats) that normally have no central pallor in their red cells. Some breeds of dogs (Shiba Inu and Akita) normally have microcytic red cells that should not be confused with spherocytes.

SPECIMEN AND PROCESSING CONSIDERATIONS

SPECIMEN: EDTA whole blood (lavender-top tube) for evaluation of gross agglutination and CBC, blood smear for evaluation

RELATIVE COST: $$ (reported as part of CBC)

PEARLS

- Microcytic red blood cells of severe iron-deficiency anemia differ from spherocytes in that microcytic red cells are hypochromic and truly microcytic (their mean corpuscular volume is decreased); spherocytes have normal red cell volume and appear hyper-chromic.
- In anemic patients, a CBC and/or fresh blood smears to screen for spherocytes (suggesting IMHA) should always be obtained before transfusion. Spherocytosis after transfusion does not discriminate between IMHA and normal post-transfusion phenomenon.
- Spherocytic anemia or IMHA may not always be accompanied by a positive Coombs' test (false-negative tests in some cases).
- Lack of spherocytes does not rule out IMHA.

AUTHOR: FIDELIA R. FERNANDEZ

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Sodium

DEFINITION

Electrolyte and the major extracellular cation. Concentration is relative to hydration status and extracellular fluid (ECF) volume but does not indicate total body Na content. Serum Na concentration essentially equals ECF Na concentration.

SYNONYMS

Na, Na^+

TYPICAL NORMAL RANGE

Dogs: 140-150 mEq/L. Cats: 150-160 mEq/L. Conversion: mEq/L = mmol/L.

PHYSIOLOGY

Serum concentration is net balance of oral intake, excretion, and water shifts between ECF and ICF (intracellular fluid). Na (and water) lost via kidneys, intestine, skin, respiratory tract. Concentration is regulated via balance of blood volume and plasma osmolality by glomerular filtration and renal tubular resorption. With hypovolemia, aldosterone promotes Na resorption, antidiuretic hormone (ADH, vasopressin) promotes water resorption. Hypoosmolality causes decreased water intake, increased urinary water excretion. Hypervolemia reduces Na resorption. Hyperosmolality promotes water intake, ADH-mediated water resorption. Water shifting from ICF to ECF dilutes serum Na.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS

- Hypovolemia; hypotonic fluid loss: vomiting, diarrhea, pancreatitis, peritonitis, osmotic diuresis, renal failure, postobstructive diuresis
- Normovolemia; pure water loss: diabetes insipidus, water deprivation, high temperature, brainstem disease
- Hypervolemia; Na gain (uncommon): salt poisoning, hypertonic fluid administration, hyperaldosteronism

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Evaluate hydration status; test for listed diseases.

CAUSES OF ABNORMALLY LOW LEVELS

- High measured osmolality: hyperglycemia, mannitol administration
- Low measured osmolality:
  - Hypovolemia: vomiting, diarrhea, pancreatitis, peritonitis, pleural effusion, uroabdomen, hypoadrenocorticism, prolonged diuretic administration, ketonuria, Na-wasting nephropathy
  - Hypervolemia: heart failure, severe hepatopathy, nephrotic syndrome, advanced renal disease (oliguric/anuric)
  - Normovolemia: hypotonic fluid therapy, psychogenic polydipsia, syndrome of inappropriate antidiuretic hormone secretion (SIADH; rare)

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Evaluate hydration status, test for listed diseases, measure plasma osmolality, measure urinary fractional Na excretion.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS

- Increase: osmotic diuretics, phosphate enema, furosemide, corticosteroids
- Decrease: furosemide, prolonged diuresis (osmotic, thiazides)

LAB ARTIFACTS THAT MAY INTERFERE: Marked hyperlipidemia/hypercholesterolemia or hyperproteinemia may decrease measured Na by electrolyte exclusion effect (method dependent). Serum osmolality is normal.

SPECIMEN: Serum (red-top tube) preferred. Heparinized plasma may be used (lithium or ammonium heparin, green-top tube).

RELATIVE COST: $

PEARLS:

- Sampling from an improperly cleared intravenous catheter commonly causes inaccurate values.
- Most reference laboratory methods are subject to electrolyte exclusion effect artifacts. Proteins and lipids are part of the "solids" component of plasma.

When their concentration in the water phase of plasma is increased (hyperproteinemia, hyperlipidemia), they displace sodium ions, resulting in a falsely low measurement of sodium in the same volume of sample fluid.

- The appearance of hypovolemia as a cause of both hypo- and hypernatremia may seem paradoxical. Loss of sodium and fluid, as may occur with diuretic overdose or vomiting, may initially result in volume depletion and a relative hypernatremia. Subsequent intracellular movement of sodium, when accompanied by volume reexpansion, can cause hyponatremia.

AUTHOR: ROBIN W. ALLISON

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Semen Analysis

DEFINITION

Assessment of male ejaculate for volume, sperm number and morphology, percent of live sperm, presence of other cells, bacteria, and, occasionally, alkaline phosphatase and carnitine concentration; used as part of assessment of male fertility

TYPICAL NORMAL RANGE

Normal total sperm count is 400 × 10^6/ejaculate (varying depending on volume of ejaculate), with 52%-90% classified as live and normal in most dogs. Motility, which is often considered an indicator of viability, should be =80%; motility patterns are random. Sperm should have single heads of uniform shape and size; free heads should be rare; tails are normally straight to slightly curved; hooked, kinked, or multiple tails are considered abnormal. It is common to see few urethral, prostatic, or squamous epithelial cells; low numbers of bacteria are also common. Alkaline phosphatase >10,000 U/L.

PHYSIOLOGY

Ejaculate is divided into three fractions. First and third fractions are mostly prostatic secretion; the second sperm-rich fraction should be used for evaluation.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY LOW LEVELS: Decreased numbers of normal viable sperm suggest testicular injury, neoplasia, or atrophy. Decreased concentration of seminal alkaline phosphatase and/or carnitine indicates obstruction of genital tubular structures.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Examination of testicle and epididymis on physical examination and using ultrasound; measurement of resting plasma testosterone.

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE: Aged sample or exposure to temperature extremes invalidates physical and biochemical analysis

SPECIMEN: Motility must be evaluated immediately; it cannot be assessed in specimens transported to a reference laboratory. Physical analysis (color, morphology, sperm count): 1 mL semen in sterile container. Alkaline phosphatase: 1 mL semen in sterile container. Store at room temperature. Specimens <2 hours old are considered best.

RELATIVE COST: $$ (physical analysis); $ (alkaline phosphate)

PEARLS

History is an important aspect of fertility assessment. Do not rely on a single test.

AUTHOR: LOIS ROTH-JOHNSON

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Schistocytes

DEFINITION

Red cell fragments that are considered to be the hallmark of microangiopathic hemolysis

SYNONYM

Schizocyte

PHYSIOLOGY

Schistocytes result from shredding of red cells as they pass through microvasculature containing fibrin thrombi or altered endothelium. Any traumatic or physical injury to red cells can lead to schistocyte formation.

CAUSES OF ABNORMALLY HIGH LEVELS: Disseminated intravascular coagulation (DIC), vasculitis, hemangiosarcoma, dirofilariasis, intravenous catheters, burns, heart valve disease, myelofibrosis, glomerulonephritis. May be seen in severe iron-deficiency anemia (increased red blood cell fragility causes fragmentation).

CLINICAL APPLICATIONS

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Evaluate patient's clinical history and physical exam, heartworm status, coagulation profile, tick titers.

IMPORTANT INTERSPECIES DIFFERENCES: Schistocytes are not typically seen in cats with DIC, possibly because their smaller red blood cells are less likely to be damaged by fibrin in vascular spaces.

SPECIMEN AND PROCESSING CONSIDERATIONS

SPECIMEN: EDTA whole blood (lavender-top tube) for CBC and blood smear evaluation

RELATIVE COST: $$ (reported as part of CBC)

PEARLS

Even small numbers of schistocytes are significant, indicating underlying microangiopathy; unlikely to be induced artifactually by smear preparation technique.

Absence of schistocytes does not rule out DIC (correlate with coagulation profile). A CBC report of *poikilocytosis* (a broad term that refers to circulating presence of any abnormally shaped RBCs) warrants pathologist review of blood smear to better define the shape change and identify any schistocytes.

AUTHOR: FIDELIA R. FERNANDEZ

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Trypsinlike Immunoreactivity

DEFINITION

Immunologic assay that detects trypsinogen, trypsin, and trypsin bound to protease inhibitors. Most detected activity due to trypsinogen.

SYNONYM

TLI

TYPICAL NORMAL RANGE

Dogs: 5-35 mg/L. Cats: 12-82 mg/L.

PHYSIOLOGY

Trypsinogen, the inactive (zymogen) form of trypsin, is produced by pancreatic acinar epithelial cells and is present in low concentration in the blood of normal patients. The assay also detects the active enzyme, trypsin, which may be increased in concentration in the blood of patients with pancreatitis.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Pancreatitis

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Not usually used for diagnosis of pancreatitis; canine -or feline-specific lipase is the preferred test and considered diagnostic. In some cases, clinical signs, diagnostic imaging results, and possibly increased serum amylase and lipase adequate for the diagnosis of pancreatitis. TLI > 50 mg/L (dogs) or >100 mg/L (cats) is consistent with pancreatitis.

CAUSES OF ABNORMALLY LOW LEVELS: Exocrine pancreatic insufficiency (EPI); severe, chronic, persistent pancreatitis or lymphocytic pancreatitis associated with parenchymal destruction

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Less than 2.5 mg/L (dogs) and <8 mg/L (cats) are diagnostic for EPI. Values between these and reference range are equivocal and may indicate loss of acinar tissue due to inflammation. Progressive immune-mediated disease (e.g., previous bout of pancreatitis or immune-mediated disease) may result in EPI. If EPI is suspected, repeat test in 4 weeks. Low levels may also indicate chronic, persistent pancreatitis.

IMPORTANT INTERSPECIES DIFFERENCES

- Cats: age-related increases associated with acinar adenomas.
- Dogs: increased values associated with inadequate nutrition/underfeeding.

SPECIMEN AND PROCESSING CONSIDERATIONS

SPECIMEN: Serum (red-top tube), non-hemolyzed, fasting (12-18 hours) sample

RELATIVE COST: $$

PEARLS

Assays are species specific. Check with reference laboratory to be sure that species-specific assays are being performed.

AUTHOR: LOIS ROTH-JOHNSON

1ST EDITION AUTHOR: FONZIE QUANCE-FITCH

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Troponins, Cardiac

DEFINITION

Troponins are intracellular myofibrillar proteins expressed in cardiac and skeletal muscle. Cardiac troponin I (cTnI) is the most diagnostically relevant.

TYPICAL NORMAL RANGE

Different diagnostic instruments assess different parts of the cTnI molecule such that normal reference ranges are instrument specific. Contact laboratory for reference range information. Sample normal ranges:

- Dogs: 0.03-0.07 ng/mL (cTnI), 0.01-0.15 ng/mL (cardiac troponin T), 0.05-0.21 ng/mL (cardiac troponin C)
- Cats: 0.03-0.16 ng/mL (cTnI), 0.05-0.22 ng/mL (cardiac troponin T)

PHYSIOLOGY

- Troponins regulate the contractility of striated muscle. They mediate the interaction between the sarcomeric proteins actin and myosin. The troponin complex is composed of three proteins: *troponin I* is the inhibitory component that prevents interaction between actin and myosin until intracellular calcium is bound by *troponin C; troponin T* is the tropomyosin-binding element that binds troponin I to the actin filament.
- The cardiac isoforms of troponins I and T are specific markers for myocardial injury because they are antigenically distinct from skeletal muscle troponins. They are found in high concentration only in cardiac myocytes.
- Cardiac troponins are released into the circulation when there is cardiac ischemia and necrosis. They increase in proportion to the degree of myocardial injury, regardless of cause. Troponins increase in the circulation within 4-6 hours after myocyte injury and may persist up to 1 or 2 weeks; renal function affects clearance. They are sensitive and specific markers of myocardial injury.
- Troponin levels may have prognostic value in dilated cardiomyopathy in dogs and correlate with heart size and survival.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Pericardial effusion caused by hemangiosarcoma or idiopathic pericarditis in dogs (serum levels greater with hemangiosarcoma, though substantial overlap), cardiomyopathy, myocardial contusion, gastric dilatation/volvulus, myocarditis, arrhythmias, structural heart disease associated with congestive heart failure in dogs and cats, hyperthyroidism, acute pulmonary thromboembolism, high-dose doxorubicin toxicity in dogs, and canine babesiosis.

SPECIMEN AND PROCESSING CONSIDERATIONS

SPECIMEN: Serum (red-top tube), heparinized plasma (green-top tube), or EDTA plasma (lavender-top tube); refrigerate or freeze at −20°C.

RELATIVE COST: $$

PEARLS

Cardiac troponin concentrations are diagnostically superior to other enzyme assessments (e.g., myocardial isoenzyme of creatine kinase) in human beings and appear to be promising, valuable detection and monitoring tools in veterinary cardiology.

AUTHOR: RUANNA GOSSETT

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Triiodothyronine (T3)

DEFINITION

Active form of iodine-containing thyroid hormone. Primary function is to increase rate of cell metabolism.

SYNONYM

3,5,3'-triiodothyroinine

TYPICAL NORMAL RANGE

Dogs: 0.5-1.8 ng/mL. Cats: 0.4-1.6 ng/mL. Conversion: ng/dL × 10 = pg/mL; ng/dL × 0.01536 = nmol/L; pg/dL × 15.4 = nmol/L = SI unit.

PHYSIOLOGY

Approximately 20% of T3 produced in the thyroid gland; the rest is from conversion of T4 to T3 in cells. More biologically active than thyroxine (T4). In circulation, 99% is protein bound. Dissociates to free T3 to enter cells. Binds to receptor proteins in peripheral tissue cells, which induces DNA translation and production of proteins associated with cell growth, oxidative phosphorylation, and membrane transport of electrolytes, resulting in an increase in metabolic rate and growth stimulation.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Hyperthyroidism; presence of autoantibodies; exogenous T3, TSH, or TRH; administration of iodine (or compounds containing iodine)

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: If hyperthyroidism suspected: other thyroid tests, imaging. If autoantibodies suspected: assess thyroglobulin autoantibody (TgAA) levels. Evaluate diet and supplements for iodine content.

CAUSES OF ABNORMALLY LOW LEVELS: Hypothyroidism, euthyroid sick syndrome

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: T4, free T4 by equilibrium dialysis, evaluate for nonthyroidal diseases.

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE: Decrease: moderate to marked hemolysis

SPECIMEN: Serum (red-top tube) or EDTA plasma (lavender-top tube). Separate serum or plasma from red blood cells as soon as possible. Store at 2°C-8°C (refrigeration).

RELATIVE COST: $$ (Usually run in conjunction with other thyroid tests; a variety of thyroid testing panels is available from most reference laboratories.)

PEARLS

T3 is of little diagnostic value. Broad overlap in T3 serum levels within euthyroid, hypothyroid, and euthyroid sick dogs. Total T3 is relatively insensitive and often nonspecific in assessment of hypothyroidism. Total and free T3 provide little additional information over total and free T4 by equilibrium dialysis. Serum T3 correlates poorly with thyroid disease.

AUTHOR: LOIS ROTH-JOHNSON

1ST EDITION AUTHOR: FONZIE QUANCE-FITCH

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150

$$$$: >$150

Triglycerides

DEFINITION

Main storage form of long-chain fatty acids

SYNONYM

Triacylglycerol

TYPICAL NORMAL RANGE

Serum levels, dogs: 20-150 mg/dL; cats: 20-90 mg/dL

PHYSIOLOGY

Three fatty acid molecules are bound (esterified) to a glycerol backbone to form a triglyceride molecule, the main lipid in adipose tissue and primary form of body fat. Primary sites of triglyceride synthesis are liver, small intestine, adipose tissue and mammary gland, but synthesis occurs in most cells. Triglycerides are transported in the blood bound to apoproteins, forming complexes called *lipoproteins.* Circulating triglyceride levels reflect a balance of absorption and synthesis by the small intestine, synthesis and secretion by hepatocytes, and uptake by adipose tissue. These processes are affected by dietary fat intake and hormones (insulin, glucagon).

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS

- Primary hyperlipidemia: idiopathic hyperlipidemia (schnauzer, beagles, and rarely in Brittany spaniels, mixed-breed dogs and cats); familial hyperchylomicronemia in cats
- Secondary hyperlipidemia: postprandial, hypothyroidism (dogs), diabetes mellitus, pancreatitis, hepatic disease, nephrotic syndrome, hyperadrenocorticism, high-fat diet, acromegaly (cats)

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Measure fasting levels (minimum 12-hour fast) to rule out postprandial hyperlipidemia. If persistent, assess for causes of secondary hyperlipidemia. If secondary hyperlipidemia is ruled out, primary hyperlipidemia is diagnosis of exclusion.

CAUSES OF ABNORMALLY LOW LEVELS: Malabsorption/maldigestion; hepatic synthetic failure (chronic hepatopathies)

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Serum trypsinlike immunoreactivity (TLI), cobalamin (vitamin B12) and folate levels, assess for panhypoproteinemia; serum bile acids (pre- and postprandial).

IMPORTANT INTERSPECIES DIFFERENCES: Hyperlipidemia may occur in cholestatic liver disease. Cats with hepatic lipidosis do not have hyperlipidemia.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS

- Increased: doxorubicin therapy, exogenous corticosteroids, megestrol acetate
- Decreased: lipid-lowering diets, supplementation with fish oils, nicotinic acid and fibric acid derivatives such as gemfibrozil

LAB ARTIFACTS THAT MAY INTERFERE: Hemolysis, lipemia, increased fluid viscosity and glycerol artificially elevate triglyceride levels.

SPECIMEN: Ensure sample collected after 12-hour fast. Serum (red-top tube), heparinized plasma (green-top tube), or EDTA plasma (lavender-top tube). Stable at 2°C-8°C for 1 week, 3 months frozen at 20°C.

RELATIVE COST: $$

PEARLS

Triglyceride levels may be measured in suspected chylous effusions. Triglyceride levels in the fluid that are greater than serum triglyceride levels in effusion indicate chylous effusion, even if the effusion is not grossly milky in appearance.

AUTHOR: RUANNA GOSSETT

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Toxoplasma gondii Serology

DEFINITION

Toxoplasmosis is a protozoan disease caused by *Toxoplasma gondii,* an intracellular parasite that infects many tissues of birds and mammals, including humans (see p. 1105).

TYPICAL NORMAL RANGE

Reported as titer values; consult with reference laboratory.

PHYSIOLOGY

Serum titers are first detectable via ELISA 1-2 weeks (immunoglobulin [Ig] M) or ≥2 weeks (IgG) after infection in dogs and cats. A fourfold increase in IgG titer over 2-3 weeks is consistent with infection. An elevated IgM titer at any time, regardless of IgG titer, is consistent with infection, but a low IgM titer does not rule out past exposure. Since infected animals harbor tissue cysts for life, a long-term measurable IgG titer is expected.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: ELISA-positive IgG with negative IgM titer most consistent with chronic exposure to *T. gondii,* although some IgM titers decrease rapidly in acute infections, as seen in 20%-85% of the cat population (geographically variable). Positive IgM with negative IgG titer most consistent with recent exposure or active infection with *T. gondii.* Positive IgG with positive IgM titer consistent with recent exposure or active infection.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: If IgG titer is positive, evaluate IgM titer or paired IgG titers (at least 2 weeks apart). Greater than fourfold increase in paired IgG titers indicates recent exposure. PCR test on cerebrospinal fluid, aqueous humor, whole blood, bronchoalveolar lavage or tracheal wash fluid, or fresh tissue to demonstrate presence of *Toxoplasma* DNA. Definitive diagnosis requires demonstration of organisms in tissue via histopathology, immunohistochemistry, and/or PCR, or rarely via animal or cell culture inoculation. Some infectious disease specialists recommend response to treatment (e.g., with clindamycin) as a diagnostic test in patients with compatible clinical signs and a positive IgM or rising IgG titer.

CAUSES OF ABNORMALLY LOW LEVELS: Negative IgG and IgM titers indicate absence of exposure or peracute infection.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: If clinical signs are suggestive of acute toxoplasmosis, reevaluate IgM and IgG titers in 3 weeks.

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE: Lipemia and hemolysis interfere with the ELISA and may cause a false-positive result.

SPECIMEN: Serum (red-top tube), 1 mL. Stable for 4 days at 4°C or for several weeks at 0°C.

RELATIVE COST: $$ (ELISA, PCR, IFA)

PEARLS

Value of a single IgG measurement in cats is highly limited because a large proportion of healthy cats (20%-85% of the population) has a positive result.

AUTHOR: PATTY J. EWING

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Total Protein (Serum)

DEFINITION

Serum proteins consist of albumin, antibodies, complement, enzymes, coagulation factors, and transport proteins. Albumin and globulin make up the majority of serum total proteins. Fibrinogen, factor V, and factor VIII are present in plasma but not in serum, because they are utilized in clot formation.

SYNONYM

Total solids

TYPICAL NORMAL RANGE

Dogs: 5.1-7.8 g/dL (g/dL × 10 = mg/mL). Cats: 5.9-8.5 g/dL (g/dL × 10 = mg/mL).

PHYSIOLOGY

The proteins in serum are important for maintaining colloid osmotic pressure (primarily albumin), buffering to maintain blood pH, hemostasis, transport of molecules (hormones, drugs, calcium, bilirubin, hemoglobin, other proteins, lipids, and metal ions), acute-phase response to inflammation, and immune response. Most of these proteins are synthesized in the liver and immune system.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Increased globulin: acute and chronic inflammation or infection (rickettsial, bacterial, viral, fungal, protozoal, parasitic), immune-mediated disease, chronic hepatic disease, nephrotic syndrome, and neoplasia (myeloma, lymphoma, lymphocytic leukemia, and rarely solitary plasma cell tumors). Increased albumin occurs with dehydration and is “relative;” increased production does not occur.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Measure serum albumin and globulin levels, assess hydration status, serum protein electrophoresis if hyperglobulinemia is absolute (normal albumin level) and repeatable.

CAUSES OF ABNORMALLY LOW LEVELS: Low albumin without a decrease in globulins occurs with protein-losing nephropathy and chronic hepatopathies. Both hypoalbuminemia and hypoglobulinemia occur with protein-losing enteropathy, whole blood loss (gastrointestinal, lacerations/trauma, other hemorrhage), exudative skin disease, massive burns, and effusive disease. Hypoglobulinemia with normal albumin occurs with decreased immunoglobulin concentration due to failure of passive transfer or inherited or acquired immune deficiency.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Measure serum albumin and globulin levels. As indicated clinically, evaluate for gastrointestinal, hepatic, renal disease.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS

- Total protein levels increased by testosterone, estrogens, growth hormone
- Total protein levels decreased by thyroxine, cortisol

LAB ARTIFACTS THAT MAY INTERFERE: Lipemia, hemolysis, and hyperbilirubinemia may artifactually increase total protein readings (globulin fraction).

SPECIMEN: Serum (red-top tube). Can be evaluated using heparinized plasma (green-top tube) or EDTA plasma (lavender-top tube). Stable for 1 month at 2°C-8°C

RELATIVE COST: $

AUTHOR: RUANNA GOSSETT

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Thyroxine (Total), Free Thyroxine by Equilibrium Dialysis

DEFINITION

Thyroxine (T4 is the major storage form of iodine-containing thyroid hormone. Its primary function is to increase the rate of cell metabolism. Free T4 (fT4 is the biologically available, non-protein-bound form of the hormone able to enter cells.

SYNONYM

T4: tetraiodothyronine

TYPICAL NORMAL RANGE

- fT4 averages approximately 2 ng/dL
- To convert: mg/dL × 10 = ng/mL; mg/dL × 12.87 = nmol/L; ng/mL × 1.287 = nmol/L (SI unit nearest 1 nmol/L).

PHYSIOLOGY

Thyroxine is highly (up to 99.9%) protein bound in circulation and therefore not biologically active. In cells, thyroxine is deiodinated to the active form of the hormone (T3). Binds to receptor proteins in cells, inducing DNA translation and production of proteins associated with cell growth, oxidative phosphorylation, and membrane transport of electrolytes, resulting in an increase in metabolic rate and growth stimulation.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Hyperthyroidism; presence of autoantibodies; exogenous T4, TSH, or TRH; administration of iodine (or compounds containing iodine)

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH

- If hyperthyroidism suspected: other thyroid tests, including follow-up testing, imaging
- If autoantibodies suspected: measure serum thyroglobulin autoantibody (TgAA) levels.
- Evaluate diet, supplements for iodine content.

CAUSES OF ABNORMALLY LOW LEVELS: Hypothyroidism, euthyroid sick syndrome.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Measure serum TSH levels, evaluate for nonthyroidal diseases.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Glucocorticoids, sulfonamides, phenobarbital, nonsteroidal antiinflammatory drugs may decrease total T4 concentration, with less (or no) effect on free T4.

LAB ARTIFACTS THAT MAY INTERFERE

- Artifactual increase of free T4 if sample is not kept cold
- Artifactual increase of free and total T4 if stored in glass tubes at 37°C

SPECIMEN: Serum (red-top tube) or EDTA plasma (lavender-top tube). Separate serum or plasma from red blood cells as soon as possible. Store at 2°C-8°C.

RELATIVE COST: $$

PEARLS

- Breed differences occur: T4 and free T4 can be markedly lower in sighthounds: small breeds tend to have higher reference intervals.
- Total T4 is a good screening test because of its sensitivity to disease but a poor confirmatory test because of its lower

specificity.
- Free T4 is not as likely to be affected by nonthyroidal illness or drugs.
- Diurnal fluctuations occur in dogs but are not predictable, up to 20% below normal reference interval.
- Free T4 is also measured by radioimmunoassay, which is cheaper but of no apparent benefit over total T4 and less accurate than free T4 by equilibrium dialysis.

AUTHOR: LOIS ROTH-JOHNSON

1ST EDITION AUTHOR: FONZIE QUANCE-FITCH

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Thyroid-Stimulating Hormone

DEFINITION

Pituitary-derived hormone that acts on the thyroid gland to produce and secrete thyroid hormones

SYNONYMS

Canine TSH (cTSH), thyrotropin, TSH

TYPICAL NORMAL RANGE

Dogs: 0.1-0.5 ng/mL (µg/dL × 10 = ng/mL). Be sure test method has been validated for dogs.

PHYSIOLOGY

TSH is released from the pituitary from stimulation by thyrotropin-releasing hormone (TRH), and it acts on the thyroid gland to stimulate synthesis and release of thyroxine (T4) and triiodothyronine (T3). T3 and T4 act as negative feedback to reduce TSH and TRH secretion.

CAUSES OF ABNORMALLY HIGH LEVELS: Hypothyroidism (primary), thyroxine supplementation

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Free T4 by equilibrium dialysis (free T4 ED) and total T4

CAUSES OF ABNORMALLY LOW LEVELS: Sensitivity of the test is not sufficient to differentiate normal from low concentrations.

IMPORTANT INTERSPECIES DIFFERENCES: Species-specific immunoassay required. No valid measurement of feline TSH available; there may be some cross-reactivity with the canine TSH assay. Canine test may detect elevated levels in cats but can not document decreased levels.

SPECIMEN AND PROCESSING CONSIDERATIONS

SPECIMEN: Serum (red-top tube) or EDTA plasma (lavender-top tube). Separate serum or plasma from red blood cells as soon as possible. Store at 2°C-8°C (refrigeration).

RELATIVE COST: $$

PEARLS

- Canine patients with low free T4 (ED) and increased cTSH concentrations are extremely likely to have hypothyroidism.
- May increase ability to assess thyroid function when evaluated in conjunction with thyroid hormone concentrations

AUTHOR: LOIS ROTH-JOHNSON

1ST EDITION AUTHOR: FONZIE QUANCE-FITCH

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Thyroglobulin Antibody

DEFINITION

Autoantibodies against thyroglobulin, the major storage form for thyroxine and tri-iodothyronine in the thyroid follicle

SYNONYM

TgAA

TYPICAL NORMAL RANGE

Results reported as negative, positive, or inconclusive.

PHYSIOLOGY

The presence of thyroglobulin antibody (TgAA) is an indicator of immune-mediated thyroiditis and homozygous carrier state for the disease.

CAUSES OF ABNORMALLY HIGH LEVELS: Immune-mediated thyroiditis; low-grade false-positive results may occur with routine vaccinations in the previous 30-40 days.

CLINICAL APPLICATIONS

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Free T4 (equilibrium dialysis). Repeat TgAA test in 2-4 months.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Thyroid supplement associated with false-negative test. Treatment should be discontinued for at least 90 days prior to testing.

SPECIMEN: Serum (red-top tube) or EDTA plasma (lavender-top tube). Separate serum or plasma from red blood cells as soon as possible. Store at 2°C-8°C (refrigeration).

RELATIVE COST: $$

PEARLS

Dogs that test positive are not recommended for breeding, owing to the hereditary nature of immune-mediated thyroiditis and resultant hypothyroidism. Many dogs may develop TgAA prior to clinically evident immune-mediated thyroiditis and hypothyroidism. Carriers (heterozygotes) are negative. Dogs with chronic disease with thyroid destruction may have negative results. Occasionally dogs may have TgAA without having hypothyroidism; TgAA should always be interpreted in conjunction with other thyroid hormone parameters.

AUTHOR: LOIS ROTH-JOHNSON

1ST EDITION AUTHOR: FONZIE QUANCE-FITCH

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Testosterone

DEFINITION

Hormone responsible for development of male characteristics

TYPICAL NORMAL RANGE

Usually, serum levels > 1 ng/mL indicate an intact male.

PHYSIOLOGY

Derived from cholesterol, primarily produced by testicular interstitial cells; ovarian theca cells, zona reticularis of the adrenal cortex, and placenta produce lesser amounts. Hematogenous distribution to target tissue; affects bone growth and muscle mass, development of spermatogenic tissue in testes, and behavior. Extratesticular production accounts for sexual behavior in castrated males or animals with ovarian or adrenal tumors.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Cryptorchid or intersex patients may have concentrations consistent with intact male.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Investigate for presence of abdominal testicle(s) or abnormal gonadal tissue.

CAUSES OF ABNORMALLY LOW LEVELS: Infertility

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Resample because cyclically low levels may occur in fertile patients; pulses of testosterone may occur throughout the day. Increased concentration over basal levels following administration of human chorionic gonadotropin (hCG) or gonadotropin-releasing hormone (GnRH) indicates functional testicular tissue.

IMPORTANT INTERSPECIES DIFFERENCES: Male cats have pulsatile secretion of testosterone and may have undetectable levels. Therefore, evaluation should be done following intramuscular injection of either GnRH or hCG as follows:

- 25 µg GnRH IM, then draw sample 1 hour later (reference interval: 17.3-41.6 nmol/L) *or*
- 250 IU hCG IM, then draw sample 1 hour later (reference interval: 10.4-31.2 nmol/L)

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: False increases due to administration of androgenic drugs such as methyltestosterone; administration of radioisotopes falsely increases values measured by radioimmunoassay; chronic administration of androgenic drugs suppresses natural production.

LAB ARTIFACTS THAT MAY INTERFERE: Delayed separation from red blood cells, collection in EDTA (lavender-top tube), and storage at room temperature falsely decrease values.

SPECIMEN: Heparinized (green-top tube) plasma or serum; separate plasma or serum from red blood cells as soon as possible; store specimen at 2°C-8°C.

RELATIVE COST: $$

PEARLS:

- Main indications are assessment of infertile male patients and to help determine whether a male without external testicles is cryptorchid or has been neutered (see p. 268).
- Presence or absence of penile spines in adult male cats helps support or refute testosterone exposure, respectively.

AUTHOR: LOIS ROTH-JOHNSON

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Taurine Blood Levels

DEFINITION

Amino acid with important role in retinal and myocardial metabolism

TYPICAL NORMAL RANGE

- Cats: <20 nmol/mL (plasma) is considered diagnostic of cardiomyopathy; cats with <60 nmol/mL should receive supplementation.
- Dogs: <40 nmol/mL (plasma) is considered low and has been associated with dilated cardiomyopathy in the cocker spaniel, golden retriever, and Newfoundland breeds (see p. 1075).
- Whole blood concentrations (and the whole blood reference ranges) are approximately double the plasma concentrations.

PHYSIOLOGY

Low blood levels of taurine have been associated with dilated cardiomyopathy in cats and certain breeds of dogs, such as cocker spaniels, retrievers, and many other breeds. Determination of plasma and/or whole blood levels of taurine may be useful in determining role in dilated cardiomyopathy and need for supplementation. Taurine-deficient cats (but not dogs) may develop degenerative retinal lesions.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY LOW LEVELS: Dietary deficiency, poor dietary bioavailability, excessive loss of metabolic precursors (cysteine), and/or familial predisposition

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Correlate with cardiac and/or ophthalmic evaluation findings.

IMPORTANT INTERSPECIES DIFFERENCES: Fasting may decrease plasma levels of taurine in feline samples; therefore, whole blood is the preferred sample for cats. Ideally, both whole blood and plasma taurine levels should be determined for dogs.

SPECIMENS AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE: Bacterial contamination may falsely decrease blood taurine levels. Delay in separating and chilling plasma or poor blood collection technique may result in falsely increased levels of plasma taurine, because taurine is released from leukocytes and activated platelets.

SPECIMEN: Collect 2 ml fresh heparinized (green-top tube) whole blood and freeze; freezing heparinized whole blood lyses RBCs and releases taurine (desirable). Alternatively, collect 1 mL of frozen heparinized plasma. Chill sodium heparin collection tube (green-top tube) and separate plasma immediately after collection in a refrigerated centrifuge. After centrifugation, transfer plasma —without disturbing the buffy coat—to red-top tube (without serum separator plug) for submission.

RELATIVE COST: $$$

PEARLS

- Dogs do not need to be eating a taurine-deficient diet to develop taurine-deficient dilated cardiomyopathy; poor bioavailability of nutritional taurine (e.g., binding by rice husks) and excess urinary excretion of taurine precursors (e.g., cystine) have been proposed as mechanisms. Reference intervals in dogs are not well established. They are suspected to be significantly higher than those in cats. Clinically normal dogs have been reported to have 77 + 2.1 (plasma) and 266 + 5.1 (whole blood) nmol/mL taurine.
- Oral taurine supplementation is inexpensive and safe.
- Low taurine levels may be used to confirm a diagnosis of cardiomyopathy but are generally not used as a screening test.

AUTHOR: SHERRY J. MORGAN

Pricing Information

$: <$20

$$: $21-75
$$$: $76-150
$$$$: >$150

Urine Specific Gravity

DEFINITION

Urine specific gravity (USG) is an estimate of urine osmolality. Concentrated urine: USG > 1.030 (dog), >1.035 (cat). Isosthenuria: USG = 1.008-1.012. Hypos-thenuria: USG < 1.008.

TYPICAL NORMAL RANGE

Normally 1.001-1.060, depending on hydration status

PHYSIOLOGY

Assessment of ability to concentrate urine. Depends on hydration status, renal function, and extrarenal influences (diuretics and other drugs, endocrine disorders, etc.).

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS

- Increased USG with dehydration may be marked but typically is an appropriate response for preservation of effective circulating volume.
- Proteinuria and glucosuria may cause falsely high estimates of value.
- 1g/dL glucosuria (between 3+ and 4+ on urine dipsticks) increases USG by 0.004-0.005.
- 1 g/dL proteinuria (4+ on urine dipstick) increases USG by 0.003-0.005

CAUSES OF ABNORMALLY LOW LEVELS

- If low USG (1.008-1.012) is concurrent with normal serum urea (BUN) and creatinine concentrations, the most likely explanation is normal formation of dilute urine to preserve euvolemia (e.g., after drinking water). No conclusion can be drawn concerning renal function, except that at least 25% of renal tubules must be functioning for BUN and creatinine levels to be normal.
- If low USG (1.008-1.012) plus azotemia, glucosuria, dehydration, polyuria, or oliguria, then renal tubular concentrating ability is impaired. Underlying causes include:
    - Decreased numbers of functional nephrons (>75% nonfunctioning nephrons); chronic kidney disease
    - Osmotic diuresis (glucosuria, ketonuria, iatrogenic, other)
    - Diabetes insipidus (central, nephrogenic)
    - Diuretics (furosemide, other loop diuretics; thiazides)
    - Aldosterone deficit (hypoadrenocorticism) or resistance (spironolactone)

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Determine hydration status, evaluate serum biochemistry values, especially urea, creatinine, phosphate, glucose, calcium, sodium, and potassium.

IMPORTANT INTERSPECIES DIFFERENCES

- Concentrating abilities vary among species: cat > dog > horse/cow.
- Adults have greater concentrating ability than neonates.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Diuretics cause USG to decrease (sodium and water excretion).

SAMPLE FOR COLLECTION AND ANY SPECIAL SPECIMEN HANDLING

NOTES: Urine, 5 mL minimum, in clean container

RELATIVE COST: $ (reported as part of urinalysis)

PEARLS

- A low USG is meaningless with respect to renal function unless it is accompanied by urea and creatinine concentrations measured on a blood sample drawn at the same time as the urine sample.
- Acute anuric renal failure may be associated with a normal USG (residual urine).
- USG in untreated diabetics is usually 1.025-1.035; isosthenuria suggests concomitant renal disease or hyperadrenocorticism.

AUTHOR: ELIZABETH G. WELLES

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Urine Protein/Creatinine Ratio

DEFINITION

Amount of protein excreted in urine compared with (ratio) the concentration of urine, as determined in a single sample collection (spot check)

SYNONYMS

UP:C ratio, UP:UC ratio

TYPICAL NORMAL RANGE

Urine protein/creatinine (UP:C) ratio in healthy individuals is <0.6 (cats) or <0.5 (dogs, 0.5-1 are borderline values).

PHYSIOLOGY

- Absolute amount of protein in a urine sample varies depending on water content (urine concentration), regardless of degree of proteinuria.
- Therefore, increased urinary protein loss can be assessed for significance when compared to the concentration of creatinine in the urine.
- Glomeruli normally allow the passage of only trace amounts of protein (if any) into the urine, with tubular reabsorption of nearly all filtered protein. Glomerular damage, renal tubular damage, or inflammation in the urinary tract can cause proteinuria and an increased UP:C.
- UP:C has traditionally been used in the diagnosis of protein-losing nephropathies (glomerulonephritis, amyloidosis), for which it remains the initial diagnostic test of choice.
- Renal tubular protein loss and associated UP:C increase may also be used as early markers of chronic kidney disease, with important treatment and prognostic implications in dogs and cats.
- Recently it has been shown that most dogs with active urinary sediment (pyuria) do not have detectable proteinuria and have normal UP:C. Those dogs with both pyuria and concurrent hematuria or bacteriuria are more likely to have proteinuria, +/—increased UP:C. Proteinuria may not be present with hematuria until the hematuria is grossly visible and then may not cause increased UP:C.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS

- Urinary tract inflammation (pyuria, hematuria, and bacteriuria) may result in modest UP:C ratio increases (e.g., 1-3), although very high values (e.g., 40) have been reported rarely in patients with bacterial cystitis.
- Tubular loss of protein may result in a UP:C ratio of 1-5.
- Glomerular loss of protein usually results in UP:C >1, usually >3, and renal amyloidosis usually has UP:C ratio >15.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Full urinalysis, serum protein concentration, serum urea and creatinine, urine bacterial culture and susceptibility

SPECIMEN AND PROCESSING CONSIDERATIONS

SPECIMEN: Urine, 2 mL minimum, in clean container

RELATIVE COST: $$

PEARLS

- Albumin is a major component of the urinary protein excreted in protein-losing nephropathy. Because it is of a similar molecular size as antithrombin (AT), a markedly increased UP:C may indicate a hypercoagulable state owing to loss of significant AT.
- The presence of an active sediment does not automatically negate the interpretation of an increased UP:C ratio.

AUTHOR: ELIZABETH G. WELLES

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Urine pH Abnormalities

DEFINITION

Urine pH higher or lower than expected based on species and diet; the negative logarithm of hydrogen ion concentration in urine. Aciduria: low urine pH (<7). Alkaluria: high urine pH (>7)

TYPICAL NORMAL RANGE

Dogs and cats: 6.0-7.5

PHYSIOLOGY

Dietary constituents influence urine pH in health.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS

- Alkaluria: expected postprandially in monogastric mammals
- Infections (usually cystitis) in dogs/cats caused by bacteria that contain/produce urease (urea is degraded to ammonia, which is a weak base and removes free hydrogen ion from urine).
- Excess base is excreted or increased acid (free hydrogen ions) is retained (renal proximal and distal tubules) in some cases of metabolic alkalosis and occasionally in cases of chronic respiratory alkalosis.
- Distal renal tubular acidosis (decreased hydrogen ion excretion in distal nephron) may result in alkaline urine or a disproportionately high urine pH (>6) compared with the blood pH (acidemia).
- Proximal renal tubular acidosis (inability to conserve bicarbonate in proximal tubules) may result in high urine pH early in the disorder.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Urine sediment examination (presence of pyuria +/− bacteria) and/or culture for bacteria.

CAUSES OF ABNORMALLY LOW LEVELS

- Aciduria: severe cases of metabolic alkalosis with hypochloridemia + hypokalemia (paradoxical aciduria, see p. 53)
- Hypokalemia (H^+ excretion in exchange for K^+ resorption in intercalated cells of distal tubules)
- Loop diuretic treatment (e.g., furosemide)
- Excretion of excess acid (H^+) in metabolic or respiratory acidosis

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Determine serum electrolyte and acid-base status (Na^+, K^+, Cl^-, HCO^-_3, and anion gap, +/− blood pH).

IMPORTANT INTERSPECIES DIFFERENCES: Dogs and cats typically have urine that is more acidic than that of herbivores.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Potassium-wasting diuretics may result in renal K^+ conservation and excess H^+ excretion (aciduria).

LAB ARTIFACTS THAT MAY INTERFERE

- Marked delay in analysis may result in urine alkalinization (urea converts to ammonia spontaneously or via urease-containing bacteria).
- Prolonged exposure to high-pH (≥9) urine may cause dipstick protein reading to be falsely increased.

SPECIMEN: Urine, minimum of 5 ml, in clean/sterile container collected by free catch, catheterization, or cystocentesis (if culture also needed). Analysis of urine should be completed within 2-3 hours after collection; otherwise, urine pH may increase with age as urea converts to ammonia.

RELATIVE COST: $

AUTHOR: ELIZABETH G. WELLES

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Urine Cortisol/Creatinine Ratio

DEFINITION

Screening test for hyperadrenocorticism that measures the ratio of urinary cortisol to creatinine excretion

TYPICAL NORMAL RANGE

- Ratios < approximately 10×10^{-6} rule out hyperadrenocorticism.
- Ratios > approximately 10×10^{-6} indicate elevated serum cortisol (adrenal or nonadrenal disease).

PHYSIOLOGY

Because urine excretion of creatinine is fairly constant, its ratio to urine cortisol excretion provides a measurement of average serum cortisol levels.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Hyperadrenocorticism, many nonadrenal diseases and physiologic conditions

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Review history and physical exam for signs of hyperadrenocorticism; adrenocorticotropic hormone (ACTH) stimulation, low-dose dexamethasone suppression test (LDDST) if indicated.

IMPORTANT INTERSPECIES DIFFERENCES: Ratio may be abnormally high in cats with hyperthyroidism.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Corticosteroid administration increases levels; ketoconazole therapy decreases levels.

LAB ARTIFACTS THAT MAY INTERFERE: Increase: anticoagulants, bilirubin

SPECIMEN: Fresh urine, 5 mL minimum, morning collection preferred. To minimize stress-associated increases in cortisol, some clinicians advocate that the client obtain the urine sample in a clean plastic container when the dog voids at home immediately prior to traveling to the veterinary hospital.

RELATIVE COST: $$

PEARLS

- Increased ratio is a sensitive but nonspecific test for hyperadrenocorticism. High ratios are associated with stress and nonadrenal disease as well as hyperadrenocorticism.
- Values within reference range strongly indicate patient does not have hyperadrenocorticism.
- Increased urinary cortisol excretion may be physiologic or pathologic.

AUTHOR: LOIS ROTH-JOHNSON

1ST EDITION AUTHOR: FONZIE QUANCE-FITCH

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Urinalysis

DEFINITION

Panel of screening tests done on urine to evaluate for inflammation, degenerative lesions, protein loss, neoplasia in the urinary tract, and systemic disease

TYPICAL NORMAL RANGE

Color: yellow; appearance: clear; pH: 6 to 7.5; specific gravity: 1.001 to >1.030 (dogs), 1.001 to >1.035 (cats); protein, glucose, ketones, bilirubin, blood, bacteria: negative (trace to 1+ bilirubinuria is normal in the dog); red blood cells, leukocytes, epithelial cells: 0 to 5 per high-power field; casts: 0 to 2 per low-power field. Some values depend on collection method.

PHYSIOLOGY

Urine constituents and composition reflect lesions of the urinary tract and may provide an indication of metabolic abnormalities.

SPECIMEN AND PROCESSING CONSIDERATIONS

LAB ARTIFACTS THAT MAY INTERFERE: Delay in specimen processing may decrease some values and increase others. See specific tests. Generally, 10 mL of urine is recommended; reference-range quantitation of urine sediment is usually based on this volume.

SPECIMEN: Fresh urine (10 mL) in sterile container. Indicate method of collection (cystocentesis, catheterization, or free catch).

RELATIVE COST: $

PEARLS

- Collection method may influence interpretation. Blood and epithelial cells in catheterized specimens or bacteria in free catch specimens may not indicate disease.
- Unless contraindicated (e.g., bleeding disorder makes risk of cystocentesis unacceptable), serum biochemistry profiles should always be accompanied by urinalysis to better understand significance of abnormalities of blood glucose, urea, creatinine, albumin, cholesterol, and electrolytes on the profile.

AUTHOR: LOIS ROTH-JOHNSON

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

von Willebrand Factor Assay

DEFINITION

Assay to detect von Willebrand disease (vWD), which results from decreased functional von Willebrand factor (vWF) and causes prolonged bleeding time and abnormal primary hemostasis

TYPICAL NORMAL RANGE

Dogs: 60%-172% of normal pooled plasma

PHYSIOLOGY

- vWF is produced by endothelial cells and megakaryocytes and circulates with factor VIII, which prolongs its stability. Stored in endothelial cells and platelet α-granules, vWF acts as a bridge between exposed subendothelial collagen and platelets and among platelets. Platelet binding of vWF triggers a cascade of hemostatic and thrombotic events. Low levels of vWF result in lack of platelet activation (see p. 1176).
- Measured by quantitative ELISA with species-specific antibodies to vWF. Multimeric analysis (separates the different vWF multimers) can distinguish between type 1 and 2 vWD. Functional assays exist but are not frequently used in the clinical setting.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Azotemia, liver disease

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: No clinical importance

CAUSES OF ABNORMALLY LOW LEVELS: Types 1, 2, and 3 vWD are the most common hereditary bleeding disorders in dogs. ELISA is typically <35% in vWD. Lack of any detectable vWF indicates type 3 vWD; vWF 30%-70% indicates a carrier.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Genetic tests to identify gene mutations to detect carriers in certain dog breeds. Any dog with factor levels < 70% is considered a carrier and not appropriate for breeding.

IMPORTANT INTERSPECIES DIFFERENCES: Feline platelets contain vWF; canine platelets do not contain significant levels. Thrombocytopenia does not affect vWF values in dogs.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Epinephrine, endotoxin, and 1-deamino-8-d-arginine vasopressin (DDAVP) can increase vWF. DDAVP will increase vWF both in dogs with type 1 vWD and in normal dogs.

LAB ARTIFACTS THAT MAY INTERFERE: Decrease: hemolysis, clotting

SPECIMEN: Collect blood in sodium citrate (blue-top tube) or EDTA (lavender-top tube). After centrifugation, plasma should be promptly collected, frozen, and shipped overnight.

RELATIVE COST: $$

PEARLS

- If the platelet counts and coagulation times are within normal limits, buccal mucosal bleeding time may help diagnose vWD. Affected patients will have prolonged buccal mucosal bleeding times.
- While DNA testing can identify carriers and is specific for the mutation responsible for the disease, it does not necessarily identify whether dogs will be clinically affected. The value obtained from factor assay better predicts the likelihood of clinical signs.

AUTHOR: DEBORAH G. DAVIS

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Warfarin

DEFINITION

Commonly used rodenticide; testing is typically for retrospective confirmation (e.g., identification and prevention of future reintoxication or for legal purposes). Note: animals suspected of active hemorrhage due to ingestion of warfarin or other anticoagulant toxicosis should be evaluated with prothrombin time (PT) or assessment of proteins inhibited by vitamin K absence/antagonism (PIVKA), because turnaround time to warfarin assay results is typically long, and it is less widely available.

SYNONYM

- First-generation compounds: warfarin, indanedione-containing rodenticides
- Second-generation compounds: cou-marin-based generics (brodifacoum, difenacoum, bromadiolone) and the indanedione, diphacinone

TYPICAL NORMAL RANGE

Consult laboratory for reference range and for inclusion of both first- and second-generation compounds in test panel.

PHYSIOLOGY

Well- but slowly-absorbed following oral administration. Peak plasma levels in 6-12 hours. Most is plasma protein bound, but high concentrations in liver, spleen, kidney. Metabolism occurs in the liver. Elimination rate depends on compound, amount ingested; may accumulate if small amounts ingested over several days. Warfarin half-life in dog plasma is 14.5 hours; the half-life of diphacinone is suspected to be days. Brodifacoum is assumed to be similar or longer than that of diphacinone. The differences in residual half-lives have important therapeutic implications. Compounds interfere with coagulation by decreasing coagulation factors II, VII, IX, and X (competitive inhibition of vitamin K epoxide-reductase).

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Ingestion of compounds or animals that have consumed compounds. Relay toxicosis (incurred from consumption of prey [e.g., rodents] that have eaten warfarin) rarely occurs with second-generation anticoagulants other than diphacinone.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Remove source; administer vitamin K; whole blood transfusion.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS: Oxyphenbutazone, phenylbutazone, diphenylhydantoin, sulfonamides, and corticosteroids increase toxicity.

SPECIMEN: Chemical detection of specific anticoagulants in vomitus or baits. Liver tissue (frozen) for postmortem diagnosis. Unclotted blood, stomach contents, intestinal content, feces, spleen, and kidney should also be submitted.

RELATIVE COST: $$ (Send-out test for most reference laboratories; additional fees may apply.)

PEARLS

- Conditions enhancing susceptibility are high dietary fat (fatty acids displace the plasma protein-bound anticoagulant), prolonged oral antibiotic therapy, biliary obstruction, liver disease, hypoalbuminemia (warfarin is highly plasma protein bound), renal disease.
- Most veterinary reference laboratories do not do rodenticide testing. When testing is offered, results are usually not available for several days. Testing is typically confirmatory rather than proactively diagnostic.

AUTHOR: SHERRY J. MORGAN

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Zinc, Serum Level

DEFINITION

Zinc is an essential trace mineral that serves as a cofactor for enzymes in many tissues. It is important in regulation of the immune response, modulation of keratogenesis, wound healing, maintenance of normal reproductive function, and acuity of taste and smell.

TYPICAL TOXIC RANGE

Dogs, cats: <2 mg/mL (serum); <30-70 ppm, wet weight (liver). Check with laboratory for values considered diagnostic of toxicity.

PHYSIOLOGY

Source is dietary. Zinc is absorbed via the intestine, metabolized in the liver, and exported to peripheral tissues.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH LEVELS: Ingestion of excessive levels of zinc phosphide (either as powder, bait). Toxicity may also result from relay toxicosis associated with eating tissues of zinc phosphide-poisoned animals or ingestion of U.S. pennies minted after 1983.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH: Vomitus/gastric lavage (phosphine gas) is actually the preferred method of diagnosis in case of toxicity. Caution: phosphine gas (faint garlic or rotten fish odor; gas is liberated in the breath of animals with zinc phosphide intoxication, such as during gastric lavage) is a public health hazard and may cause severe/permanent respiratory injury to veterinary personnel or bystanders.

CAUSES OF ABNORMALLY LOW LEVELS: Malnutrition, malabsorption, animals on total parenteral nutrition

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS LOW: Skin biopsy if zinc-deficient dermatosis is suspected

IMPORTANT INTERSPECIES DIFFERENCES: Zinc-responsive dermatosis occurs in dogs. Familial form (Alaskan malamutes, Siberian huskies) and from affecting puppies fed zinc-deficient or oversupplemented diets. Lethal acrodermatitis is a rare inherited disorder of bull terriers that does not respond to zinc supplementation and is invariably fatal.

SPECIMEN AND PROCESSING CONSIDERATIONS

SPECIMEN

- Serum: because of the use of zinc stearate to coat rubber, serum samples must be drawn in all-glass or all-plastic syringes, and all-glass or all-plastic vials must be used for transport.
- Toxicity: test for toxic metabolite, phosphine gas. Submit frozen vomitus or gastric lavage in airtight containers.

RELATIVE COST: $$$

PEARLS

- In zinc phosphide toxicity, there may be a characteristic acetylene odor to the gastric contents; may be bloody.
- Zinc phosphide causes emesis in dogs and cats, so fatal intoxication is not frequent. Ingestion with a meal enhances toxicity by promoting conversion to zinc phosphine gas.
- Ingested pennies may be detected radiographically.

AUTHOR: SHERRY J. MORGAN

Pricing Information

$: <$20
$$: $21-75
$$$: $76-150
$$$$: >$150

Introduction to Laboratory Tests

Overview

This section regroups over 150 diagnostic tests that are used widely in small-animal practice. Information is drawn from both basic science and applied clinical medicine to provide a brief summary of each test. The facts and interpretations necessary to understand these tests under most circumstances are included, and additional detail can be found in specific references (see below).

Each topic is organized in a consistent manner. Sections for each entry include:

DEFINITION

a concise explanation of the nature of the test.

SYNONYMS

when applicable, other names by which the test is known.

TYPICAL NORMAL RANGE

a broad reference interval for normal results. Exact ranges are generally laboratory specific and may even be population or test kit specific. The ranges published here should be considered only an approximate guide.

PHYSIOLOGY

a brief description of the natural processes underlying the analyte being measured and specific application of the test.

CLINICAL APPLICATIONS

CAUSES OF ABNORMALLY HIGH/ LOW LEVELS:

the principal differential diagnoses for values falling outside the normal range.

NEXT DIAGNOSTIC STEP TO CONSIDER IF LEVELS HIGH/LOW:

recommended tests or procedures that typically are indicated if the current test is not the definitive test of choice.

IMPORTANT INTERSPECIES DIFFERENCES:

relevant physiologic or test-associated variation.

SPECIMEN AND PROCESSING CONSIDERATIONS

DRUG EFFECTS ON LEVELS:

alterations in test results that may be expected when a patient is receiving certain medications.

LAB ARTIFACTS THAT MAY INTERFERE:

extraneous factors that may produce a false reading and should be considered by the clinician when interpreting test results.

SPECIMEN:

the sample required to perform the test.

RELATIVE COST:

a price scale is included to provide a relative indication of test costs. Necessarily, the exact cost will vary from one laboratory or institution to another and one geographic region to another, and changes over time will alter these values within any laboratory. Nevertheless, by comparing tests to each other according to their costs, the price scale can provide a relative sense of the expense

associated with each test. The scale used is based on costs of tests submitted to a full-service reference laboratory in North America in 2009, as follows:

$: <$20
$$: $21-75
$$$: $76-150
$$$: >$150

PEARLS:

tips, important reminders, or explanations generally acquired through experience. These are clinically important but otherwise often escape publication.

SUGGESTED ADDITIONAL READING

TEXTBOOKS

Allison RW, Meinkoth JH, editors: Clinical pathology and diagnostic techniques, Vet Clin North Am Small Anim Pract 37:203–402, 2007.

Feldman EC, Nelson RW: Canine and feline endocrinology and reproduction, ed 3, St Louis, 2004, Saunders.

Greene CE, editor: Infectious diseases of the dog and cat, ed 3, St Louis, 2006, Saunders.

Latimer KS, Mahaffey EA, Prasse KW, editors: Duncan and Prasse's veterinary laboratory medicine clinical pathology, ed 4, Ames, IA, 2003, Iowa State University Press.

Meyer DJ, Harvey JW, editors: Veterinary laboratory medicine: interpretation and diagnosis, ed 3, St Louis, 2004, Saunders.

Stockham SL, Scott MA, editors: Fundamentals of veterinary clinical pathology, ed 2, Ames, IA, 2008, Blackwell.

Thrall MA, Baker DC, Campbell TW, et al: Veterinary hematology and clinical chemistry, Baltimore, 2004, Lippincott Williams & Wilkins.

JOURNALS

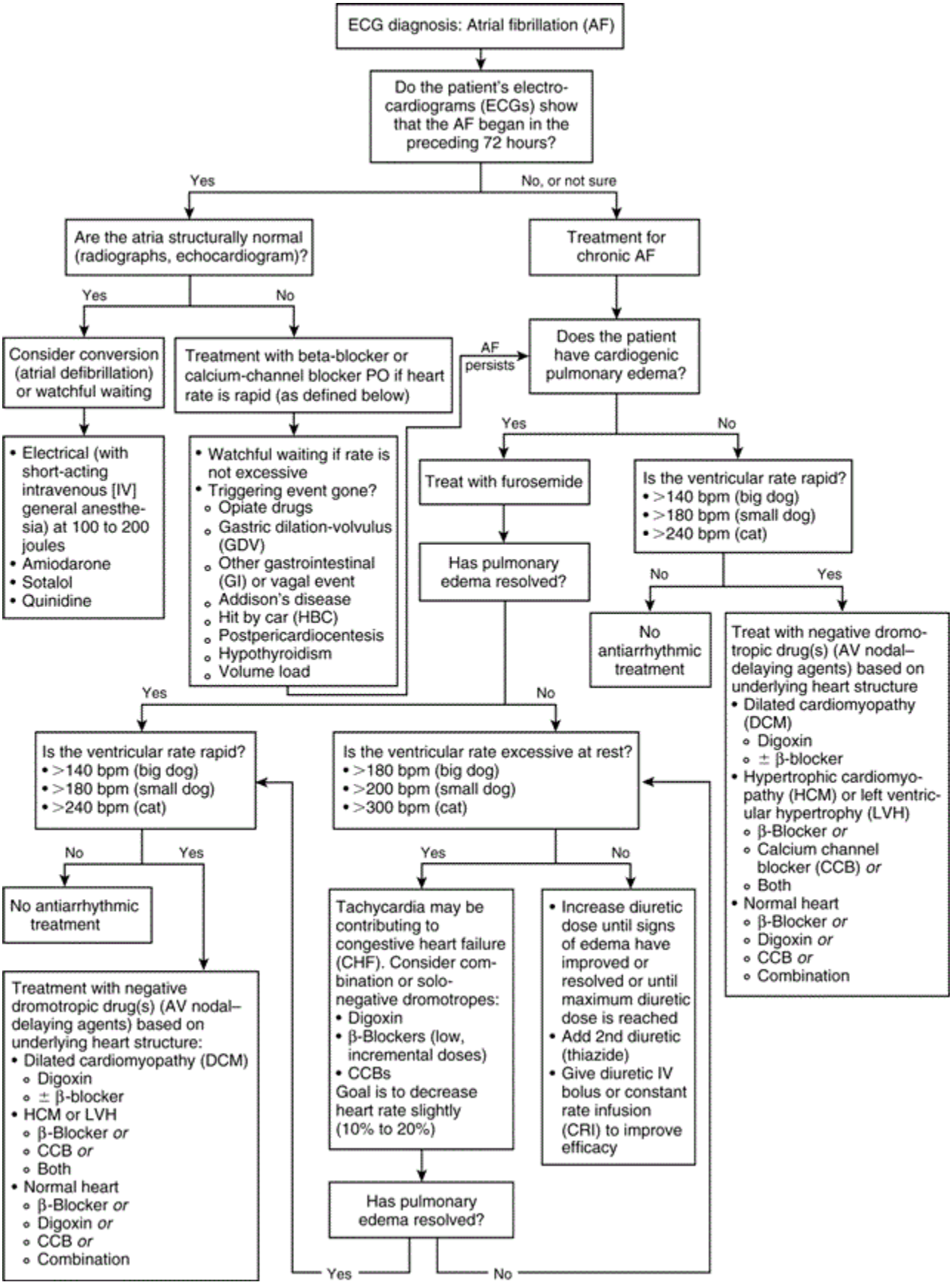
Journal of the American Animal Hospital Association

Journal of the American Veterinary Medical Association

Journal of Veterinary Diagnostic Investigation

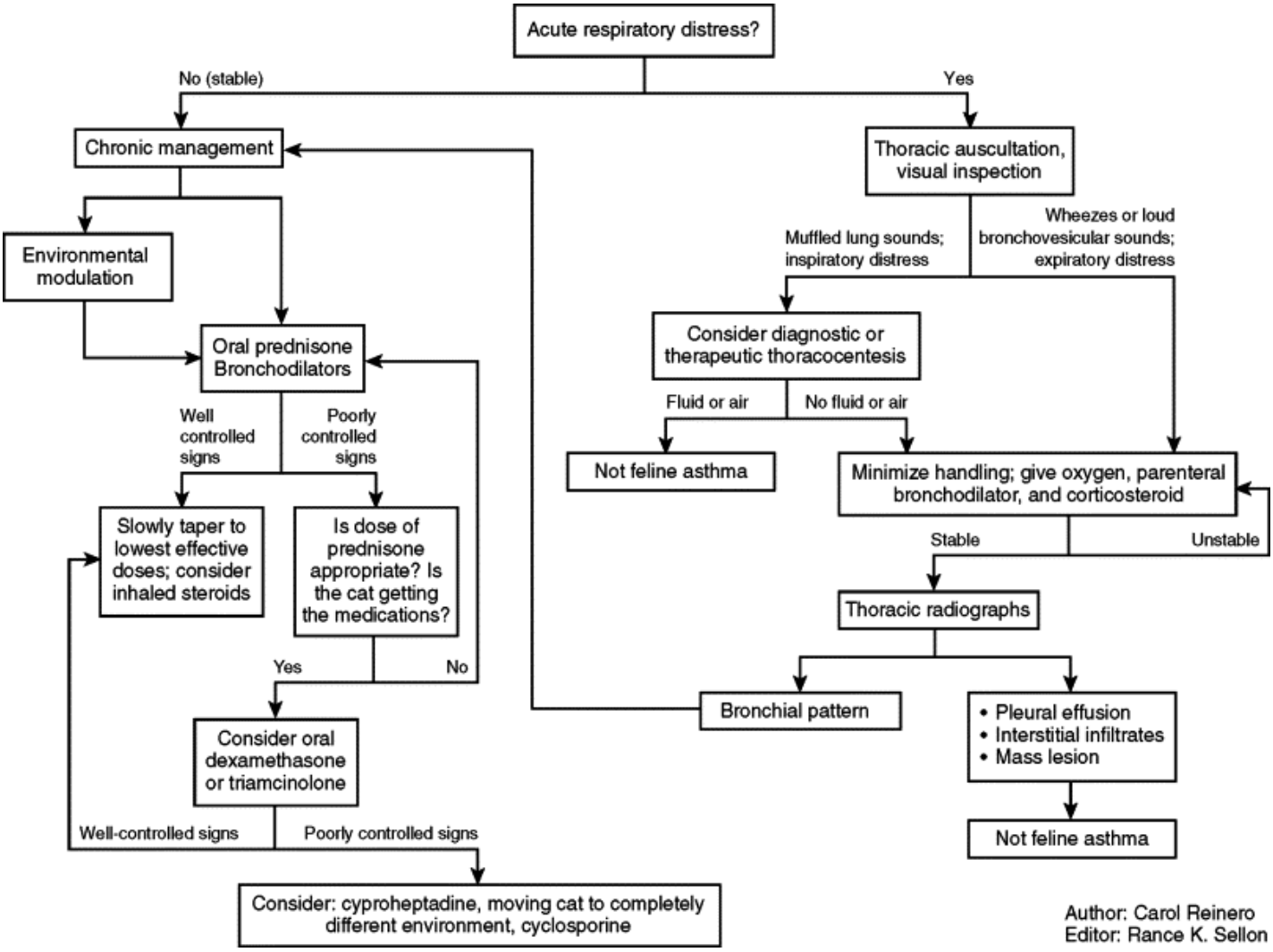
Journal of Veterinary Internal Medicine Veterinary Clinical Pathology

Atrial Fibrillation



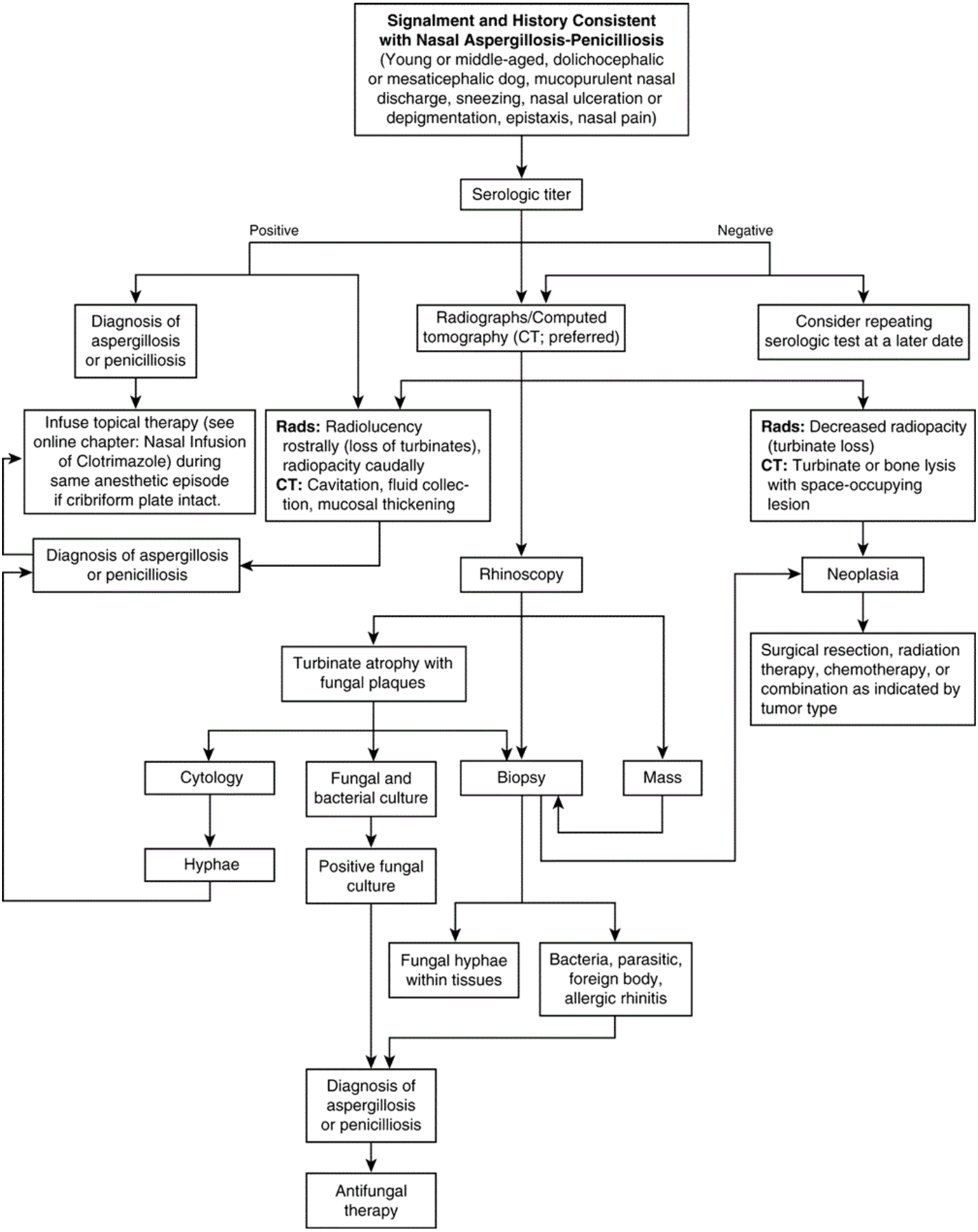
From Ettinger SJ, Feldman EC: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, WB Saunders.

Asthma



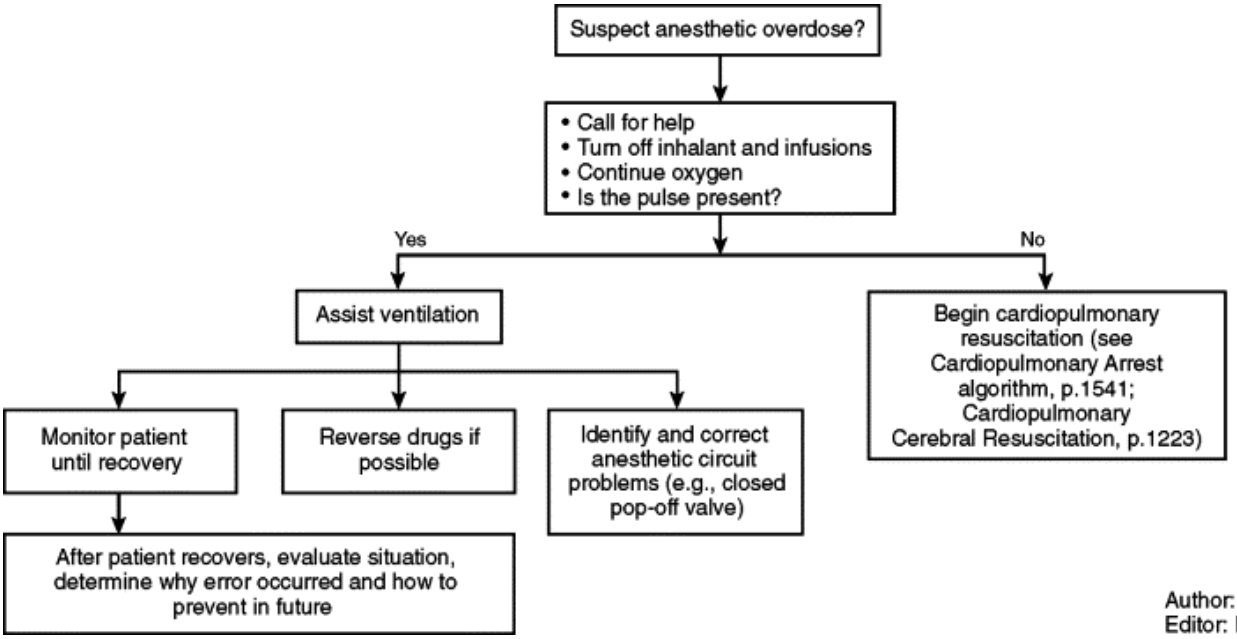
Author: Carol Reinero
Editor: Rance K. Sellon

Aspergillosis (Nasal)



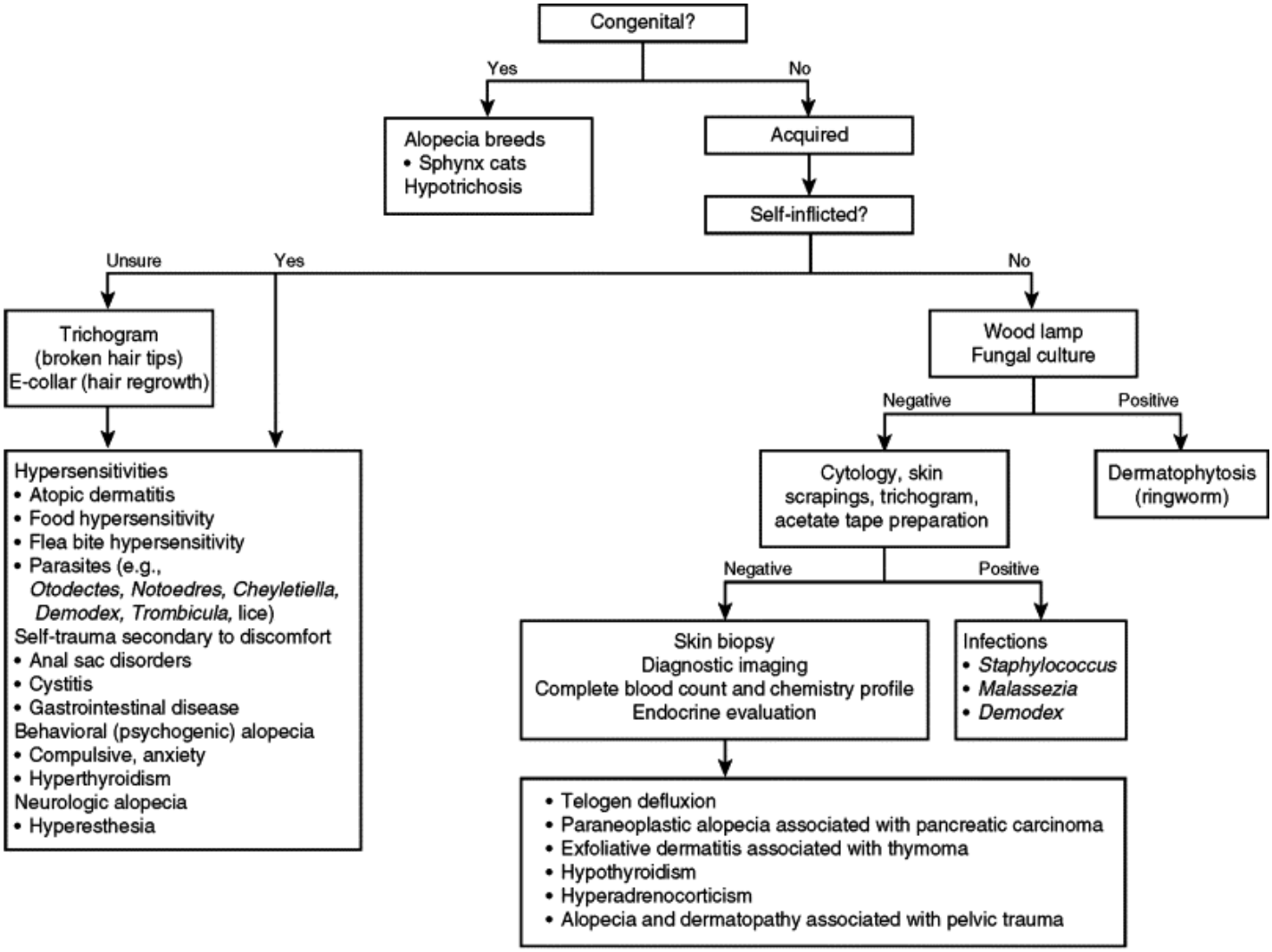
Modified from Greene CE: Infectious diseases of the dog and cat, ed 3, St Louis, 2006, WB Saunders.

Anesthetic Complications



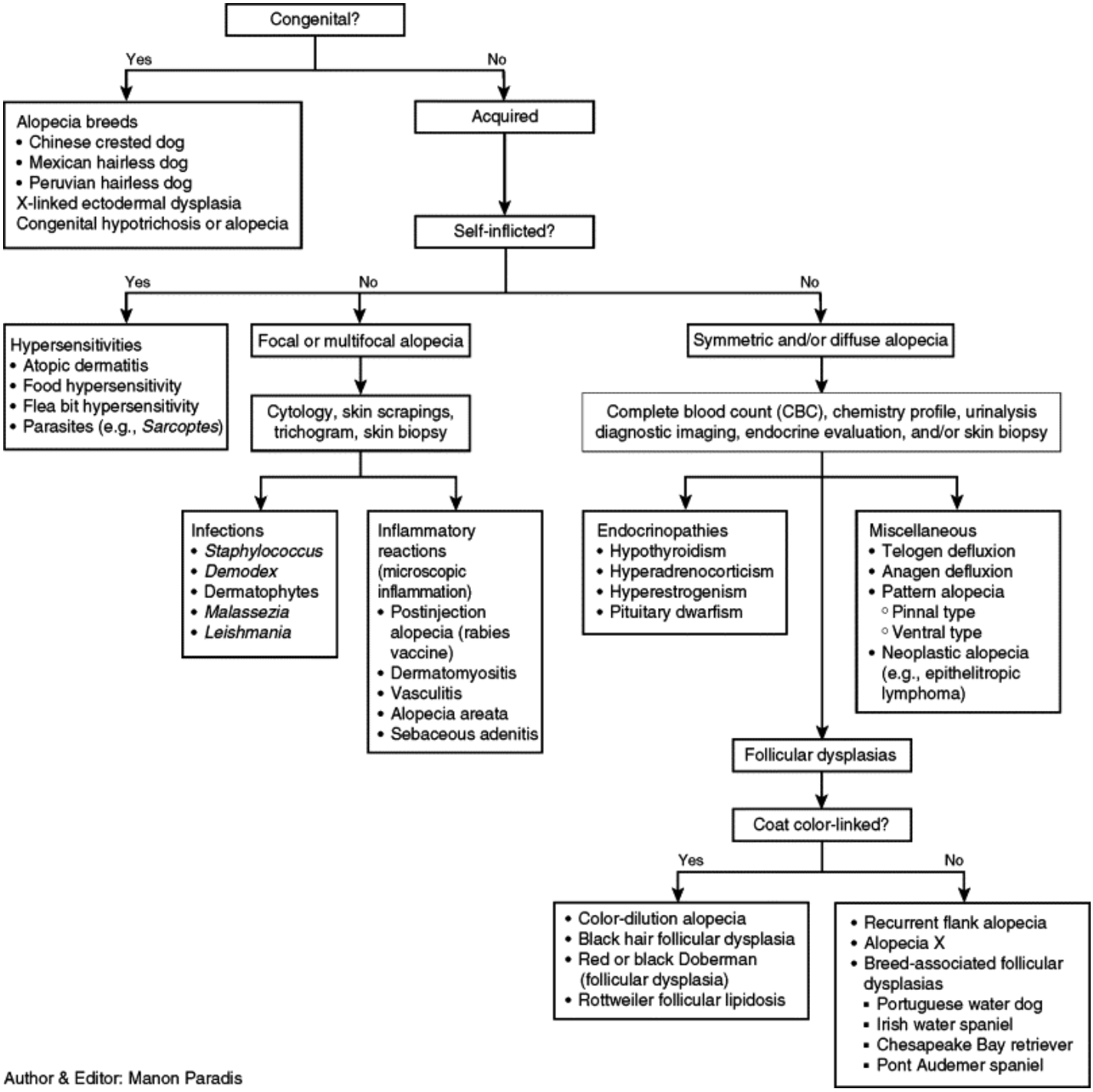
Author: Scott P. Shaw
Editor: Elizabeth Rozanski

Alopecia, Feline



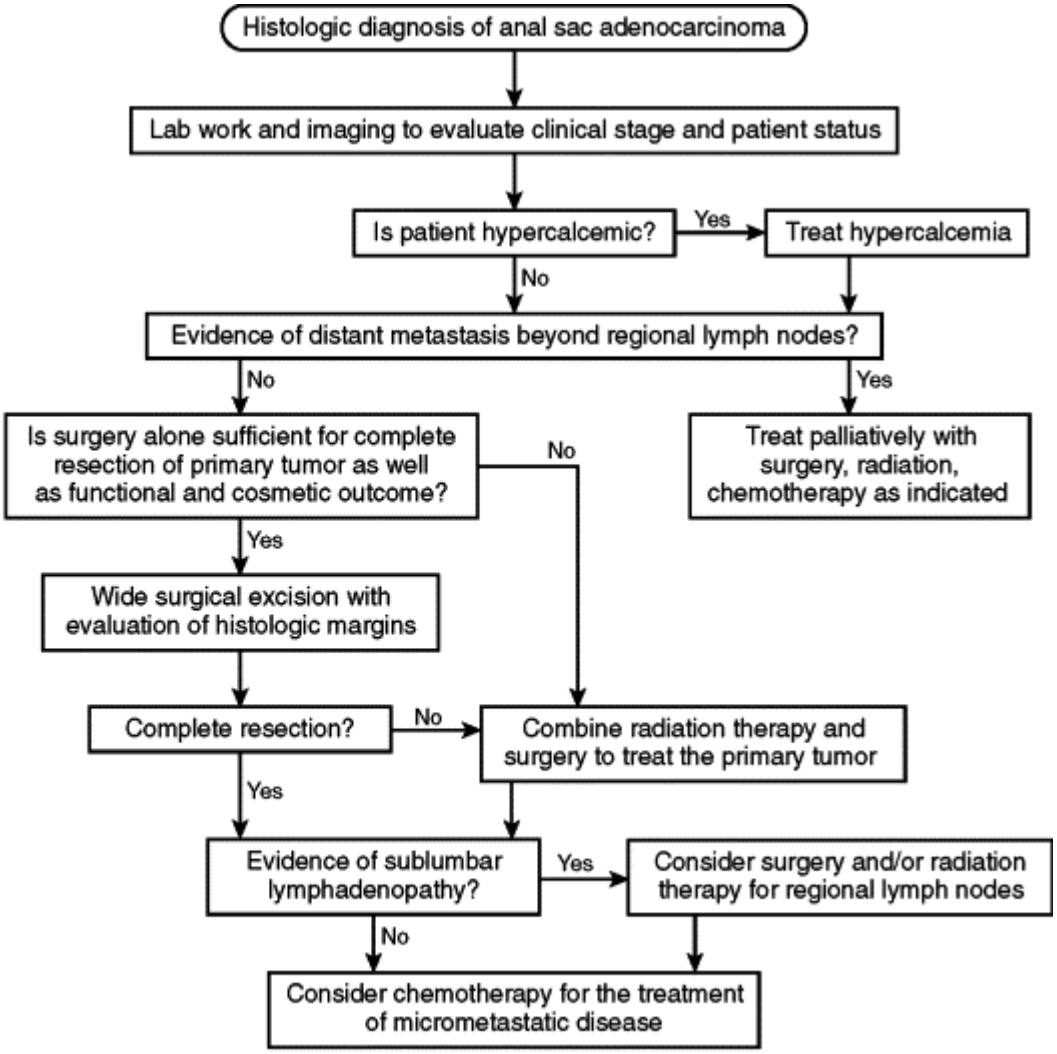
Author & Editor: Manon Paradis

Alopecia, Canine



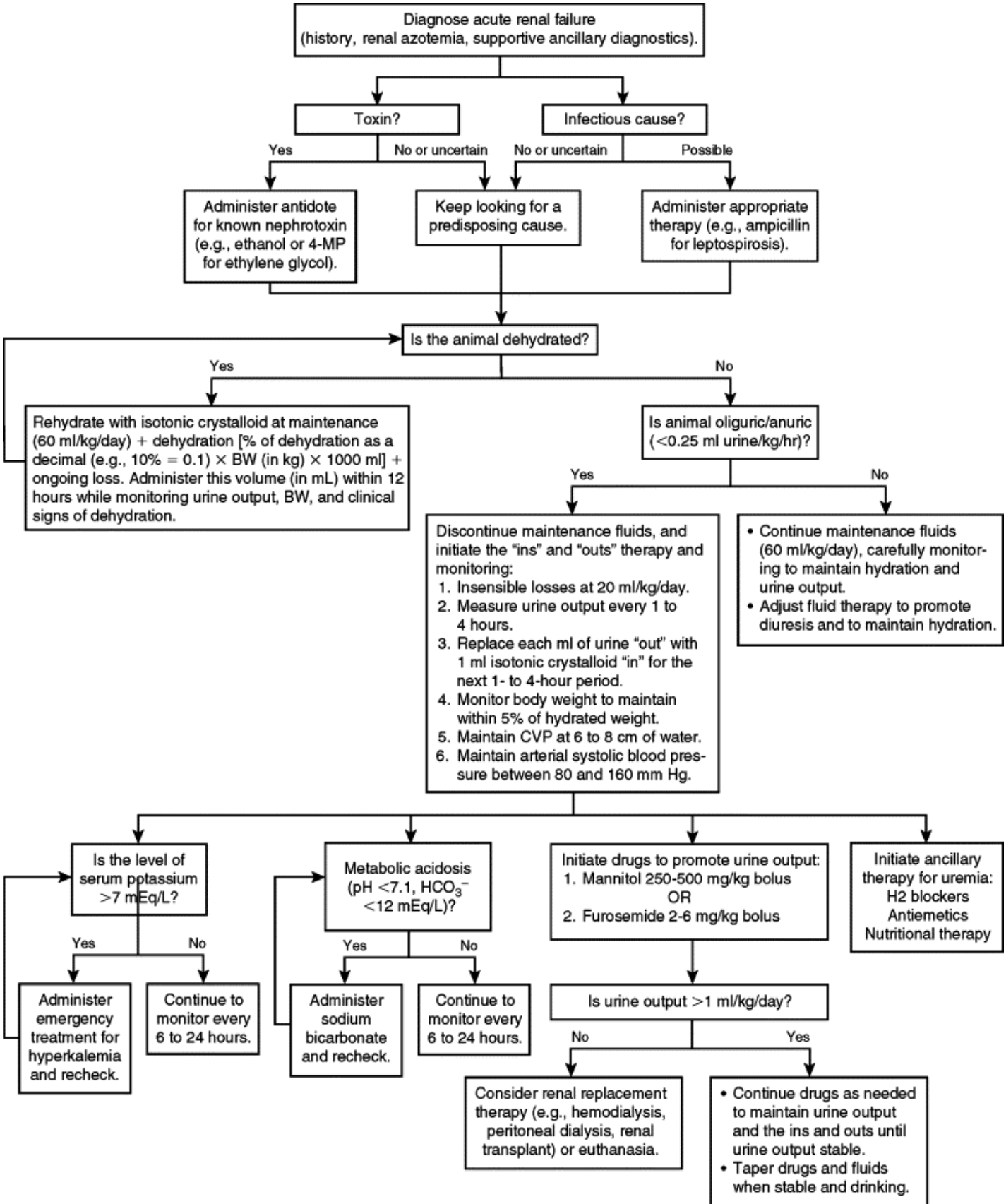
Author & Editor: Manon Paradis

Adenocarcinoma of the Anal Sacs



Author: Elizabeth A. McNiel
Editor: Kenneth M. Rassnick

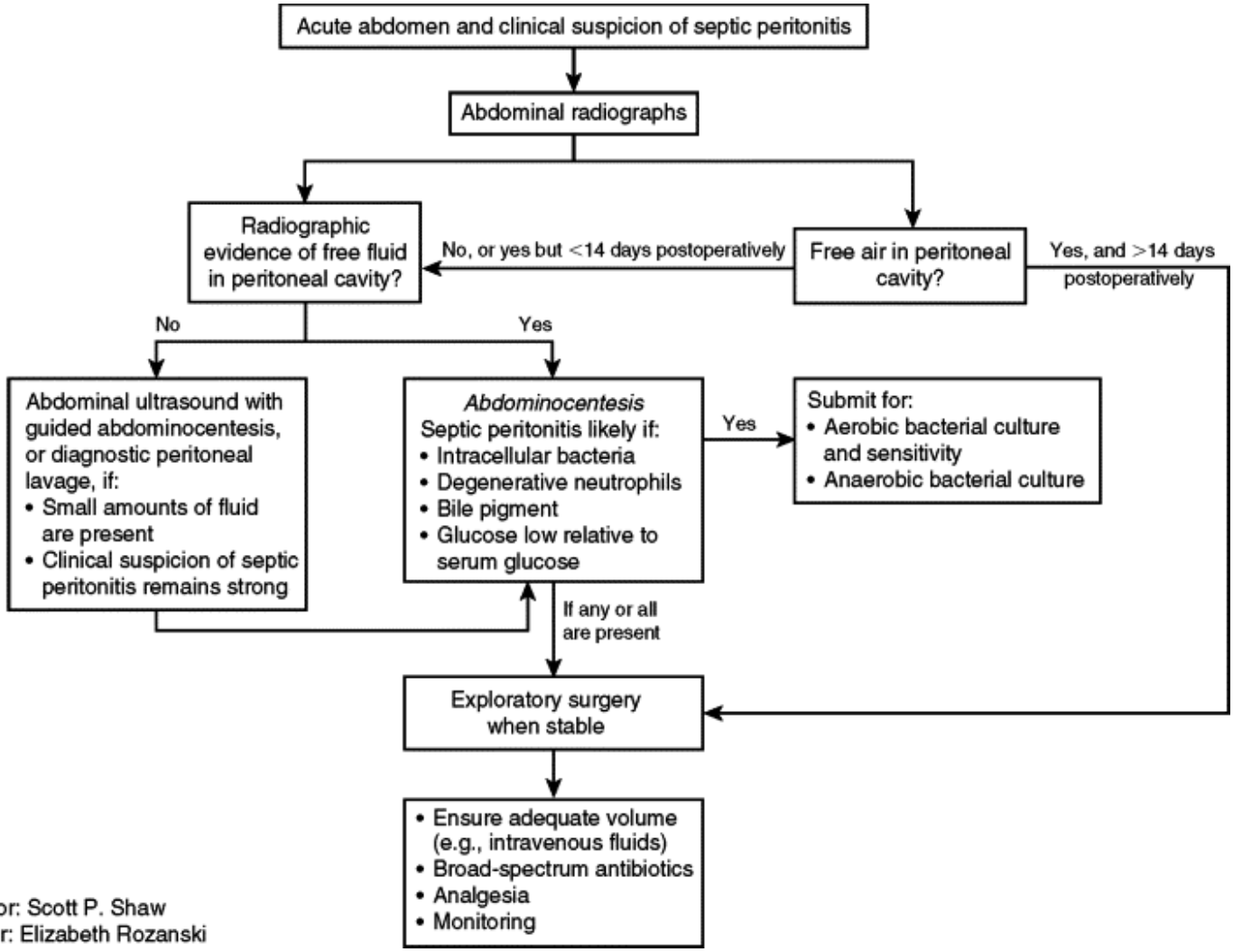
Acute Renal Failure



4-MP, 4-methylpyrazole; *BW,* body weight; *CVP,* central venous pressure.

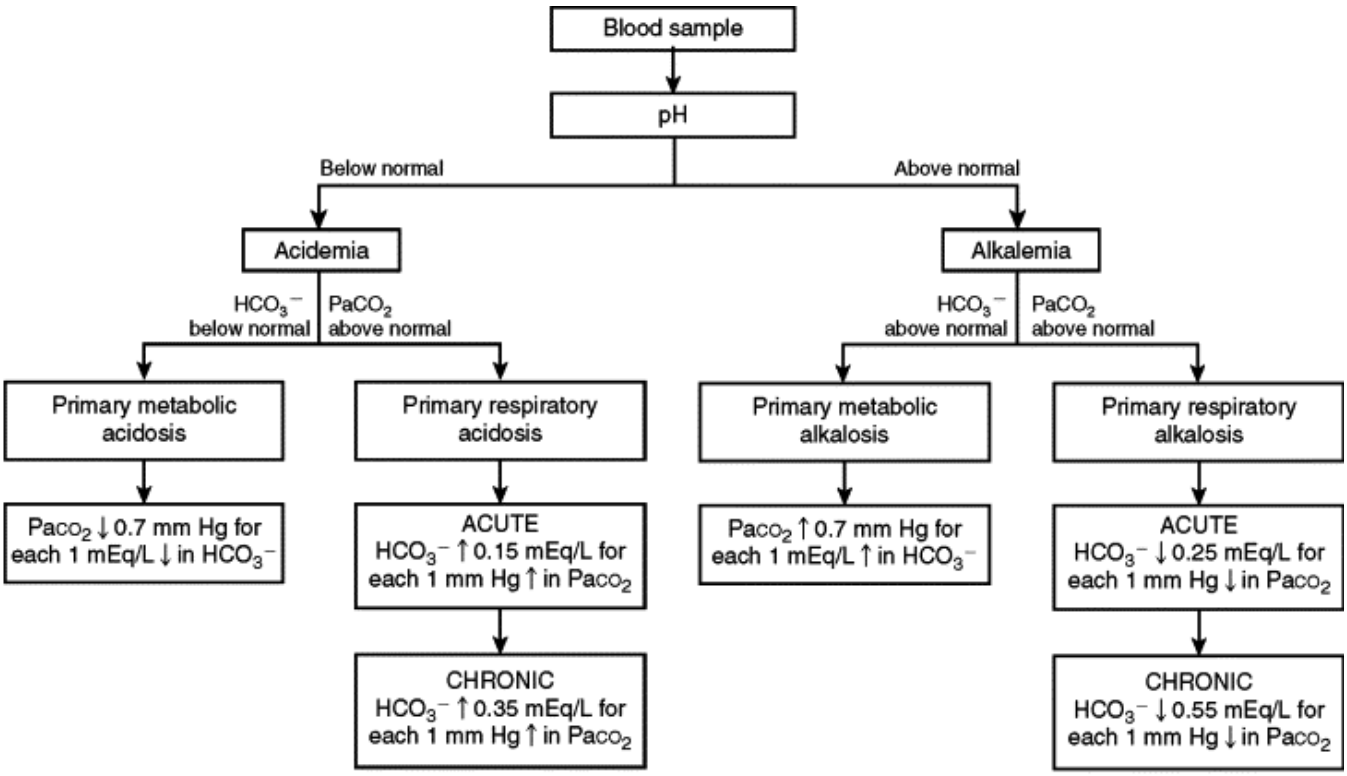
Author: Marie E. Kerl
Editor: Leah A. Cohn

Acute Abdomen



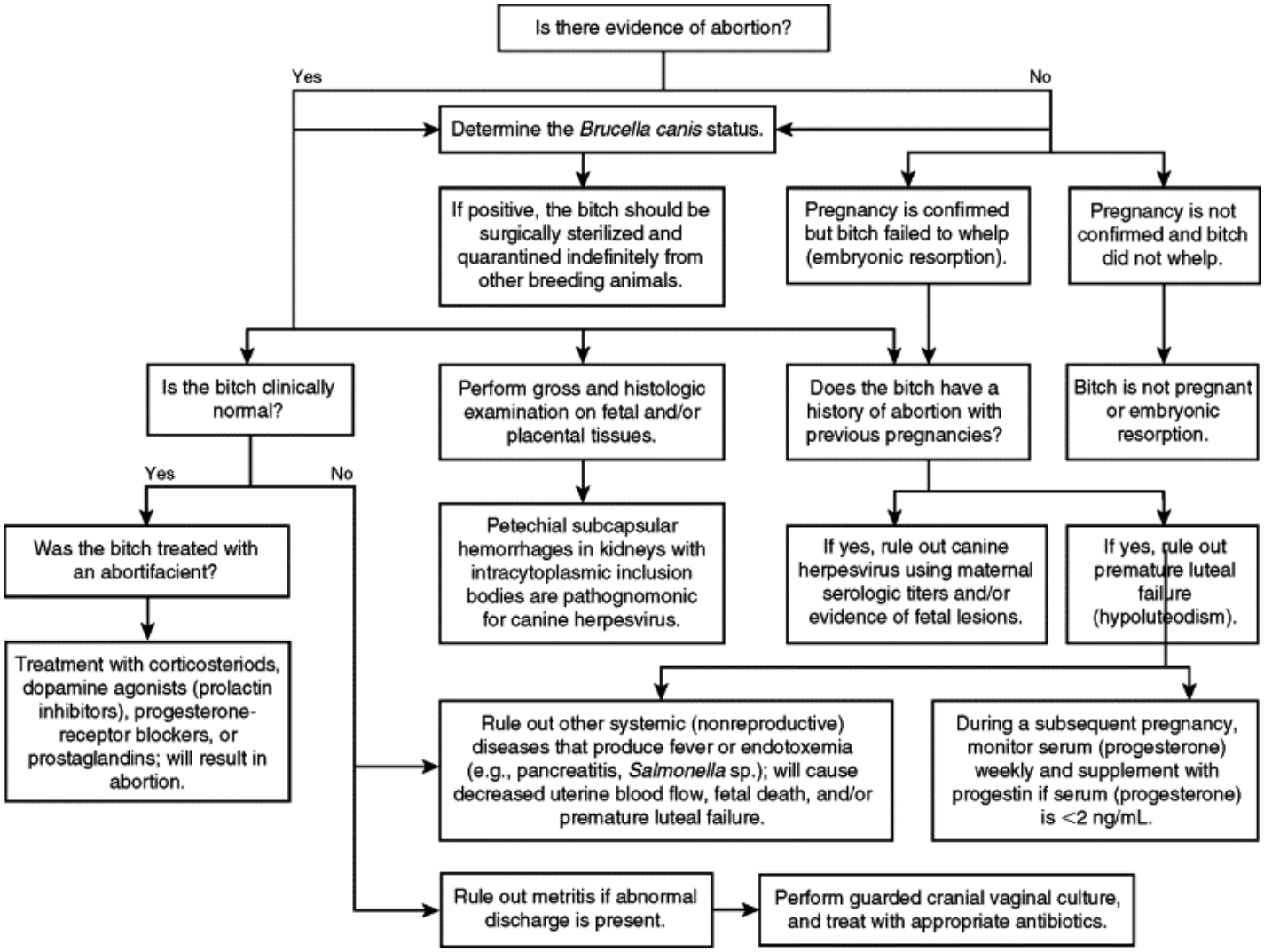
Author: Scott P. Shaw
Editor: Elizabeth Rozanski

Acid-Base Disorders



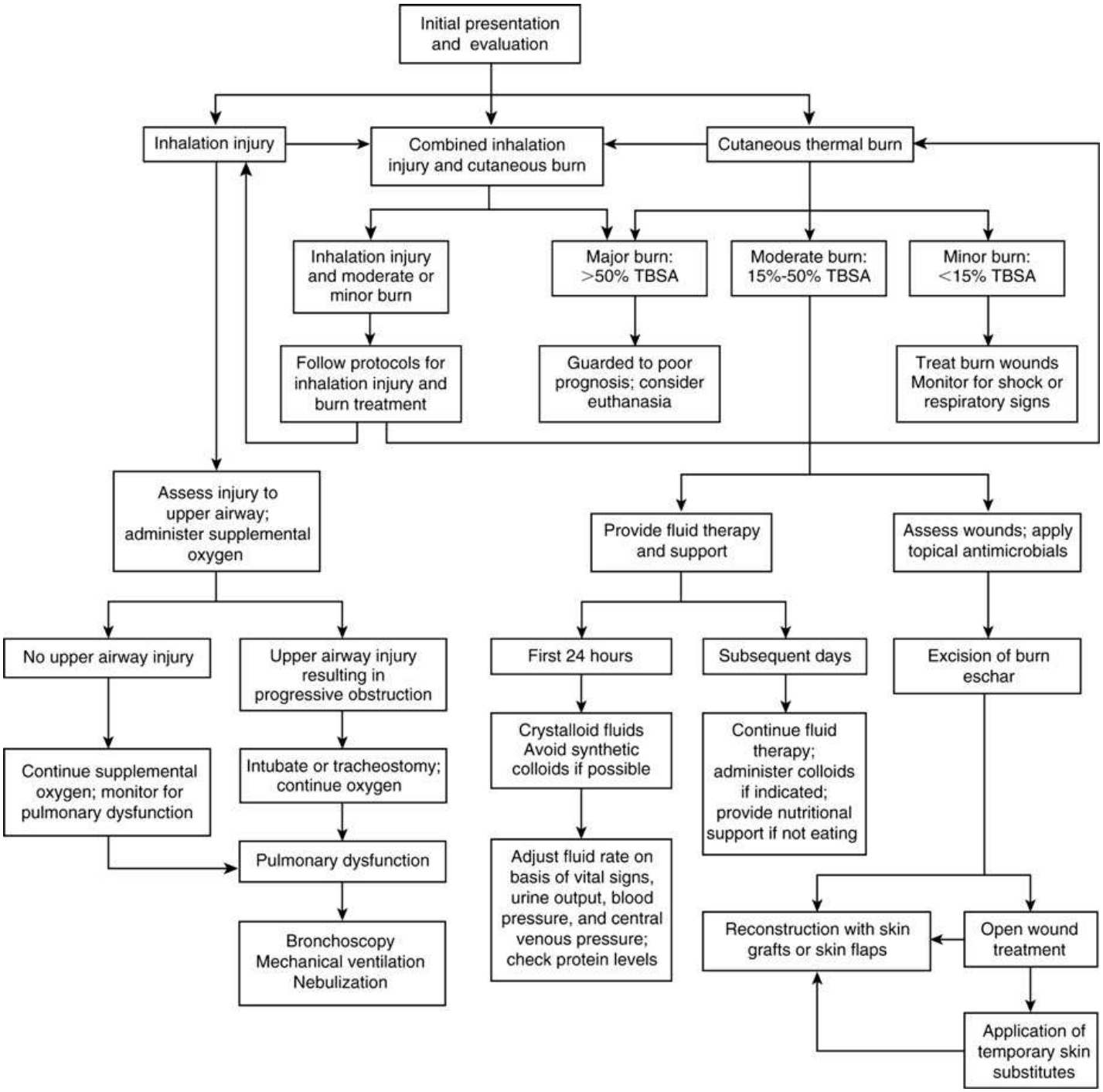
From Slatter DH: Textbook of small animal surgery, ed 3, St Louis, 2003, WB Saunders.

Abortion: Diagnostic Approach to Abortion in the Dog



Author: Wenche Farstad
Editor: Michelle Kutzler

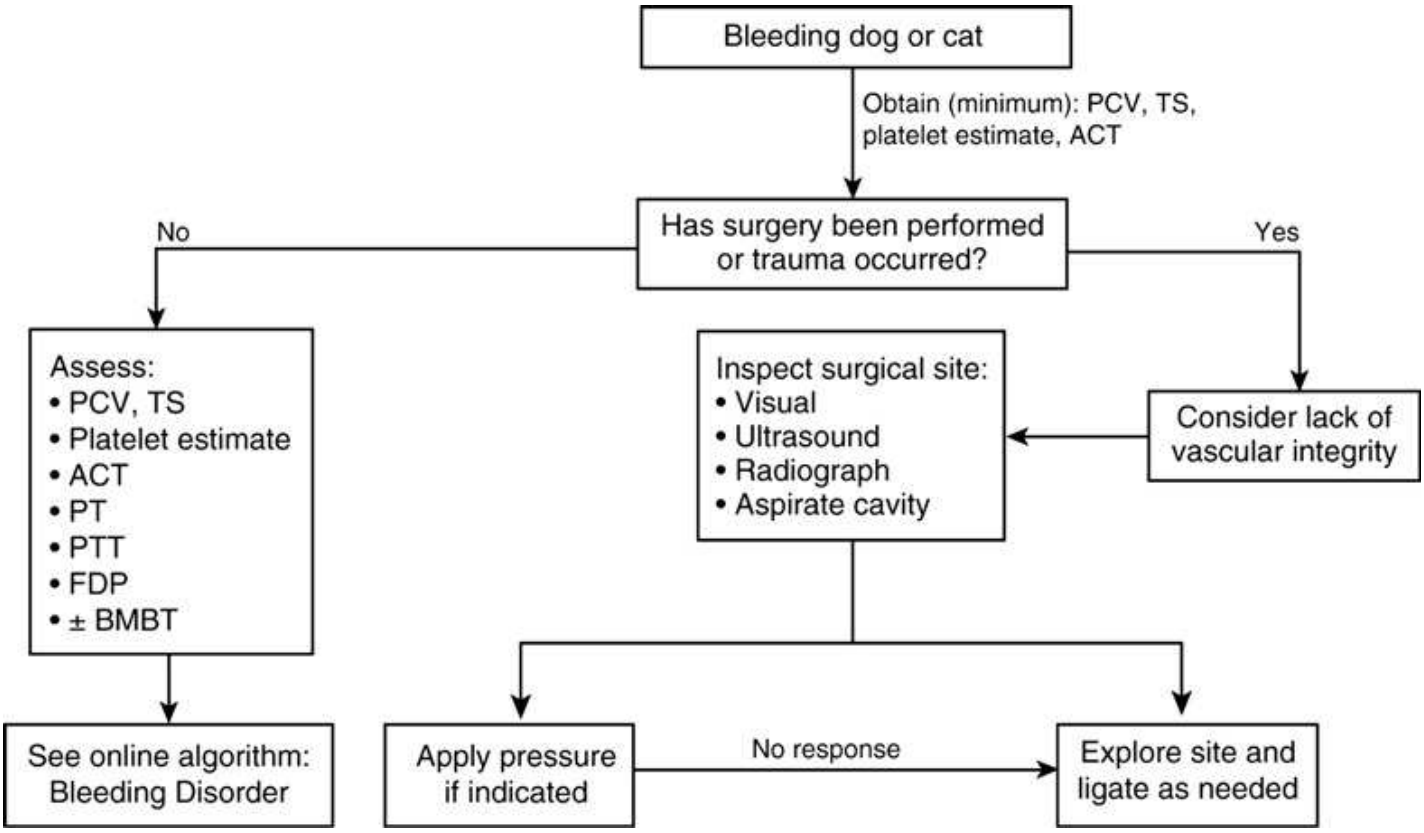
Burns and/or Smoke Inhalation



TBSA, Total body surface area.

Modified from Slatter DH: Textbook of small animal surgery, ed 3, St Louis, 2003, WB Saunders.

Bleeding Patient: Initial Approach

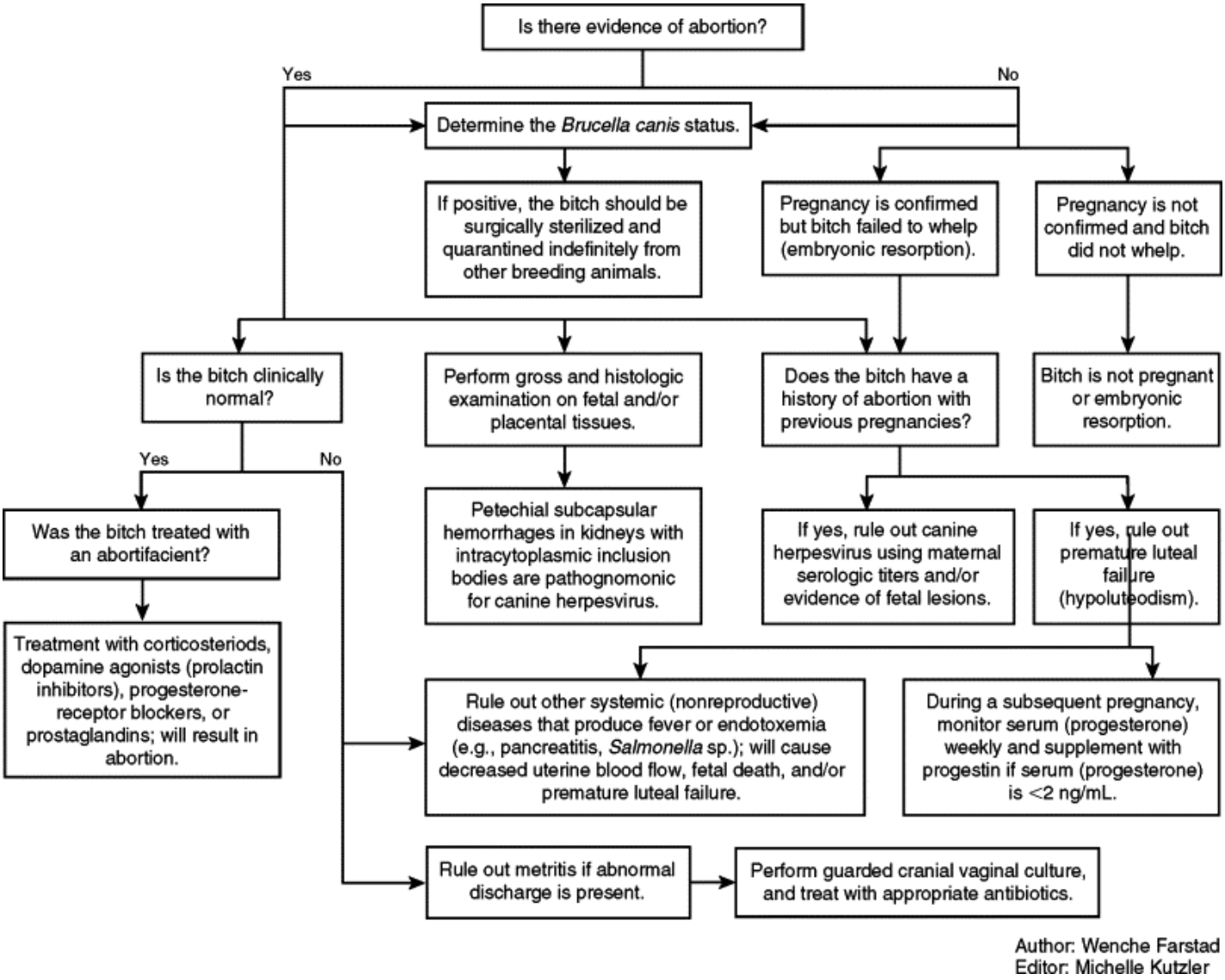


ACT, Activated clotting time; *BMBT,* buccal mucosal bleeding time; *FDP,* fibrin(ogen) degradation products;

PCV, packed cell volume; *PT,* prothrombin time; *PTT,* partial thromboplastin time; *TS,* total solids

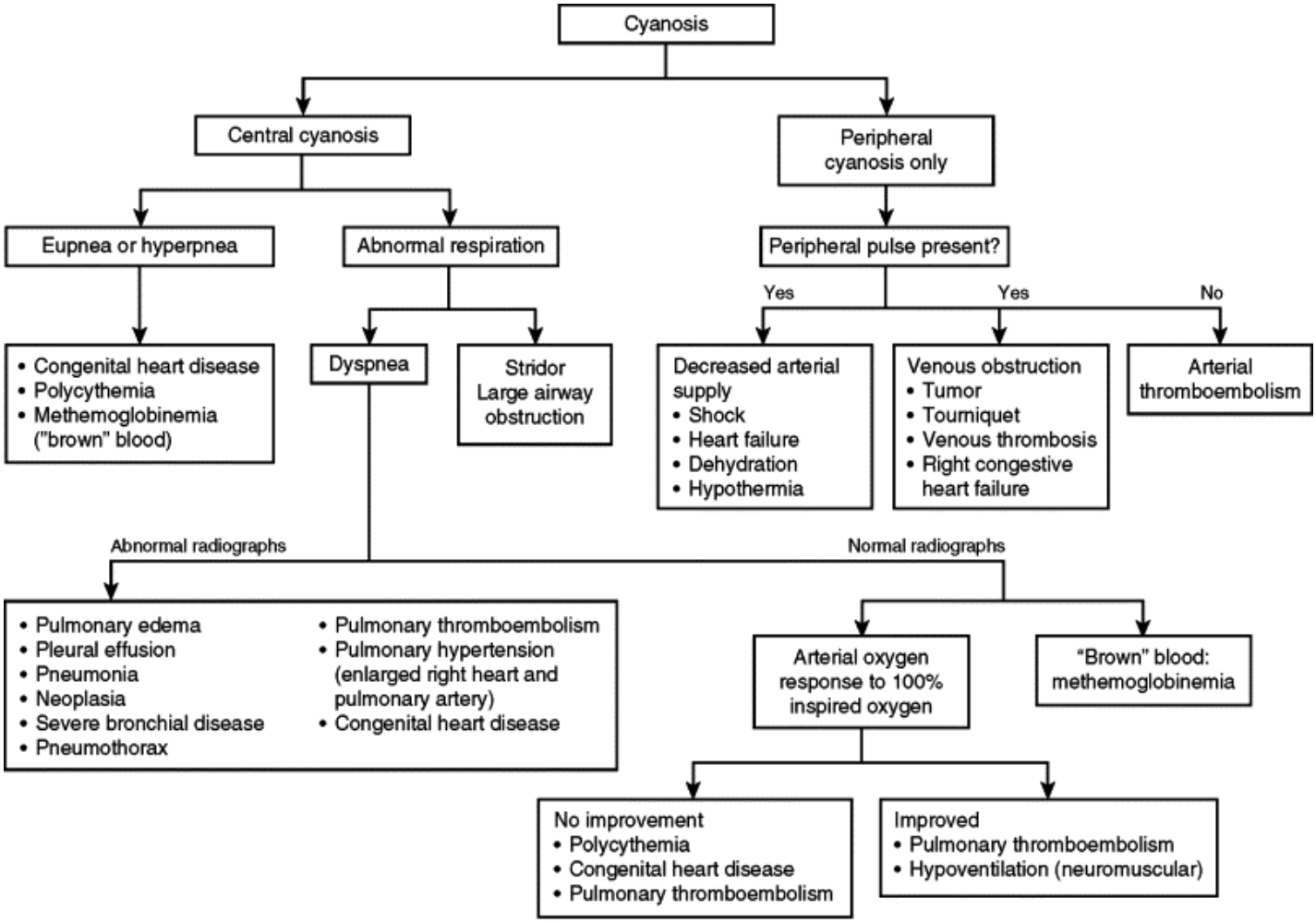
Modified from Slatter DH: Textbook of small animal surgery, ed 3, St Louis, 2003, WB Saunders.

Bleeding Disorder



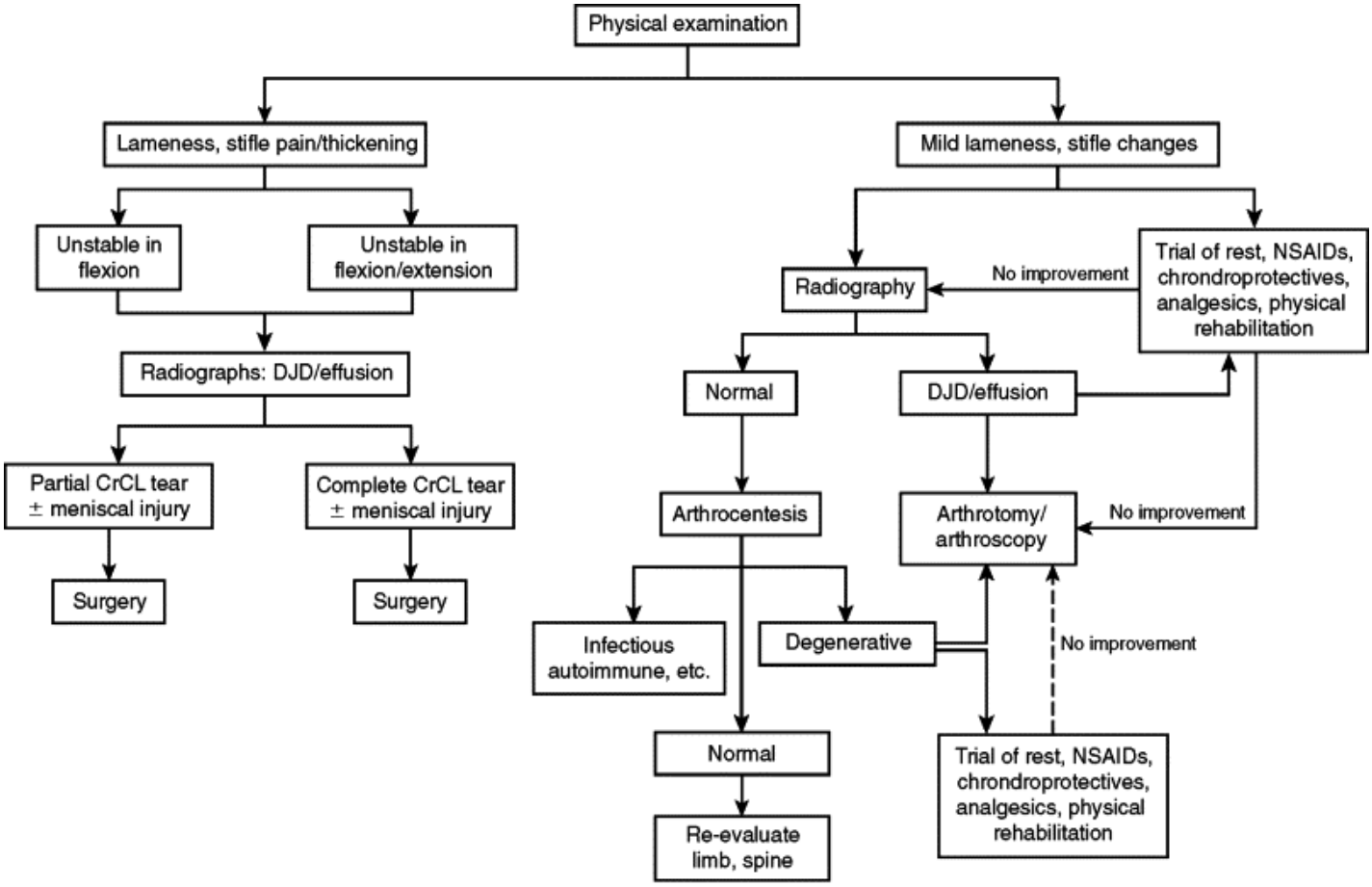
From Ettinger SJ, Feldman EC: Textbook of veterinary internal medicine, ed 7, St Louis, 2010, Elsevier.

Cyanosis



From Ettinger SJ, Feldman EC: Textbook of veterinary internal medicine, ed 7, St Louis, 2010, Elsevier.

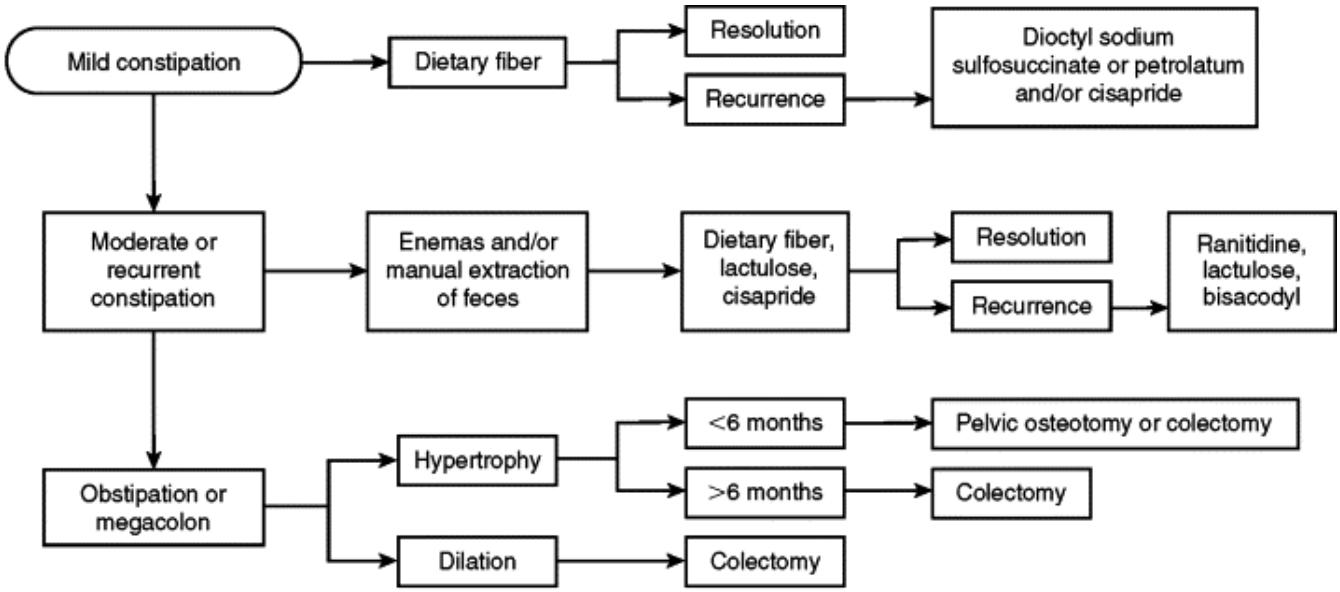
Cranial Cruciate Ligament Injury



NSAIDs, Nonsteroidal antiinflammatory drugs; *DJD,* degenerative joint disease, *CrCL,* cranial cruciate ligament.

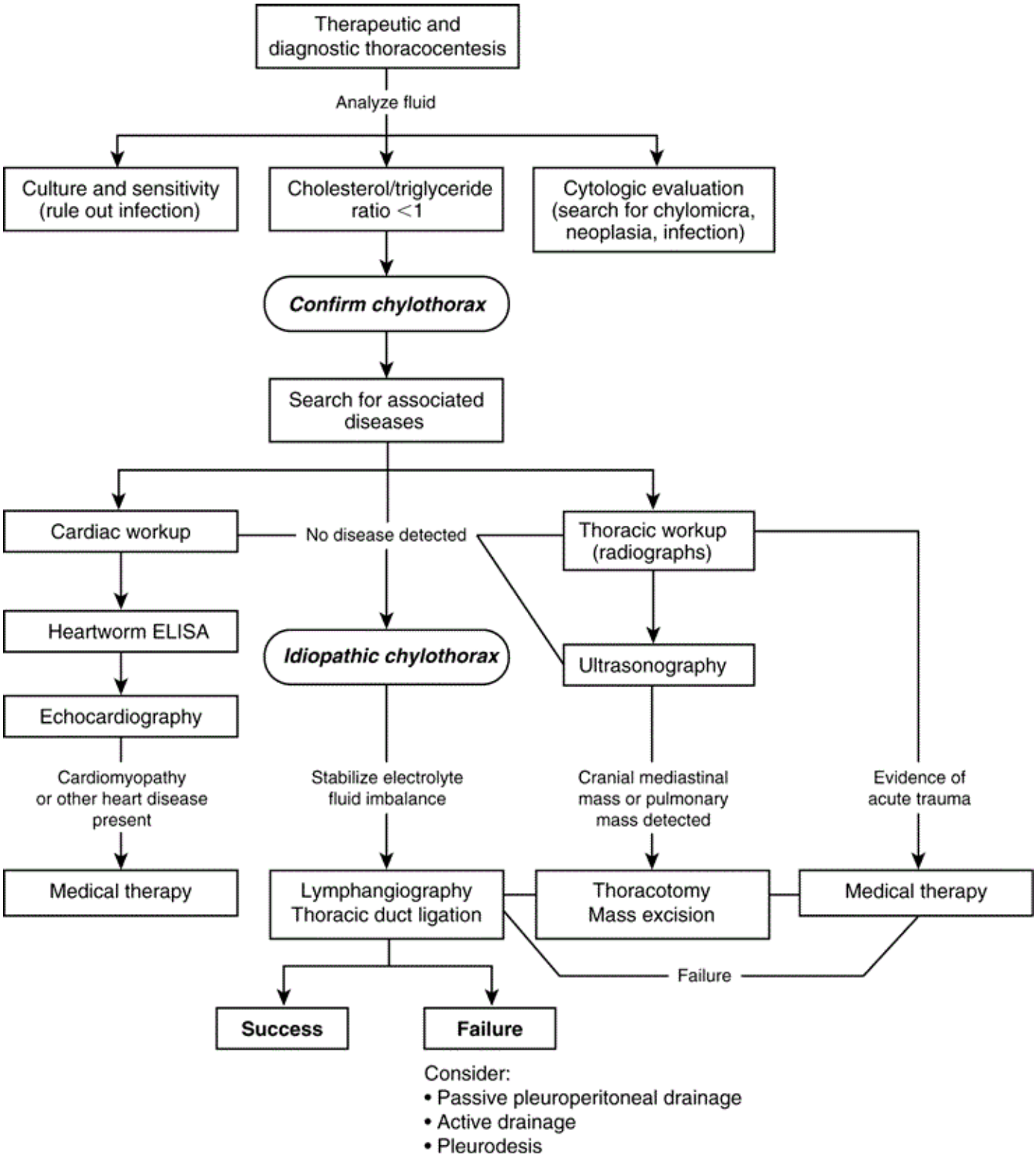
Author & Editor: Joseph Harari

Constipation, Obstipation, and Megacolon



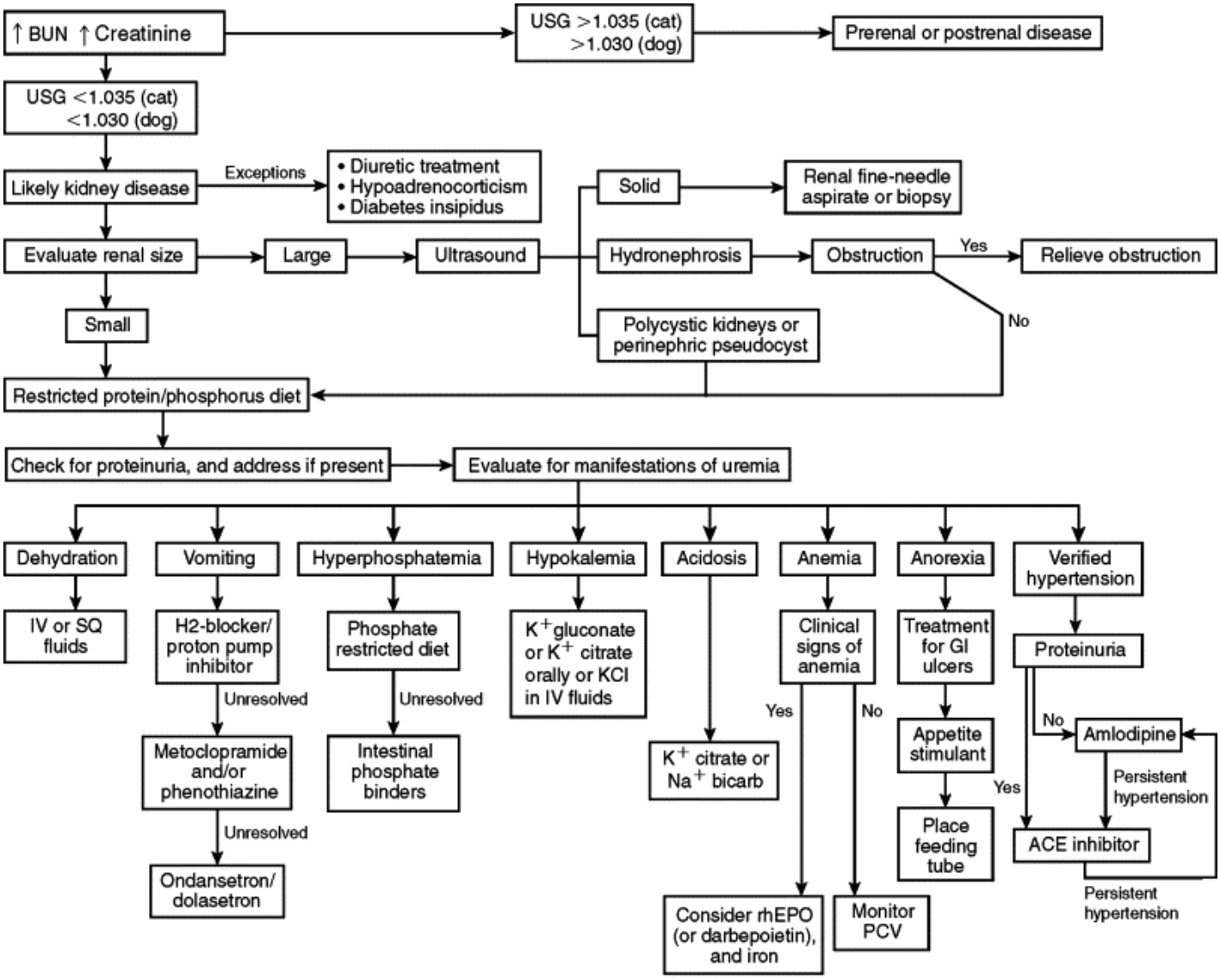
From Slatter DH: Textbook of small animal surgery, ed 3, St Louis, 2003, WB Saunders.

Chylothorax



From Bonagura JD: Kirk's current veterinary therapy XII, St Louis, 1995, WB Saunders.

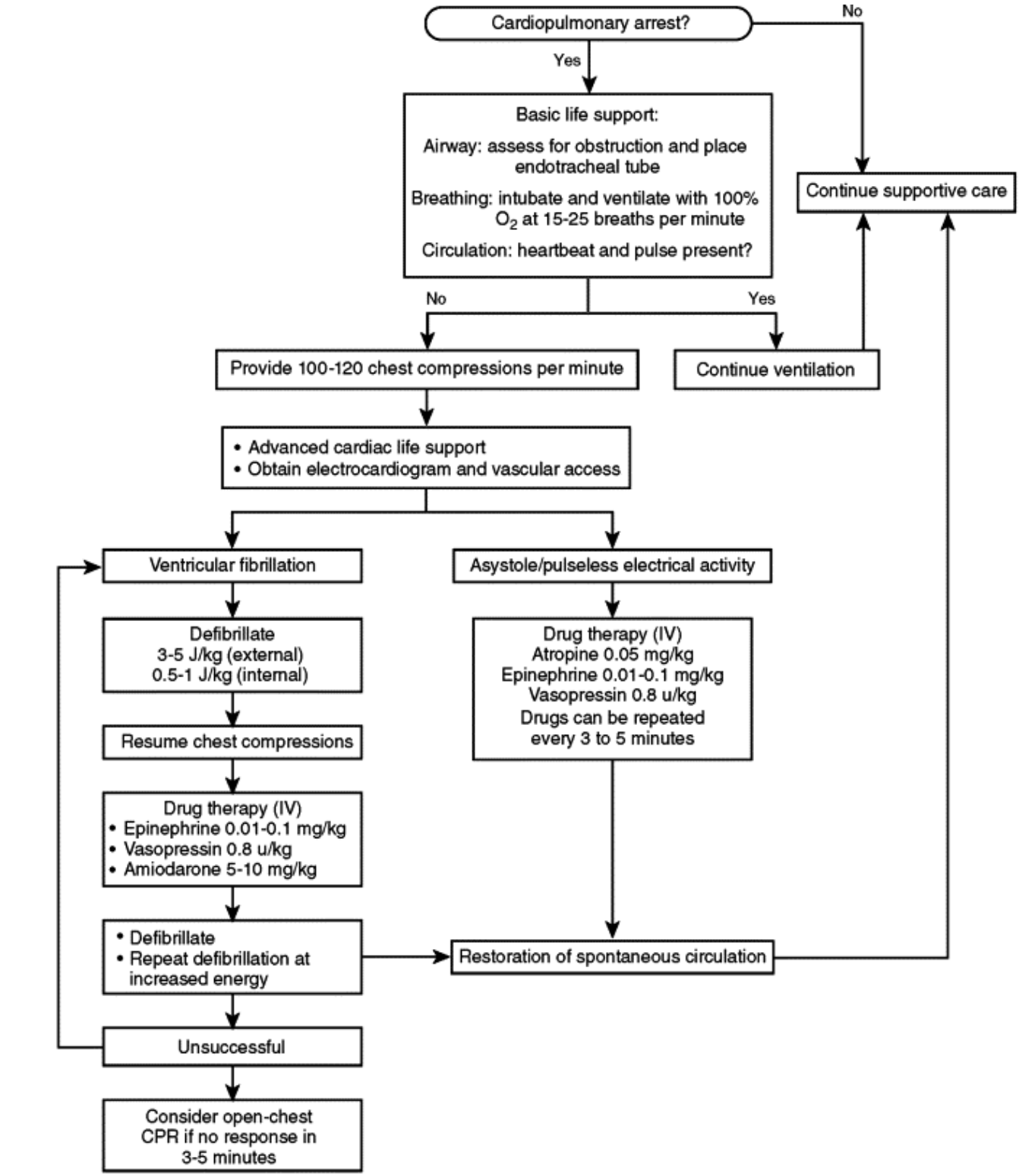
Chronic Kidney Disease: Management



ACE, Angiotensin-converting enzyme; *Bicarb,* bicarbonate; *BUN,* blood urea nitrogen; *GI,* gastrointestinal; *IV,* intravenous; *PCV,* packed cell volume; *rhEPO,* recombinant human erythropoietin; *SQ,* subcutaneous, *USG,* urine specific gravity.

Author: Cathy Langston
Editor: Leah A. Cohn

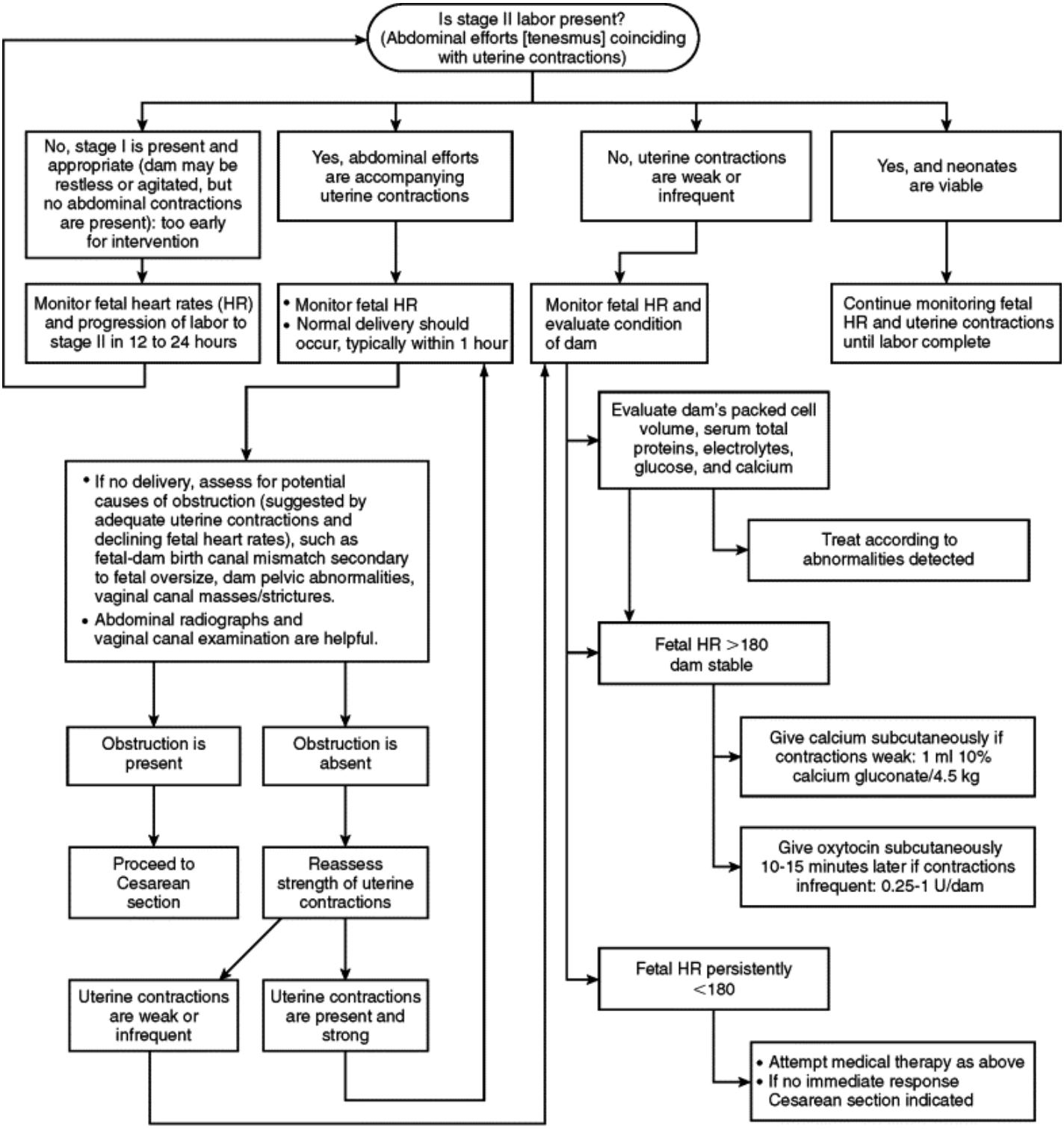
Cardiopulmonary Arrest



Author: Scott P. Shaw
Editor: Elizabeth Rozanski

See also Cardiopulmonary Cerebral Resuscitation (p. 1223)

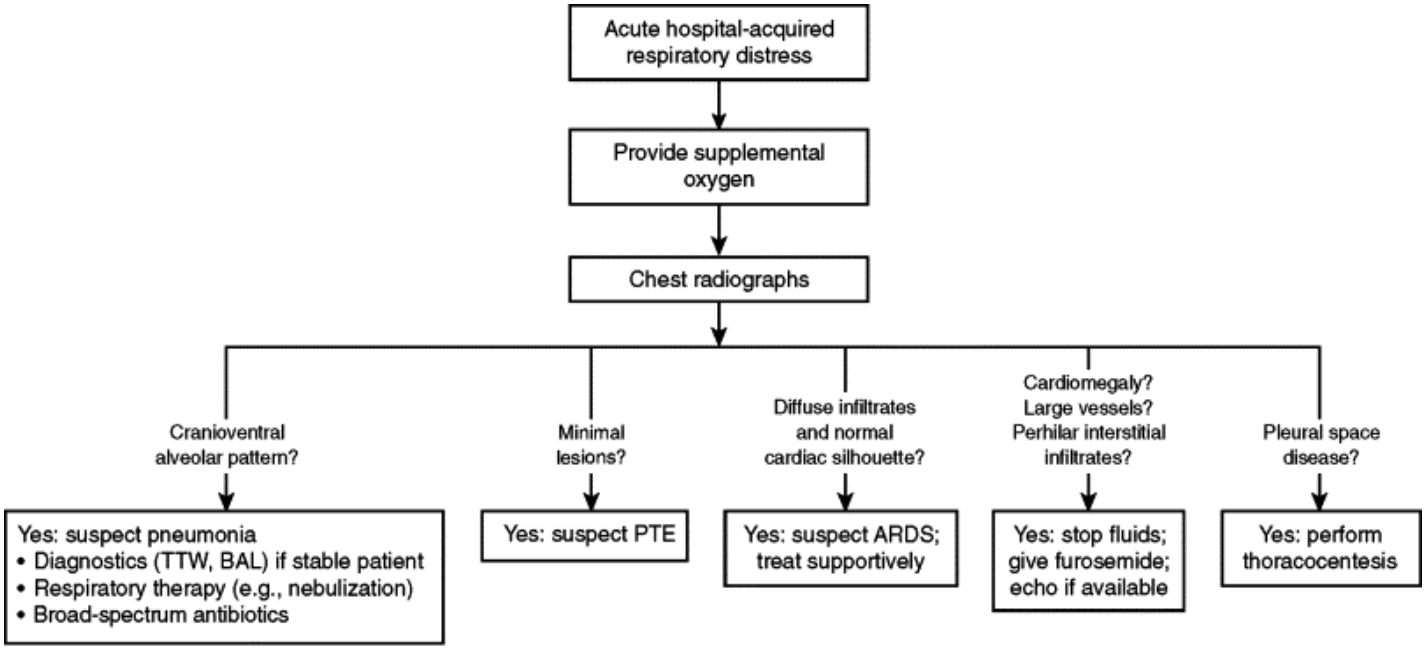
Dystocia



HR, Heart rate.

Author: Autumn P. Davidson
Editor: Michelle A. Kutzler

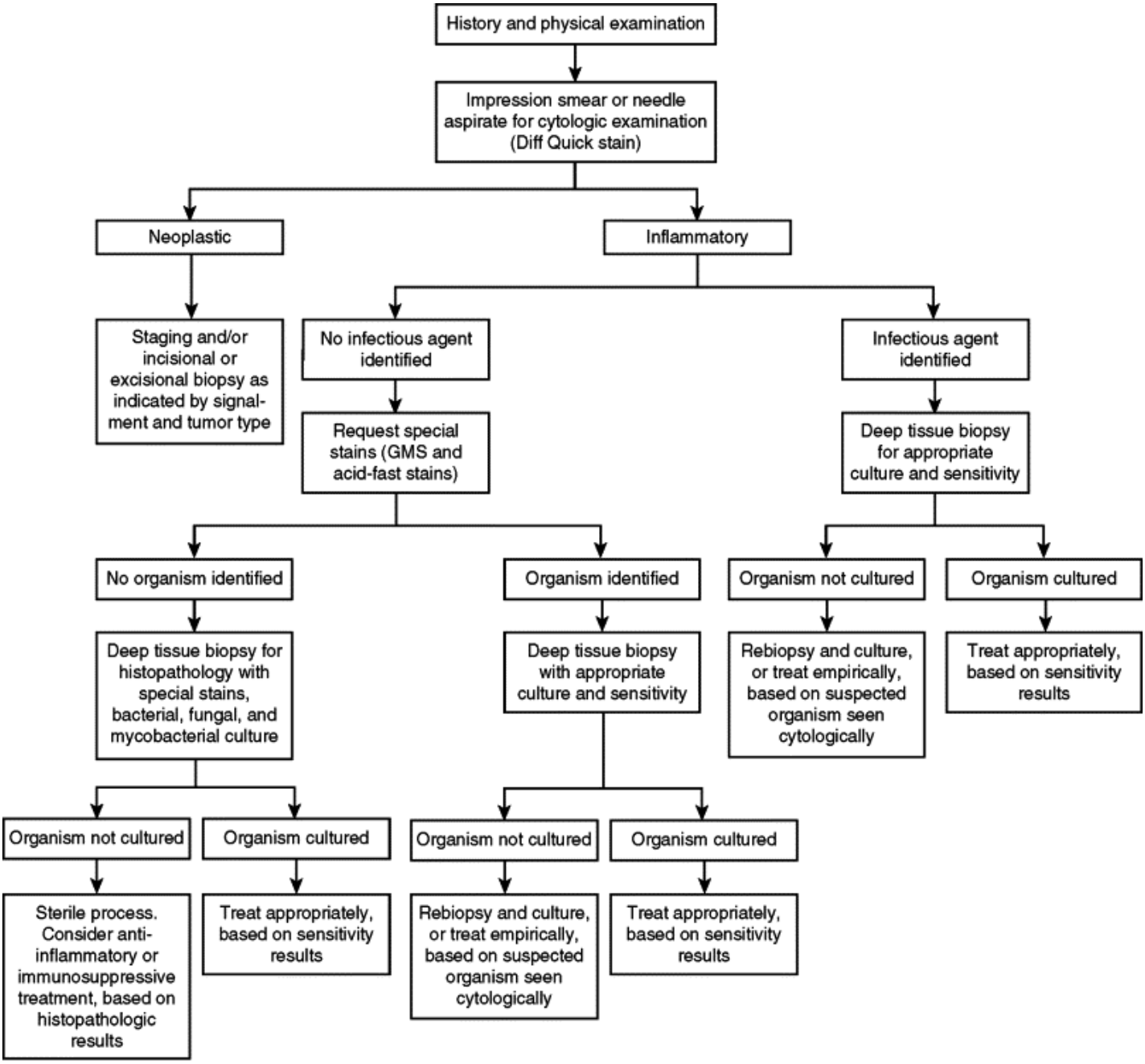
Dyspnea and Respiratory Distress: Hospital-Acquired



ARDS, Acute respiratory distress syndrome; *PTE,* pulmonary thromboembolism; *TTW,* transtracheal wash; *BAL,* bronchoalveolar lavage.

Author: Scott P. Shaw
Editor: Elizabeth Rozanski

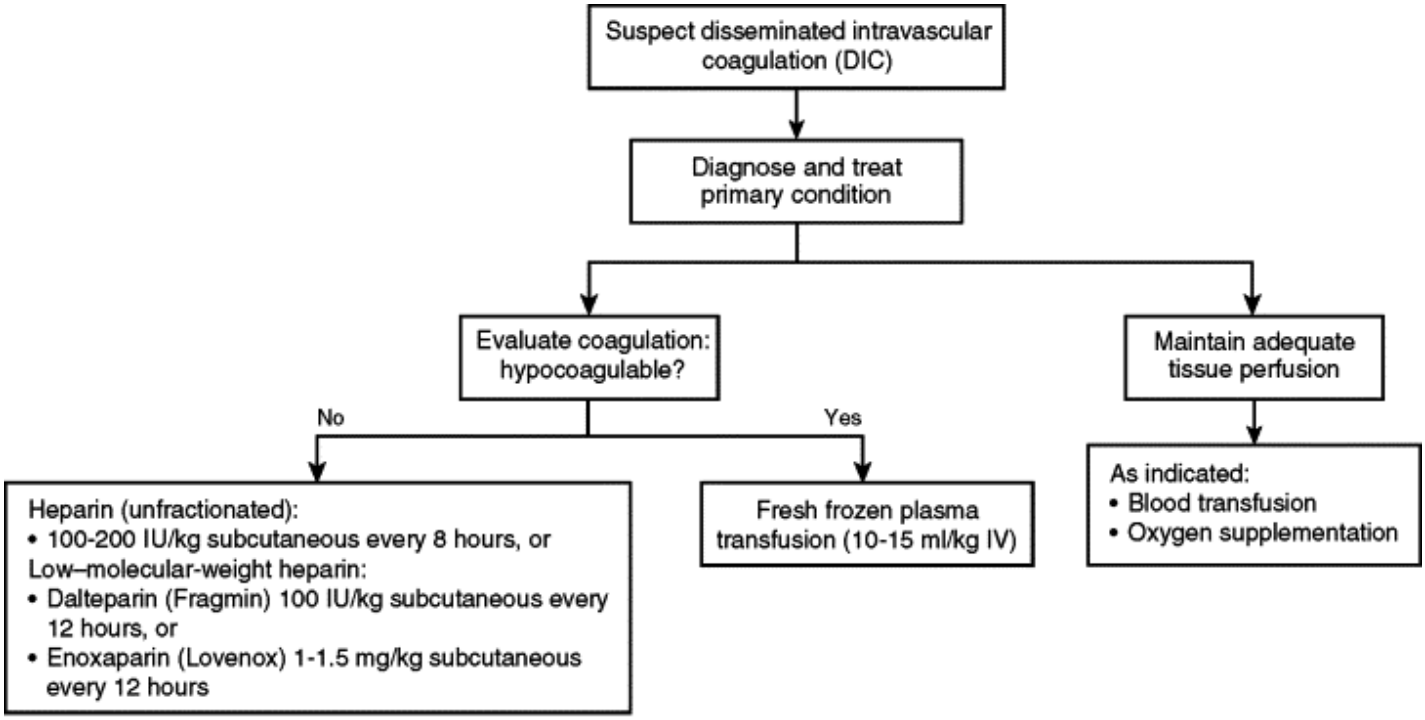
Draining Tracts, Cutaneous



GMS, Gömöri methenamine silver.

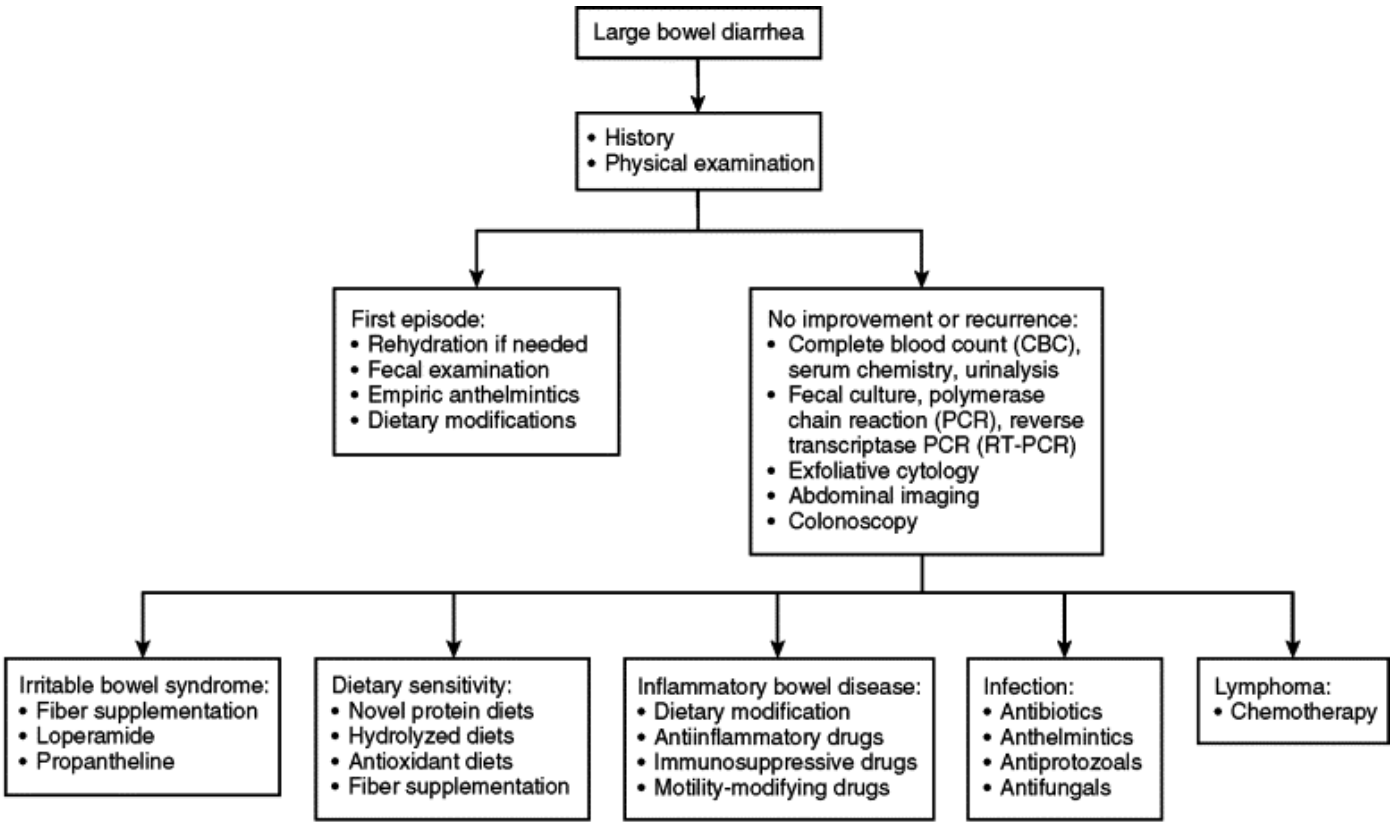
Author: Andrew Lowe
Editor: Manon Paradis

Disseminated Intravascular Coagulation



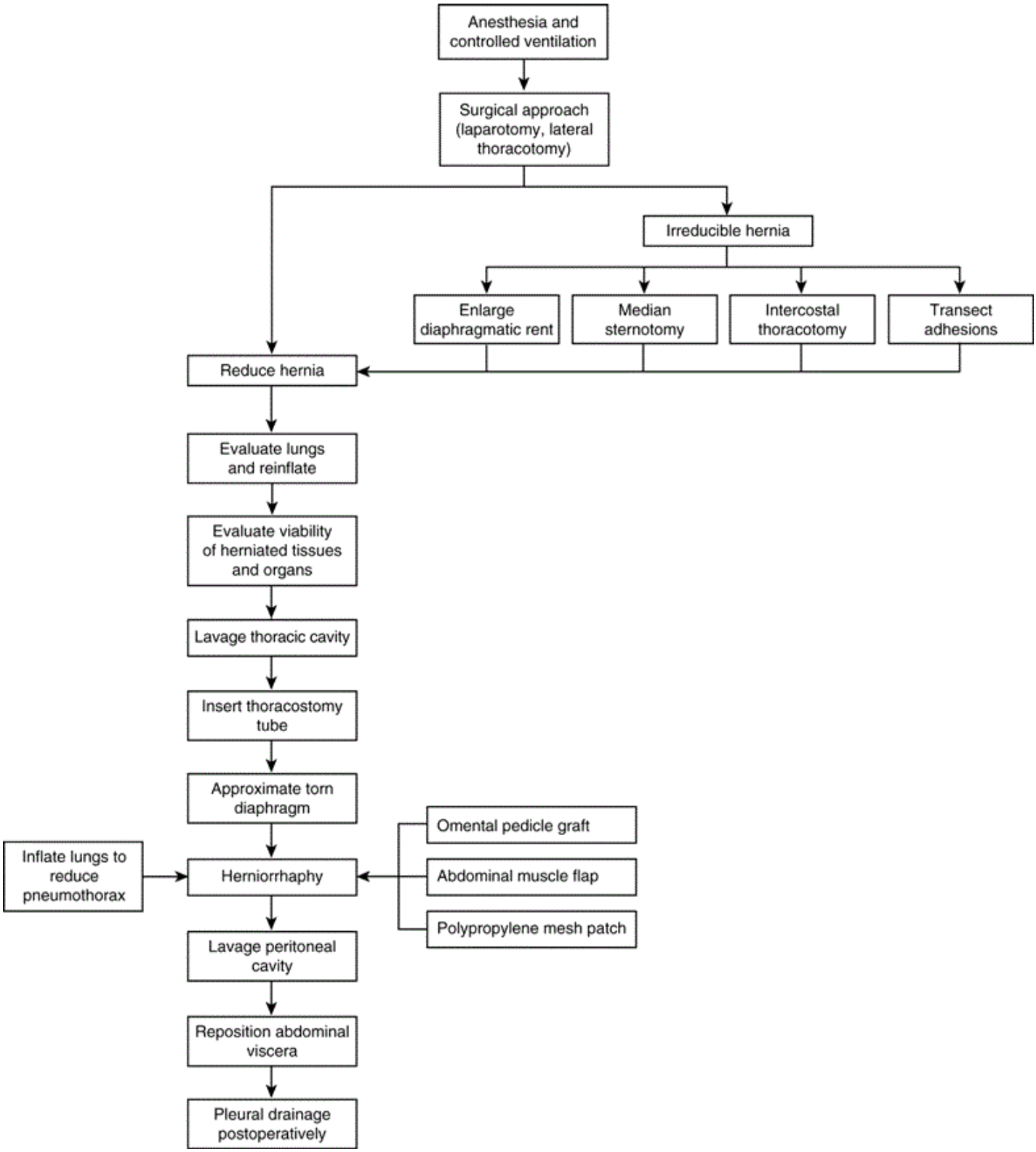
Author: Scott P. Shaw
Editor: Elizabeth Rozanski

Diarrhea, Large Bowel



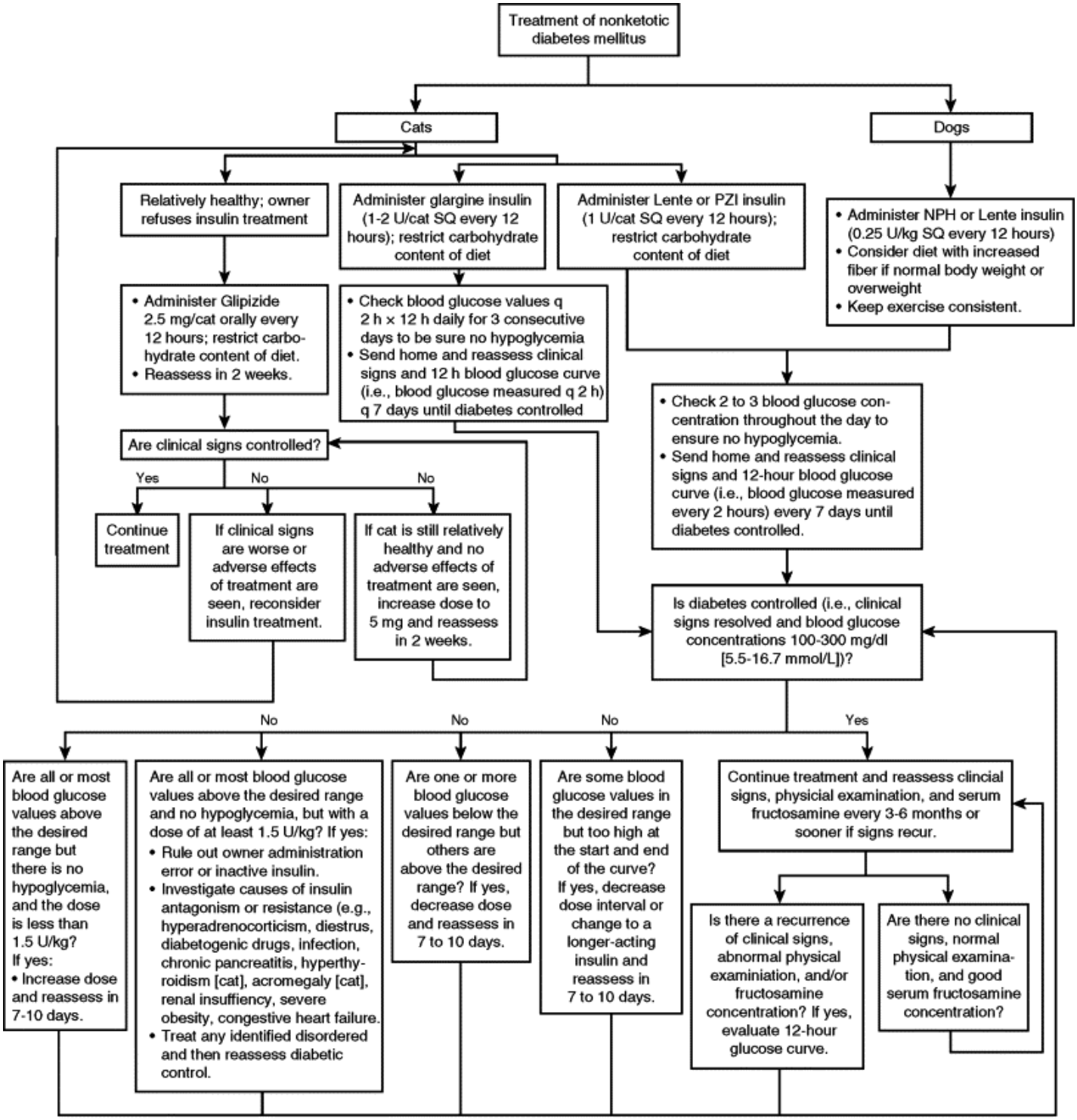
From Ettinger SJ, Feldman EC: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, WB Saunders.

Diaphragmatic Hernia



Modified from Slatter DH: Textbook of small animal surgery, ed 3, St Louis, 2003, WB Saunders.

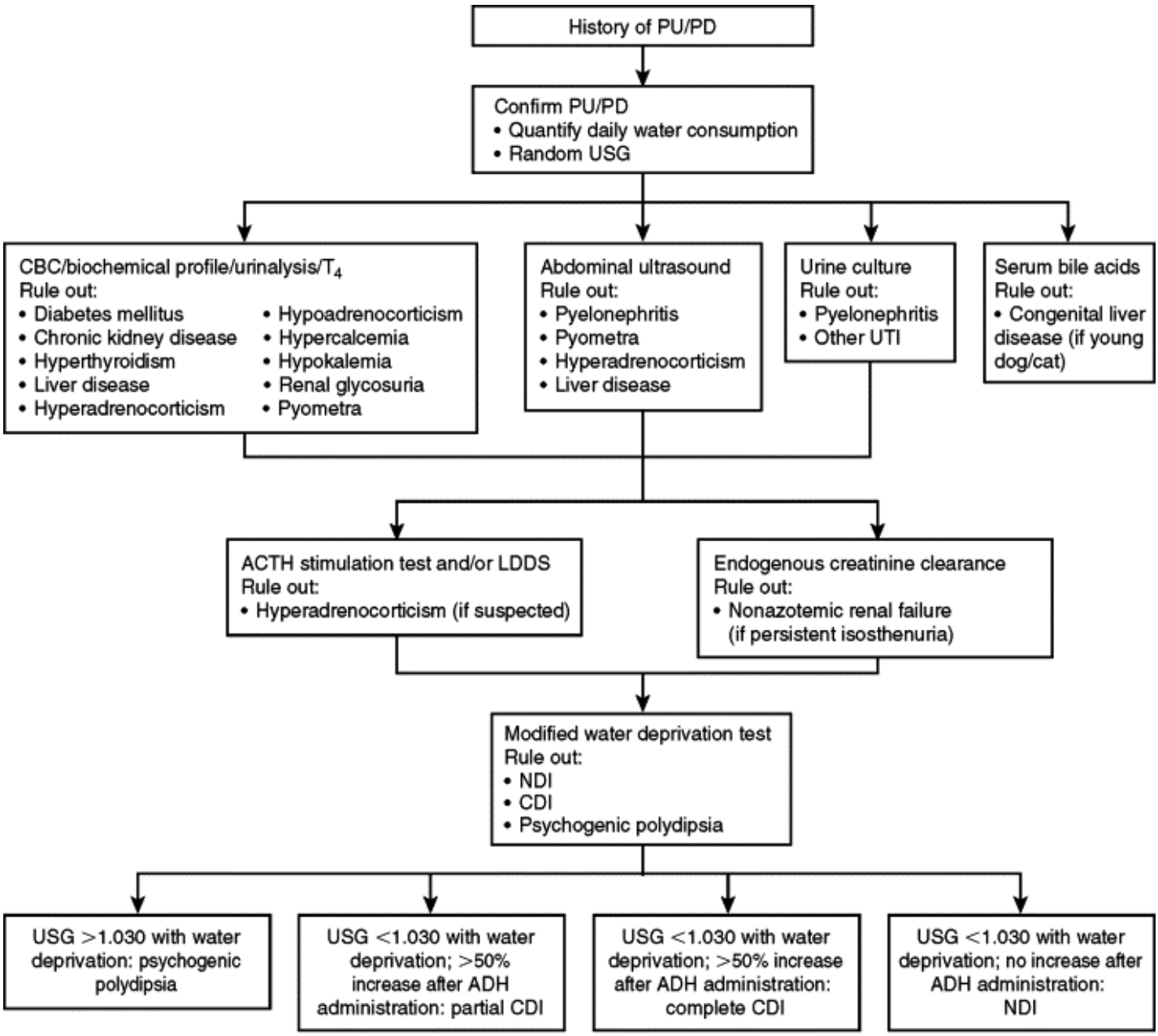
Diabetes Mellitus



NPH, Neutral protamine Hagedorn; *PZI*, protamine zinc insulin; *SQ*, subcutaneous.

Author & Editor: Sherri Ihle

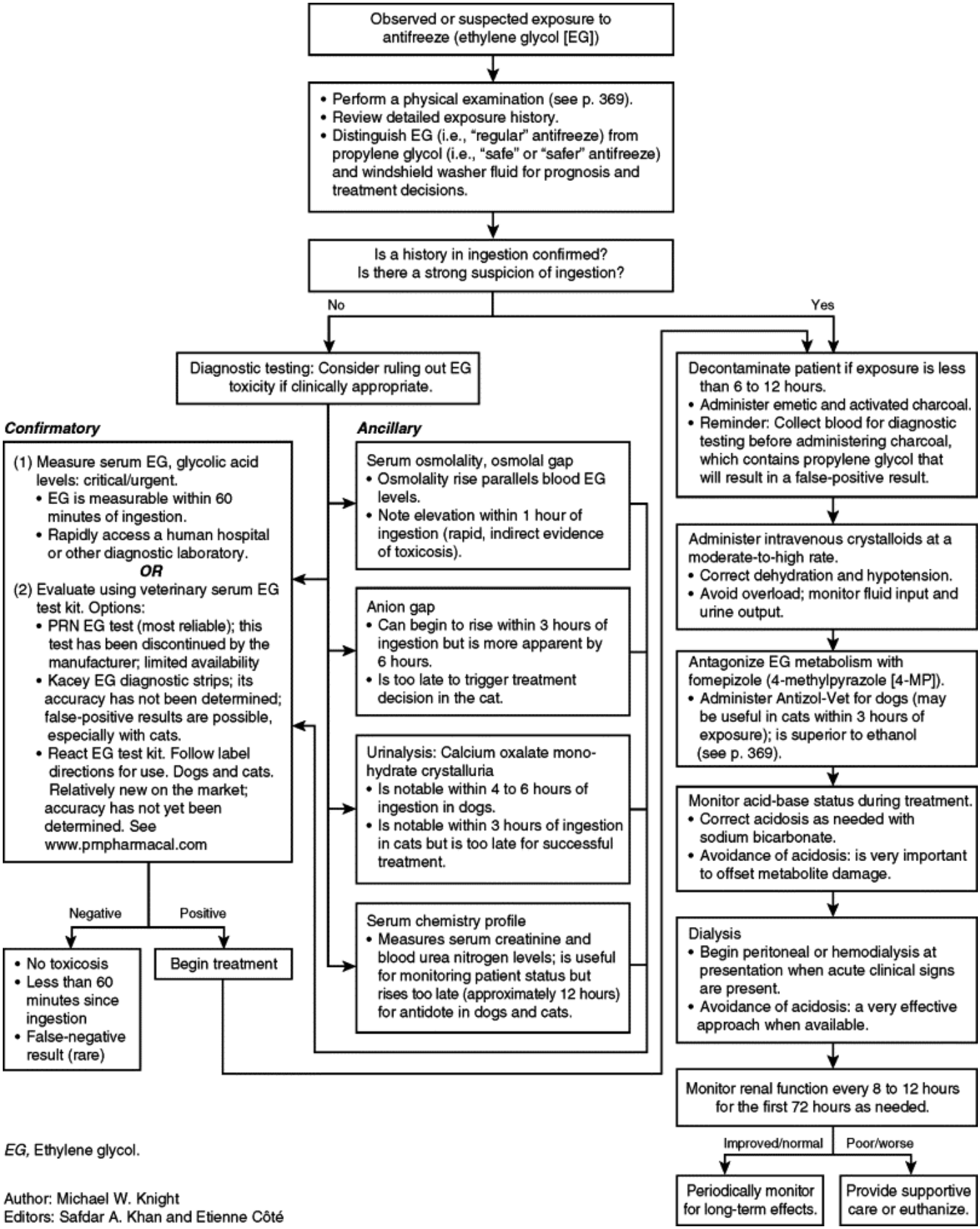
Diabetes Insipidus



ACTH, Adrenocorticotropic hormone; *ADH,* antidiuretic hormone; *CBC,* complete blood count; *CDI,* central diabetes insipidus; *LDDS,* low-dose dexamethasone suppression test; *NDI,* nephrogenic diabetes insipidus; *PU/PD,* polyuria/polydipsia; *USG,* urine specific gravity; *UTI,* urinary tract infection.

Author: Sarah L. Naidoo
Editor: Sherri Ihle

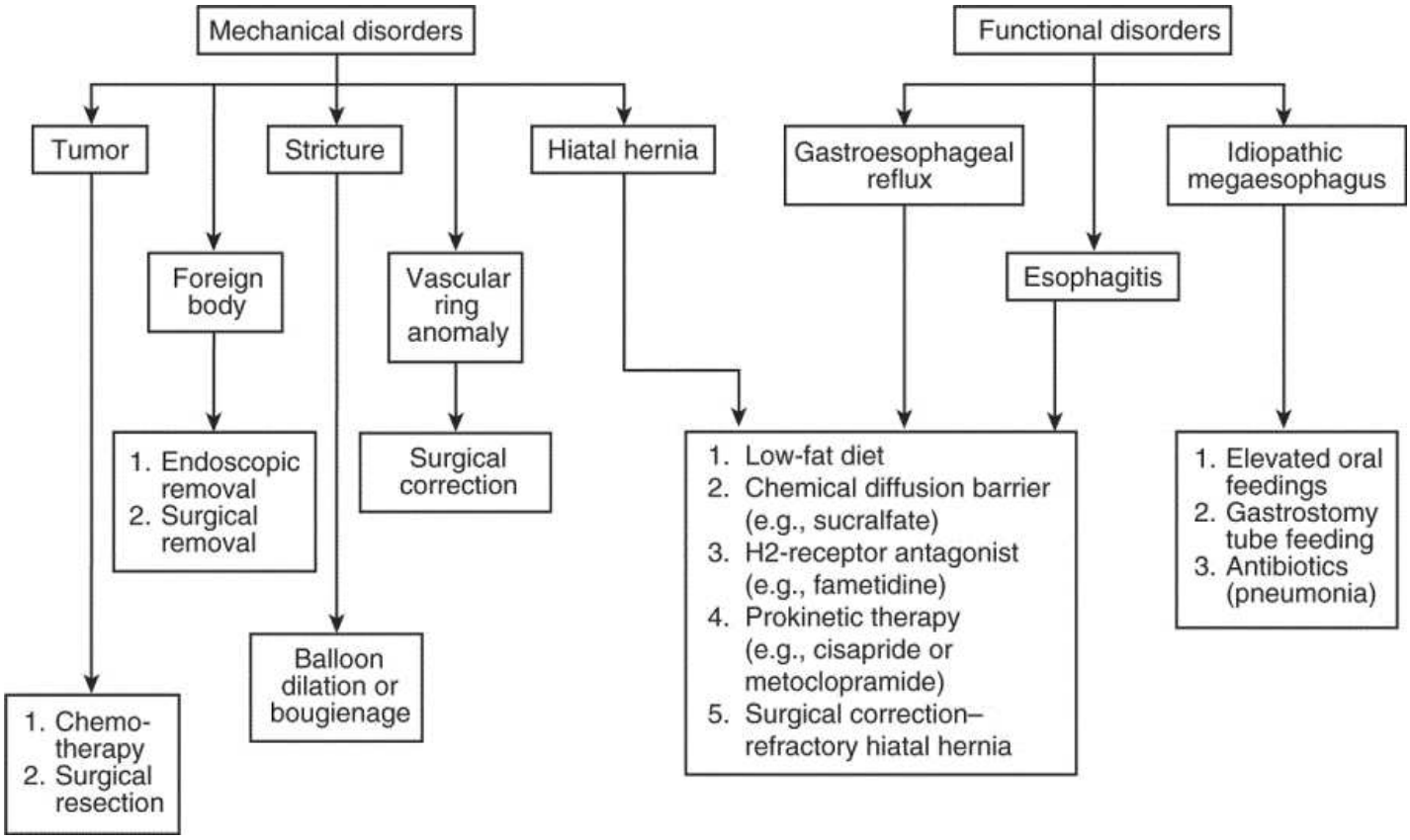
Ethylene Glycol Intoxication



EG, Ethylene glycol.

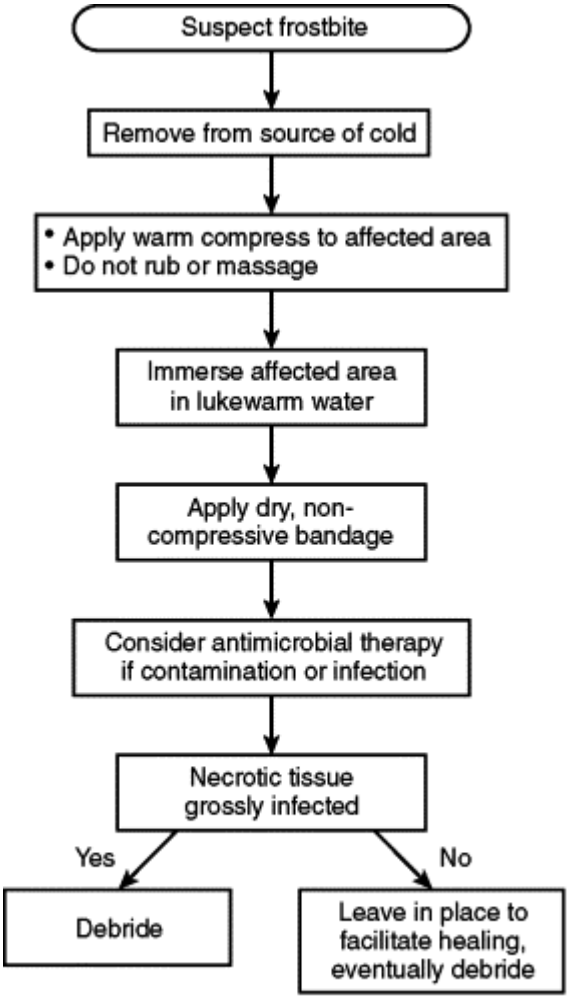
Author: Michael W. Knight
Editors: Safdar A. Khan and Etienne Côté

Esophageal Motility Disorder: Treatment



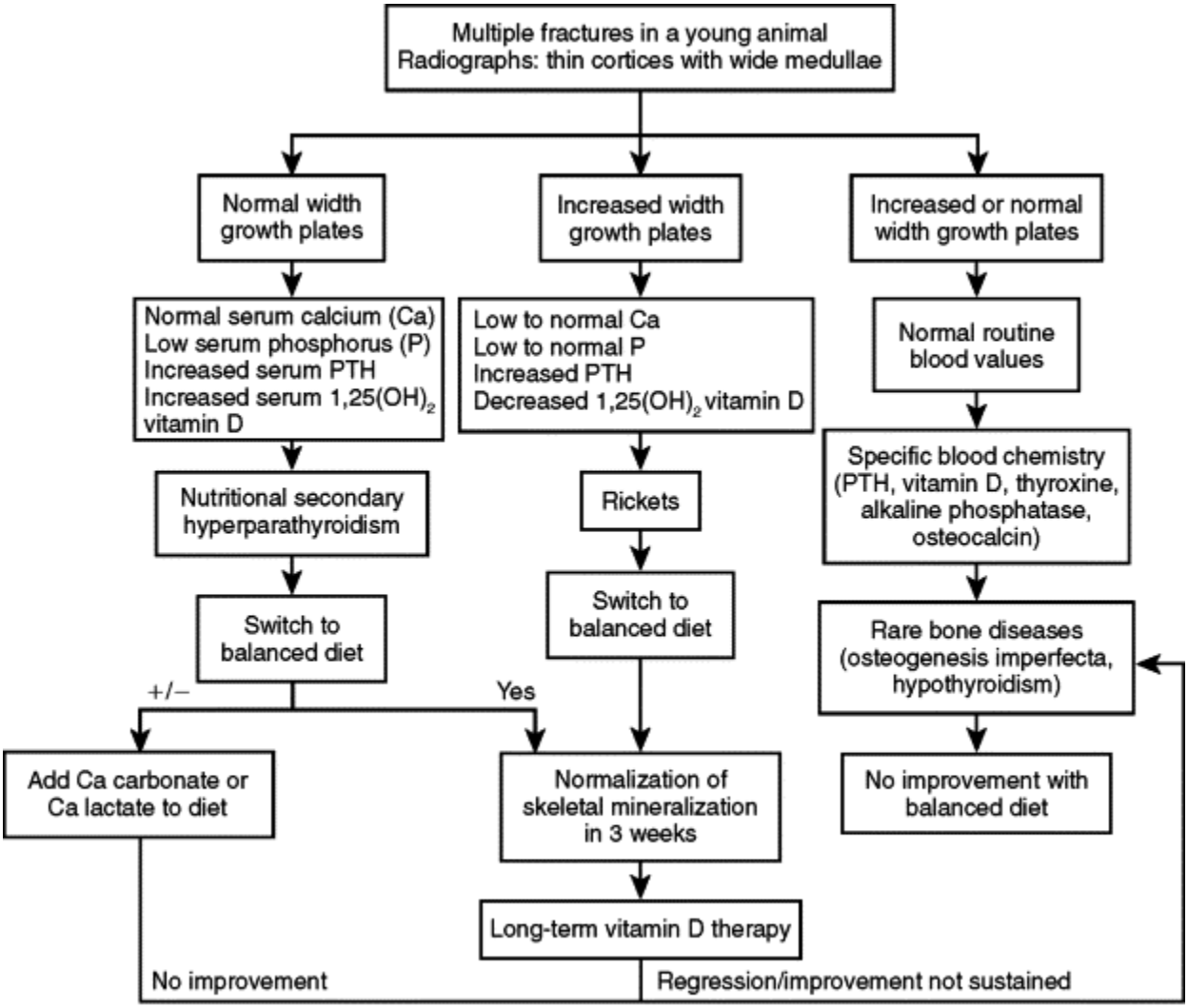
Modified from Slatter DH: Textbook of small animal surgery, ed 3, St Louis, 2003, WB Saunders.

Frostbite



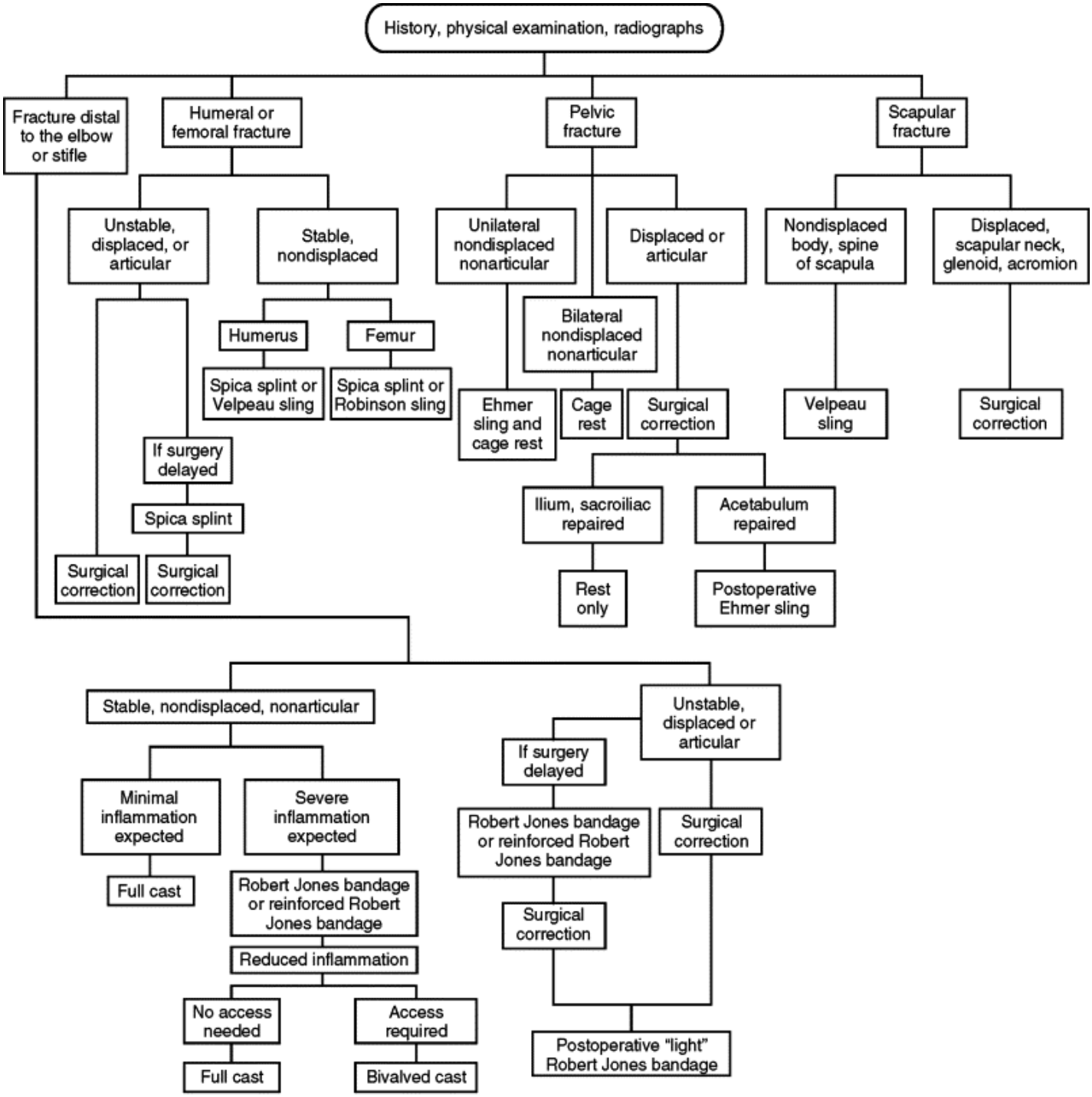
Author: Scott P. Shaw
Editor: Elizabeth Rozanski

Fractures Pathologic



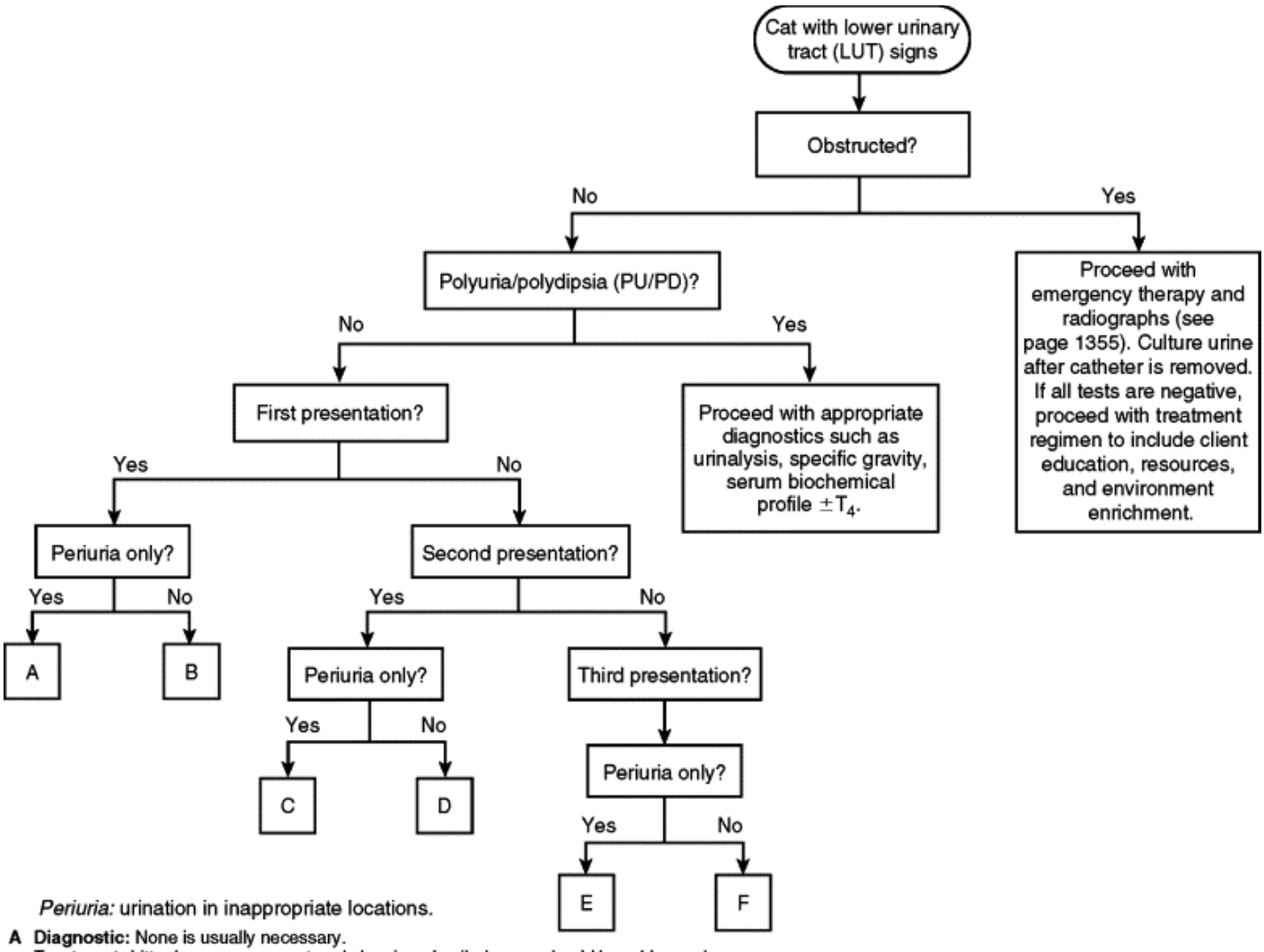
From Ettinger SJ, Feldman EC: Textbook of veterinary internal medicine, ed 7, St Louis, 2010, Elsevier.

Fracture Management



From Slatter DH: Textbook of small animal surgery, ed 3, St Louis, 2003, WB Saunders.

Feline Lower Urinary Tract Signs



Periuria: urination in inappropriate locations.

A **Diagnostic:** None is usually necessary.
Treatment: Litter box management and cleaning of soiled areas should be addressed.
Medications: No medications are recommended.

B **Diagnostic:** A radiograph should be considered, especially if hematuria is present.
Treatment: If the radiograph is negative, therapy should include analgesia for 2 to 3 days during the acute episode. Litter box management and cleaning of soiled areas should be addressed.
Medications: No medications are recommended.

C **Diagnostic:** A urinalysis is recommended. If submaximal urine specific gravity is present, then appropriate diagnostics are needed.
Treatment: If diagnostic tests are negative, then the resource checklist* should be reviewed and additional areas that were not previously addressed should be incorporated.
Medications: Pheromone therapy is recommended.

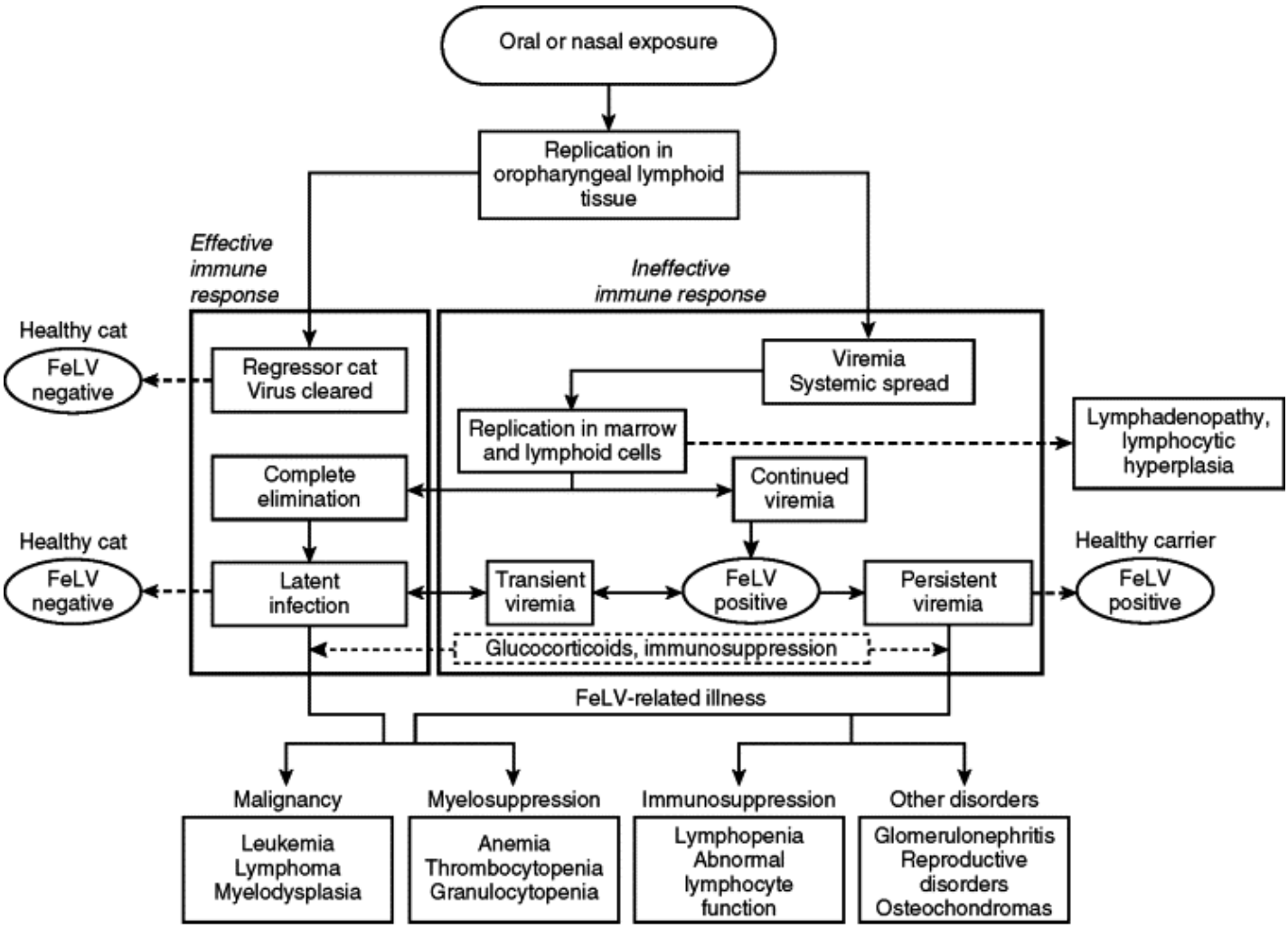
D **Diagnostic:** A radiograph, urinalysis, and urine culture are recommended.
Treatment: If all tests are negative, analgesia should be provided for 2 to 3 days during acute episode. Canned food is encouraged for the cat in addition to litter box management and cleaning of soiled areas. The cat's urine specity gravity is monitored for 3 to 4 weeks to assess the cat's water intake.
Medications: Pheromone therapy is recommended.

E **Diagnostic:** A urinalysis should be performed if it has not already been done. Radiographs, urine culture, and biochemical profile are also recommended.
Treatment: If all tests are negative, then the resource checklist* is formally reviewed and those areas that have not already been addressed should be incorporated. Further information for cleaning soiled areas should be provided. Additional resources (web sites, books) on how to provide an enhanced indoor environment for cats should be provided to clients. Intercat conflict issues should also be addressed.
Medications: Pheromone therapy should be used in conjunction with behavior-altering medications such as tricyclic antidepressants (TCAs) or buspirone. The medication should be taken for 4 weeks; if no improvement is seen, a referral for further diagnostics and consultation should be considered.

F **Diagnostic:** A radiograph, a urinalysis, and a urine culture should be performed. A complete blood count (CBC) and biochemical profile should also be submitted. If all tests are negative, a contrast study or abdominal ultrasound of the bladder and urethra should be considered to rule out radiolucent calculi and other mass lesions.
Treatment: If all diagnostics are negative, analgesia should be provided for 2 to 3 days during acute episode. In addition to canned food, ensure that water consumption is sufficient. Water should be viewed as a "drug," and the cat's urine specific gravity should be monitored (goal: submaximal concentration, e.g., urine specific gravity < 1.040) to evaluate water intake. The resource checklist* should be formally reviewed, and those areas that have not already been addressed should be incorporated. Additional resources (web sites, books) on how to provide an enhanced indoor environment for cats should be provided to clients. Intercat conflict issues should also be addressed. Follow up and support for clients are essential.
Medications: Phermonotherapy should be used in conjunction with behavior-altering medications such as TCAs or anxiolytics. Medication should be taken for 4 weeks; if no improvement is seen, a referral for further diagnostics such as a cystoscopy should be considered.

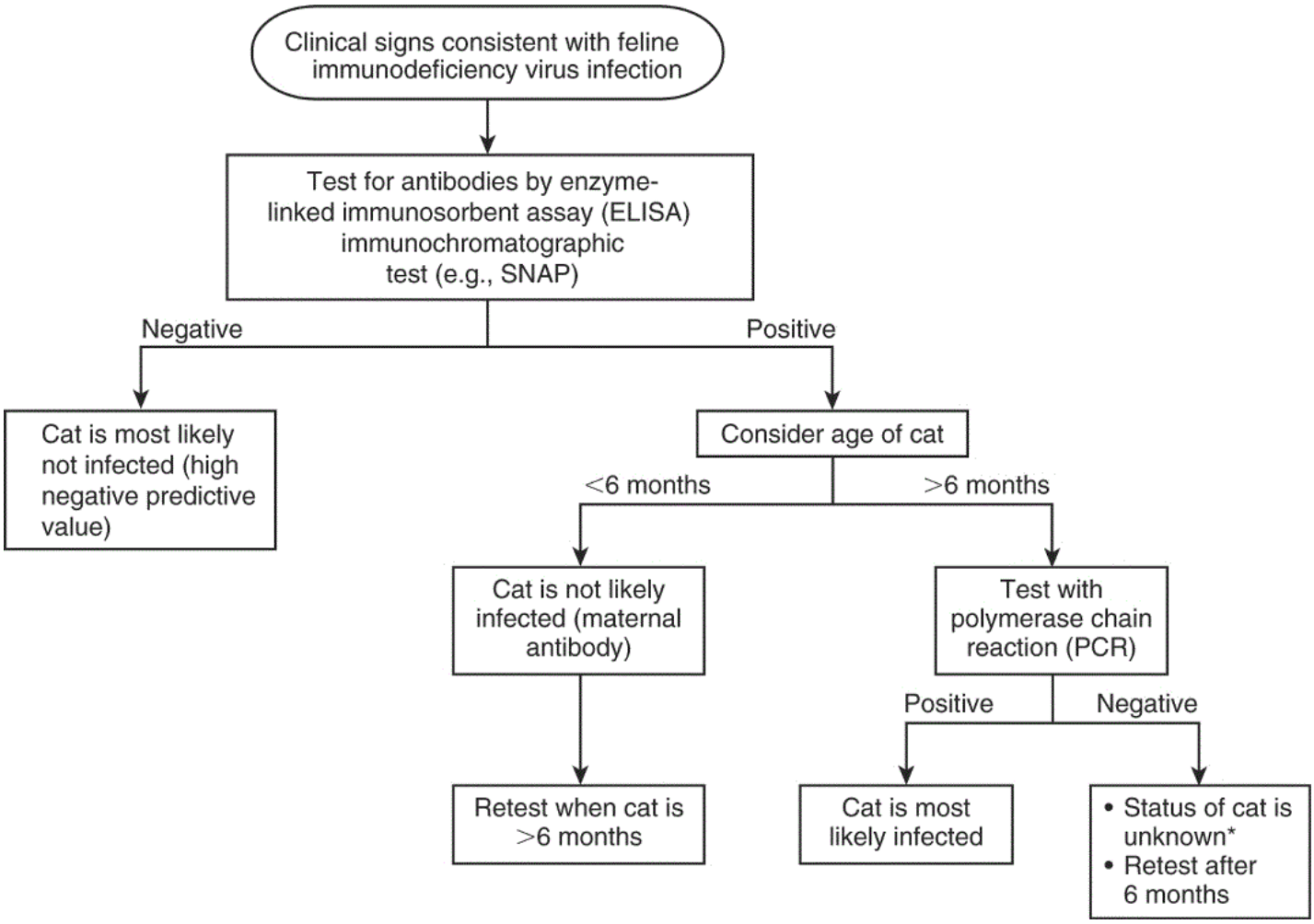
Modified from Ettinger SJ, Feldman EC: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, WB Saunders.
*Additional materials available at www.indoorcat.com. Resource checklist:
www.vet.ohio-state.edu/assets/pdf/hospital/indoorcat/Client%20Resource%Checklist%20and%20Action%20Plan.pdf.

Feline Leukemia Infection



From Greene CE: Infectious diseases of the dog and cat, ed 3, St Louis, 2006, WB Saunders.
FeLV, Feline leukemia virus.

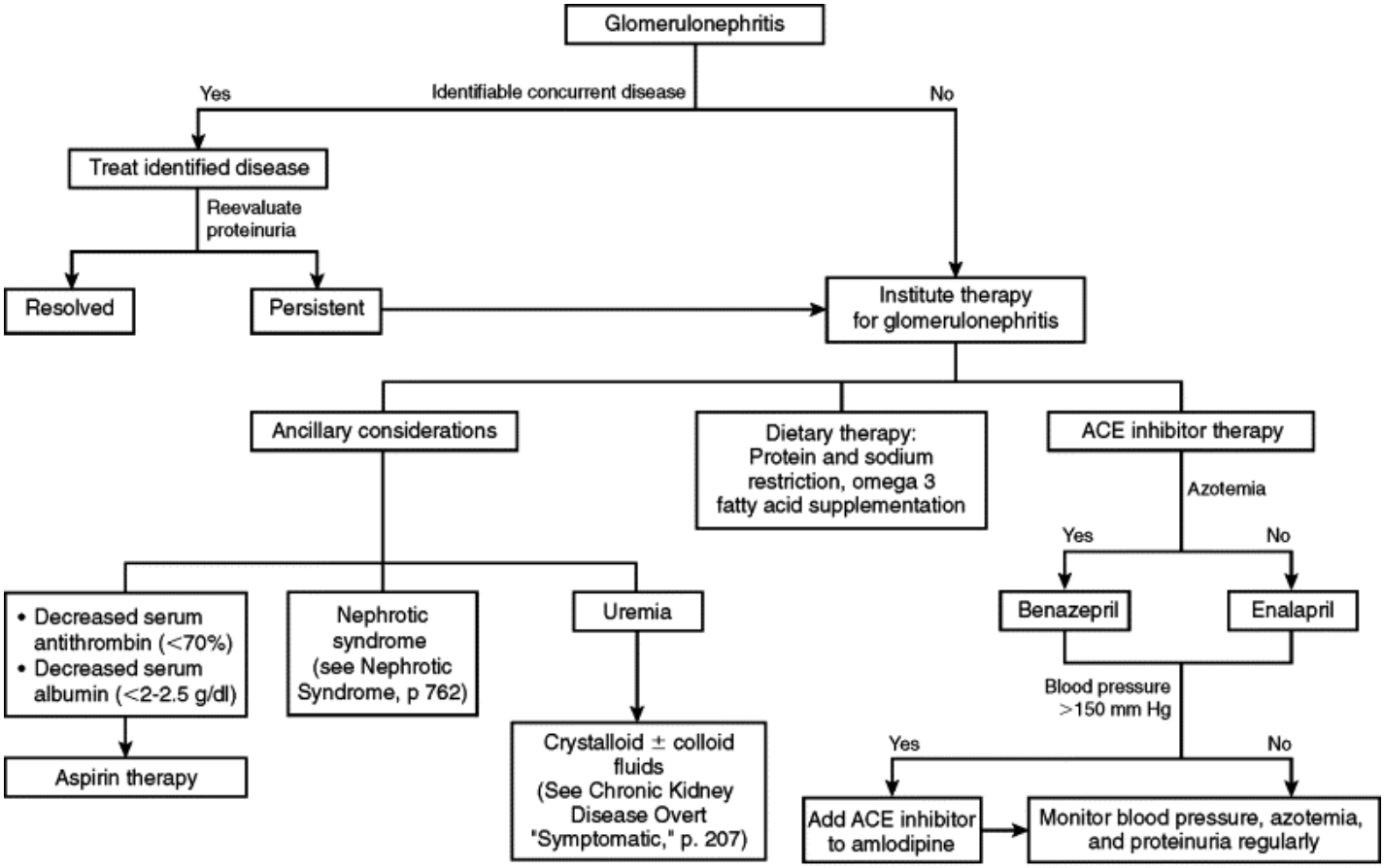
Feline Immunodeficiency Virus Infection



*Cats can have positive results due to early infection, or vaccination (and no infection).

Modified from Ettinger SJ, Feldman EC: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, WB Saunders.

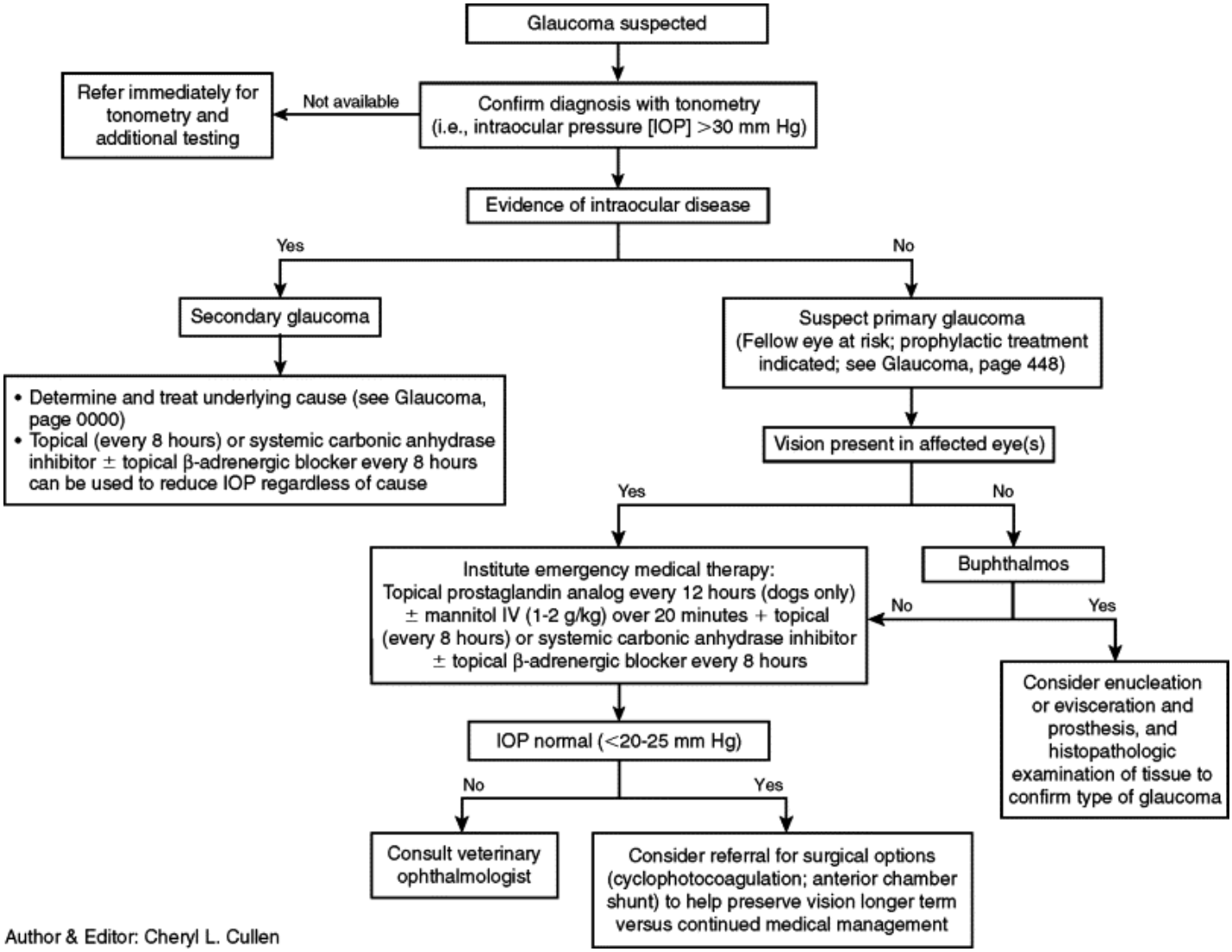
Glomerulonephritis: Management



ACE, Angiotensin-converting enzyme.

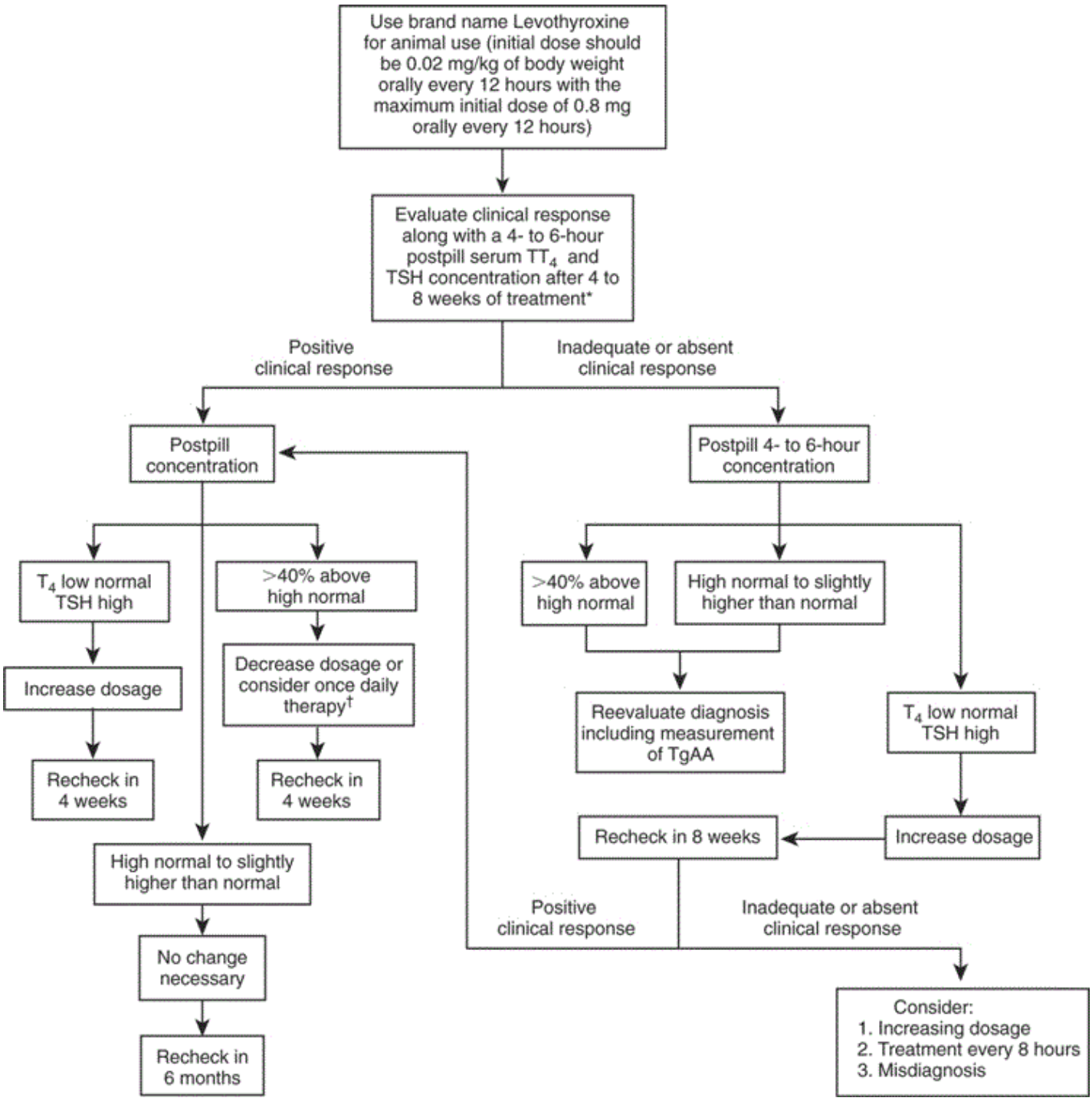
Author: Anne M. Dalby
Editor: Leah A. Cohn

Glaucoma



Author & Editor: Cheryl L. Cullen

Hypothyroidism Treatment



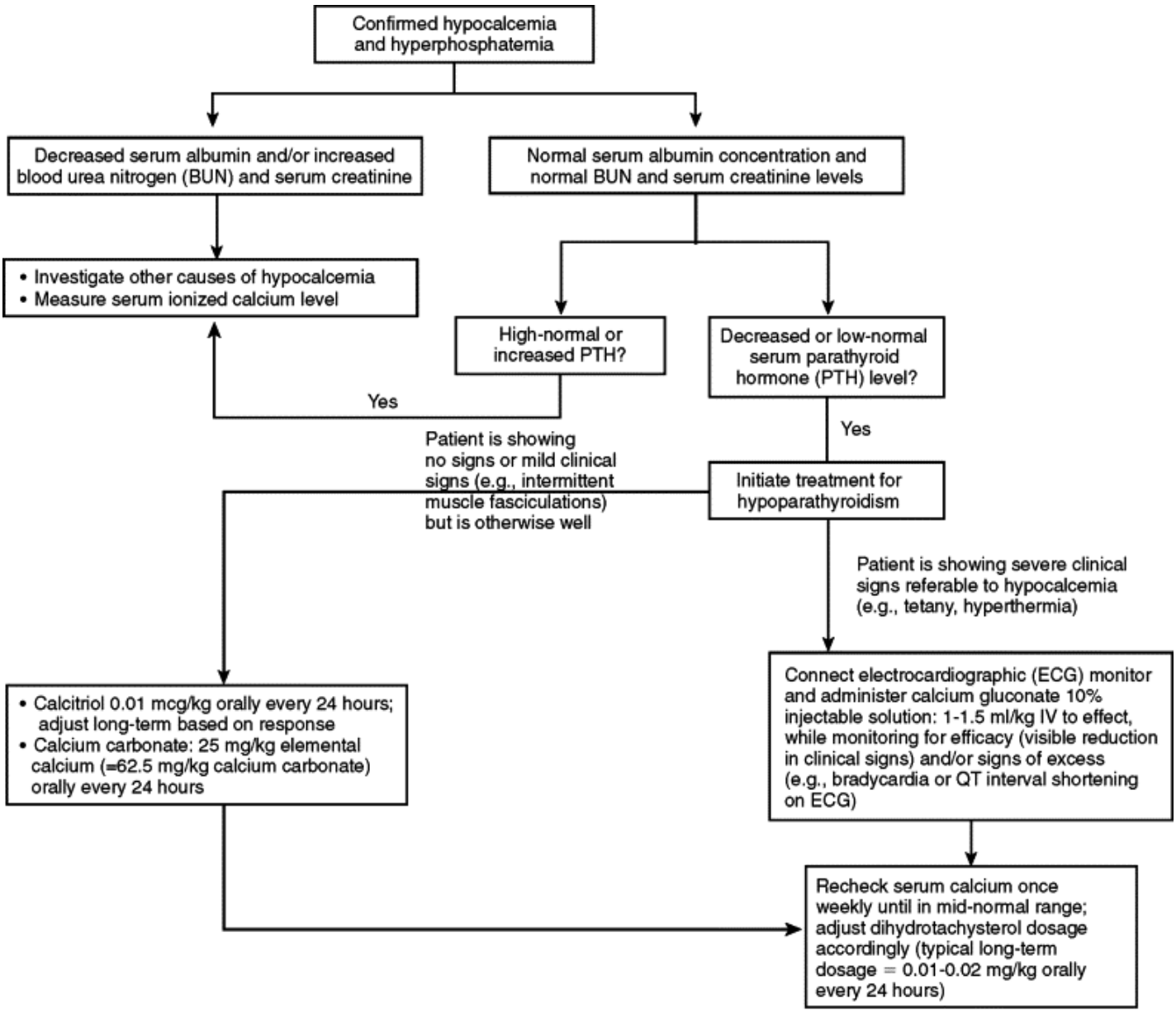
T4, Thyroxine; *TT4,* total serum thyroxine concentration; *TgAA,* serum thyroglobulin autoantibodies.

*Serum free T4 by equilibrium dialysis can also be measured.

†Prepill serum T4 also recommended if daily therapy is administered.

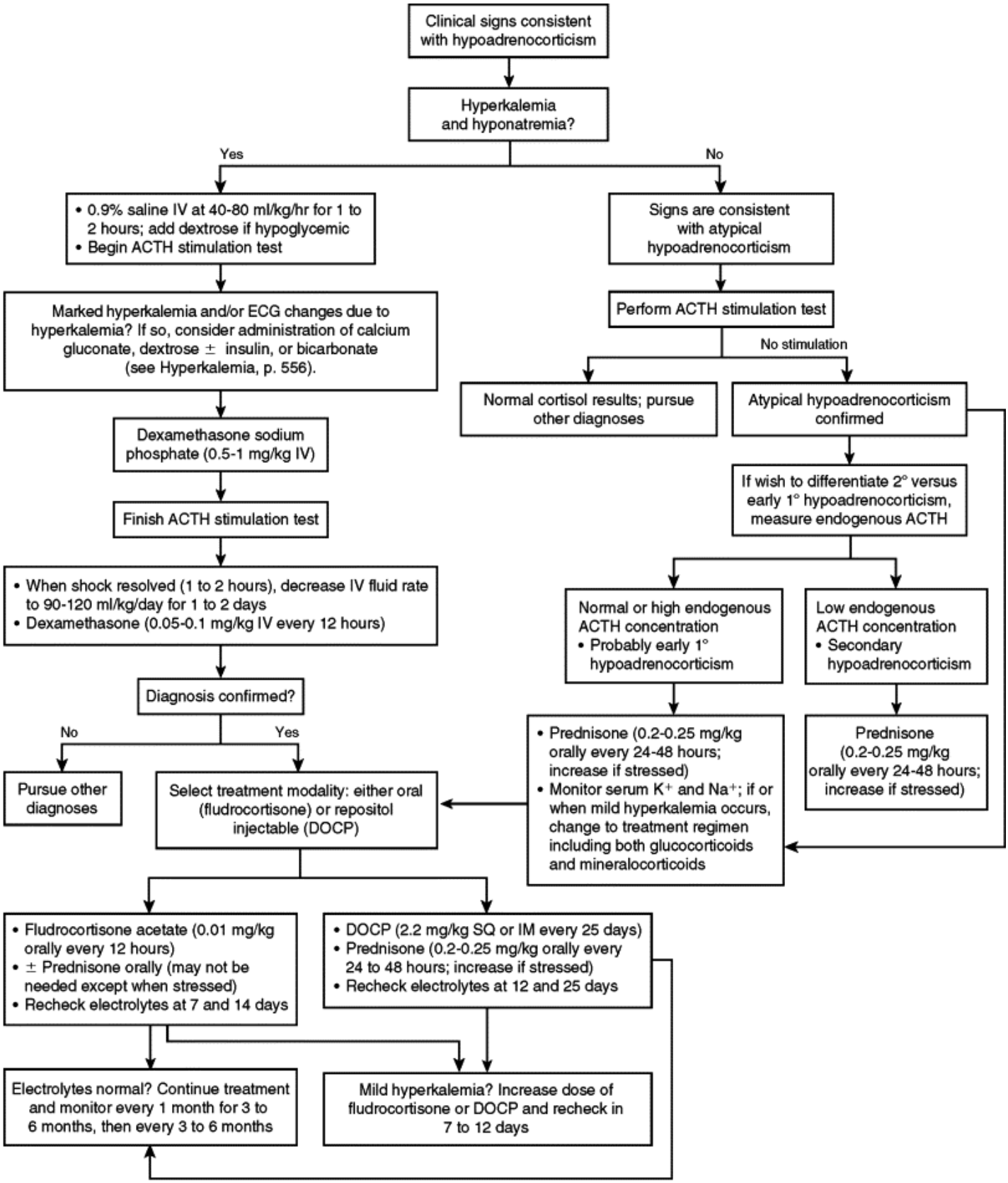
From Ettinger SJ, Feldman EC: Textbook of veterinary internal medicine, ed 7, St Louis, 2010, Elsevier.

Hypoparathyroidism: Management



Author: Cary L. M. Bassett
Editor: Sherri Ihle

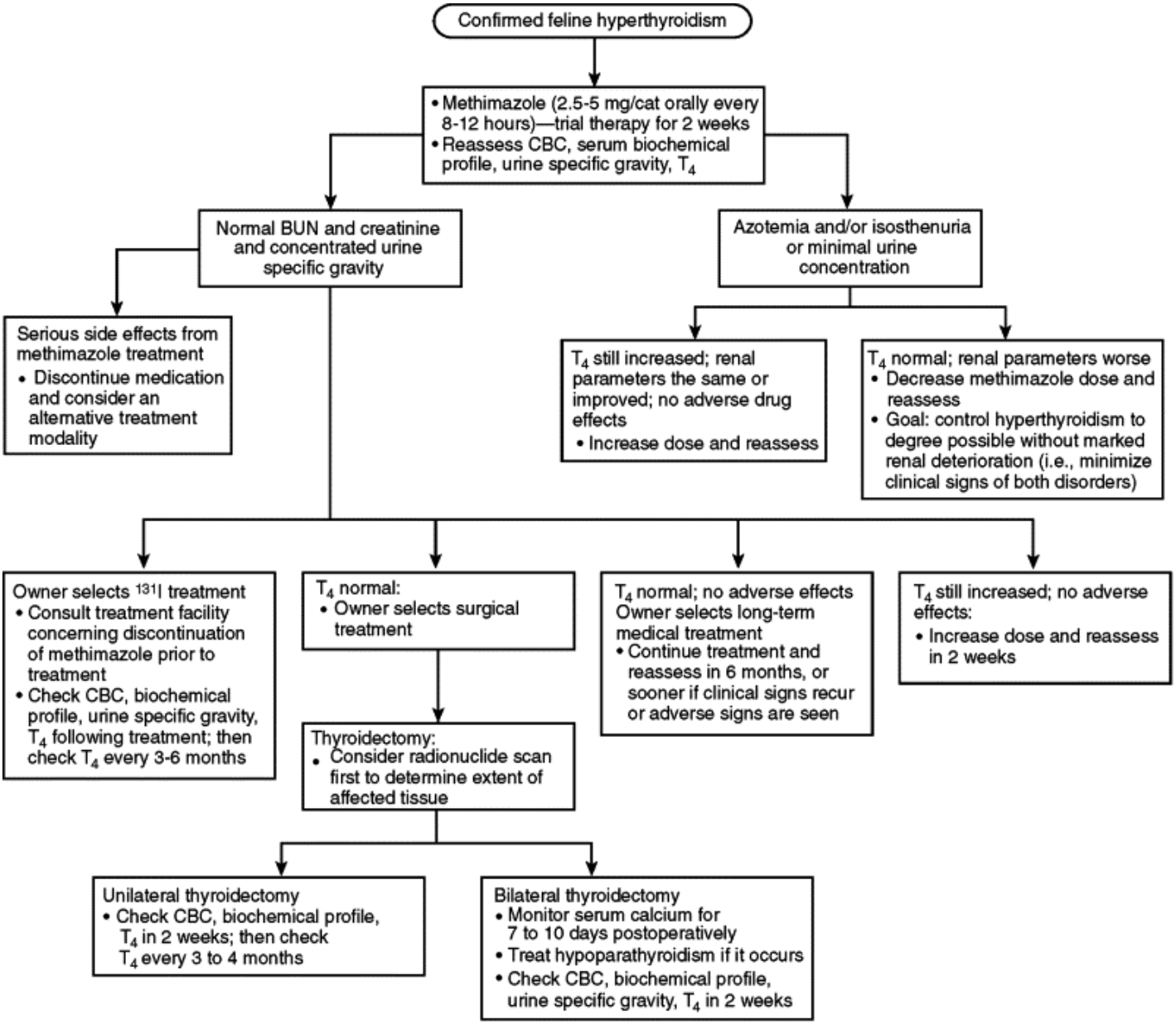
Hypoadrenocorticism



ACTH, Adrenocorticotropic hormone; *DOCP,* desoxycorticosterone pivalate.

Author: Cary L. M. Bassett
Editor: Sherri Ihle

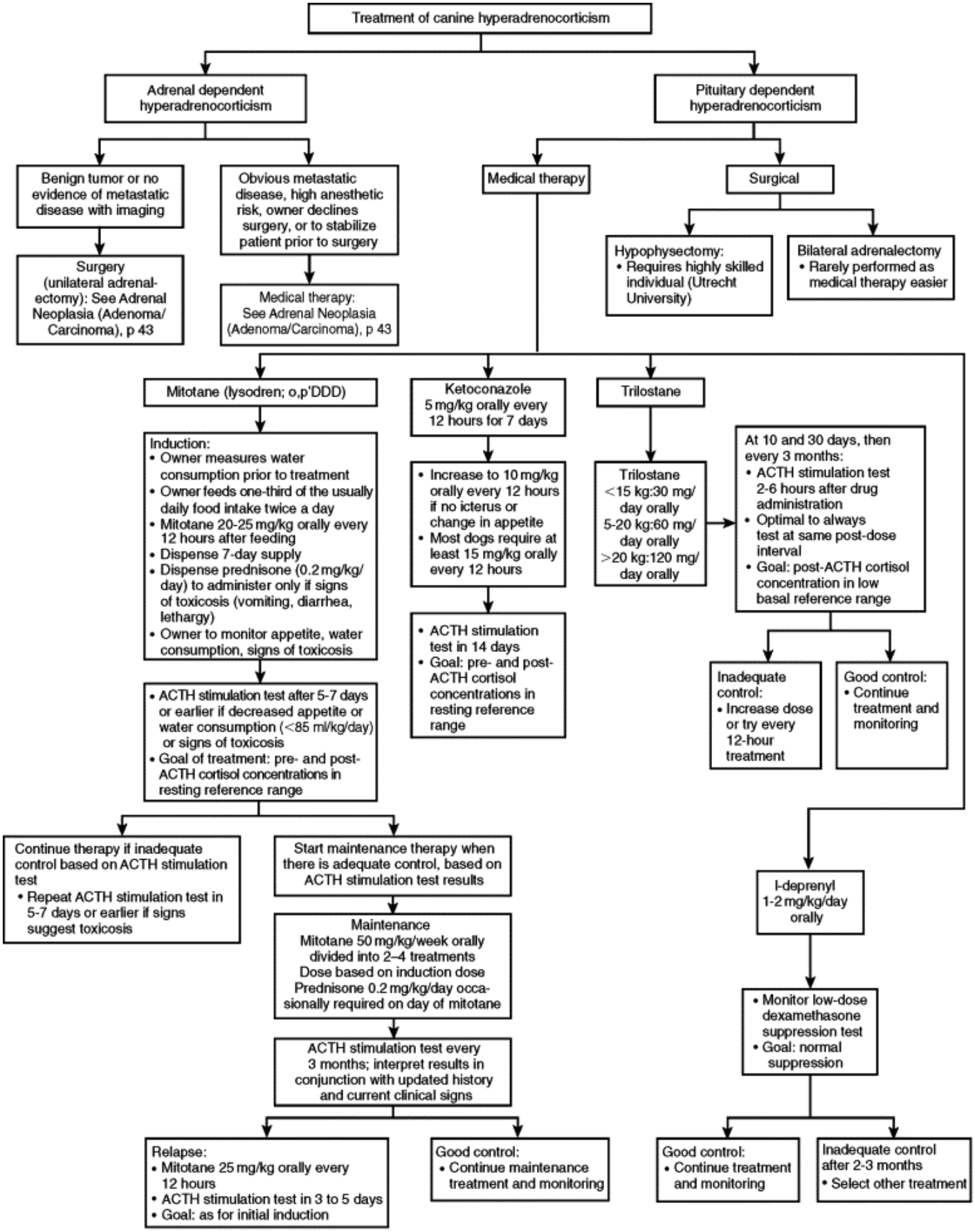
Hyperthyroidism: Treatment



CBC, Complete blood count; *BUN,* blood urea nitrogen.

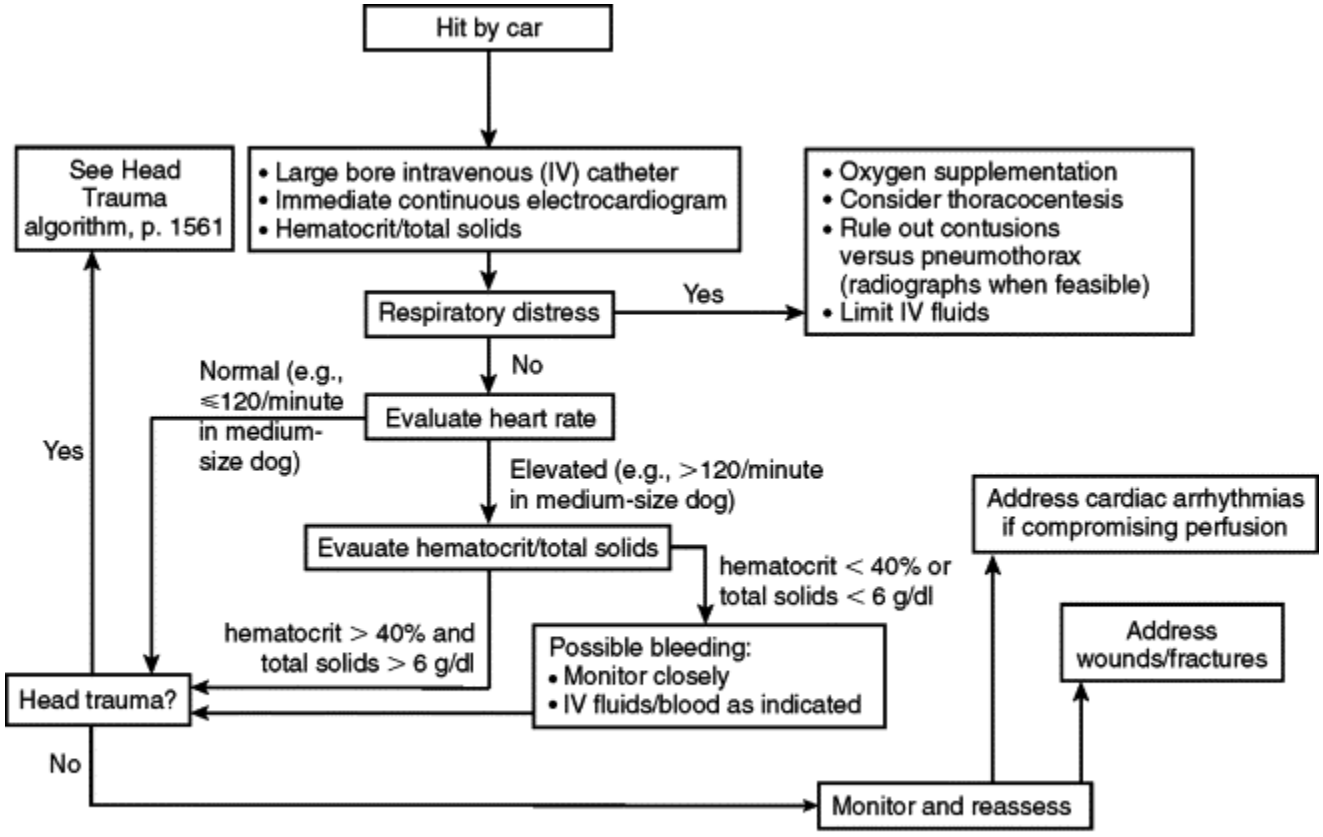
Authors: Sherri Ihle and Kristi L. Graham
Editor: Sherri Ihle

Hyperadrenocorticism: Treatment



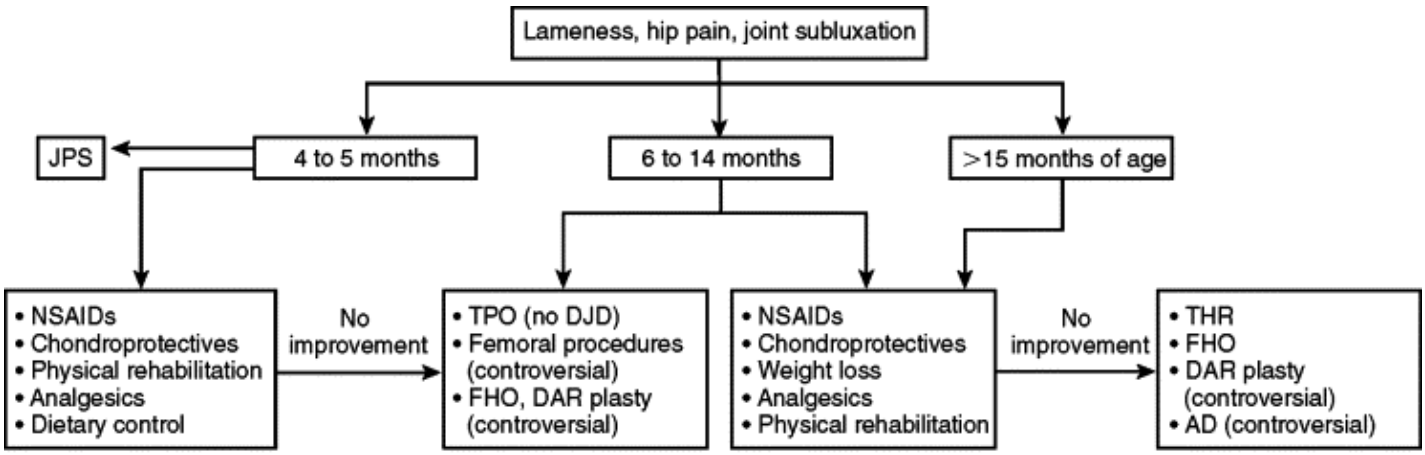
Author: Kate Hill
Editor: Sherri Ihle

Hit by Car



Author: Scott P. Shaw
Editor: Elizabeth Rozanski

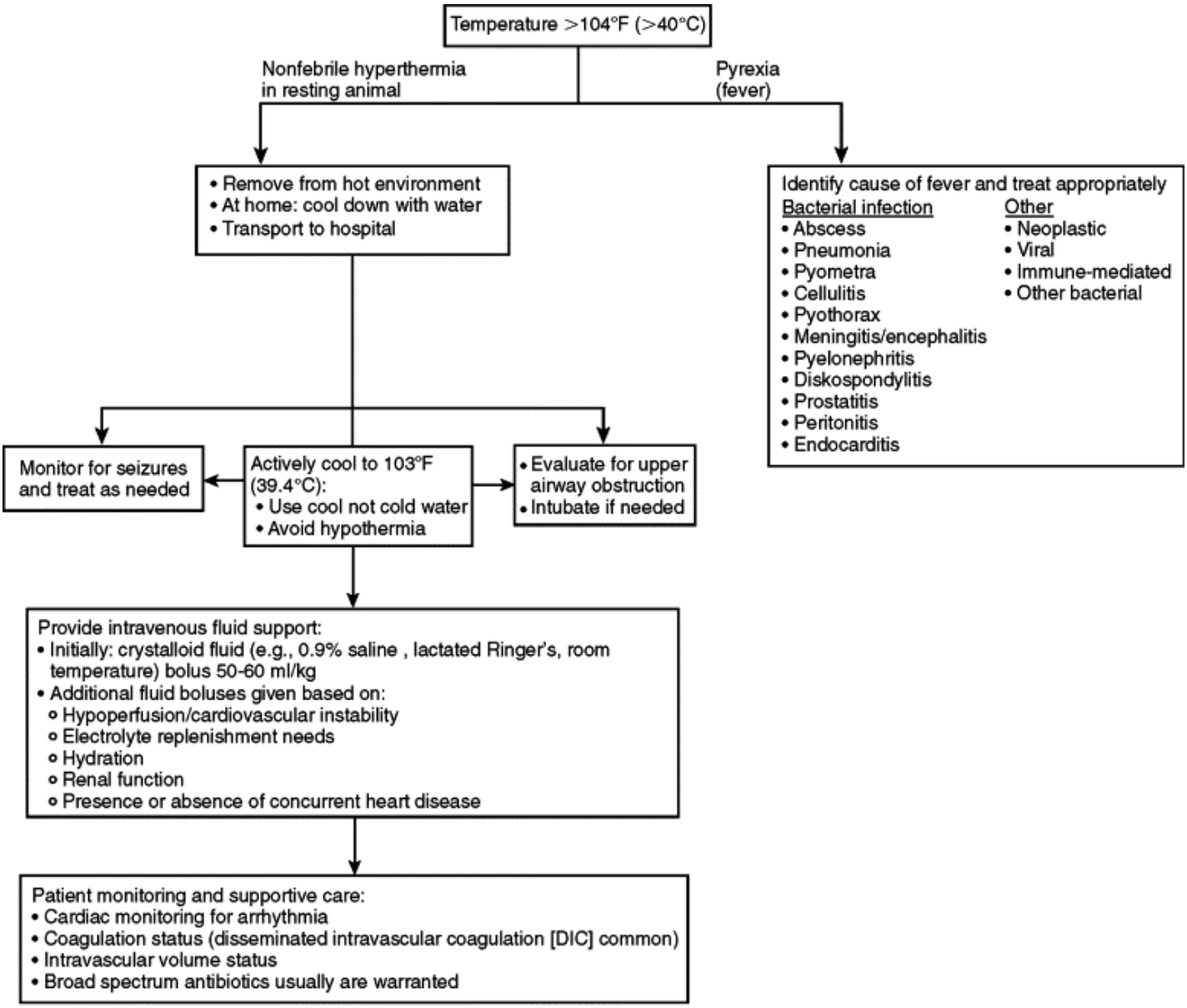
Hip Dysplasia



JPS, Juvenile pubic symphysiodesis; *TPO,* triple pelvic osteotomy; *THR,* total hip replacement; *FHO,* femoral head/neck ostectomy; *DAR* plasty, dorsal acetabular rim arthroplasty; *NSAIDs,* non-steroidal anti-inflammatory drugs; *AD,* acetabulum denervation.

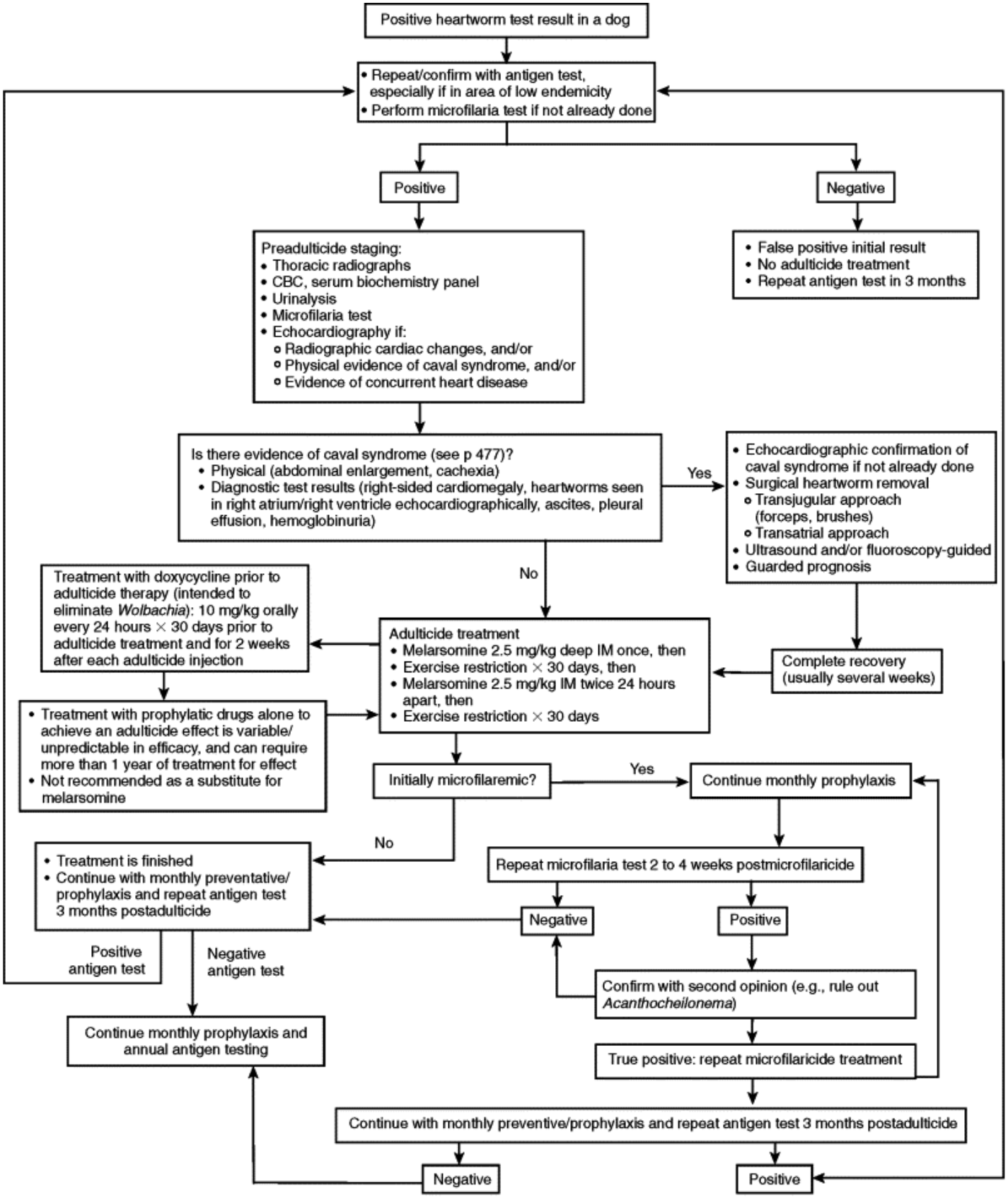
Author & Editor: Joseph Harari

Heat Stroke—Hyperthermia



Author: Scott P. Shaw
Editor: Elizabeth Rozanski

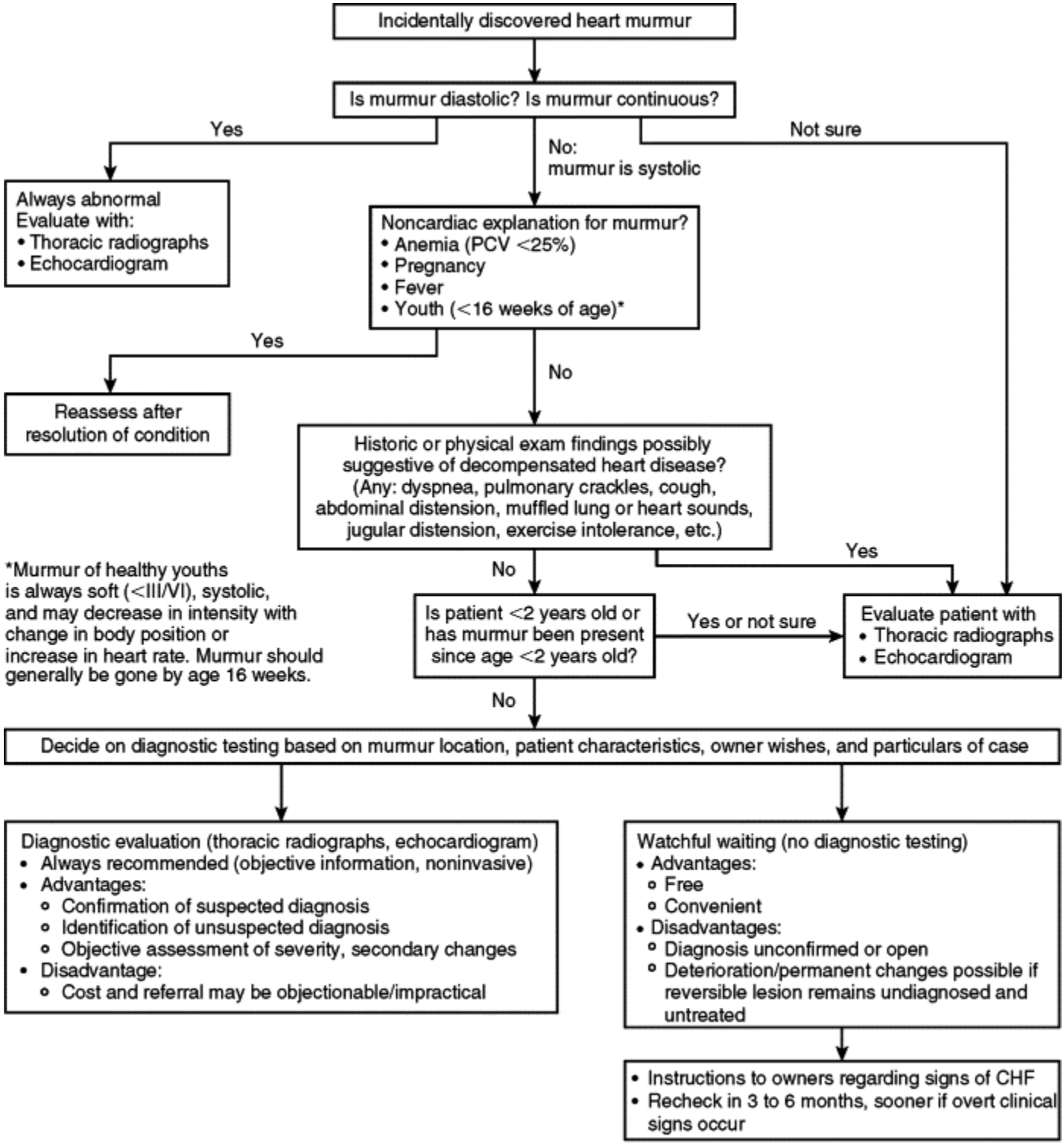
Heartworm Management



CBC, Complete blood count; *IM,* intramuscular.
Additional information available on the American Heartworm Society Web site: www.heartwormsociety.org.

Author & Editor: Etienne Côté

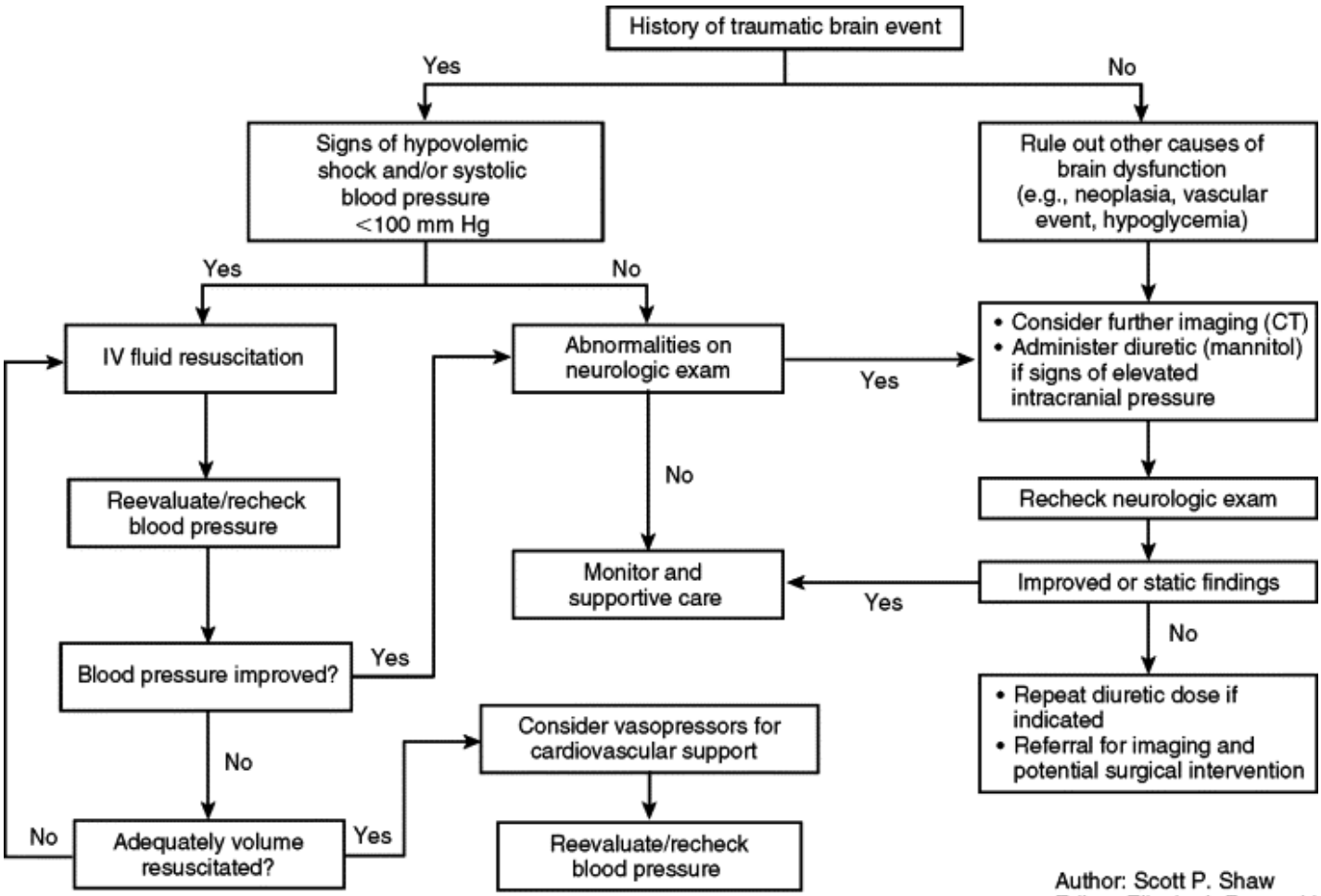
Heart Murmur: Incidental Finding ("Asymptomatic")



PCV, Packed cell volume; *CHF,* congestive heart failure.

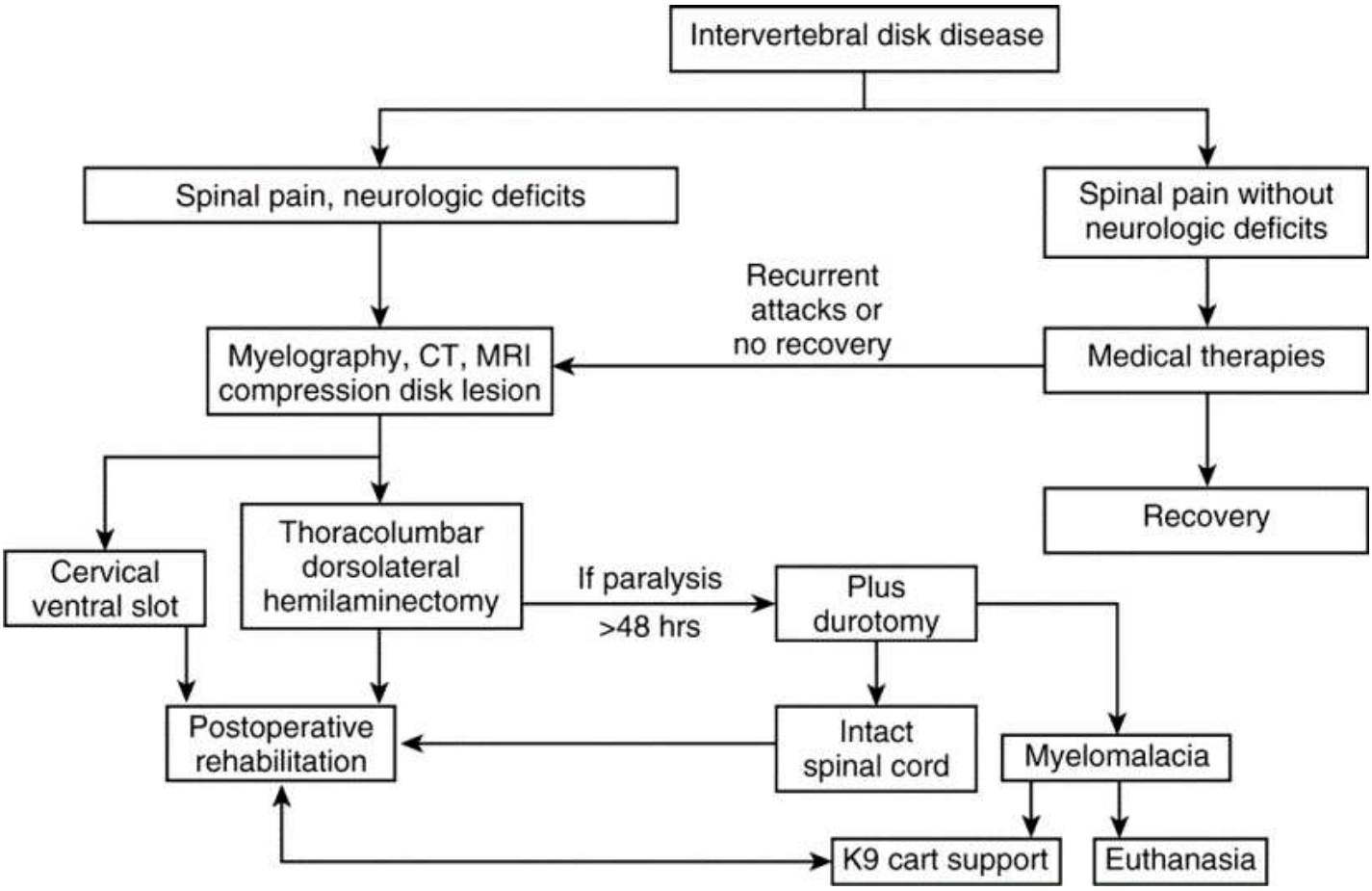
Author & Editor: Etienne Côté

Head Trauma



Author: Scott P. Shaw
Editor: Elizabeth Rozanski

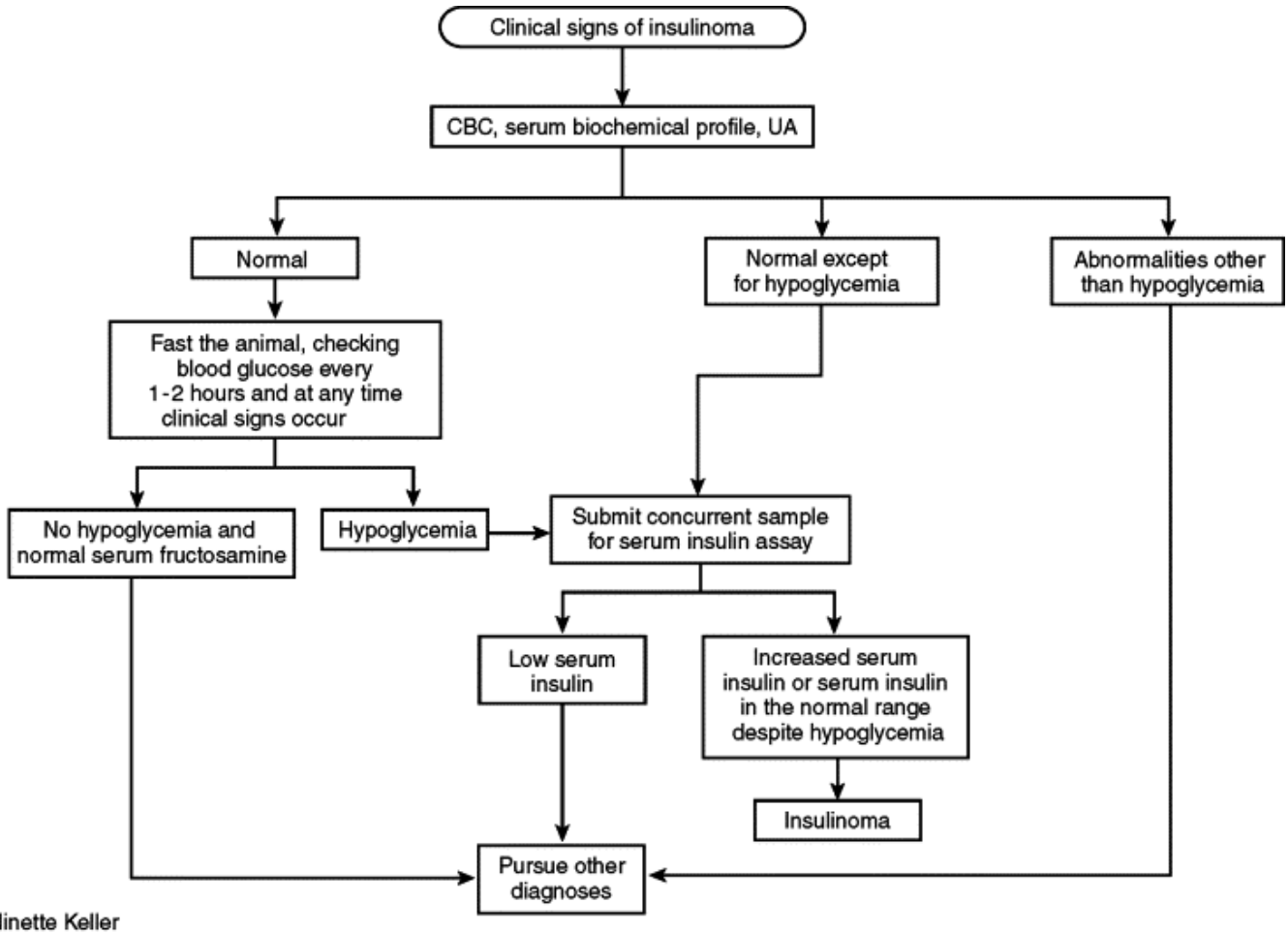
Intervertebral Disk Disease



CT, Computed tomography; *MRI,* magnetic resonance imaging; *K9,* canine.

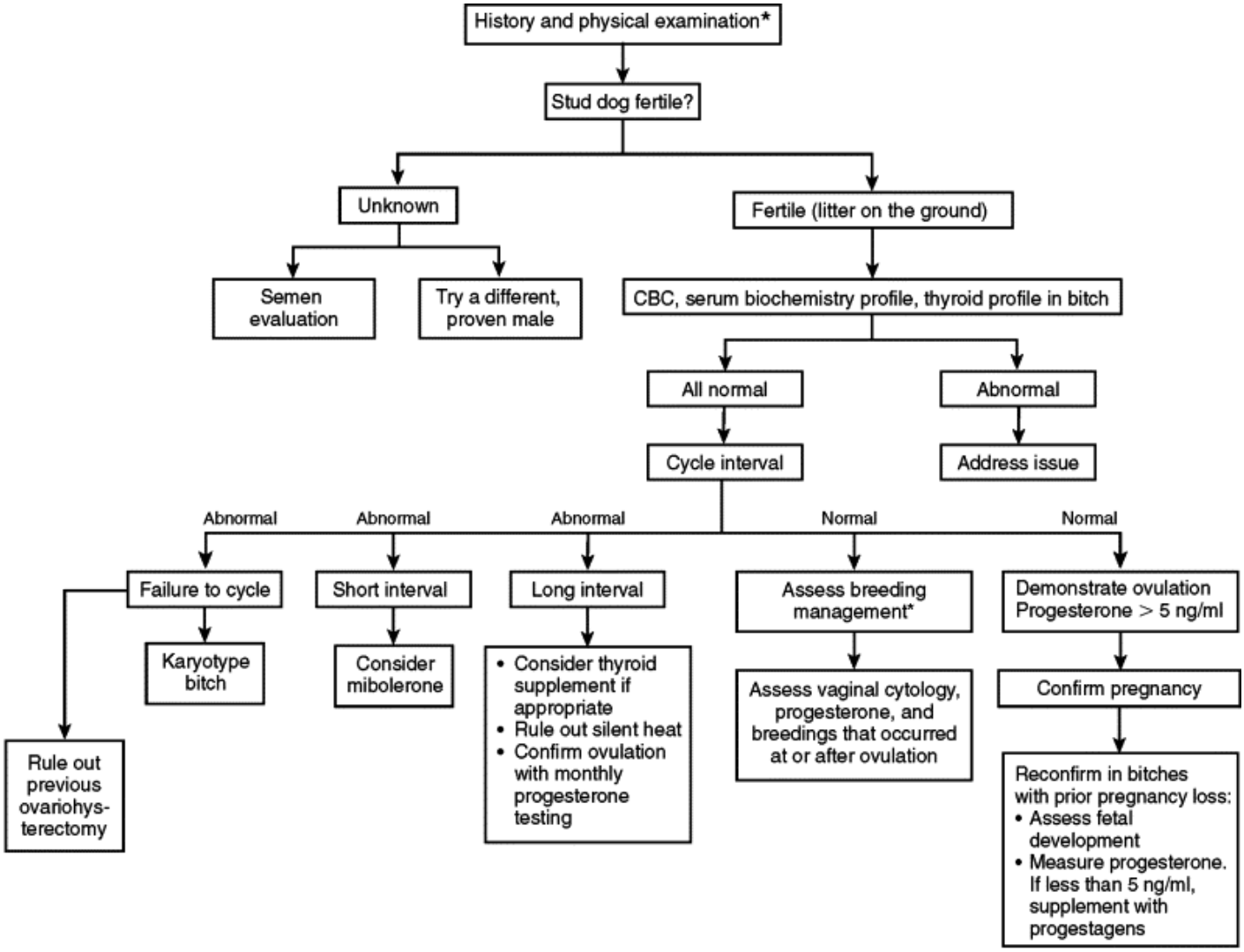
Author & Editor: Joseph Harari

Insulinoma: Diagnosis



Author: Ninette Keller
Editor: Sherri Ihle

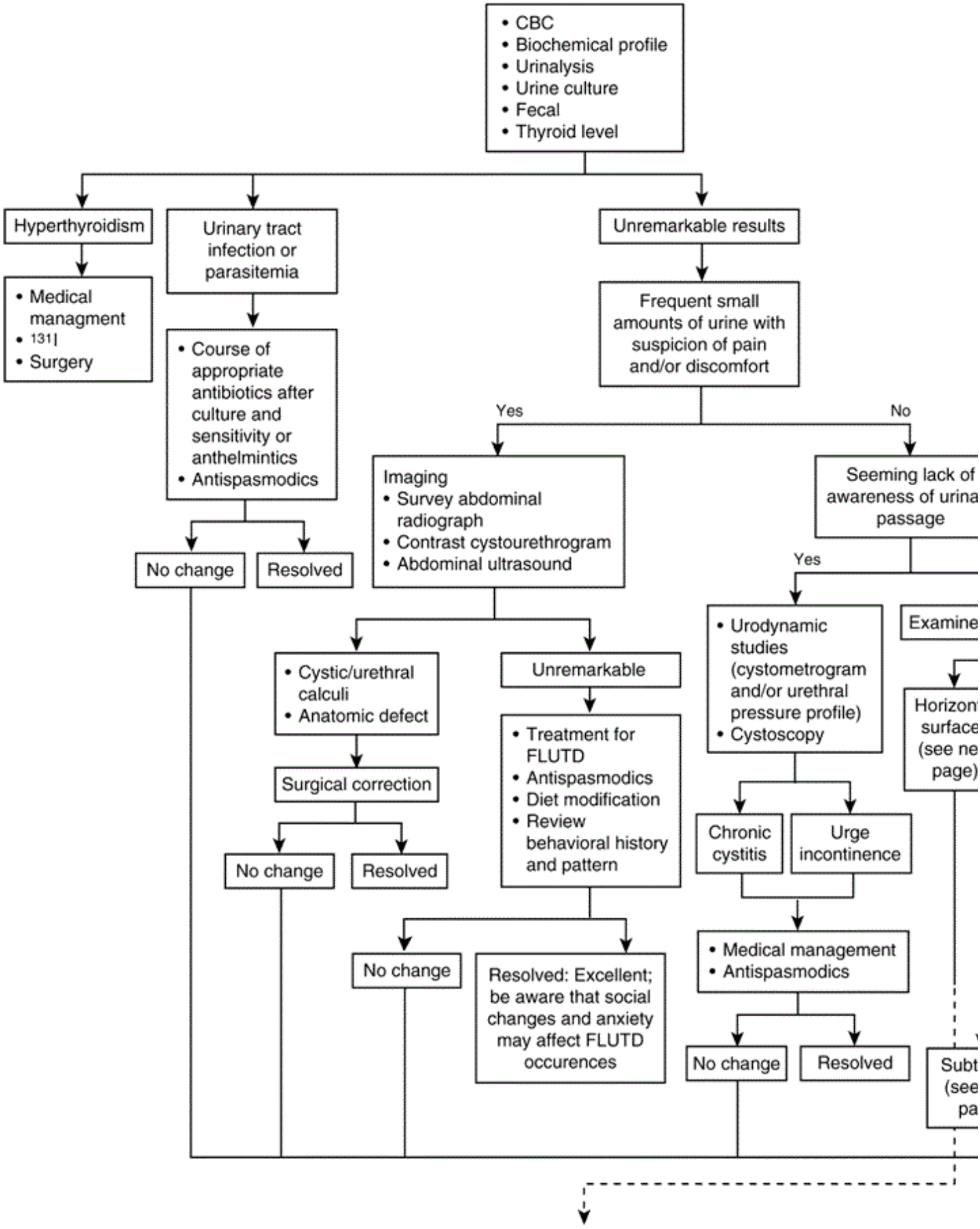
Infertility in the Canine Female: Keys to Solving Infertility Problems



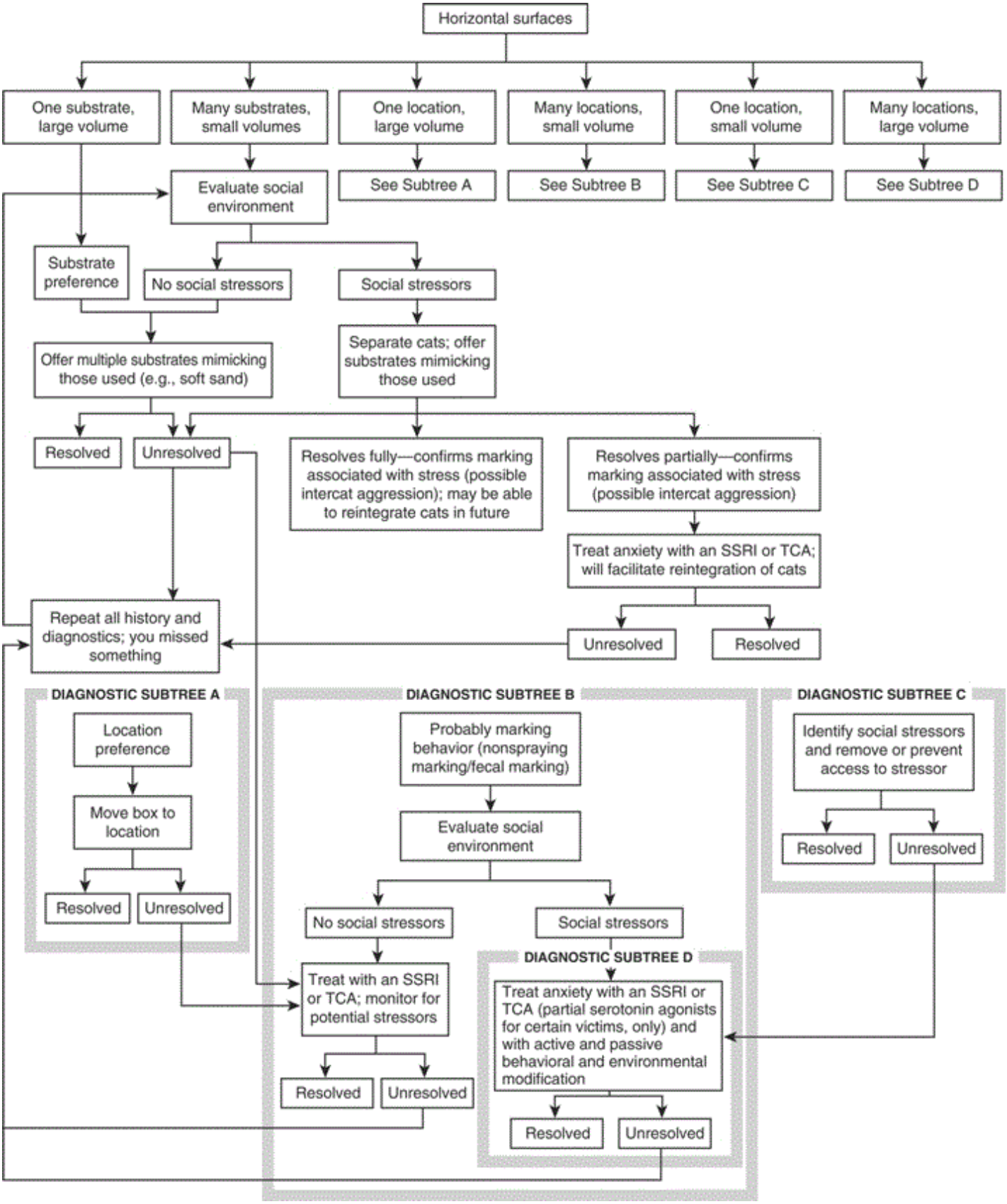
* Most important.

Author: Frances O. Smith
Editor: Michelle A. Kutzler

Inappropriate Elimination, Cat



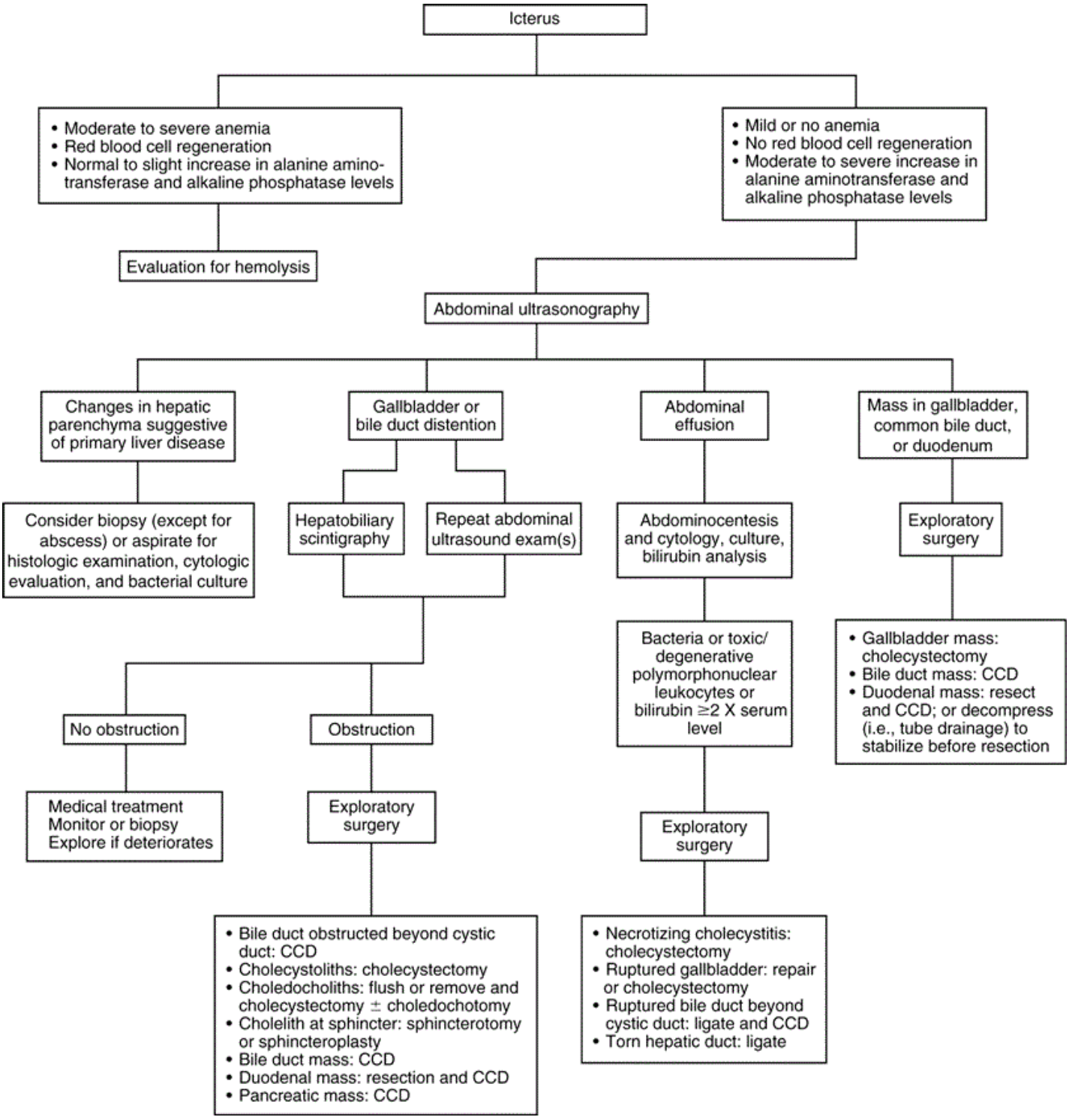
CBC, Complete blood count; *FLUTD*, feline lower urinary tract disease.



SSRI, Selective serotonin reuptake inhibiting drug (e.g., fluoxetine, paroxetine); *TCA,* tricyclic antidepressants (e.g., amitriptyline, nortriptyline, clomipramine).

Author & Editor: Karen L. Overall

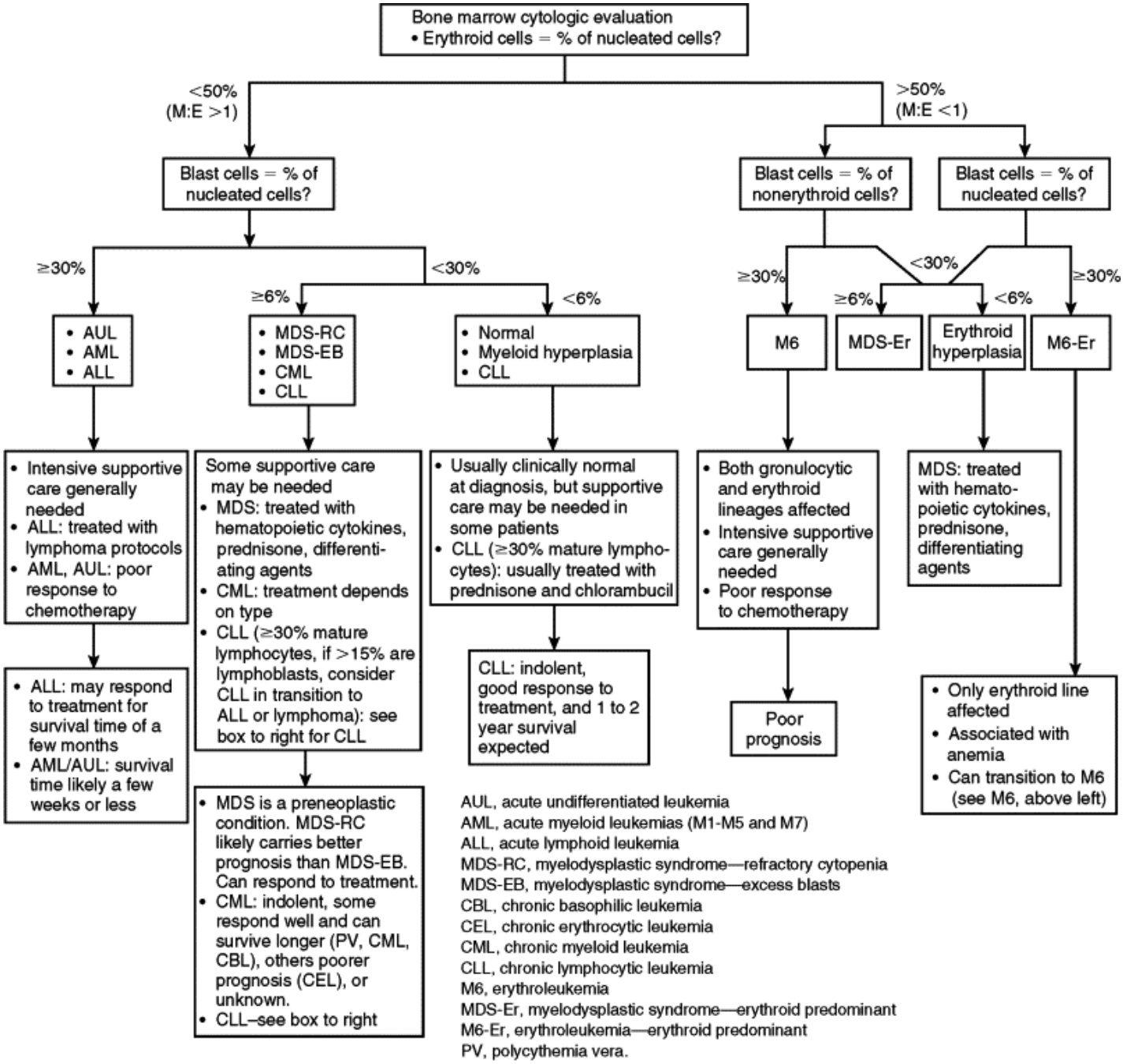
Icterus: Management



CCD, Cholecystoduodenostomy.

Modified from Slatter DH: Textbook of Small Animal Surgery, ed 3, St Louis, 2003, WB Saunders.

Leukemias: Classification and Treatment

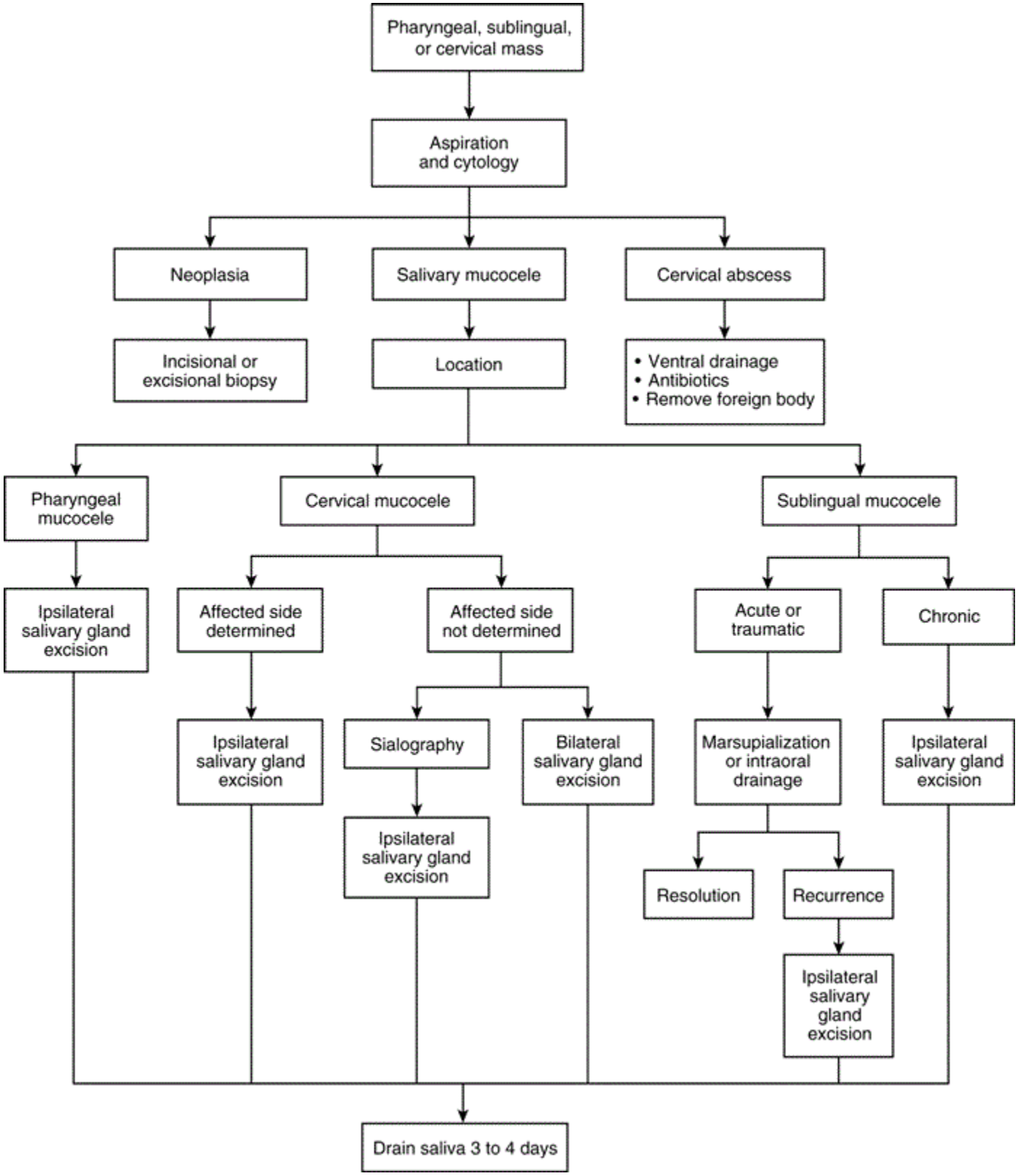


AUL, acute undifferentiated leukemia
AML, acute myeloid leukemias (M1-M5 and M7)
ALL, acute lymphoid leukemia
MDS-RC, myelodysplastic syndrome—refractory cytopenia
MDS-EB, myelodysplastic syndrome—excess blasts
CBL, chronic basophilic leukemia
CEL, chronic erythrocytic leukemia
CML, chronic myeloid leukemia
CLL, chronic lymphocytic leukemia
M6, erythroleukemia
MDS-Er, myelodysplastic syndrome—erythroid predominant
M6-Er, erythroleukemia—erythroid predominant
PV, polycythemia vera.

Author: Nicole C. Northrup
Editor: Kenneth M. Rassnick

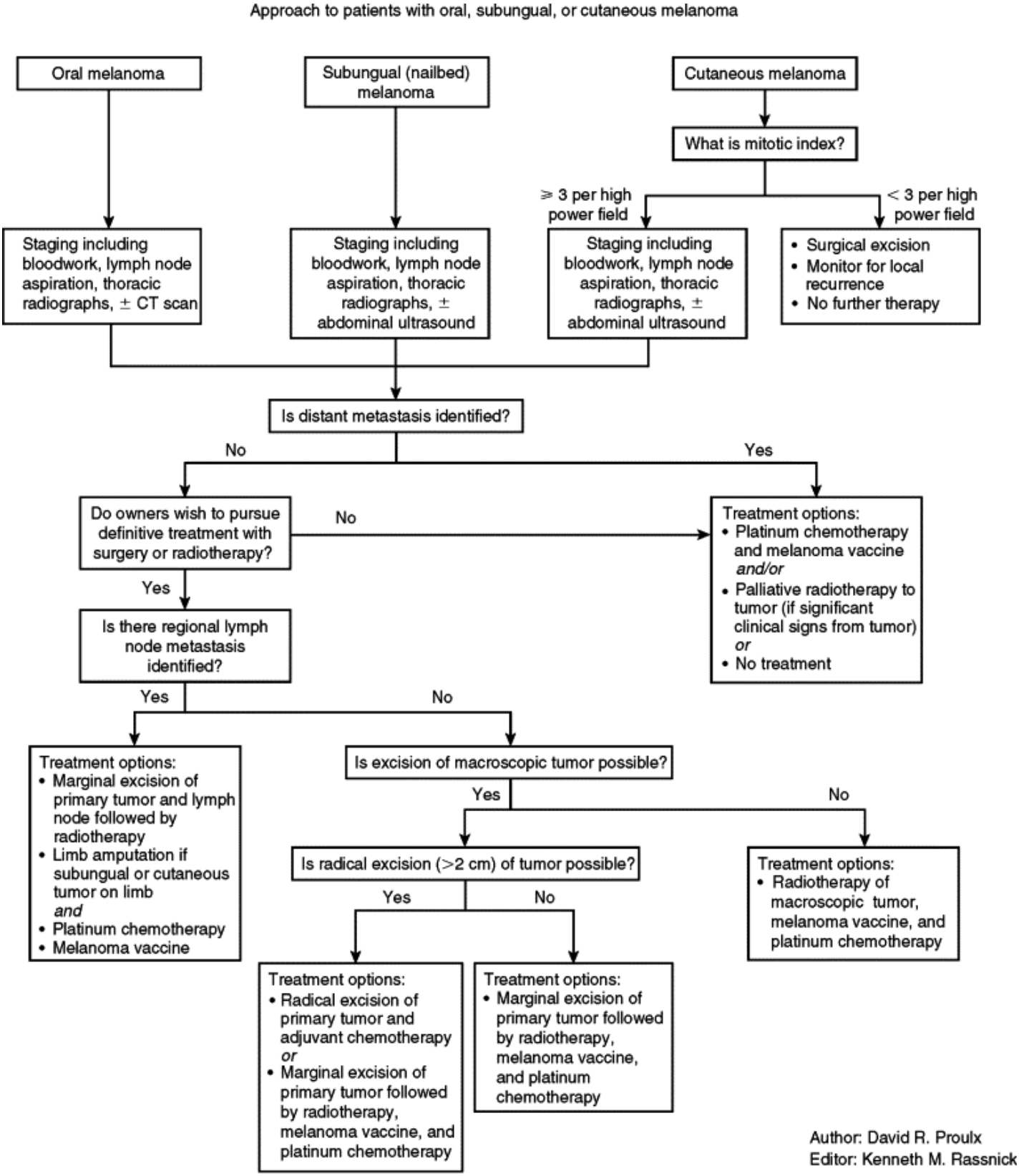
Based on the Animal Leukemia Study Group criteria for classification of acute myeloid leukemias in dogs and cats, and modified from Jacobs RM, Messick JB, Valli VE: Tumors of the hemolymphatic system. In Meuten DJ (ed): Tumors in domestic animals, ed 4, Ames, IA, 2002, Iowa State Press, pp 119-198.

Mucocele, Salivary



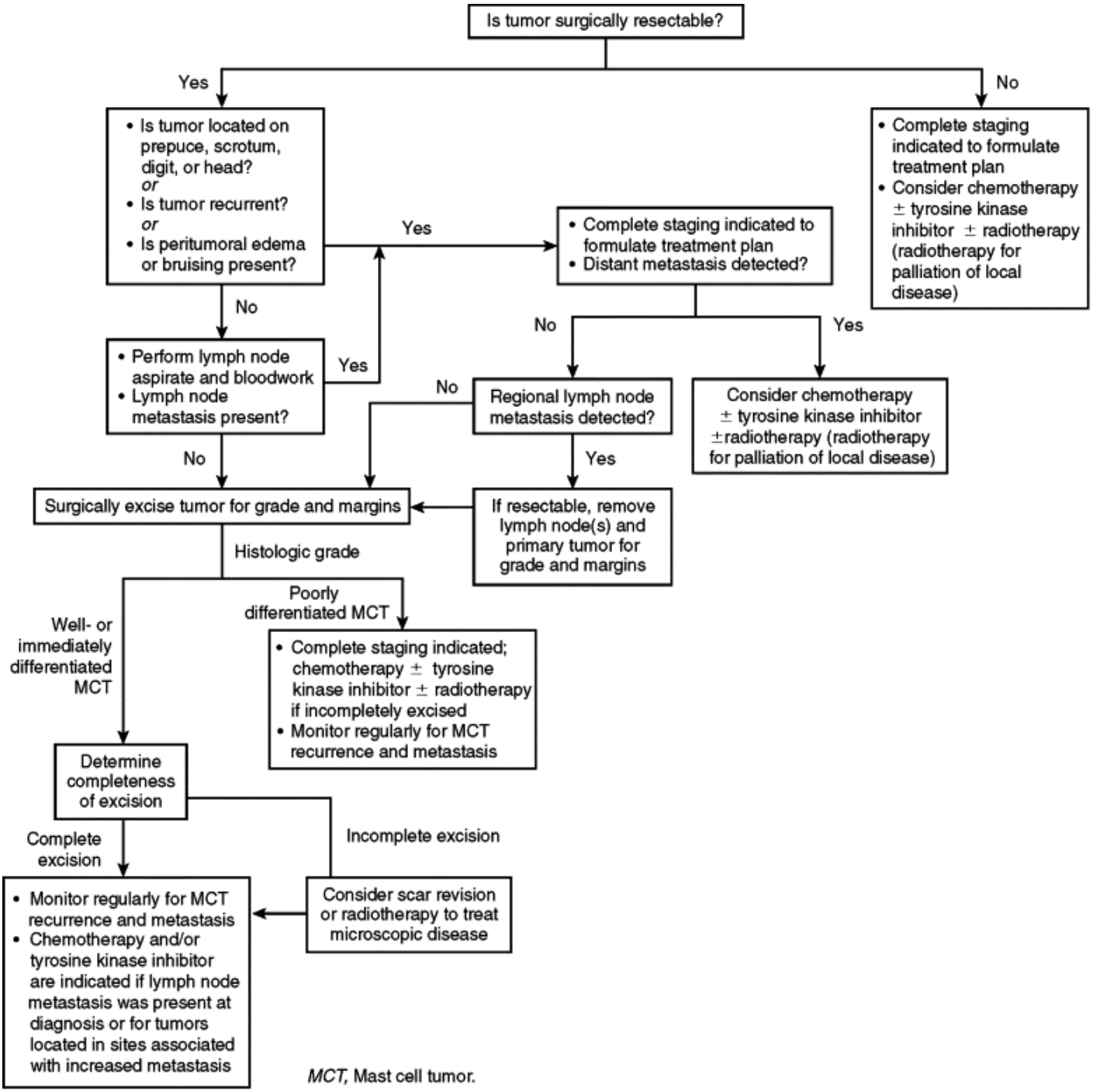
Modified from Ettinger SJ, Feldman EC: Textbook of veterinary internal medicine, ed 7, St Louis, 2010, WB Saunders.

Melanoma



CT, Computed tomography.

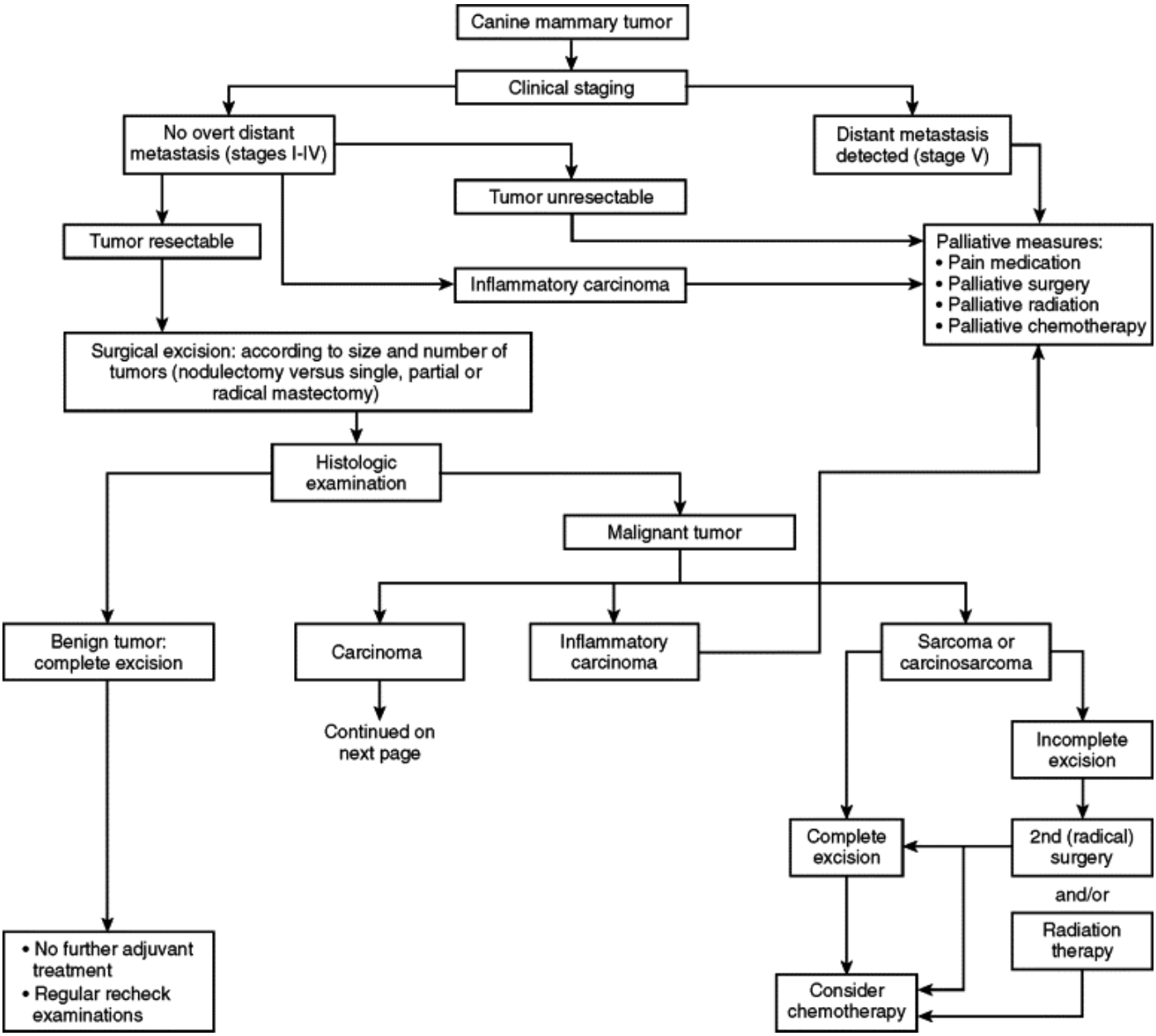
Mast Cell Tumor in the Dog

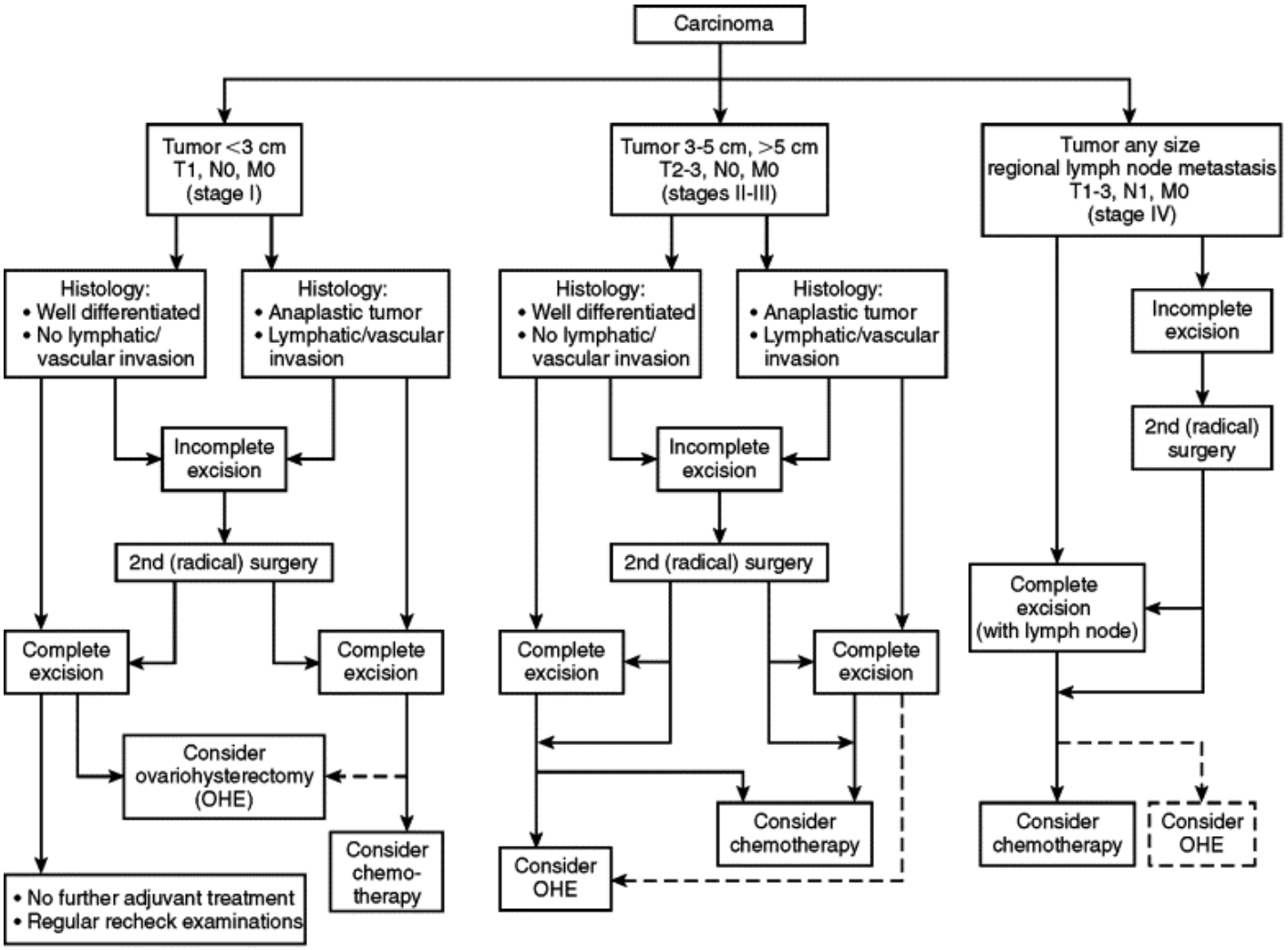


MCT, Mast cell tumor.

Author: Tracy Gieger
Editor: Kenneth M. Rassnick

Mammary Gland Tumors, Dog

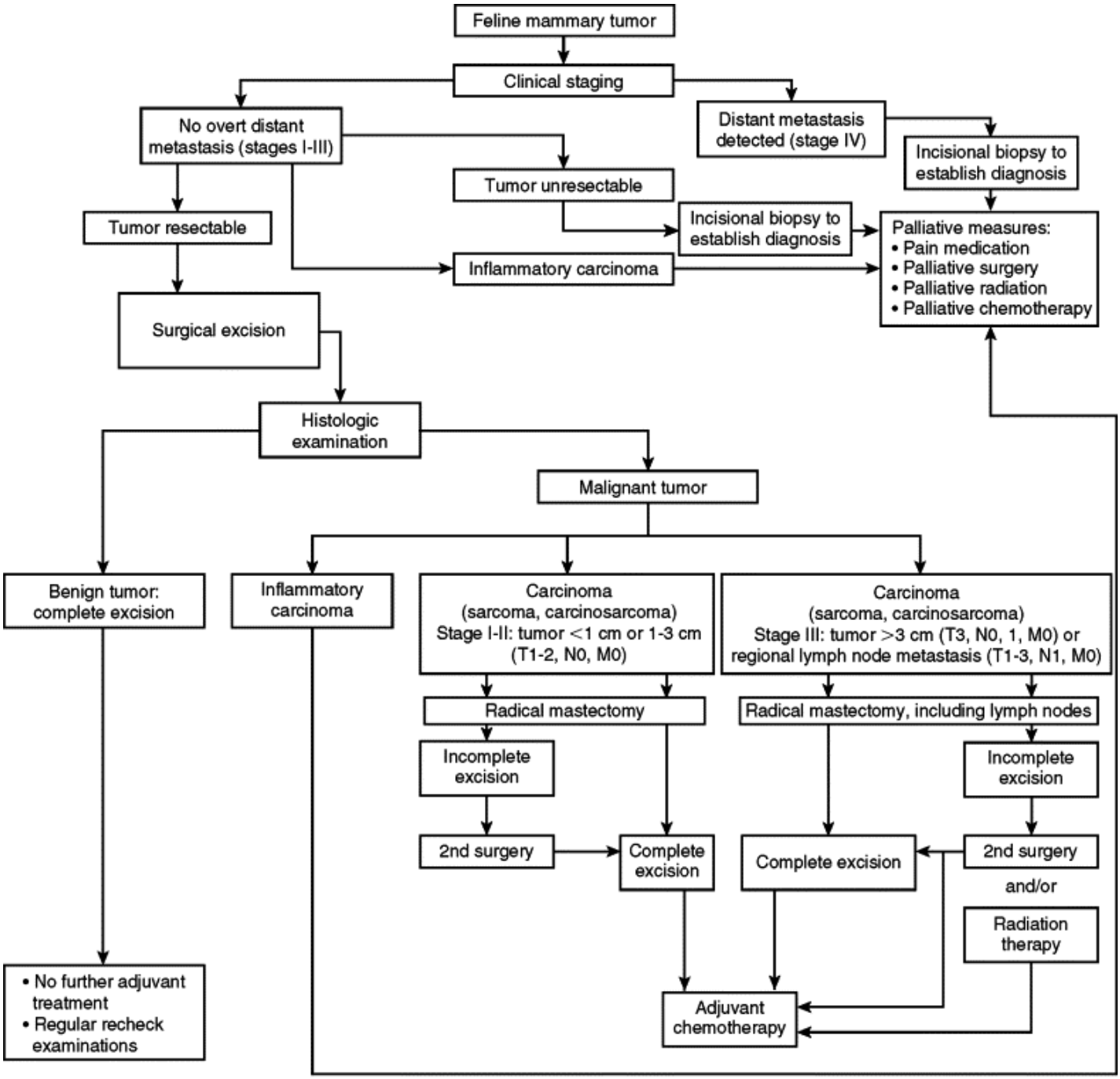




Dashed lines represent possible but nonessential courses of action.

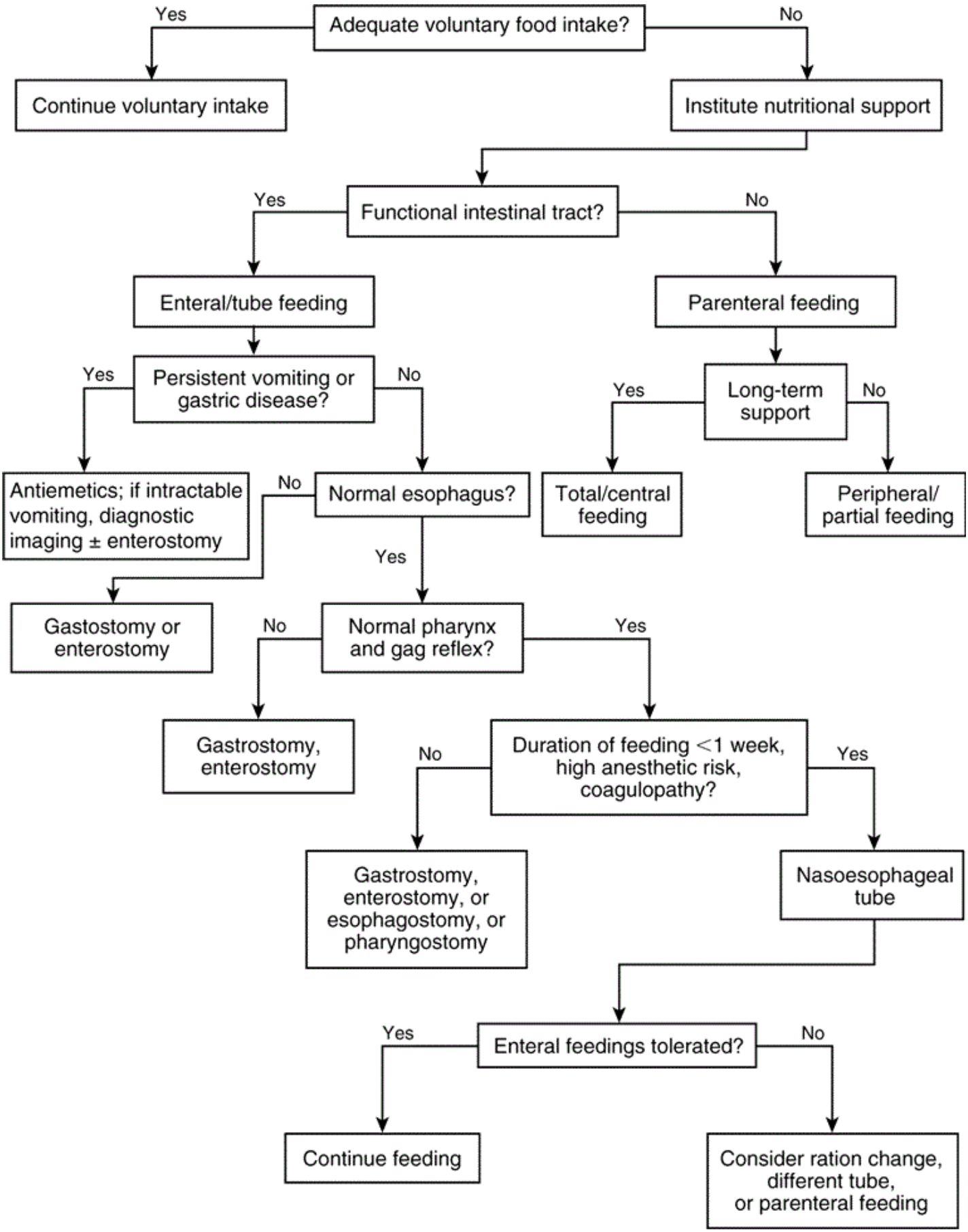
Updated & edited: Kenneth M. Rassnick
Ist Edition Author: Daniela Simon

Mammary Gland Tumors, Cat



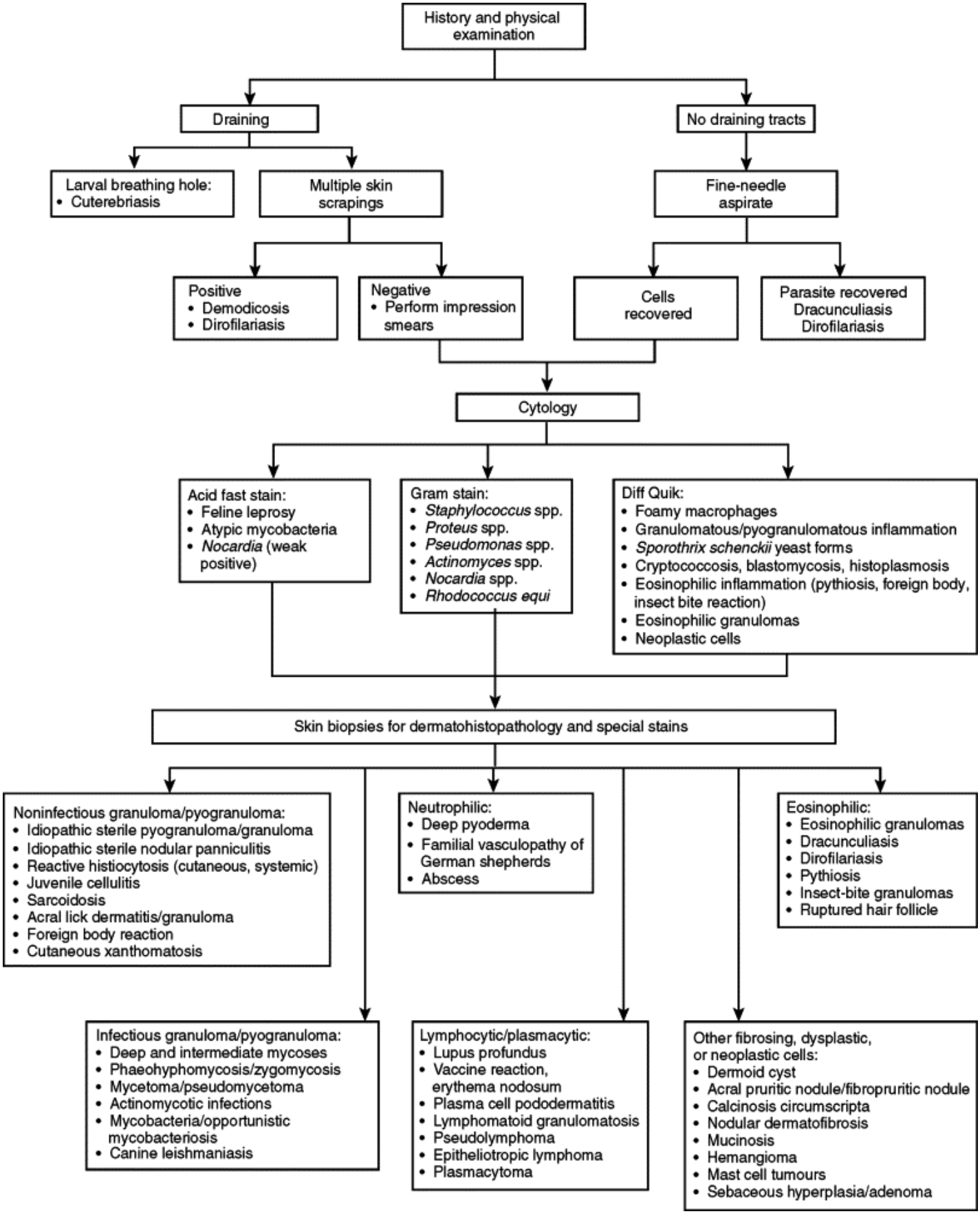
Updated & edited: Kenneth M. Rassnick
1st Edition Author: Daniela Simon

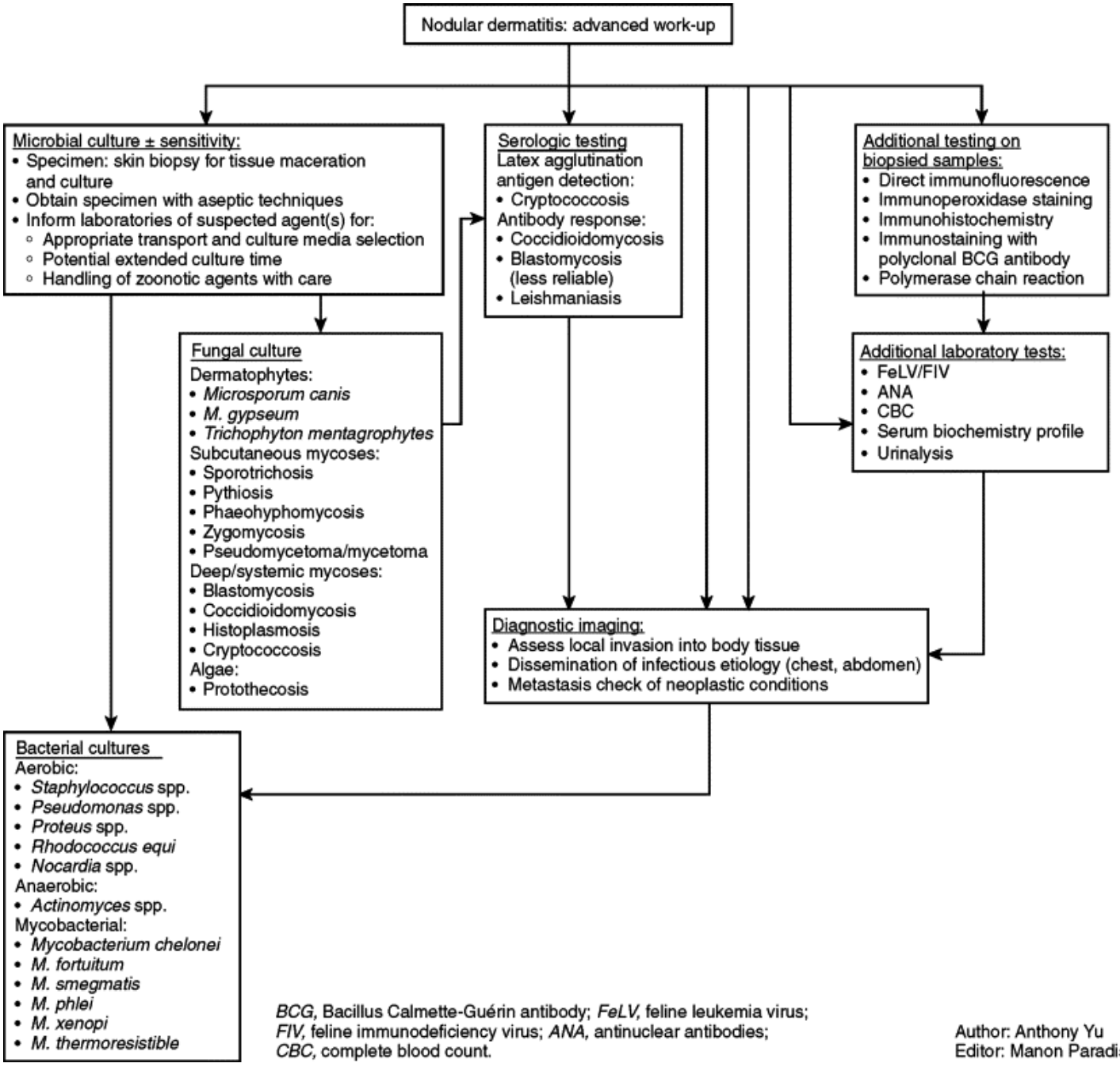
Nutritional Support, Decision-Making



Modified from Slatter DH: Textbook of small animal surgery, ed 3, St Louis, 2003, WB Saunders.

Nodular Dermatosis

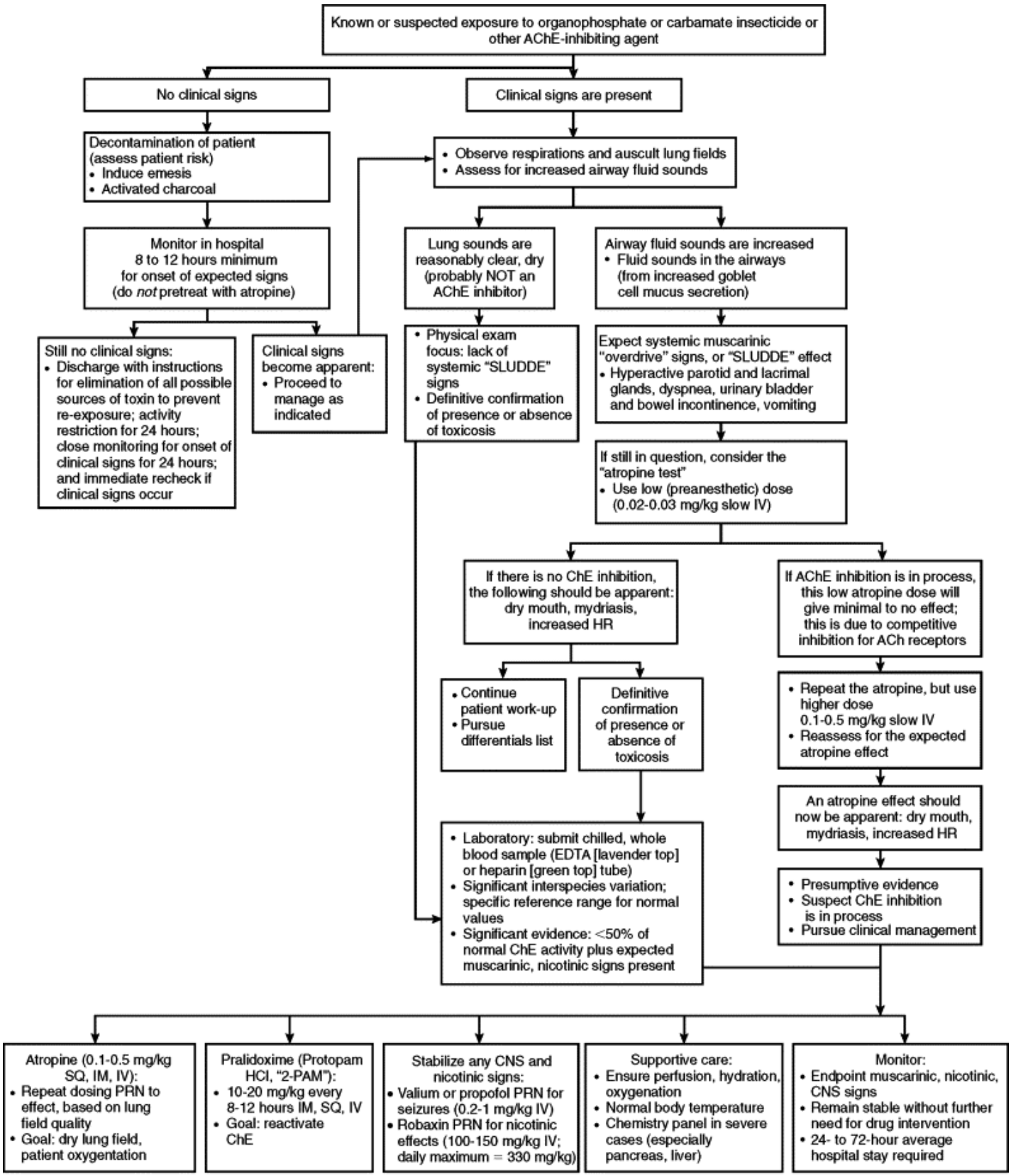




BCG, Bacillus Calmette-Guérin antibody; *FeLV,* feline leukemia virus; *FIV,* feline immunodeficiency virus; *ANA,* antinuclear antibodies; *CBC,* complete blood count.

Author: Anthony Yu
Editor: Manon Paradis

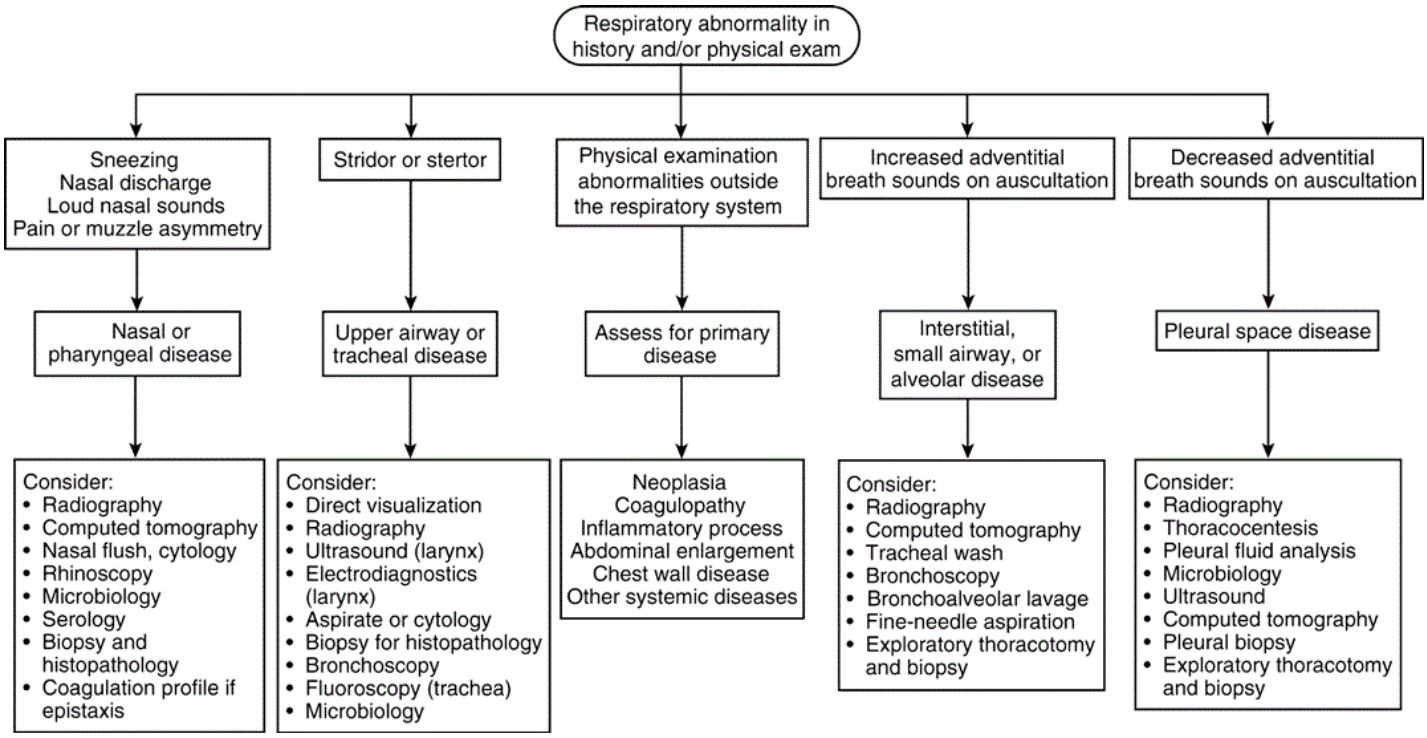
Organophosphate and Carbamate Toxicity



ACh, Acetylcholine; *AChE,* Acetylcholinesterase, cholinesterase; *CNS,* central nervous system; *HR,* heart rate; *IV,* intravenous; *IM;* intramuscular; *PRN,* as needed; *SQ,* subcutaneous; *SLUDDE,* salivation, lacrimation, urination, diarrhea, dyspnea, emesis.

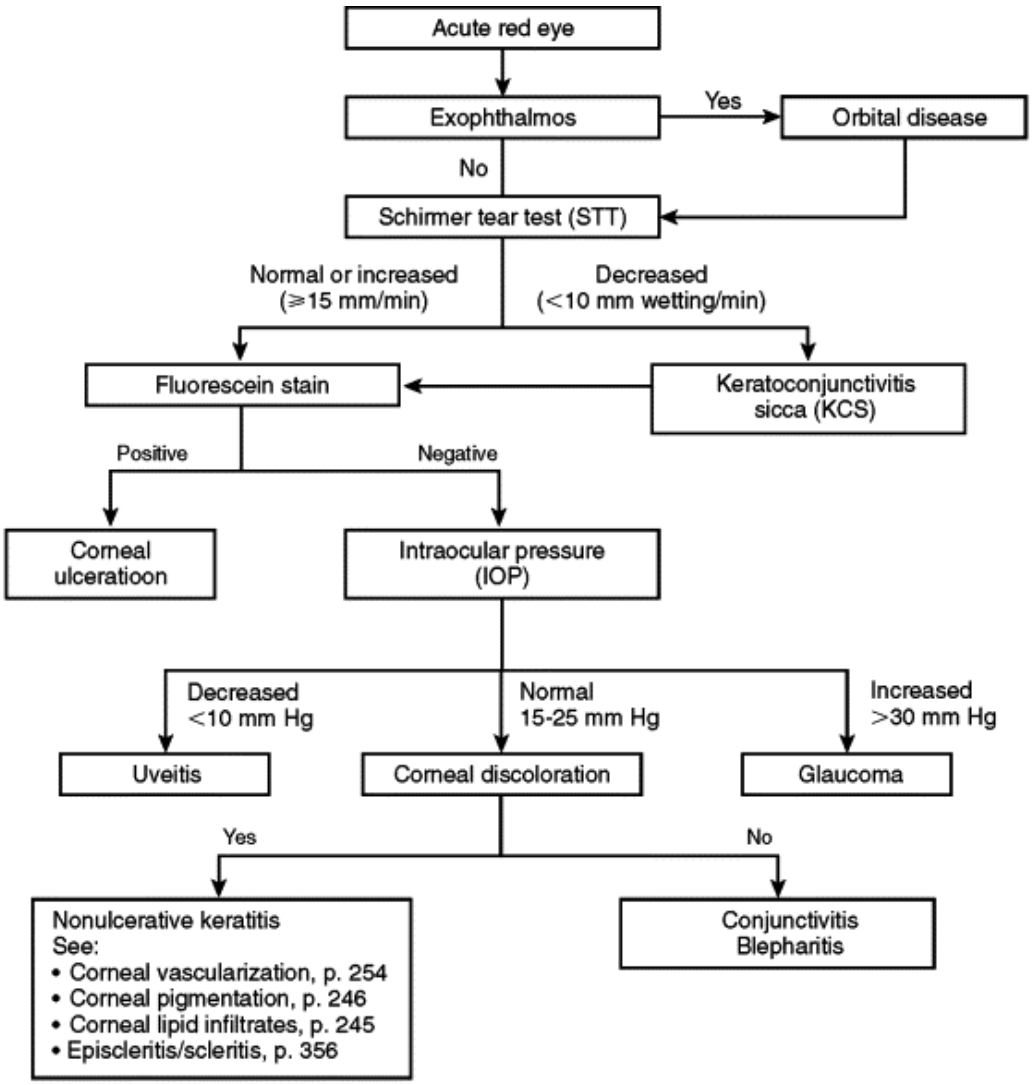
Author: Michael W. Knight
Editor: Safdar A. Khan

Respiratory Signs



Modified from Ettinger SJ, Feldman EC: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, WB Saunders.

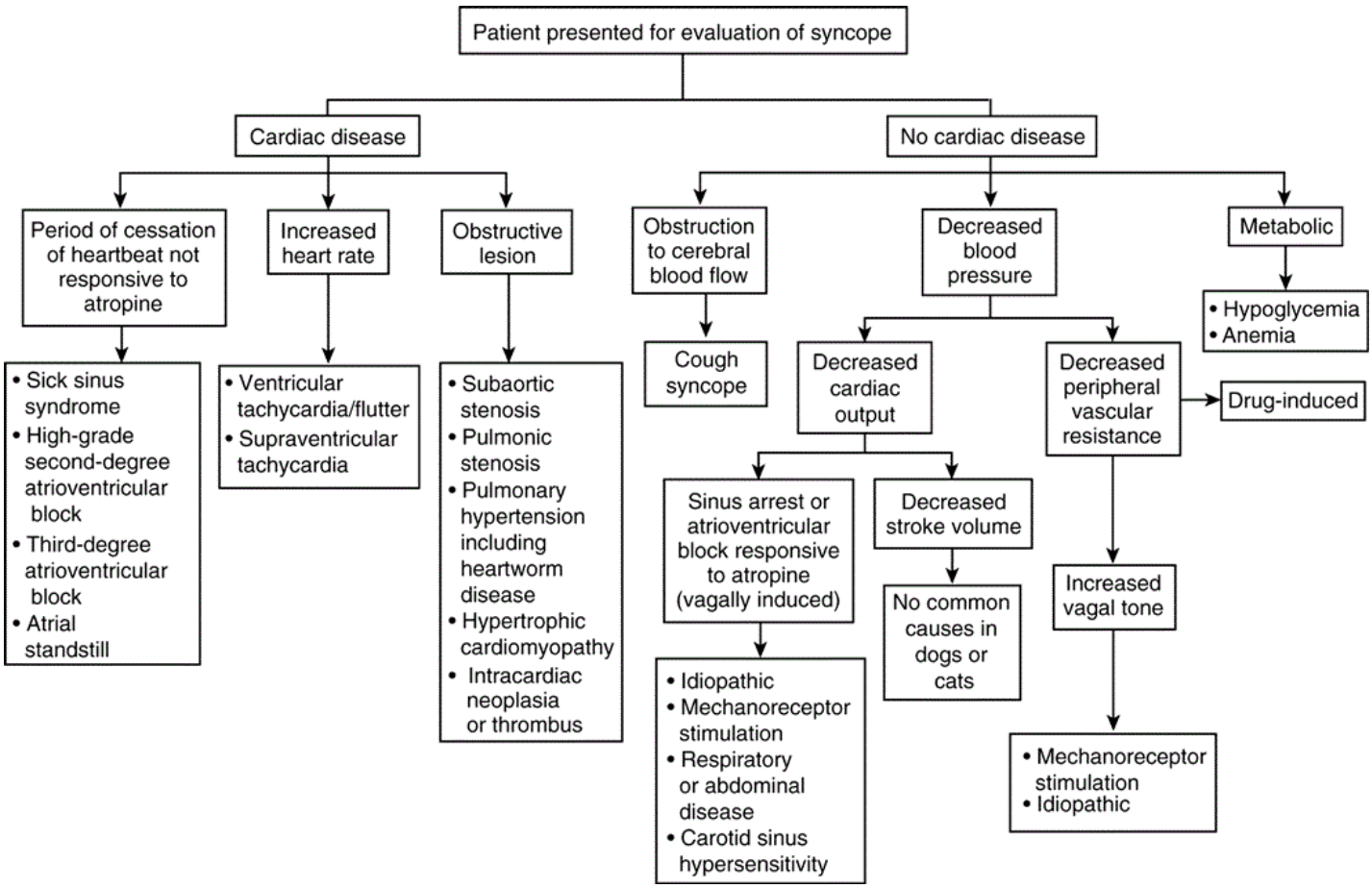
Red Eye, Acute



Note: STT values ≥ 10 but <15 mm wetting/minute may be normal or indicative of early KCS; IOPs between 10-15 and 25-30 mm Hg may be normal for some animals (interpret STT values and IOPs in light of other ophthalmic findings).

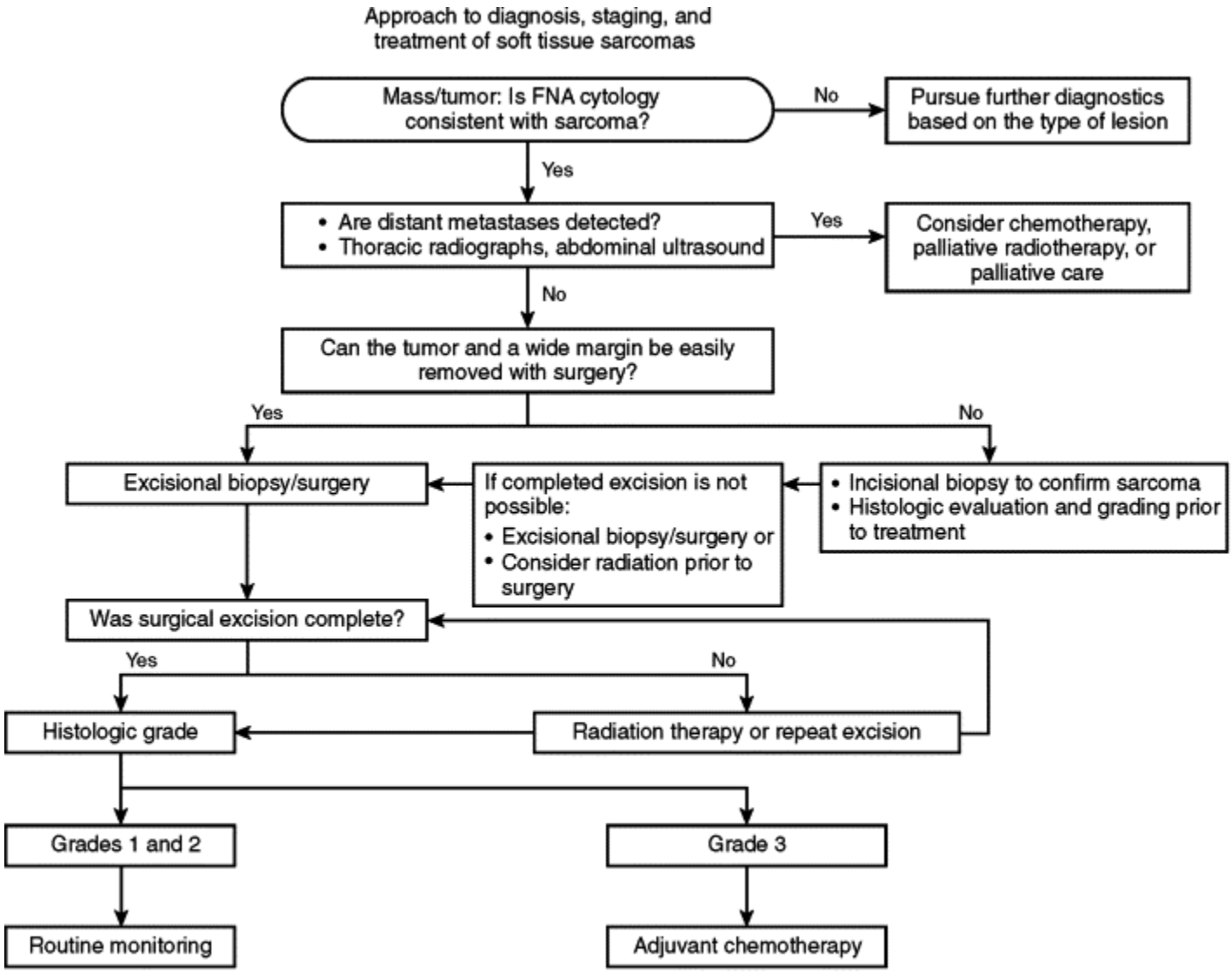
Author & Editor: Cheryl L. Cullen

Syncope



Modified from Kittleson MD, Kienle RD: Small animal cardiovascular medicine, St Louis, 1999, Mosby.

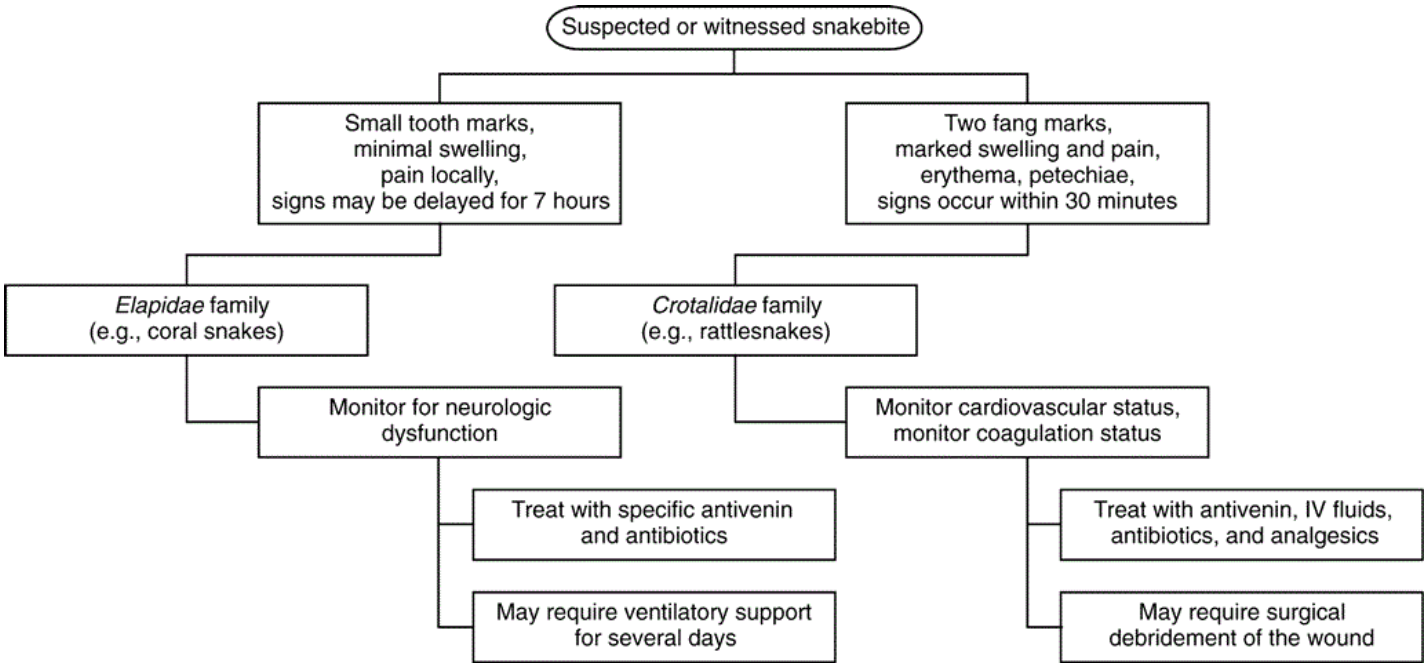
Soft Tissue Sarcoma



FNA, Fine needle aspiration.

Author: John Farrelly
Editor: Kenneth M. Rassnick

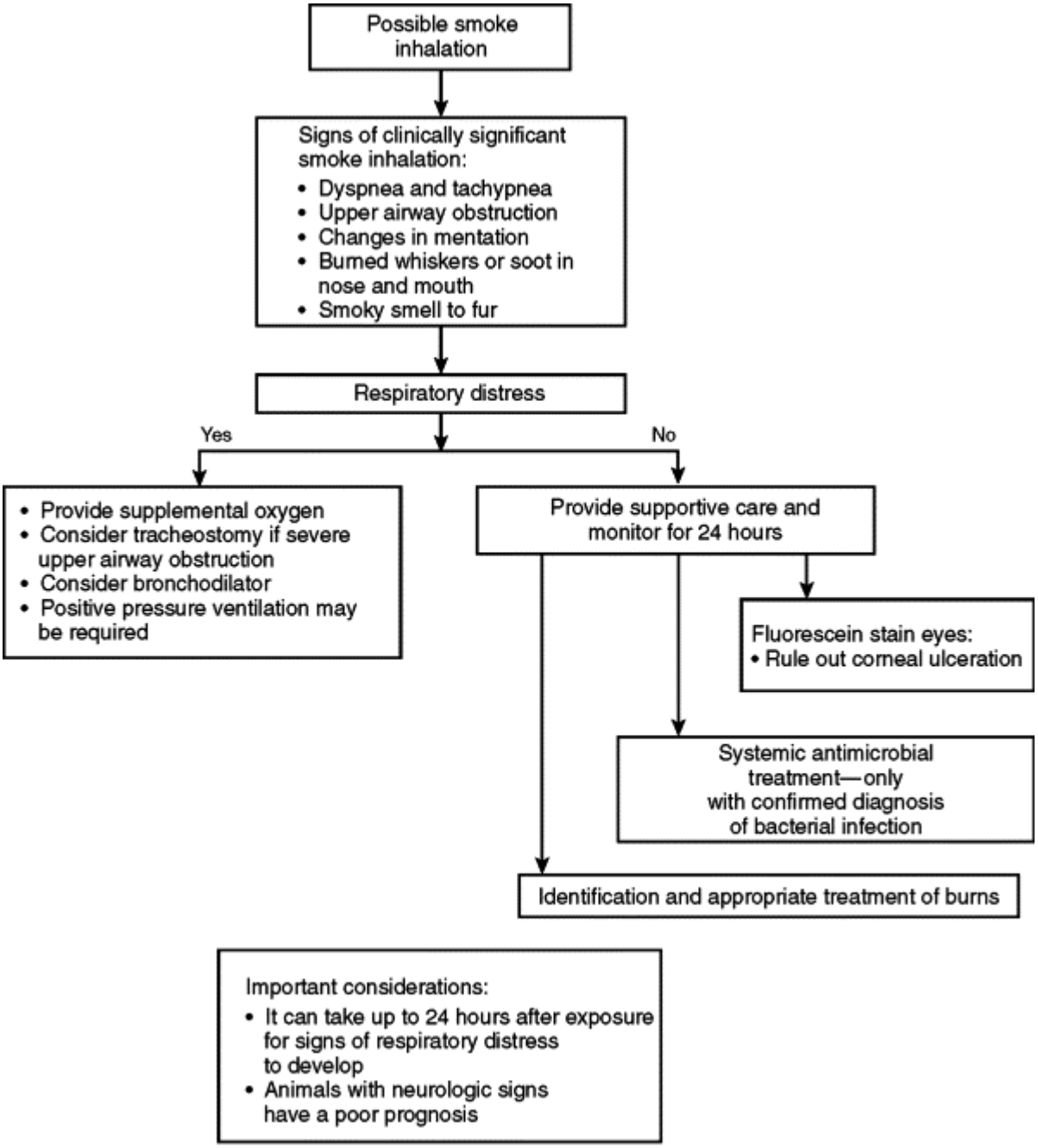
Snakebite



Author: April Paul

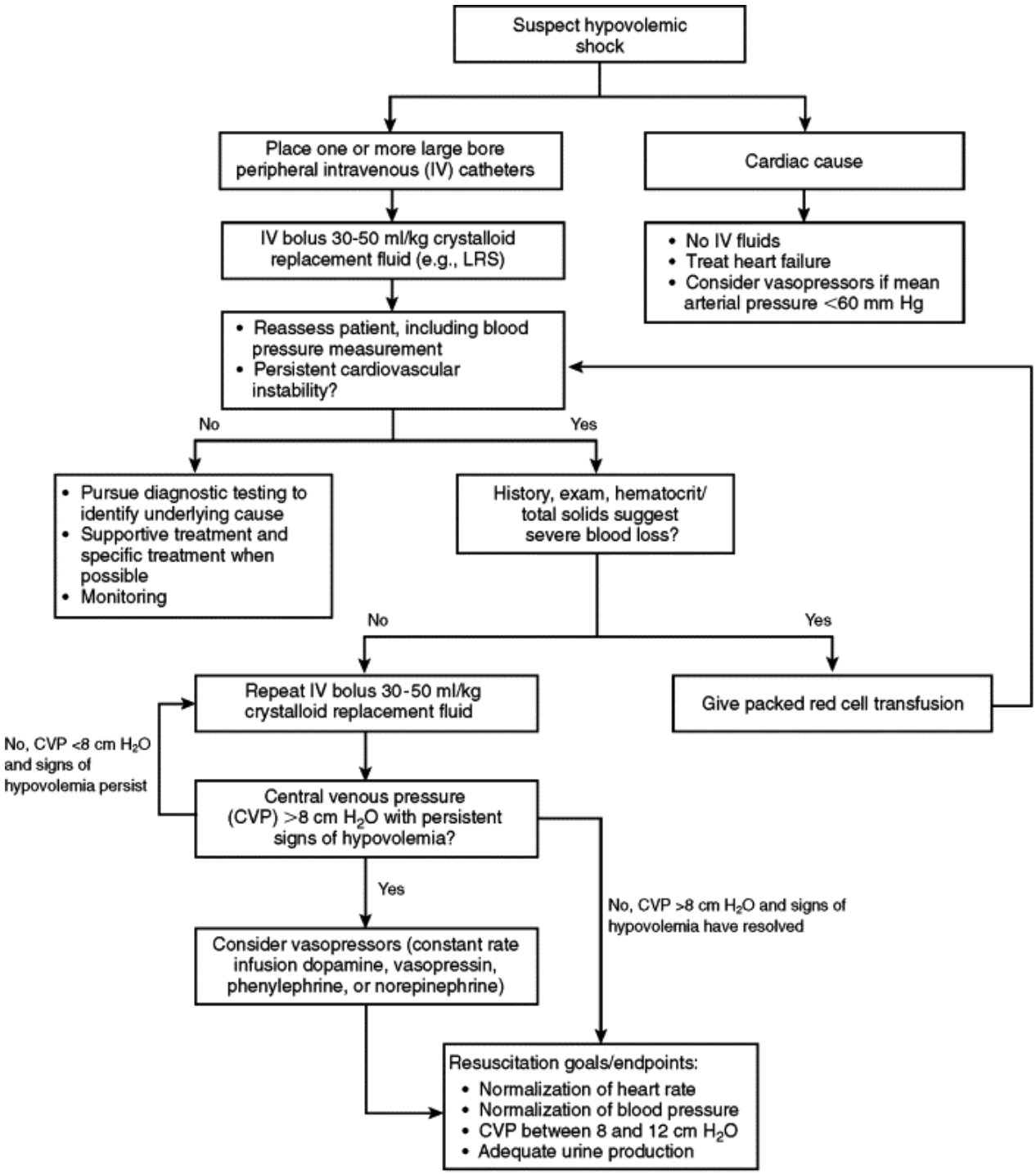
Editor: Elizabeth Rozanski

Smoke Inhalation



Author: Scott P. Shaw
Editor: Elizabeth Rozanski

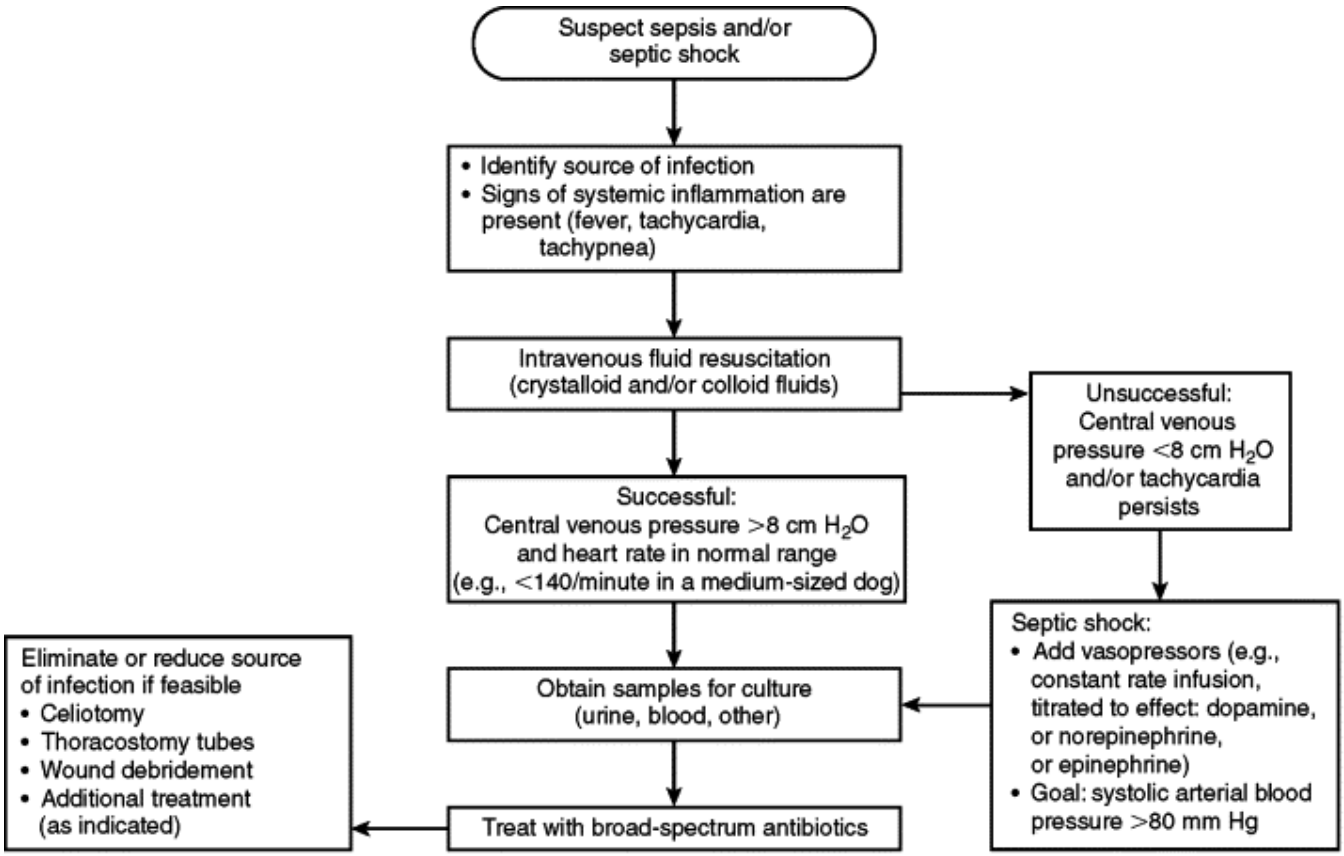
Shock, Hypovolemic



LRS, Lactated Ringer's solution.

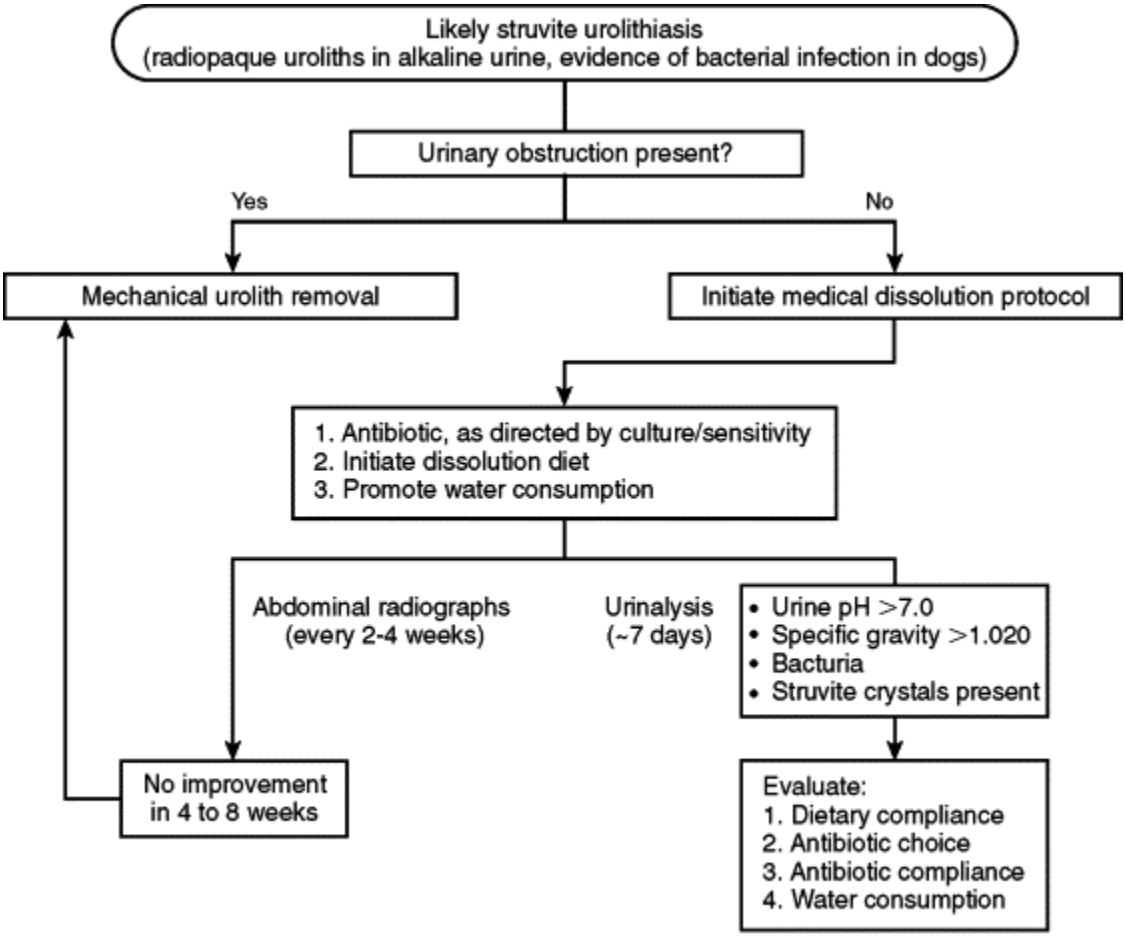
Author: Scott P. Shaw
Editor: Elizabeth Rozanski

Sepsis and Septic Shock



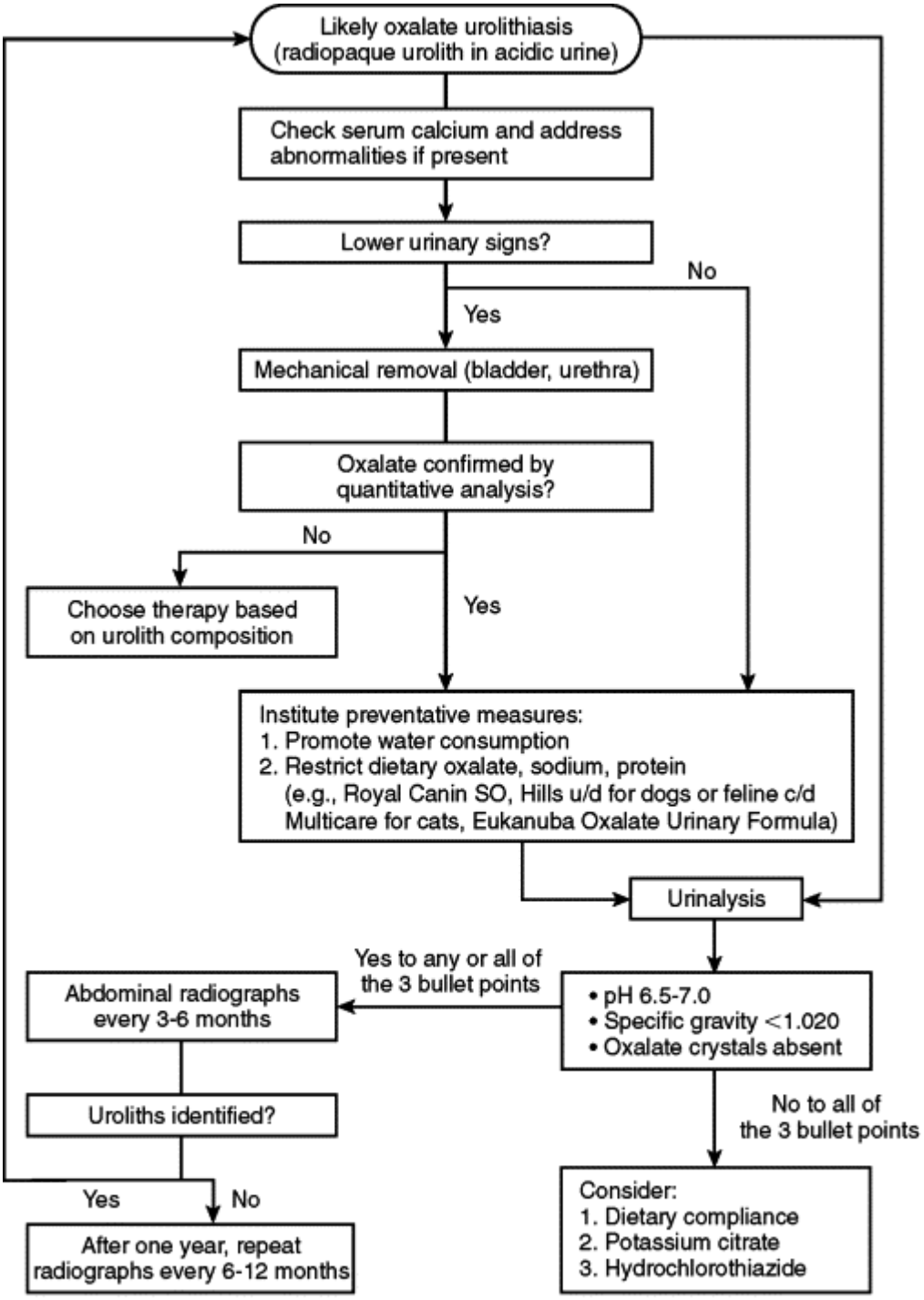
Author: Scott P. Shaw
Editor: Elizabeth Rozanski

Uroliths, Struvite



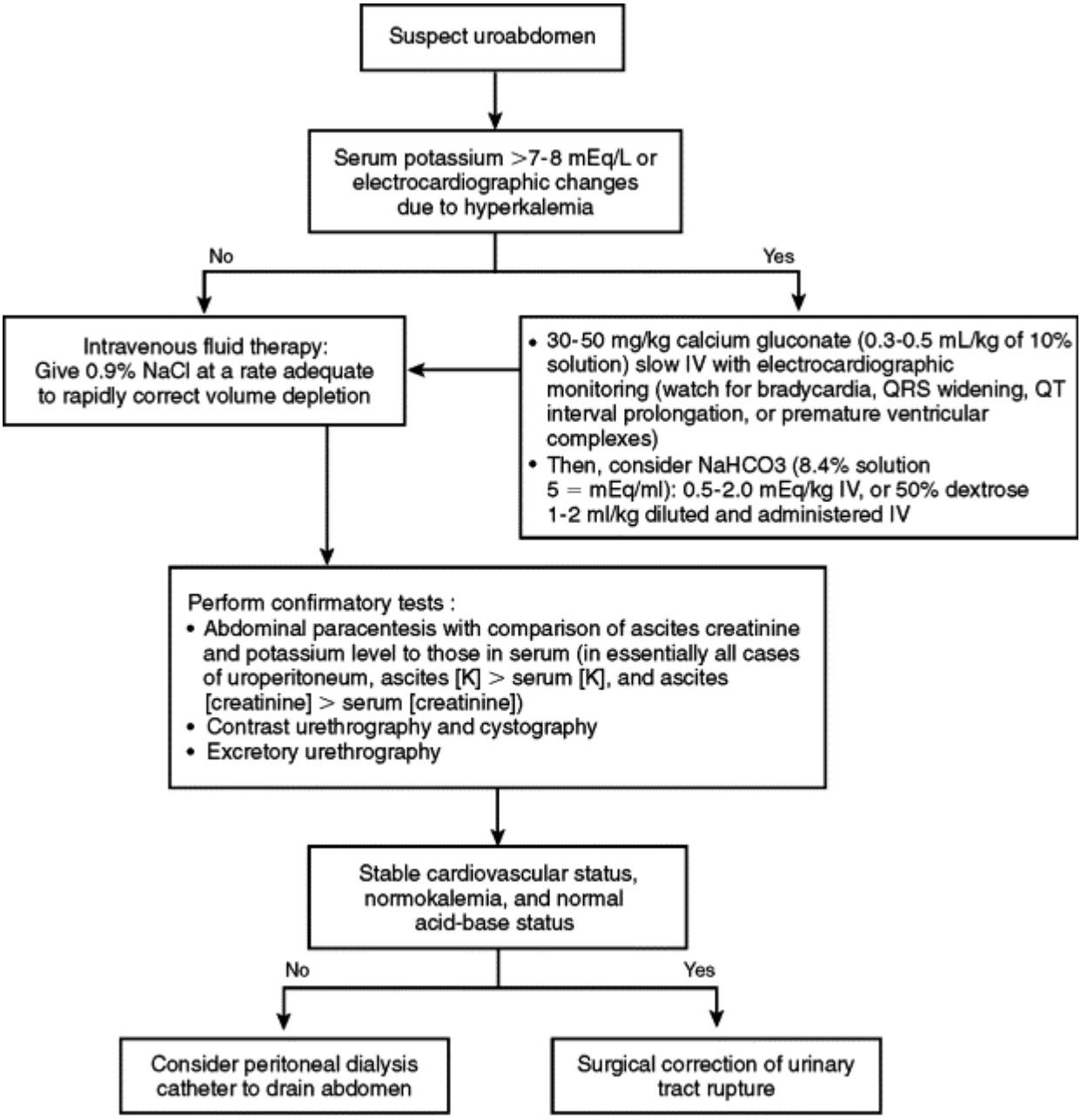
Author: Karen K. Faunt
Editor: Leah A. Cohn

Uroliths, Oxalate



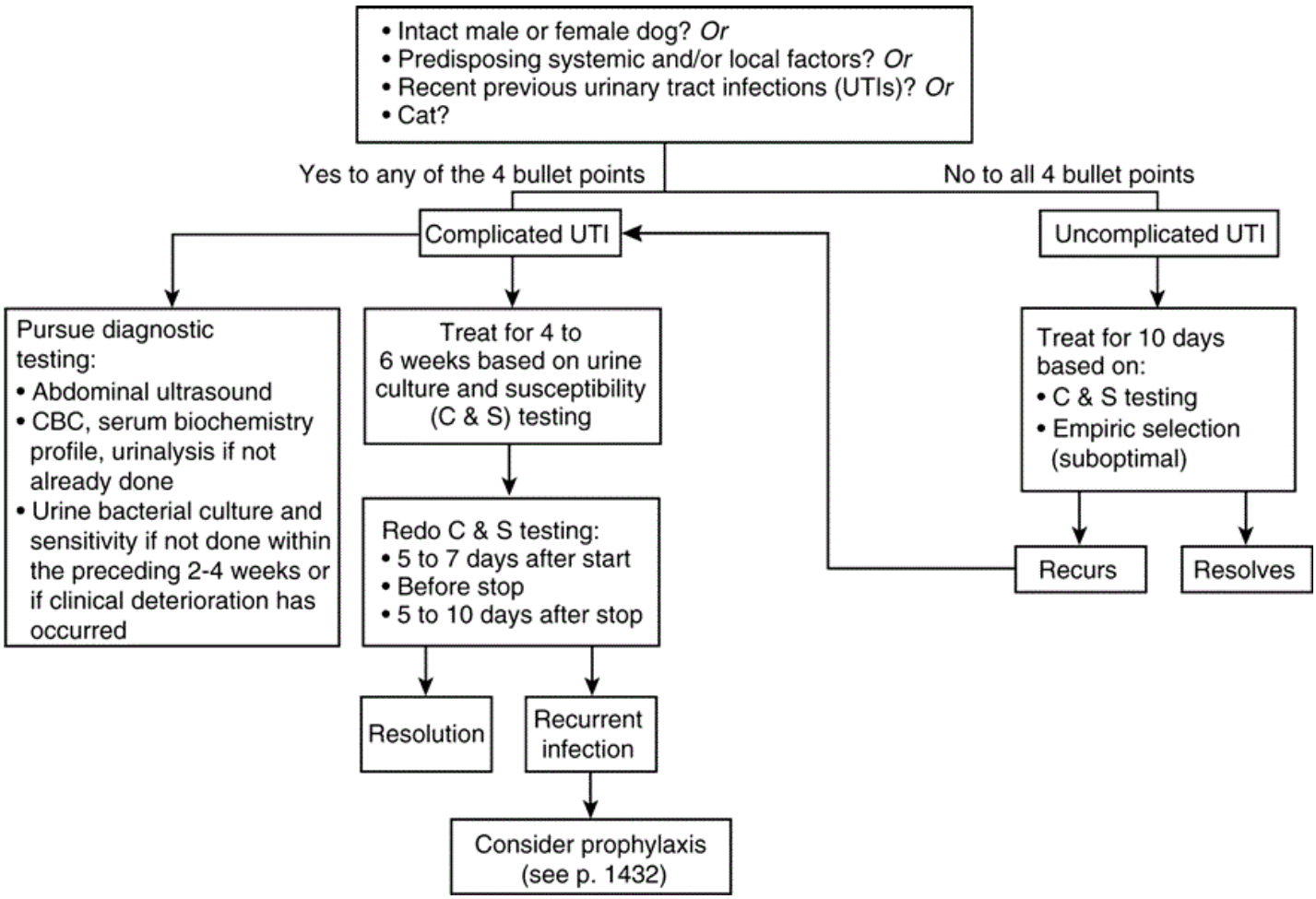
Author: Karen K. Faunt
Editor: Leah A. Cohn

Uroabdomen



Author: Scott P. Shaw
Editor: Elizabeth Rozanski

Urinary Tract Infection



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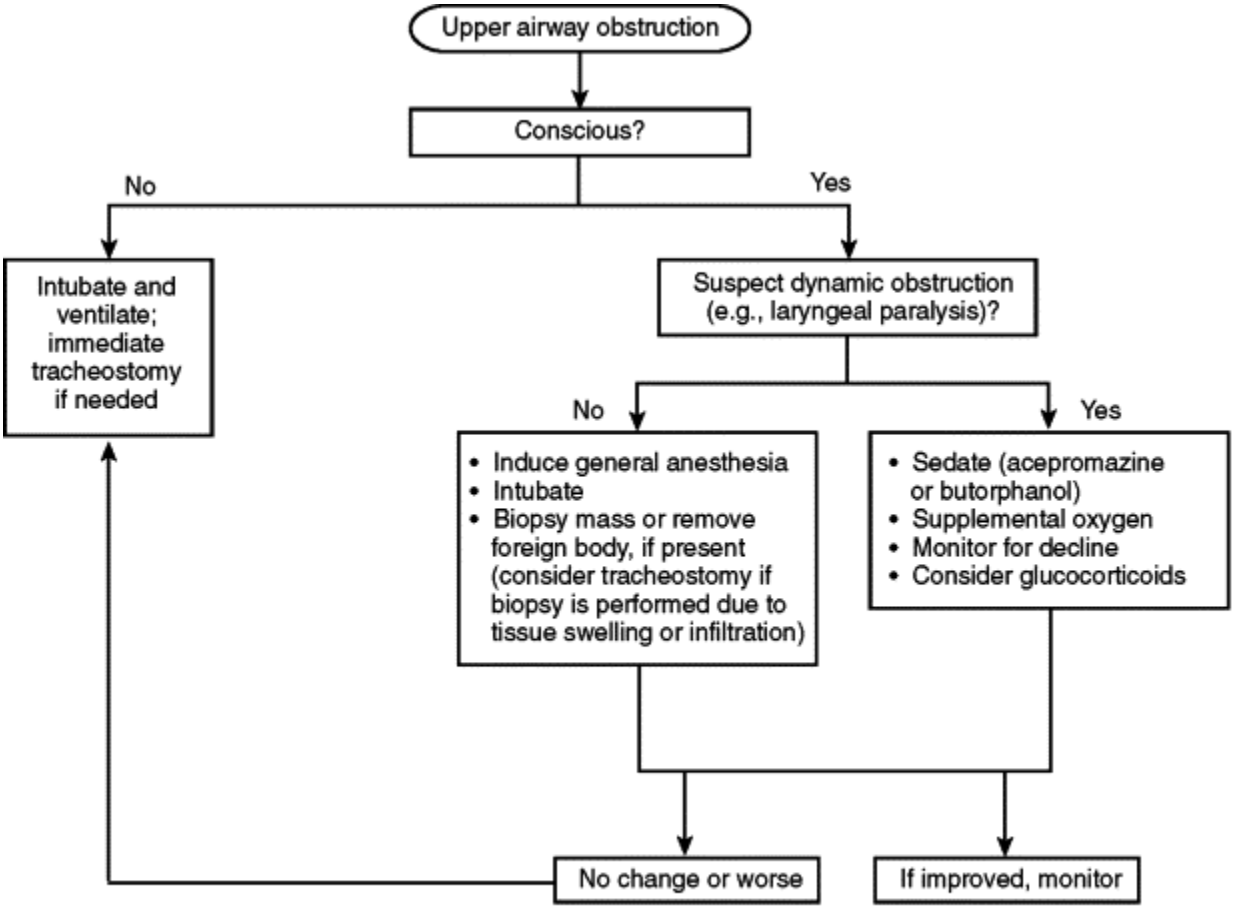
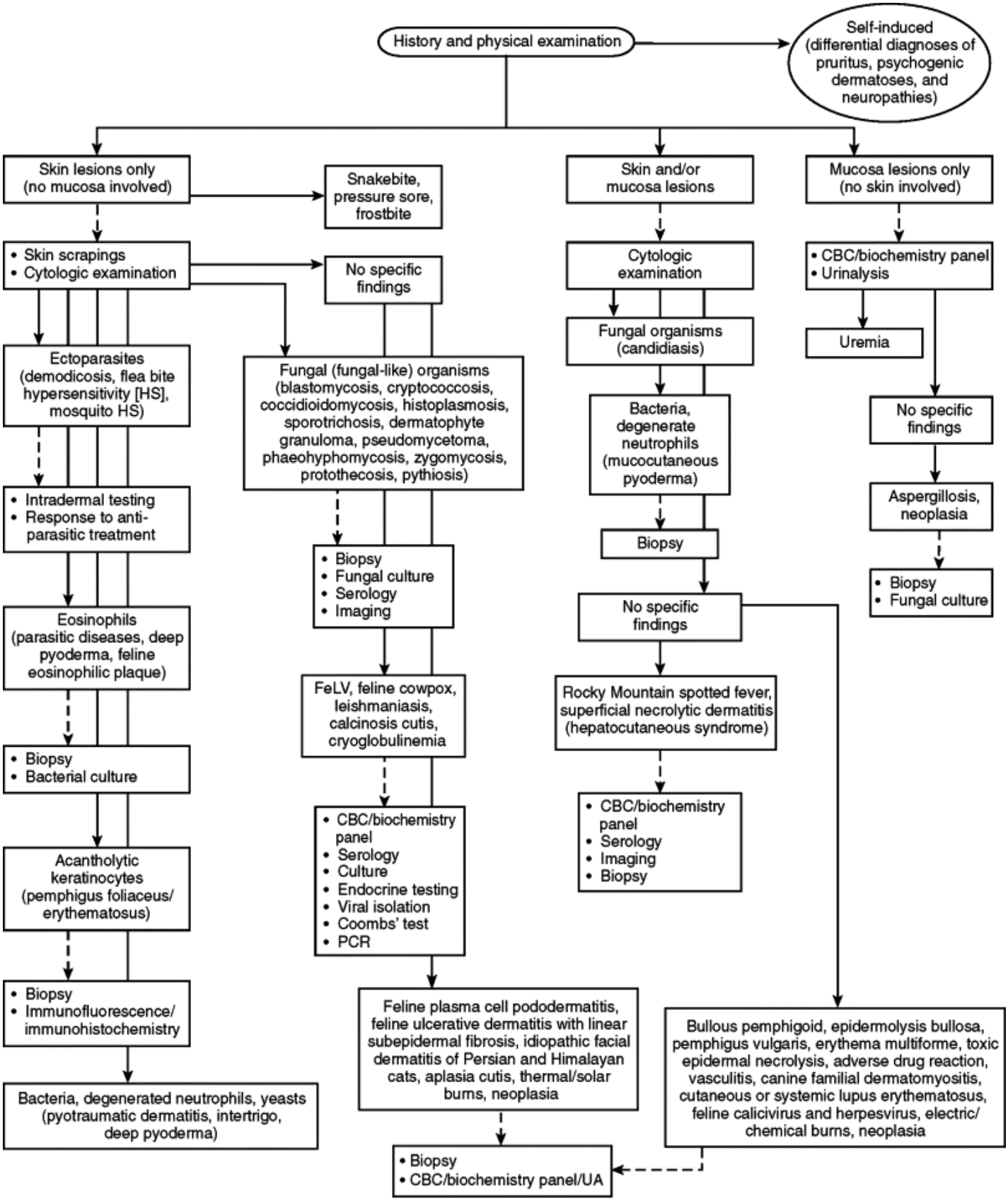
Upper Airway Obstruction/Choking



Author: Scott P. Shaw
Editor: Elizabeth Rozanski

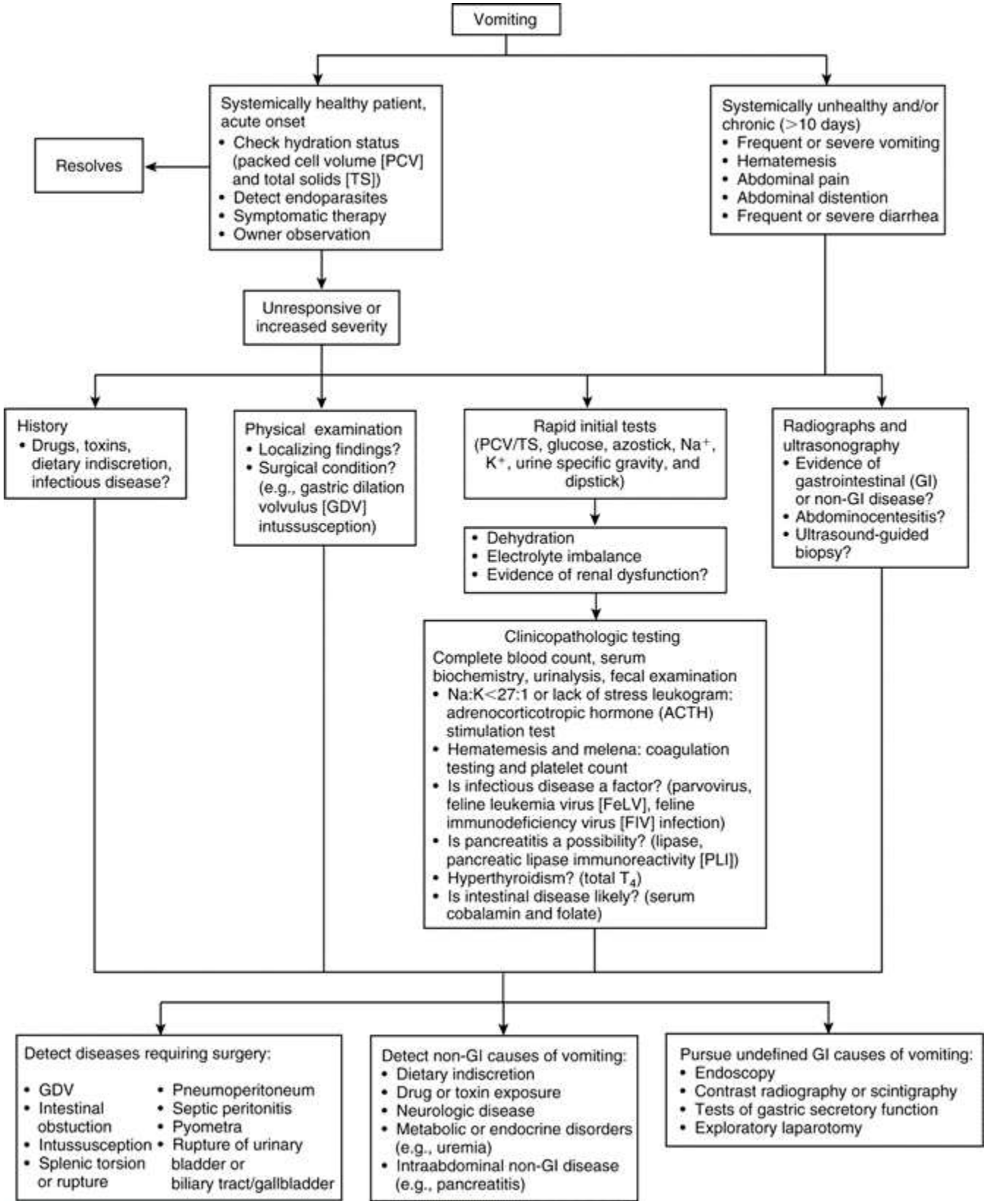
Ulcerative and Erosive Dermatoses



CBC, Complete blood count; *FeLV,* feline leukemia virus; *HS,* hypersensitivity; *PCR,* polymerase chain reaction; *UA,* urinalysis.
Dashed lines indicate diagnostic procedures.

Author: Frédéric Sauvé
Editor: Manon Paradis

Vomiting



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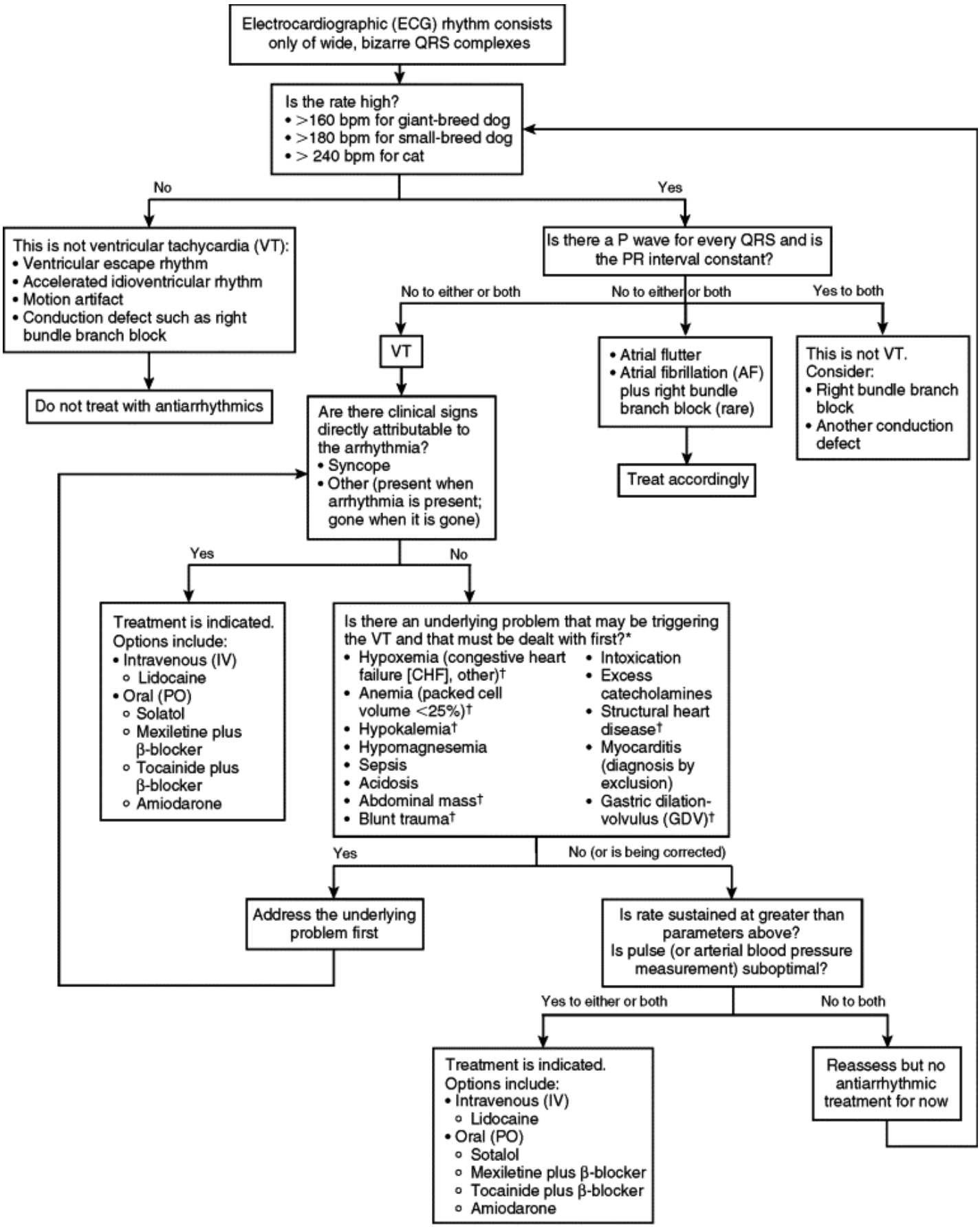
Ventricular Tachycardia: Management



Modified from Ettinger SJ, Feldman EC: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, WB Saunders.

*Virtually any medical problem, if severe enough, can cause ventricular arrhythmias.

†Most common.

Clinical Algorithms

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Introduction to Drug Formulary

EDITOR

* **Etienne Côté, DVM, DACVIM (Cardiology, Small Animal Internal Medicine)**

* The editor acknowledges and appreciates the work of Stephen J. Ettinger, DVM, DACVIM (Cardiology, Small Animal Internal Medicine), FACC, FAHA and Wayne S. Schwark, DVM, MSc, PhD, who, together with the editor, were redactors of this section in the previous edition. Thanks also to Drs. Justin Allen, Kirstie Barrett, Valerie Case, Crystal Doyle, and Ali Gorgi for providing suggestions and information on new medications.

The drugs listed in this formulary represent a compilation of the more commonly used therapeutic agents in small-animal practice, without implying endorsement (or lack thereof) of specific medications. Not all drugs used in veterinary practice are included, and clinicians may infrequently or never use some of those listed.

Drugs are organized in alphabetical order by generic names, with trade names in parentheses under the generic title, and the drugs also are listed alphabetically by brand name, with a cross-reference. A brief description of the drug's actions or indications is also provided. Canine and feline dosages are given individually. Note that *total dose* is the amount given to an animal in each single dose (in contrast to dose per kilogram body weight) and not the total amount of drug given for the full course of treatment. The fifth column, entitled Comments, describes commonly seen side effects, specific important observations, or other characteristics that are particularly important to the clinician. A sixth column, entitled How the Drug Is Supplied, includes commonly available sizes and formulations. Abbreviations used in the formulary are first defined on this page for the reader's reference.

Entries that are preceded by letters or modifiers are listed according to the principal word in the name of the drug. For example, L-asparaginase is listed under the letter *A,* DL-methionine is listed under the letter *M,* and *S*-adenosyl methionine is also listed under the letter *M.* Entries that are preceded by numbers are listed without the number (e.g., 4-methylpyrazole is listed under M).

While every effort has been made to include clinically useful, important, and accurate information, a comprehensive review of the details of individual drugs is too voluminous to be listed in this format. Therefore, it remains the prescriber's and clinician's responsibility to ensure that the particulars of any drug are appropriate for the intended application. The clinician should recheck drug dosages for accuracy as well as for specific indications, contraindications, and warnings. Drugs are listed not only by their licensed uses but also by commonly practiced uses. Again, the clinician needs to identify the specific and recommended indications for each drug by reviewing relevant information (e.g., product insert, primary sources) before prescribing, recommending, or using a drug.

Drugs, dosages, comments, and side effects are taken from several sources: (1) the clinical experience of the editor and previous redactors of this formulary; (2) drug-related information from the other sections of this textbook; (3) Ettinger SJ, Feldman, EC: Textbook of veterinary internal medicine, ed 6, St Louis, 2005, Saunders; (4) PDR Staff: Physician's desk reference, ed 64, Williston, VT, 2009, PDR Network; (5) Plumb DC: Veterinary drug handbook, ed 6, Ames, Iowa, 2008, Blackwell; (6) Kirk RW, Bonagura JD, editors: Current veterinary therapy IX-XIV, Philadelphia and St Louis, 1986-2008, Saunders; (7) Greene CE, editor: Infectious diseases of the dog and cat, ed 3, St Louis, 2006, Saunders; and (8) websites medlineplus.gov, www.medicinenet.com, www.drugs.com, and www.rxlist.com.

ABBREVIATIONS

AA: amino acid
ACE: angiotensin-converting enzyme
ACS: American Chemical Society
ACT: activated coagulation time
ACTH: adrenocorticotropic hormone
APTT: activated partial thromboplastin time
AV: atrioventricular
BM: bone marrow
BP: blood pressure
BUN: blood urea nitrogen
BW: body weight
C: capsules
C-II: class 2 controlled drug
C-III: class 3 controlled drug
C-IV: class 4 controlled drug
CA: carbonic anhydrase
CBC: complete blood count
CDI: central diabetes insipidus
CDS: cognitive dysfunction syndrome
CHF: congestive heart failure
CLL: chronic lymphocytic leukemia
CNS: central nervous system
COX: cyclooxygenase
CRI: constant rate infusion
D5W: sterile 5% dextrose in water
DCM: dilated cardiomyopathy
DIC: disseminated intravascular coagulation
DJD: degenerative joint disease
DOCA: deoxycorticosterone acetate
ECG: electrocardiogram
EDTA: ethylenediamine tetraacetic acid
EPA: U.S. Environmental Protection Agency
ER: extended release
ES: extra strength
FAIDS: feline immunodeficiency virus–induced acquired immunodeficiency syndrome
FDA: U.S. Food and Drug Administration

FeLV: feline leukemia virus
FIP: feline infectious peritonitis
FIV: feline immunodeficiency virus
G-: gram negative
G+: gram positive
GABA: γ-aminobutyric acid
GI: gastrointestinal
h: hour
HDDST: high-dose dexamethasone suppression test
HM: human medicine
HPA: hypothalamic-pituitary-adrenal
HR: heart rate
HW: heartworm
I: injectable
IBD: inflammatory bowel disease
IC: intracardiac
ICU: intensive care unit
IHA: immune-mediated hemolytic anemia
IM: intramuscular
IP: intraperitoneal
ITP: immune-mediated thrombocy topenia
IU: international unit(s)
IV: intravenous
KCS: keratoconjunctivitis sicca
LDDST: low-dose dexamethasone suppression test
LES: lower esophageal (gastroesophageal) sphincter
LRS: lactated Ringer's solution
MAO: monoamine oxidase
MVO_2: myocardial oxygen consumption
NDI: nephrogenic diabetes insipidus
NPH: isophane
NSAID: nonsteroidal antiinflammatory drug
O: topical ointment
OO: ophthalmic ointment
OS: ophthalmic solution
OTC: over-the-counter, nonprescription item
P: powder
PCV: packed cell volume
PDH: pituitary-dependent hyperadrenocorticism
PO: per os; oral
PP: polyphagia
PRN: as needed
PSS: physiologic saline solution
PT: prothrombin time
PTE: pulmonary thromboembolism
PU/PD: polyuria and polydipsia
q: every
RA: rheumatoid arthritis
RAAS: renin-angiotensin-aldosterone system
RBC: red blood cell
RS: regular strength
S: oral solution
SIBO: small-intestinal bacterial overgrowth/antibiotic-responsive enteritis
SLE: systemic lupus erythematosus
SQ: subcutaneous
SVT: supraventricular tachycardia
T: tablet
$T_{1/2}$: serum half-life
T_3: triiodothyronine
T_4: thyroxine
TCC: transitional cell carcinoma
tbsp: tablespoon ((=15 mL)
tsp: teaspoon ((=5 mL)
TVT: transmissible venereal tumor
Tx: treatment
U: unit(s)
USP: U.S. Pharmacopeia
UTI: urinary tract infection
V/D: vomiting/diarrhea
VM: veterinary medicine
vWF: von Willebrand factor
WBC: white blood cell

TABLE VI-1

Drug Formulary

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
2-PAM	*(see pralidoxime)*				
4-methylpyrazole, 4-MP	*(see fomepizole)*				
5-ASA	*(see mesalamine)*				
5-FU	*(see fluorouracil)*				
Abelcet	*(see amphotericin B, liposomal encapsulated)*				
Acarbose (Precose)	Oral hypoglycemic drug used for treating diabetes mellitus; α-glucosidase inhibitor	12.5-25 mg per dog PO for initial dose; if ineffective, may increase to 50-100 mg per dog if no adverse effects	12.5 mg per cat PO q 12 h	Adverse effects (diarrhea, weight loss) common: 35% of dogs	25, 50, 100 mg T HM
Accolate	*(see zafirlukast)*				
Accutane	*(see isotretinoin)*				
Acepromazine (acetylpromazine, PromAce, AtraVet, “ace”)	Sedation, preanesthetic, central antiemetic	Premedication or as part of sedative protocol; 0.03-0.15 mg/kg SQ, IM, IV; as oral sedative (e.g., prior to travel): 0.5-1 mg/kg PO	Same	Oversedation causes CNS depression; in old or systemically ill animals, use at fraction of low dose (e.g., ¼) or not at all; do not use in animals with seizures or hypotension; breed sensitivities; has no anxiolytic or analgesic properties on its own (travel); hypotensive agent	5, 10, 25 mg T; 10 mg/mL I VM
Acetaminophen (Tylenol, Excedrin, Feverall, Liquiprin, Midol, Pamprin, Panadol, Percogesic, Tempra, Bromo-Seltzer, paracetamol, and most “aspirin-free” preparations)	Antipyretic, analgesic	10-20 mg/kg PO q 12 h	Do not use	Toxic to cats (methemoglobinemia); gastric irritation; hepatotoxicity if overdose; analgesic, not antiinflammatory	Many sizes T OTC
Acetazolamide (Diamox)	Glaucoma, CA inhibitor	2-10 mg/kg PO q 8 h	2-10 mg/kg PO q 8 h	Hypokalemia, panting, acidosis	125, 250 mg T, C HM
Acetylcysteine (Mucomyst)	1. Acetaminophen toxicosis in cats 2. Decrease bronchial secretion viscosity 3. Collagenase-complicated corneal ulcers	1. Same as for cats 2. Nebulize as 2% solution q 12 h 3. One drop 2%-10% solution q 2-4 h in eye	First dose 140 mg/kg PO, then 70 mg/ kg PO q 6 h for 3-7 treatments; may be given as slow bolus IV	Tastes bad, bronchospasm possible, conjunctivitis if prolonged topical use	100, 200 mg/mL, I HM
Acetylsalicylic acid (ASA, aspirin)	Analgesia, antiinflammatory, antipyretic, DIC, antithrombotic via decreased platelet aggregation	10-25 mg/kg PO q 8-24 h; 0.5 mg/kg PO q 12 h as antithrombotic	Per cat: 40.5-81 mg (10-20 mg/kg) PO q 48-72 h; minidose: 5 mg (1 mg/kg) PO q 72 h	Anorexia-nausea, GI irritation, gastric ulcer, bleeding, platelet dysfunction, anemia; doses higher than minidose are *less* anticoagulant in dogs	81, 300, 600 mg, T OTC
Acitretin (Soriatane)	Synthetic retinoid for keratinization disorders in specific breeds (e.g., cocker spaniels)	0.5-1.32 mg/kg PO q 24 h	—	Teratogenic; excreted in milk; adverse effects similar to etretinate	10, 25 mg T HM
ACTH gel (Acthar, corticotropin)	Provocative agent for diagnosis of hyperadrenocorticism or	2 IU/kg IM, obtain blood preinjection and at 2 hours postinjection	Per cat (IM); 10 IU, obtain blood preinjection and	Rare allergic reaction, do not give IV	40, 80 IU/mL I HM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
	hypoadrenocorticism	for cortisol levels	1 & 2 hours postinjection		
ACTH-like solution, aqueous (tetracosactrin, cosyntropin, Cortrosyn)	Provocative agent for diagnosis of hyperadrenocorticism or hypoadrenocorticism; appears superior to ACTH gel but more costly	Standard dose: 250 mcg/ dog (0.25 mg/dog) once, IV or IM. Low dose: 5 mcg/kg (0.005 mg/kg) IV once; with either protocol, obtain blood preinjection and at 1 hour postinjection for cortisol levels	Per cat: 0.125 mg IM or IV total dose; obtain blood preinjection and at 30 and 60 minutes postinjection	Costly; however, low dose and standard dose are equally effective when used IV; also remains effective if diluted, fractionated, and frozen for use at low dose (dogs) (Peterson ME: J Am Vet Med Assoc 224:198-199, 2004)	250 mcg (0.25 mg) per ampule I HM
Acthar	*(see ACTH gel)*				
Actigall	*(see ursodeoxycholic acid)*				
Actinomycin D (dactinomycin, Cosmegen)	Antineoplastic drug, part of chemotherapy protocols	0.5-1 mg/m^2 slow IV q 3 weeks		Lymphoma reinduction; myelotoxicity and GI adverse effects possible; vesicant (extravasation injury risk)	0.5 mg vial I HM
Activated charcoal (Toxiban, Requa)	GI adsorbent	1 g/5 mL water: give 10 mL of slurry/ kilogram PO; best administered via stomach tube	1 g/5 mL water: give 10 mL of slurry/ kilogram PO; best administered via stomach tube	Do not induce vomiting; inhalation pneumonia may occur; follow with cathartic.	VM HM (various)
Adenosyl methionine, *S*-	*(see methionine, S-adenosyl)*				
Adequan	*(see glycosaminoglycan, polysulfated)*				
Adrenalin	*(see epinephrine)*				
Adriamycin	*(see doxorubicin)*				
Adrucil	*(see fluorouracil)*				
Advantage	*(see imidacloprid)*				
Advil	*(see ibuprofen)*				
Aglepristone (Alizine, RU-534)	Progesterone receptor antagonist	10 mg/kg SQ q 24 h × 2 doses. For progestin-induced acromegaly, continue once weekly × 3 doses.	—	Not licensed or widely used in the United States, abortifacient	30 mg/mL I VM
Albendazole (Valbazen)	*Giardia;* other endoparasites	25-50 mg/kg PO q 12 h for maximum 5 days	15-25 mg/kg PO q 12 h for 5 days	May cause BM suppression at recorded dosages; 4 doses total (2-day course) recommended for giardiasis; up to 10-21 days for *Paragonimus*	300 mg/g (paste) S VM
Albeta	*(see methionine, DL-)*				
Albon	*(see sulfadimethoxine)*				

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Albuterol (Ventolin, Proventil, Volmax, salbutamol)	Immediate but short-acting β_2-adrenergic agonist bronchodilator	0.02-0.05 mg/kg (20-50 mcg/kg) PO q 8-12 h Inhalant: 1 puff PRN, up to q 12 h	1 puff PRN	Beneficial effect lasts <4 hours; restlessness, muscle tremors; use with caution in patients where sympathetic drive could be harmful (e.g., heart disease, hypertension, hyperthyroidism, seizure disorders)	2, 4, 5 mg T, 0.4 mg/mL S, 6.8, 17 g inhalation canisters (0.1 mg [100 mcg] per puff) HM
Aldactazide	*(see hydrochlorothiazide/ spironolactone)*				
Aldactone	*(see spironolactone)*				
Alendronate (Fosamax)	Bisphosphonate Hypercalcemia	0.5-1 mg/kg PO q 24 h		Application for dental resorption in cats investigational	5, 10, 35, 40, 70 T 1 mg/mL S HM
Aleve	*(see naproxen)*				
Alkeran	*(see melphalan)*				
Allopurinol (Zyloprim)	Urate urolithiasis Leishmaniasis	10 mg/kg PO q 8 h, then reduce to 10 mg/kg PO q 24 h after 1 month	None	q 8 h Tx for 30 days then q 24 h	100, 300 mg T HM
Alprazolam (Xanax)	Benzodiazepine Separation anxiety	0.02-0.04 mg/kg PO q 4-6 h PRN	0.0125-0.025 mg/kg PO q 12-24 h	Feline dose range of 0.125-0.25 mg/kg published in other sources represents a 10-fold excess and should not be used	0.25, 0.5, 1, 2 mg T HM
Altace	*(see ramipril)*				
AlternaGEL	*(see aluminum hydroxide)*				
Aluminum hydroxide (Amphojel, AlternaGEL)	Phosphate binder, antacid	Initially, 10-30 mg/kg PO q 8-12 h; titrate based on PO4 to 10-90 mg/kg PO q 6-12 h; 5-10 mL/ dog	Same dose; per cat: approx. 1-3 mL PO q 8-12 h	May cause metabolic alkalosis; Amphojel = 64 mg $Al(OH)_3$/mL; AlternaGEL = 120 mg $Al(OH)_3$/mL; decreases absorption of concurrent drugs (e.g., tetracyclines, ketoconazole)	OTC, S HM
Amantadine (Symmetrel)	NMDA antagonist analgesic drug	3-5 mg/kg PO q 24 h	3-5 mg/kg PO q 24 h	New agent with little published clinical use; safety and efficacy profiles undetermined	100 mg C, 10 mg/ mL S HM
AmBisome	*(see amphotericin B, liposomal encapsulated)*				
Amicar	*(see aminocaproic acid)*				
Amiglyde-V	*(see amikacin)*				
Amikacin (Amikin, Amiglyde-V)	Aminoglycoside, G+ and G− agent	10-20 mg/kg q 24 h or 5-10 mg/kg q 12 h IV, IM, SQ	Same	Nephrotoxic, ototoxic, neuromuscular blockade, poor GI absorption	50 mg/mL I VM
Amikin	*(see amikacin)*				

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Amino acids 3% and glycerin injection with electrolytes (ProcalAmine)	Partial parenteral nutrition; superficial necrolytic dermatitis/ hepatocutaneous syndrome	Maintenance rate	Maintenance rate	Essential and nonessential amino acids, carbohydrates, and electrolytes for IV infusion; see Parenteral Nutrition, p. 1322	IV solution bags, S
Aminocaproic acid (Amicar)	Antiprotease activity for degenerative myelopathy	15 mg/kg PO q 8 h	—	Limited information on side effects or benefits	500, 1000 mg T, 250 mg/mL S, 250 mg/mL I HM
Aminopentamide (Centrine)	Antispasmodic, cholinergic blocking agent, similar to atropine	0.01-0.03 mg/kg PO, IM, SQ q 8-12 h	0.01-0.03 mg/kg PO, IM SQ q 8-12 h	Dryness of the mouth, atropine-like side effects; contraindicated in GI obstruction, GI infection/toxin, glaucoma, heart disease, tachycardia	0.2 mg T, 0.5 mg/ mL I VM
Aminophylline	Bronchodilator, diuretic (very mild)	5-10 mg/kg PO, IV q 8-24 h	2-6 mg/kg PO q 12-24 h	Hyperexcitability, tachycardia, gastric irritation, PU/PD, anorexia; therapeutic serum level = 10-20 mcg/mL, administer IV slowly	100-200 mg T, 25 mg/mL I HM
Aminopropazine (Jenotone)	Used in urethral obstructions, smooth muscle relaxant	2.2-4.4 mg/kg IM q 12-24 h	Per cat: 6.25-12.5 mg IM q 12-24 h for 48 hours	Do not use with cystic atony; contraindicated in hypotension	25 mg T, 25 mg/mL I VM
Amiodarone (Cordarone)	Type III antiarrhythmic agent for serious/life-threatening ventricular tachyarrhythmias	10 mg/kg PO q 12 h for 1 week (loading), then 8 mg/kg PO q 24 h	—	Photosensitivity, liver necrosis, keratopathy, positive Coombs' test; may be proarrhythmic	100, 200, 400 mg T 50 mg/mL I HM
Amitraz (Mitaban)	Demodicosis, mites, ticks	5-10 mL/gallon H_2O, dip dog; air dry; = 0.025 to 0.05% solution; use 3× /wk on feet, with a fresh solution of 0.5 mL in 30 mL propylene glycol or mineral oil	—	CNS depression; wear gloves when applying; requires multiple dips; transient pruritus noted; small breeds more susceptible; use in ventilated areas and in accordance with relevant regulations (e.g., EPA)	19.9% solution for dilution and topical skin application VM
Amitriptyline HCl (Elavil)	Separation anxiety–related disorders, destructive disorders, feline inappropriate elimination; tricyclic antidepressant; long onset to clinical benefit	1.1-4.4 mg/kg PO q 12-24 h	Per cat: 2.5-5 mg total dose (0.5-1 mg/kg) PO q 12-24 h	Sedation, psychosis, anticholinergic side effects; caution if seizure history, glaucoma, dysuria	10, 25, 50, 75, 100, 150 mg T HM
Amlodipine (Norvasc)	Long-acting calcium channel blocking agent for hypertension	0.0625-0.25 mg/kg PO q 24 h	0.125-0.25 mg/kg PO q 24 h	Somnolence, hypotension	2.5, 5, 10 mg T HM
Ammonium chloride (Uroeze)	Urinary acidifier	20-50 mg/kg PO q 12 h	20-40 mg/kg PO q 12 h	Poor palatability, GI signs; contraindicated in liver disease and renal failure; granules = 200 or 400 mg in ¼ tsp	500 mg T, HM; 400 mg T; 200, 400 mg per ¼ tsp P VM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Amoxicillin (Amoxitabs, Amoxi-drops, Robamox-V)	Penicillin class antibiotic, G+ (some G−) and anaerobic antibacterial agent	10-20 mg/kg PO, SQ, IM, IV q 8-12 h	Same	Penicillin contraindications	50, 100, 150, 200, 400 mg T, 25, 50 mg/mL S VM, HM
Amoxicillin/clavulanic acid (Clavamox, Augmentin)	*(see amoxicillin);* no penicillinase inactivation	10-20 mg/kg PO q 12 h	Same	Penicillin sensitivity, vomiting in cats; tablets must remain in foil until used	62.5, 125, 250, 375 mg T; 50 mg/mL S VM, HM
Amoxitabs	*(see amoxicillin)*				
Amphojel	*(see aluminum hydroxide)*				
Amphotericin B (Fungizone)	Systemic mycoses	Test dose (monitor for acute febrile reaction) = 0.25 mg/kg IV; if okay, then 0.5 mg/kg in D5W given IV CRI 3 times weekly for 2-4 months; do not exceed 5-10 mg/kg	Test dose (monitor for acute febrile reaction) = 0.1 mg/kg IV; if okay, then 0.1-0.25 mg/kg in 5-20 mL of D5W given slowly IV 3 times weekly for up to 6 weeks	Nephrotoxic; monitor BUN: pretreat with antiemetics; extravasation injury, anaphylaxis possible; may administer at lower dosage SQ in 0.45% saline plus 2.5% dextrose; combination with oral azoles to decrease dose/toxicity	50 mg/vial (or 100 mg/vial [Abelcet]) I HM
Amphotericin B, liposomal encapsulated (AmBisome, Abelcet)	Blastomycosis, histoplasmosis, cryptococcosis, coccidioidomycosis	0.5 mg/kg IV test dose; then 1-2.5 mg/kg IV, q 48 h; recommended cumulative dose = 12 mg/kg	—	Anaphylaxis possible; less nephrotoxic than aqueous amphotericin B (as already described)	50 mg/vial I HM
Ampicillin	Penicillin class antibiotic; routine G+ and anaerobic infections, some G−	10-20 mg/kg PO, SQ, IM, IV q 8 h	Same	Penicillin contraindications, phlebitis; trihydrate (Polyflex) for IM or SQ use only	125, 250, 500 mg C; 125 mg/5 mL S; 1, 3, 6 g vials I VM, HM
Ampicillin + sulbactam (Unasyn)	Beta lactamase–inhibiting-penicillin combination	20-50 mg/kg IM or IV	Same	Broad-spectrum antibacterial typically for in-hospital/ intensive care use. Dosage reflects total dose (e.g., a vial contains 1.5 grams; 1 gram = ampicillin and 0.5 grams = sulbactam, but product is dosed based on 1.5 grams)	1.5, 3 g vials I HM
Amprolium (Corid)	Enteric coccidiostat	Per pup: 100 mg total dose q 24 h in food or water (not both) for 10 days; per adult dog: 300 mg total dose q 24 h in food or water (not both) for 10 days	—	Overdosage causes CNS disturbances; thiamine is antidote	9.6% S VM
Amrinone (Inocor)	Low-output systolic myocardial failure; phosphodiesterase inhibitor	1-3 mg bolus IV, then 0.01-0.1 mg/kg/min (10-100 mcg/kg/min) IV CRI	—	Tachycardia, anxiety; monitor pulse and BP	5 mg/mL I HM
Anafranil	*(see clomipramine)*				
Ancef	*(see cephalosporin antibiotics)*				

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Ancobon	*(see flucytosine)*				
Ancotil	*(see flucytosine)*				
Anipryl	*(see selegiline)*				
Antirobe	*(see clindamycin)*				
Antisedan	*(see atipamezole)*				
Antivert	*(see meclizine)*				
Antizol-Vet	*(see fomepizole)*				
Anzemet	*(see dolasetron)*				
Apomorphine	Induction of vomiting	0.03 mg/kg IV or ¼-½ tablet in conjunctival sac (flush out after onset of emesis)	Same	Do not use if decreased consciousness; do not use in cases of corrosive poisoning; periocular irritation	6 mg T VM, HM
Apresoline	*(see hydralazine)*				
Aqua-Mephyton	*(see vitamin K1)*				
ARA-C	*(see cytosine arabinoside)*				
Aranesp	*(see darbepoetin)*				
Arava	*(see leflunomide)*				
Aredia	*(see pamidronate)*				
Arixtra	*(see fondaparinux)*				
Artificial tears ointment (Adapt, Lacrilube)	Used for insufficient tear production or with decreased blinking	1 drop in affected eye PRN	Same	Hypersensitivity	OTC HM
ASA	*(see acetylsalicylic acid)*				
Asacol	*(see mesalamine)*				
Ascorbic acid (vitamin C)	Acetaminophen-induced methemoglobin toxicity, copper hepatotoxicity	Per dog: 100-500 mg PO, total dose q 8 h	30 mg/kg PO, SQ, IM, IV q 6 h for acetaminophen toxicity	Caution in urolithiasis	500 mg/mL I; 50, 100, 25, 500 mg, 1 g T HM, OTC
Ascriptin	*(see acetylsalicylic acid)*				
l-asparaginase (Elspar)	Induction therapy for lymphoreticular neoplasms, ITP	400 IU/kg IM, IP once or as part of a protocol; or 10,000-20,000 IU/m^2 IM, IP, SQ	Same	Allergic reactions; anaphylaxis; pretreat with antihistamines; pancreatitis; coagulopathies See pp. 671, 677 for body surface area (m^2 to body weight) conversion chart.	10,000 IU/vial I HM
Aspirin	*(see acetylsalicylic acid)*				
Atabrine	*(see quinacrine)*				
Atarax	*(see hydroxyzine)*				
Atenolol (Tenormin)	β1-adrenergic blockage; supraventricular tachyarrhythmias, systemic hypertension, hypertrophic cardiomyopathy	0.25-1 mg/kg PO q 24 h to q 12 h	Per cat: ¼-½ of 25-mg tab PO total dose, q 24 h to q 12 h	Hypotension, depression, β-blockade induced CHF, inappetence, bradycardia; generally start at low dose and	25, 50, 100 mg T HM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
				titrate up as necessary	
Atipamezole (Antisedan)	Synthetic α2-adrenergic antagonist; used for reversing analgesic-sedative effects of medetomidine or dexmedetomidine	0.025-0.1 mg/kg IV or IM; volume of dose is same as volume of (dex)medetomidine administered; reduce dose if >1 hour since (dex)medetomidine	Same	Return to normal state may not be immediate	5 mg/mL I VM
Ativan	*(see lorazepam)*				
Atopica	*(see cyclosporine)*				
Atovaquone (Mepron)	Antiparasitic drug; part of protocol for babesiosis	13.3 mg/kg PO q 8 h × 10 days		Coadministered with azithromycin 10 mg/kg PO q 24 h. May be cost-prohibitive.	150 mg/mL S HM
Atracurium (Tracrium)	Neuromuscular-blocking paralytic agent	0.2 mg/kg IV, then 4-9 mcg/kg/min IV CRI PRN	Same	Adjust as needed based on respirations (excess) and skeletal muscle movement (inadequate); no analgesia	10 mg/mL I HM
Atravet	*(see acepromazine)*				
Atropine SO4	Parasympatholytic, anticholinergic; preanesthetic agent, organophosphate toxicity; supraventricular bradyarrhythmia; atropine response test	0.02-0.044 mg/kg IM, SQ, IV. Atropine response test: give IV only, and recheck ECG after 2-15 minutes. For organophosphate poisoning, give 0.2-2 mg/kg IV, IM, or SQ (give ¼ dose IV and the remainder IM or SQ)	Same	Tachycardia, mydriasis, ileus, photophobia, dysuria; do not use in CHF unless bradycardia is present	0.54 mg/mL I VM various HM
Atropine sulfate ophthalmic solution or ointment	Used when pupillary dilation is desired (e.g., uveitis)	1 drop in affected eye q 12-24 h	Same: 1 drop in affected eye q 12-24 h	Atropine side effects; contraindicated in the presence of glaucoma; cats may salivate	0.5, 1% OO; 0.5, 1, 2, and 3% OS HM
Augmentin	*(see amoxicillin/clavulanic acid)*				
Auranofin (triethylphosphine gold; Ridaura)	Gold salt used in treatment of autoimmune disease	0.1-0.2 mg/kg PO q 12 h		Veterinary experience with efficacy and side effects is very limited	3 mg C HM
Aurothioglucose (Solganal)	Pemphigus complex, autoimmune diseases, rheumatoid arthritis	Week 1: 0.1 mg/kg IM single dose; week 2: 0.2 mg/kg single dose; then 1 mg/kg once a week IM, decreasing to once a month for maintenance immunosuppression	Per cat, week 1: 1 mg IM; week 2: 2 mg IM; then 1 mg/kg once a week IM, decreasing to once a month	Blood dyscrasias, renal and hepatotoxicity, neuritis-encephalitis, cutaneous toxicity, pain at injection site, many others	50 mg/mL I HM
Avapro	*(see irbesartan)*				
Avlosulfon	*(see dapsone)*				
Axid	*(see nizatidine)*				
Azactam	*(see aztreonam)*				

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Azathioprine (Imuran)	Immunosuppressive agent (SLE, RA, immune-mediated hepatopathies, pemphigus, polymyositis, ITP, IHA, etc.)	1-2 mg/kg PO q 24-48 h	Do not use: toxic	Monitor CBC; BM suppression (leukopenia, thrombocytopenia); rarely hepatotoxic; use chemo precautions when handling or administering	50 mg T HM
Azidothymidine (AZT, zidovudine, Retrovir)	Antiretroviral agent	—	5-15 mg/kg PO q 12 h for 21 days	Monitor for anemia	100 mg C; 300 mg T; 10 mg/mL S HM
Azithromycin (Zithromax)	Broad-spectrum static macrolide antibiotic; refractory respiratory infections, other infections	5-10 mg/kg PO q 24 h for 1-5 days	5 mg/kg PO q 24 h for 1-5 days; pulse therapy or longterm treatment possible (weeks)	Resistant infections, GI effects, perishable (oral solution expires after 1 week despite refrigeration)	250, 600 mg T; 20, 40 mg/mL S HM
Azium	*(see dexamethasone)*				
AZT	*(see azidothymidine)*				
Aztreonam (Azactam)	Beta-lactam antibiotic; IV use in G− sepsis	30 mg/kg IV q 6-8 h		Limited information in clinical veterinary medicine	500 mg, 1g, 2g I HM
Azulfidine	*(see sulfasalazine)*				
Bactrim	*(see trimethoprim/ sulfamethoxazole)*				
Bactrovet	*(see sulfadimethoxine)*				
BAL	*(see dimercaprol)*				
Banamine	*(see flunixin meglumine)*				
Baytril	*(see enrofloxacin)*				
BCNU	*(see carmustine)*				
Benadryl	*(see diphenhydramine)*				
Benazepril (Fortekor, Lotensin)	ACE inhibitor, vasodilator, CHF therapy; glomerulopathy; systemic hypertension (usually in conjunction with other Tx; ineffective as antihypertensive monotherapy)	0.25-0.33 mg/kg PO q 24 h	0.25 mg/kg PO q 24 h	Dual renal-hepatic elimination; sedation, anorexia (both very rare); monitor potassium, renal and liver values; veterinary formulation not available nor approved in the United States	5, 20 mg VM (Canada, Europe, others); 5, 10, 20, 40 mg T HM
Bentyl	*(see dicyclomine)*				
Benzapen	*(see penicillin-benzathine)*				
Benzoyl peroxide (Oxydex, Pyoben)	Acne, cornification disorders/seborrhea, pyoderma, pruritus	Shampoo PRN; leave on skin for 10 minutes and rinse. Gel: apply topically q 8-12 h	Shampoo PRN; leave on skin for 10 minutes and rinse. Gel: apply topically q 8-12 h	Bleaches fabric; may be skin irritant	OTC, VM, HM
Benztropine mesylate (Cogentin)	Priapism	0.015 mg/kg IV		Anticholinergic, antihistaminic drug most proven in horses	1 mg/mL I HM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
				with priapism. Must be given within 6 hours of onset of priapism for efficacy.	
Berenil	*(see diminazene)*				
Betamethasone (Betasone, Celestone)	Injectable or topical long-acting steroid	0.1-0.4 mg/kg IM; apply ointment topically PRN up to q 8 h	Apply ointment topically PRN up to q 8 h	Glucocorticoid adverse effects; 7-10 times the potency of prednisolone	2, 5 mg/mL I, VM; 0.6 mg T; 3 mg/mL I HM
Betapace	*(see sotalol)*				
Betasone	*(see betamethasone)*				
Bethanechol (Urecholine)	Bladder atony (nonobstructive), cholinergic agent	Per dog: 5-25 mg PO total dose q 8 h, or 2.5-15 mg SQ q 8 h	Per cat: 2.5-5 mg PO total dose q 12 h	Do not use with obstruction or areflexic bladder; GI adverse effects possible	5, 10, 25, 50 mg T HM
Biaxin	*(see clarithromycin)*				
BiCNU	*(see carmustine)*				
Biosol	*(see neomycin)*				
Bisacodyl (Dulcolax)	Laxative (stimulant and cathartic)	5-20 mg/dog PO q 24 h	5 mg/cat PO q 24 h	Short-term use only; may cause cramping, diarrhea	5 mg T OTC, HM
Bismuth subsalicylate (Pepto-Bismol)	GI tract protectant, antidiarrheic, *Helicobacter* protocols	1 mL per 4 kg BW PO up to q 6 h	Same with caution due to salicylate composition	Side effect (uncommon): vomiting; causes stool to develop dark grey or black discoloration	17, 35 mg/mL S; 262 mg T OTC, HM
Blenoxane	*(see bleomycin)*				
Bleomycin (Blenoxane)	Antineoplastic agent	10 U/m^2 IV or SQ q 24 h × 3 days, then 10 U/m^2 q 7 days; maximum total = 200 U/m^2 See pp. 671, 677 for body surface area to body weight conversion chart.		Other described uses in dogs include vincristine-resistant transmissible venereal tumor and intralesional use in acanthomatous ameloblastoma. Acute (hyperthermia, vomiting) and delayed (epithelial) toxicoses.	15 U vial I HM
Blood products	From typed donors: 1. Whole fresh; or packed RBCs 2. Fresh frozen plasma. 3. Fresh frozen plasma, initial dose (then PRN) 4. Fresh frozen plasma dose that raises plasma albumin 1 g/dL 5. For coagulation factors 6. Cryoprecipitate for vWF, hemophilia A, fibrinogen deficiencies	1. 5-22 mL/kg slowly IV; rapid if active hemorrhage is present 2. 6-10 mL/kg IV 3. 45 mL/kg IV 4. 6-10 mL/kg IV 5. 1 unit (225 mL)/10 kg BW IV	Same	Precautions are detailed in respective chapters (see Transfusion Reactions, p. 1111; Transfusion Therapy p. 1347)	VM, I
Bonine	*(see meclizine)*				

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Bovine polymerized hemoglobin	*(see hemoglobin glutamer)*				
Brethine	*(see terbutaline)*				
Brevibloc	*(see esmolol)*				
British anti-Lewisite	*(see dimercaprol)*				
Bromide (KBr-generic)	Anticonvulsant	20-35 mg/kg PO q 24 h; divide q 12 h if GI upset; may load initially with 50 mg/ kg PO with food q 6 h × 48 h; lower dosage with concurrent phenobarbital; titrate using serum levels	Do not use; may trigger severe airway disease (asthma-like) in cats	Used with other antiepileptic drugs or alone; may increase sedation, weakness; dietary chloride should be constant to avoid altering rate of elimination; pancreatitis reported sporadically	400 mg/mL S VM
Bromocriptine (Parlodel)	Dopamine agonist prolactin inhibitor; causes luteolysis	Pyometra: 0.03 mg/kg PO q 8 h for 10 days; pregnancy termination: 0.01-0.05 mg/kg PO q 8 h for 3-4 days		Used in conjunction with prostaglandin F2α inhibitor; adverse side effects include nausea, neurologic signs, mainly seen at higher dose; abortifacient	2.5, 5 mg T HM
Bromo-Seltzer	*(see acetaminophen)*				
Budesonide (Entocort)	Glucocorticoid with minimal systemic effects due to topical GI distribution and rapid first-pass hepatic metabolism; inflammatory bowel disease	Per dog: 1-6 mg PO total dose, q 24-48 h; for noninfectious colitis: ½ to 1 enema (based on body size) per rectum q 24 h after defecation		Dosing limited by formulation (one-size unbreakable capsule); capsule dissolution designed for human ileum, unproven in VM	1, 3 mg C; 2 mg enema HM
Bufferin	*(see acetylsalicylic acid)*				
Bunamidine (Scolaban)	*Taenia, Dipylidium, Echinococcus*	25-50 mg/kg PO once; fast 3 hours before and after administration	Same	V/D rarely observed	100, 200, 400 mg T VM
Buprenex	*(see buprenorphine)*				
Buprenorphine HCl (Buprenex)	Opiate agonist: analgesia Sedative for medical procedures	0.01-0.02 mg/kg (10-20 mcg/kg) IV, IM 0.0075-0.01 mg/kg (7.5-10 mcg/kg) IV, IM	0.005-0.01 mg/kg (5-10 mcg/kg) IV, IM	Respiratory depression; use cautiously in aged or debilitated patients; neuroleptanalgesia when used with diazepam or acepromazine	0.324 mg/mL I HM
BuSpar	*(see buspirone)*				
Buspirone (BuSpar)	Anxiolytic agent; urine spraying, aggression, repetitive behaviors	Per dog: 2.5-10 mg PO total dose q 8-12 h	Per cat: 2.5-5 mg PO total dose q 12-24 h	Caution when used with hepatic or renal disease; may induce CNS stimulation or depression	5, 10, 15 mg T HM
Busulfan (Myleran)	Antineoplastic agent; leukemias	3-4 mg/m^2 PO q 24 h See pp. 671, 677 for body surface area to body weight conversion chart.		Uncommonly used, myelosuppression risk	2 mg T HM
Butazolidin	*(see phenylbutazone)*				

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Butorphanol tartrate (Torbutrol, Torbugesic, Stadol)	Cough suppressant, narcotic agonist/ antagonist, analgesia, sedative	Analgesia, sedation: 0.2-1 mg/kg PO, IM, SQ q 12 h to q 6 h; 0.1-0.2 mg/kg IV; antitussive: 0.5-1 mg/kg PO q 6-12 h	Analgesia, sedation: 0.1-0.4 mg/kg, SQ, IM, IV q 6-12 h	Vomiting, sedation; possible overexcitement in cats	1, 5, 10 mg T; 1 mg/mL, 10 mg/ mL I VM, HM
B vitamins	*(see thiamine, cobalamin)*				
Cabergoline (Dostinex)	Dopamine agonist prolactin inhibitor; causes luteolysis	Pyometra: 0.005 mg/kg PO q 24 h for 10 days; pregnancy termination: 0.005 mg/kg PO q 8 h for 3-4 days	—	Abortifacient	0.5 mg T HM
Calan	*(see verapamil)*				
Calcet	*(see calcium gluconate)*				
Calciferol	*(see ergocalciferol)*				
Calcijex	*(see calcitriol)*				
Calcimar	*(see calcitonin)*				
Calcitonin (Calcimar, Miacalcin)	Reduces serum calcium in hypercalcemic states, especially cholecalciferol toxicosis	4-8 IU/kg IV, IM, SQ q 12 h	4-8 IU/kg IV, IM, SQ q 12 h	Injections are irritating; GI upset possible	200 IU/mL I HM
Calcitriol (Rocaltrol, Calcijex)	Vitamin D analog; hypocalcemia	0.02 mcg/kg PO q 24 h (hypoparathyroidism) or 0.002-0.004 mcg/ kg PO q 24 h (adjunct treatment of chronic renal failure/ renal secondary hyperparathyroidism) titrate according to response	Same	Rapid onset of action and shorter duration of activity (days) versus other drugs (e.g., DHT). Caution re. ng/kg versus mcg/ kg dosage; avoid 1000-fold dosing error	0.25-, 0.5 mcg C; 1 mcg/mL S
Calcium carbonate (Titralac, Tums)	Hypocalcemia, adjunct treatment	1-4 g/day PO	Same	Could cause alkalosis	OTC, HM
Calcium chloride (10% solution)	Ventricular asystole	0.1 mL/kg IV slowly, or IC	Same		100 mg/mL I HM
Calcium citrate (Citracal)	Calcium supplementation	20 mg/kg/day, with meals	10-30 mg/kg PO q 8 h with meals		950 mg (contains 200 mg calcium T HM, OTC
Calcium EDTA (Versenate, Edetate, Havidote)	Lead, zinc, and other metal poisoning	25 mg/kg SQ q 6 h for 5 days maximum; dilute in 5% D5W or 0.9% saline	Same	Empty gut of lead prior to use; injection may be painful despite dilution; potentially nephrotoxic	200 mg/mL I HM
Calcium gluconate (Calcet)	Critical hypocalcemia, ventricular asystole	50-200 mg/kg IV slowly over 15-30 minutes, up to q 6 h; 50-150 mg Ca^{++}/kg per day in continuous IV infusion; oral: 150-250 mg/kg PO q 8 h	Same	Arrhythmias; monitor ECG and overt response to treatment during infusion; V/D; dystrophic calcification	100 mg/mL (10% solution) I HM
Caninsulin	*(see insulin)*				
Caparsolate	*(see thiacetarsemide)*				
Capoten	*(see captopril)*				

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Capstar	*(see nitenpyram)*				
Captan powder 50% (Orthocide)	Dermatomycoses	Mix 2 tbsp per gallon of water, and apply topically every 3-7 days; do not rinse after applying	Same	May induce contact sensitization in humans	VM
Captopril (Capoten)	Vasodilator, CHF, hypertension, ACE inhibitor	0.5-1.5 mg/kg PO q 8-12 h	Per cat: 3.125-6.25 mg PO q 12 h total dose	Hypotension-depression, anorexia, V/D; could exacerbate renal failure; less effective and shorter duration of action than most other ACE inhibitors	12.5, 25, 50, 100 mg T HM
Carafate	*(see sucralfate)*				
Carbaryl	Cholinesterase inhibitor for fleas, ticks, cheyletiellic mange	Use as a dip every 7-14 days; do not rinse off; spray q 48 h	Same	Do not use on animals under 4 weeks old; cholinesterase toxicity, treat with atropine and bathing; may stain hair yellow	0.5%-2% topical solution VM
Carbazole	*(see carbimazole)*				
Carbenicillin (Geocillin, Geopen, Pyopen)	Bacterial infections, broad-spectrum penicillin derivative	40-100 mg/kg IV, IM, SQ q 6-8 h (carbenicillin sodium; systemic infections); 10-33 mg/kg PO q 8 h (carbenicillin indanyl disodium; UTI)	Same, but do not exceed 55 mg/kg with parenteral formulation	*(see penicillin)*	382 mg T; 1, 2, 5, 10, 20, 30 g I HM
Carbimazole (Carbazole)	Hyperthyroidism; is metabolized to methimazole		Per cat: 5 mg PO total dose, q 8-12 h; titrate after 1-3 weeks based on response	Adverse effects similar to methimazole; not available nor approved in United States	5, 20 mg T HM
Carboplatin (Paraplatin)	Antineoplastic for many carcinoma and sarcoma therapies	300 mg/m^2 IV in D5W over 15 minutes every 3 weeks for 4 treatments See pp. 671, 677 for body surface area to body weight conversion chart.	200 mg/m^2 IV in D5W over 15 minutes every 4 weeks See pp. 671, 677 for body surface area to body weight conversion chart.	Myelosuppression; expensive; advantageous to *cis*-platinum (renal); use chemo precautions when handling or administering	50, 15, 450 mg I HM
Cardioxane	*(see dexrazoxane)*				
Cardizem	*(see diltiazem)*				
Cardoxin	*(see digoxin)*				
Caricide	*(see diethylcarbamazine)*				
Carmustine (BCNU)	Antineoplastic agent; gliomas, CNS lymphoma	50 mg/m^2 IV q 6 weeks See pp. 671, 677 for body surface area to body weight conversion chart.		Used in CNS malignancies because crosses blood-brain barrier; GI, myelotoxicity possible, risk heightened with cimetidine (avoid cotreatment); infused over 1-2 h, corrosive	33 mg/mL in 3 mL vial I HM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
				if extravascular	
L-carnitine	AA transports fatty acids into mitochondria for energy metabolism; some dilated cardiomyopathy cases; feline hepatic lipidosis	50-100 mg/kg PO q 8 h	50-100 mg/kg PO q 24 h for hepatic lipidosis	Expensive in big dogs; to be used with other Tx; effects uncertain	250, 500 mg T/C; 100 mg/mL S HM
Carprofen (Rimadyl)	NSAID with analgesic and antipyretic effects	2 mg/kg PO q 12 h	—	Hepatotoxicity; do not use with bleeding disorders, inflammatory bowel disease, or GI ulcers; monitor liver values; do not use with corticosteroids or ASA; may decrease ACE inhibition	25, 75, 100 mg T VM
Carvedilol (Coreg)	α1-blocking agent with nonselective β-blockade; used in CHF and primary tachycardias	0.1-0.2 mg/kg PO q 24 h starting dose; may increase to 0.4 mg/kg PO q 12 h	Unknown	Lethargy; GI signs; iatrogenic relapse of CHF; if prior CHF, begin at low dose and increase slowly over several weeks; possible danger in asthmatics	3.125, 6.25, 12.5, 25 mg T HM
Cascara sagrada	Laxative	1-5 mg per dog PO q 24 h			100, 325 mg HM OTC
Castor oil	Irritant cathartic	8-30 mL PO	4-10 mL PO	Gripping catharsis may develop; do not use if obstructed or atonic	OTC, HM
CCNU	*(see lomustine)*				
CeeNu	*(see lomustine)*				
Cefa-Drops	*(see cefadroxil)*				
Cefadroxil (Cefa-Tabs, Cefa-Drops, Duricef)	First-generation cephalosporin antibiotic	22 mg/kg PO q 8 h	Same	First-generation cephalosporin; mainly active against G+	50, 100, 200 mg 1 g T; 50 mg/mL S, VM; 1 g T; 500 mg C; 25, 50, 100 mg/mL S HM
Cefa-Tabs	*(see cefadroxil)*				
Cefixime (Suprax)	Third-generation cephalosporin antibiotic	5-10 mg/kg PO q 12-24 h		Lower end of dosage range is used for cystitis	200, 400 T 20 mg/ mL S HM
Cefotaxime (Claforan)	Third-generation cephalosporin; G+ and G− organisms and many anaerobes	20-40 mg/kg slow IV q 8 h for 7 days	Same	Pain if injected IM; BM toxicity uncommon	500 mg, 1, 2, 10 g I HM
Cefotetan (Cefotan)	Second-generation cephalosporin antibiotic	30 mg/kg IV, SQ q 8 h			1, 2, 10 g vials I HM
Cefovecin (Convenia)	Long-acting injectable cephalosporin antibiotic	8 mg/kg SQ q 14 days	Same	Labeled for bacterial dermatitis but used extensively off-label. Extended elimination: 95% of dogs have therapeutic plasma cefovecin levels for	80 mg/mL I VM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
				7-14 days after one injection	
Cefoxitin (Mefoxin)	Cephamycin grouped with second-generation cephalosporins; some G+, G−, and anaerobic bactericidal activity	10-30 mg/kg IV q 6-8 h	Same	Pain if injected IM; BM toxicity uncommon	1, 2, 10 g vials I HM
Cefpodoxime (Simplicef, Vantin)	Once-daily oral third-generation cephalosporin antibiotic	5-10 mg/kg PO q 24 h	Same	Most common usage is for bacterial dermatitis	100, 200 mg T VM, HM; 10, 20 mg/ mL S HM
Ceftazidime (Ceptaz, Fortaz, Tazicef)	Third-generation cephalosporin antibiotic mainly indicated for G− sepsis	30 mg/kg IV q 8-12 h	Same		0.5, 1, 2, 6 g vials I, HM
Ceftiofur (Naxcel)	Third-generation cephalosporin	2.2-4.4 mg/kg SQ q 12-24 h	Same	—	1, 4 g vials I VM
Ceftriaxone (Rocephin)	Third-generation cephalosporin antibiotic; CNS infections	15-50 mg/kg IV q 12 h		May also be used for bacterial endocarditis in dogs	250, 500 mg; 1, 2 g vials I
Celestone	*(see betamethasone)*				
CellCept	*(see mycophenolate mofetil)*				
Centrine	*(see aminopentamide)*				
Cephalosporin antibiotics	Broad-spectrum bactericidal; β-lactamase inactivation although second- and third-generation more resistant	10-30 mg/kg PO, SQ, IM, IV q 12 h to q 6 h; review each product for specific dosage, handling, and administration	Same	GI side effects, penicillin contraindications; possibly nephrotoxic at high dosages or if used with aminoglycoside antibiotics	250, 500 mg C; 25, 50, 100 mg/mL S; 1, 2, 20 g vials I VM, HM
Cephulac	*(see lactulose)*				
Ceptaz	*(see ceftazidime)*				
Cerenia	*(see maropitant)*				
Cestex	*(see epsiprantel)*				
Cetirizine (Zyrtec)	Antihistamine; allergic disorders	5-10 mg/dog (up to maximum 2 mg/kg) PO q 12 h	5 mg/cat PO q 24 h		5, 10 mg T 1 mg/mL S HM
Charcoal	*(see activated charcoal)*				
Chemet	*(see succimer)*				
Cheque	*(see mibolerone)*				
Chitosan-based phosphate binder (Epakitin)	Hyperphosphatemia associated with chronic kidney disease	1 gram/5 kg body weight PO q 12 h	Same	Contains lactose, calcium carbonate, chitosan, and hydrolyzed soy protein	50, 150 g P VM
Chlorambucil (Leukeran)	Lymphoreticular neoplasia, chronic lymphocytic leukemia, macroglobulinemia, feline IBD	2 mg/m^2 PO q 24 h for 3 weeks beyond remission; then 1.5 mg/m^2 PO q 24 h for 15 days and then every third day; or 0.1-0.2 mg/kg PO q 24-72 h	1.5 mg/m^2 PO q 24 h as for dog, or 0.1 mg/kg PO q 48-72 h; or total dose per cat 2 mg/ cat PO q 48 h	BM suppression; usually a second-line agent often used with prednisone and/or other agents; use chemo precautions when handling or	2 mg T HM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
				administering; do not break or crush tablets	
Chloramphenicol (Chloromycetin)	Broad-spectrum bacteriostatic agent: *Mycoplasma, Rickettsia, Chlamydia,* and anaerobic bacteria; excellent lipid solubility (intracellular access) 1% ophthalmic ointment: corneal ulcers and infections; 0.5% ophthalmic solution: corneal ulcers and infections	30-50 mg/kg PO, IV, IM, SQ q 8 h; OO/ OS apply to eye q 6 h	15-50 mg/kg PO, IV, IM, SQ q 12 h; OO/OS apply to eye q 4-8 h	Hepatic microsomal enzyme inhibitor; may potentiate some Tx, use caution; do not use with "cidal" agents; monitor CBC and chemistries; caution in pregnancy/ neonates; avoid human exposure; risk of irreversible human BM suppression	100 mg/mL I; 100, 250, 500 mg; 1 g T VM, HM 1% OO, 0.5% OS VM, HM
Chlorhexidine 0.5% (Nolvasan)	Topical antiseptic shampoo Topical antiseptic solution	Shampoo every 3-7 days Dilute the solution 1:10 with water, and apply to lesions q 8-12 h	Same	—	OTC, HM, VM
Chloromycetin	*(see chloramphenicol)*				
Chlorothiazide (Diuril)	Diuretic/hypotensive, nonhormonal Tx for CDI and NDI, urolithiasis —decreased calcium elimination	20-40 mg/kg PO q 12 h	Same	Hyponatremia, hypokalemia; use cautiously with digitalis	250, 500 mg T; 50 mg/mL S HM
Chlorpheniramine (Chlor-Trimeton, ChlorTripolon)	Decongestant, antihistamine, antipruritic	Per dog: 2-8 mg PO total dose, q 8-12 h	Per cat: 1-2 mg PO total dose, q 8-12 h	May cause drowsiness or restlessness; anticholinergic side effects	10 mg/mL I; 0.4 mg/mL S; 2, 4, 8, 12 mg T OTC, HM
Chlorpromazine (Thorazine)	Tranquilization, antiemetic	Oral tranquilization: 1-3 mg/kg PO up to q 6 h Sedation: 0.1-1 mg/kg SQ, IM Antiemetic: 0.5 mg/kg IM or IV up to q 6 h	Same	Severe CNS depression with overdosage; may potentiate seizures; use sparingly or not at all in older or systemically ill patients; hypotension	10, 25, 50, 100, 200 mg T; 2 mg/ mL S; 25 mg suppository; 25 mg/mL I HM
Chlorpropamide (Diabexan, Diabinese)	Oral hypoglycemic; also potentiates renal action of ADH (diabetes insipidus)	10-40 mg/kg PO q 24 h		Variable clinical response; investigational use in VM at this time	100, 250 mg T HM
Chlorulon	*(see chorionic gonadotropin human)*				
Chlor-Trimeton	*(see chlorpheniramine)*				
ChlorTripolon	*(see chlorpheniramine)*				
Choledyl	*(see oxtriphylline)*				
Chorionic gonadotropin, human (hCG, Chorulon)	Male infertility; cryptorchidism/ testicular descent	Cryptorchidism: 100-1000 IU IM q 3-4 days × 4 Tx. Male infertility: 500-1000 IU IM q 2 weeks		Male infertility indication: notably if testicular degeneration is present or to increase libido prior to mating or collection	1000 IU/mL I VM
Chronulac	*(see lactulose)*				
Cialis	*(see tadalafil)*				
Ciloxan	*(see ciprofloxacin)*				

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Cimetidine (Tagamet)	H2 receptor antagonist, esophagitis, gastric reflux, chronic gastritis, GI tract ulceration, hypergastrinemia, effects of mast cell tumors	5-10 mg/kg PO q 6-12 h; 5 mg/kg IV q 8 h	2.5-5 mg/kg PO q 8-12 h	Hepatic microsomal enzyme inhibitor; administer slowly IV	200, 300, 400, 800 mg T; 60 mg/ mL S; 150 mg/mL I HM
Ciprofloxacin (Cipro, Ciloxan)	Fluoroquinolone antibacterial agent, broad-spectrum "cidal"; *Mycoplasma*	5-15 mg/kg PO q 12 h	—	Incompletely bioavailable in dogs; see other fluoroquinolone comments under *Enrofloxacin*	100, 250, 500, 750 mg T HM
Cisapride (Propulsid, Prepulsid)	Prokinetic serotonergic for feline megacolon; gastroesophageal reflux; first- and second-degree GI motility disorders	0.1-0.5 mg/kg PO q 8-12 h	Per cat: 2.5-5 mg total dose PO q 8-12 h	Requires adjunctive Tx as stool softener, does not increase gastric secretions; increases esophageal peristalsis; reported to be associated with ventricular arrhythmias in HM and no longer available on the human market; toxic interaction with ketoconazole, cimetidine, macrolide antibiotics	10, 20 mg T; 1 mg/ mL S HM
Cisplatin (Platinol)	Solid carcinomas, osteosarcoma	50-70 mg/m^2 IV every 3-5 weeks; pretreat with IV fluids 12 hours before and after Tx. Intracavitary: same protocol, using 50 mg/m^2 dose diluted into 250 mg 0.9% sterile NaCl and administered into the peritoneal or pleural space immediately after effusion evacuation	None: do not use	Use antiemetic agent; BM suppression; renal toxicity; fatal pulmonary edema in cats; anaphylaxis; use chemo precautions when handling or administering	10 and 50 mg vials I HM
Citracal	*(see calcium citrate)*				
Citrate	*(see potassium citrate)*				
Claforan	*(see cefotaxime)*				
Clarithromycin (Biaxin)	Broad-spectrum macrolide antibacterial; resistant respiratory or skin infections	5-10 mg/kg PO q 12 h	Same	GI, liver disturbances; BM toxicity rarely	250, 500, mg T; 25, 50 mg/mL S HM
Clavamox	*(see amoxicillin/clavulanic acid)*				
Clemastine fumarate (Tavist products, Contac products, many others)	Antihistamine; allergic skin disease, other allergies, mast cell tumor	0.05-0.1 mg/kg PO q 12 h	0.3-0.6 mg/cat PO q 12 h	Lethargy/drowsiness or restlessness; caution: other active ingredients in OTC combo formulations	1.34, 2.8 mg T HM OTC
Cleocin	*(see clindamycin)*				
Clindamycin (Cleocin, Antirobe)	Lincosamide antibiotic, G+, *Streptococcus, Staphylococcus,*	5-10 mg/kg PO q 12 h; toxoplasmosis: 5-20 mg/kg PO q 12 h	Same; toxoplasmosis: 12.5-25 mg/kg PO q 12 h	May cause V/D and very rarely hepatotoxicity; do not use with erythromycin	150 mg/mL I: 25, 75, 150 mg C; 25 mg/mL S

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
	anaerobes, *Bacteroides,* toxoplasmosis, neosporosis, babesiosis, osteomyelitis			or chloramphenicol; oral solution has unpleasant taste	VM, HM
Clofazimine (Lamprene)	Mycobacterial infections		1 mg/kg PO q 24 h up to daily maximum of 4 mg/kg	Efficacy and safety poorly established in VM	50, 100 mg C HM
Clomicalm	*(see clomipramine)*				
Clomipramine (Anafranil, Clomicalm)	Separation anxiety, acral lick dermatitis; tricyclic antidepressant agent	1-2 mg/kg PO q 12 h	0.5-1 mg/kg PO q 24 h	Do not use in breeding dogs or if dog is receiving or has received MAO inhibitors (e.g., Anipryl, amitraz, etc.); vomiting, lethargy, diarrhea, and polydipsia are adverse reactions most often noted; caution in animals with GI motility or seizure disorders	5, 20, 40, 80 mg T VM
Clonazepam (Klonopin)	Seizure disorders, panic disorders, sedation	0.5 mg/kg PO q 8-12 h; titrate as required to effect	1/8-¼ of 0.5 mg tablet PO as feline appetite stimulant	Second-line seizure Tx; sedation, duration of action in dogs may be short (few hours)	0.5, 1, 2 mg T HM
Clopidogrel (Plavix)	Antiplatelet drug, thienopyridine drug	—	18.75 mg/cat PO q 24 h	Emerging application in cats at risk of thromboembolism. Clinical efficacy/safety promising but unproven.	75 mg T HM
Cloprostenol (Estrumate)	Abortifacient for mismating (early, prior to ossification of fetal bones)	1-2.5 mcg/kg SQ, q 24-48 h for 5 days	Same	Dilute 1:10 with sterile 0.9% NaCl for accurate dosing	250 mcg/mL I VM
Clorazepate (Tranxene)	Second- or third-line antiepileptic drug; benzodiazepine	0.5-1 mg/kg PO q 8 h	0.5-1 mg/kg PO q 8 h	New agent; safety and efficacy profile poorly defined at this time	3.75, 7.5, 15 mg T HM
Clotrimazole (Veltrim, Lotrimin, Mycelex)	Used topically for nasal aspergillosis; also externally for *Malassezia* and other fungi	PRN to fill nasal cavity for nasal aspergillosis (follow precautions and protocol) See p. 1308	—	Intranasal administration requires preplacing catheters surgically or via endoscope; use propylene glycol preparation for this indication	10 mg/mL topical solution OTC, HM
Coal tar (0.5% to 8%)	Shampoo; cornification disorders/seborrhea, dermatitis, eczema, keratolytic	Bathe every 3-14 days; leave in contact with skin for 10 minutes and rinse thoroughly	Same	May irritate skin	VM
Cobalamin (vitamin B12, cyanocobalamin)	Used for treating vitamin B12 deficiency from exocrine pancreatic disease, SIBO, and in giant schnauzers	Total dose: 250-1200 mcg (0.25-0.12 mg) per dog, SQ once weekly × 6 weeks, then q 14 d × 6 weeks, then PRN	Total dose: 125-250 mcg (0.125-0.25 mg) per cat IM, SQ; dosing schedule as for dogs		1000 mcg/mL (= 1 mg/mL) I HM, VM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Codeine	Opiate antitussive	1-2 mg/kg PO PRN up to q 6 h		May cause sedation at higher doses; schedule C-II	15, 30, 60 mg T 3 mg/mL S HM
Cogentin	*(see benztropine)*				
Colace	*(see dioctyl sodium sulfosuccinate)*				
Colchicine	Hepatic fibrosis	0.03 mg/kg/day PO q 24 h	No reported use	Not well described; GI effects, BM toxicity, teratogenicity possible	0.5, 0.6 mg T HM
Colony-stimulating factor	*(see filgrastim)*				
Comfortis	*(see spinosad)*				
Compazine	*(see prochlorperazine)*				
Conofite	*(see miconazole)*				
Convenia	*(see cefovecin)*				
Cordarone	*(see amiodarone)*				
Coreg	*(see carvedilol)*				
Corid	*(see amprolium)*				
Corticotropin	*(see ACTH gel)*				
Cortrosyn	*(see ACTH-like solution, aqueous)*				
Cosequin	*(see glucosamine-chondroitin sulfate)*				
Cosmegen	*(see actinomycin D)*				
Cosyntropin	*(see ACTH-like solution, aqueous)*				
Coumadin	*(see warfarin)*				
Covera	*(see verapamil)*				
Cuprimine	*(see penicillamine)*				
Cyanocobalamin	*(see cobalamin)*				
Cyclophosphamide (Cytoxan, Neosar)	Lymphoreticular tumors, solid carcinomas, immune-mediated disease	50 mg/m^2 (or 2 mg/kg) PO, 4 days on, 3 days off, or use q 48 h; or 200-300 mg/m^2 IV q 3 weeks See pp. 671, 677 for body surface area to body weight conversion chart.	Same	GI signs; BM suppression; hemorrhagic cystitis, especially with higher (weekly) dose; alopecia; use with caution; use chemo precautions when handling or administering (see Chemotherapy; Adverse Reactions, p. 188); do not crush or break tablets. Caution: cyclosporine brand name almost identical (Neosar versus Neoral)	25, 50 mg T; 100, 200, 500 mg and 1 and 2 g vials I HM
Cyclosporine-ophthalmic (Optimmune)	T-lymphocyte inhibitor; KCS in dogs	0.2% ophthalmic ointment or solution in oil base; use one drop/short (¼-in) strip	Do not use	May be ophthalmic irritant; monitor for infections	HM, VM, OO, OS; 4 mL olive oil and 1 mL cyclosporine

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
		q 12 h in affected eye(s) until improvement occurs, then q 24 h			
Cyclosporine-systemic (Sandimmune, Atopica, Neoral)	IHA, ITP, perianal fistula, atopic dermatitis, feline necrotizing gingivitis, renal transplantation, other immunosuppressive purposes	Emulsion forms: (Neoral, Atopica): 2-5 mg/kg PO q 12 h (2-5 mg/kg PO q 24 h if concurrent ketoconazole administration) Nonemulsion form: (Sandimmune, very rarely available now): 5-10 mg/kg PO q 12 h (5-10 mg/kg PO q 24 h if concurrent ketoconazole administration) 2-3 mg/kg slow IV over 4 hours q 12 h; dilute to 1 mg/mL in D5W or 0.9% NaCl before IV administration	Same; cats should have a negative *Toxoplasma* titer to qualify for treatment	Adjust dose to attain good clinical response and 200-500 ng/mL blood level (for autoimmune diseases; 300-800 ng/mL for renal transplant patients). Oral doses based on greater absorption of emulsion forms versus nonemulsion forms; can cause nephrotoxicity (protein-losing nephropathy), gingival hyperplasia; anaphylaxis possible with IV; little clinical experience with IV to date. Caution: cyclophosphamide brand name is almost identical (Neoral versus Neosar)	25, 50, 100 mg C; 100 mg/mL S; 50 mg/mL I, HM; 10, 25, 50, 100 mg C VM
Cypip	*(see diethylcarbamazine)*				
Cyproheptadine (Periactin)	Serotonin and H1 antagonist: Appetite stimulant via hypothalamic action Feline pica Antihistamine Urine spraying Add-on for feline asthma	1 mg/kg PO q 8-12 h	Total dose = 1-4 mg/ cat PO q 12-24 h	Can cause excitability or depression, especially at higher doses; vomiting, aggressiveness	4 mg T; 0.4 mg/mL S HM
Cystorelin	*(see gonadotropin-releasing hormone)*				
Cytarabine	*(see cytosine arabinoside)*				
Cytobin	*(see triiodothyronine)*				
Cytomel	*(see triiodothyronine)*				
Cytosar	*(see cytosine arabinoside)*				
Cytosine arabinoside (Cytarabine, Cytosar, ARA-C)	Antineoplastic, lymphoma protocol	100 mg/m^2 SQ or slow IV q 24 h for 2-4 days	Same	Leukopenia-BM suppression, GI toxicity, reconstituted vial good for 48 hours; use along with cancer protocol; use chemo precautions when handling or administering	100, 500 mg, 1 and 2 g vials I HM
Cytotec	*(see misoprostol)*				
Cytoxan	*(see cyclophosphamide)*				
Dacarbazine (DTIC)	Melanoma, sarcoma	800-1000 mg/m^2 IV, CRI (8 hours) every 3-4 weeks	Not recommended	GI toxicity, BM suppression, extravasation injury	100, 200 mg vials, I

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
					HM
Dactinomycin	*(see actinomycin D)*				
Dalteparin	*(see heparin, low-molecular-weight)*				
Danazol (Danocrine)	Modified androgen; used for ITP, IHA; anabolic; used for prostatic hypertrophy or androgen-dependent neoplasia	5-10 mg/kg PO q 12 h	5 mg/kg PO q 12 h	Adjunctive Tx for ITP and IHA; hepatotoxicity; BM toxicity possible; immunosuppressive response may take weeks or months; androgen effects faster	50, 100, 200 mg C HM
Danocrine	*(see danazol)*				
Dantrolene (Dantrium)	Skeletal muscle relaxant; malignant hyperthermia	2-3 mg/kg IV; 1-5 mg/kg PO q 8 h	0.5-2 mg/kg PO q 12 h		100 mg C 0.33 mg/ mL I HM
Dapsone (Avlosulfon)	1. Antibacterial, antiinflammatory agent used for some skin disorders 2. Antiprotozoal/ antimycobacterial effects	1. 1 mg/kg PO q 8 h 2. 1 mg/kg PO q 8 h initially until remission, then 0.3 mg/kg maintenance	Rarely used in this species; 1 mg/kg PO q 24 h and 8 mg/kg PO q 24 h have been reported	Hepatotoxicity and BM suppression may occur early in therapy; hemolysis, GI signs, skin eruptions possible	25 and 100 mg T HM
Daranide	*(see dichlorphenamide)*				
Daraprim	*(see pyrimethamine)*				
Darbepoetin (Aranesp)	Erythropoietin analog; considered less antigenic; anemia of chronic kidney disease	0.45 mcg/kg SQ once weekly at first, then q 2-3 weeks adjusted for maintenance	Same	Considered less antigenic in dogs and cats than recombinant human erythropoietin	25, 40, 60, 100, 150, 200, 300, 500 mcg vials or preloaded syringes I HM
DDAVP	*(see desmopressin acetate)*				
DDVP	*(see dichlorvos)*				
DEC	*(see diethylcarbamazine)*				
Decadron	*(see dexamethasone)*				
Deca-Durabolin	*(see nandrolone decanoate)*				
Decholin	*(see dehydrocholic acid)*				
Decoquinate (Deccox)	Hepatozoonosis	20 mg/kg (or 1 teaspoon/10 kg mixed in food) PO q 12 h		Administer for 2 years, or until PCR testing is negative, to inhibit development of merozoites released from tissue cysts	6% preparation (60 g decoquinate per kg of product) oral premix VM
Dectomax	*(see doramectin)*				
Deferoxamine (Desferal, DFO)	Iron chelator; treatment of iron toxicity	10-15 mg/kg/hr IV CRI, then titrate based on serum iron levels. Alternatively, if CRI not possible, give 10-40 mg/kg IM q 8 h for	—	Arrhythmia, hypotension, wheezing if CRI too rapid; hypocalcemia, thrombocytopenia possible; do not use	500 mg vials I HM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
		24-72 hours, based on serum iron levels		in cases of renal failure; potential teratogen	
Dehydrocholic acid (Decholin)	Used to stimulate bile flow	10-15 mg/kg PO q 8 h for 7-10 days	Same	Do not use with biliary obstruction	HM
Delmadinone (Tardak)	Benign prostatic hyperplasia	1.5 mg/kg IM or SQ: 2 injections 8 days apart; may repeat 1 dose 1 month later		Remission of clinical signs in 83% of dogs.	10 mg/mL I VM
Demadex	*(see torsemide)*				
Demerol	*(see meperidine HCl)*				
Denosyl	*(see methionine, S-adenosyl)*				
Depakene	*(see valproic acid)*				
Depakote	*(see valproic acid)*				
Depen	*(see penicillamine)*				
Depo-Medrol	*(see methylprednisolone acetate)*				
Depo-Provera	*(see medroxyprogesterone acetate)*				
Deprenyl	*(see selegiline)*				
Deracoxib (Deramaxx)	COX-2-inhibiting NSAID drug; for treatment of osteoarthritis, perioperative pain management	1-2 mg/kg PO q 24 h (long-term use); 3-4 mg/kg PO q 24 h (max 7 days)	—	GI signs (vomiting, anorexia)	25, 75, 100 mg chewable T VM
Deramaxx	*(see deracoxib)*				
Dermathycin	*(see thyrotropin)*				
Derm caps	*(see fatty acid nutritional supplement)*				
DES	*(see diethylstilbestrol)*				
Desferal	*(see deferoxamine)*				
Desitin	*(see zinc oxide)*				
Desmopressin acetate (DDAVP)	Vasopressin analog (1-desamino-8-D-arginine-vasopressin) to manage central diabetes insipidus, von Willebrand disease	1-4 drops intranasally or in subconjunctival sac, q 6-24 h (diabetes insipidus) or 1-2 mcg/kg SQ, q 24 h to q 12 h; 0.1 mg/kg PO q 8 h (tablets)	Oral dose: 0.25-0.5 mg/cat PO q 8-12 h (tablets)	Rhinorrhea, hypersensitivity reactions, water retention; use nasal spray form topically (1.5-4 mcg/drop); 40 times stronger than parenteral (4 mcg/mL)	10 mcg/spray (= 0.1 mL) in 2.5- or 5-mL bottles; 4 mcg/mL I; 0.1 and 0.2 mg, T HM
Desoxycorticosterone pivalate (DOCP) (Percorten-V)	Replacement therapy for mineralocorticoid deficiency (hypoadrenocorticism); each 25 mg releases 1 mg DOCA/day for 21-26 days	1 mL/12 kg, q 25 days (i.e., 2 mg/kg) IM or SQ	—	Titrate dosage to effect; monitor serum electrolytes; no glucocorticoid activity; may require oral prednisolone 0.2-0.4 mg/kg per day as adjunctive therapy	25 mg/mL I VM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Dexamethasone (Azium, Dexate, Decadron); Dexamethasone sodium phosphate (SP)	Potent glucocorticoid for antiinflammatory, immune suppression, hypoadrenocorticism, shock, pituitary-adrenal axis testing	Antiinflammatory: 0.1-0.2 mg/kg per day PO, SQ, or IV; immunosuppressive: 0.2-0.4 mg/kg per day PO, SQ, or IV; long-term oral: q 48 h best. Hypoadrenocorticism: 0.1-0.8 mg/kg IV (initial treatment; e.g., hypovolemic shock), but maintenance = <0.1 mg/kg PO PRN up to q 24 h. LDDST = 0.01 mg/kg IV; HDDST = 0.1 mg/kg IV	Same	HPA axis suppression, multiorgan steroid effects; very high CNS doses (e.g., 4-8 mg/ kg) of unproven clinical benefit and almost always associated with short-term adverse effects (e.g., severe GI bleeding): if more than several consecutive days of treatment, taper dose gradually before stopping	0.25, 0.5, 0.75, 1, 1.5, 2, 4, 6 mg T; 2, 8, 16 mg/mL I (dexamethasone); 4, 10, 20, 24 mg/mL I (dexamethasone SP) VM, HM
Dexasporin ophthalmic solution or ointment (Maxitrol)	Neomycin, polymyxin, and dexamethasone combination used for steroid-responsive ophthalmic inflammation where a combined antibiotic is desirable	1 drop in affected eye q 6-12 h	1 drop in affected eye q 6-12 h	Steroids are contraindicated in some specific eye diseases (e.g., corneal ulcers, feline herpetic keratitis); systemic corticosteroid side effects are possible	0.05% ointment, 0.1% solution HM
Dexate	*(see dexamethasone)*				
Dexdomitor	*(see dexmedetomidine)*				
Dexedrine	*(see dextroamphetamine)*				
Dexmedetomidine (Dexdomitor)	α2-agonist sedative-analgesic	Sedation/analgesia: 375 mcg/m^2 IV or 500 mcg/m^2 IM Preanesthetic: 125 mcg/m^2 IM	20-40 mcg/kg IM	Dextroenantiomer of medetomidine (levo-is inactive); therefore, double potency of medetomidine, but prepared at half concentration of medetomidine, so volume administered is same as medetomidine. See pp. 671, 677 for body surface area to body weight conversion chart. Reversal agent is atipamezole.	0.5 mg/mL (= 500 mcg/mL) I VM
Dexrazoxane (Zinecard, Cardioxane)	EDTA derivative that protects against doxorubicin-induced cardiomyopathy; may also be used for doxorubicin extravasation lesions	10:1 ratio to doxorubicin dose (i.e., administer 10 times more dexrazoxane [in mg] than doxorubicin); IV CRI over 30 minutes, begun 45 minutes prior to doxorubicin		Myelosuppression possible	250 and 500 mg vials I HM
Dextran (Rheomacrodex)	Hypovolemia, plasma volume expander	Approximately 20 mL/ kg IV, titrated to effect	Same	Platelet dysfunction, hemorrhage, circulatory overload	6% dextran in PSS or D5W I HM
Dextroamphetamine (Dexedrine)	Amphetamine; narcolepsy, hyperkinesis	5-10 mg total dose per dog PO q 8 h; 0.2-1.3 mg/kg PO PRN	—	CII drug	5 mg T; 5, 10, 15 mg ER C HM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Dextromethorphan	Antitussive	0.5-2 mg/kg PO q 8 h	Same	Usually in association with other drugs (i.e., OTC cough syrup [e.g., Robitussin]); efficacy questioned; avoid with moist/ productive coughs; avoid aspirin-containing or acetaminophen-containing combination in cats (OTC)	Many OTC, HM
Dextrose 50%	Hypoglycemia	Administer 1-5 mL IV for hypoglycemic crisis; dilute with sterile water or 0.9% NaCl (3-5× the volume) before administering	1 mL IV for hypoglycemic crisis; dilute as for dogs	Dilution decreases viscosity and reduces risk of perivascular injury if extravasation; repeated dosing in insulinoma may worsen insulin secretion	50% dextrose = 500 mg/mL VM
DFO	*(see deferoxamine)*				
DHT	*(see dihydrotachysterol)*				
Diabinese	*(see chlorpropamide)*				
Diabeta	*(see glyburide)*				
Diabexan	*(see chlorpropamide)*				
Diamox	*(see acetazolamide)*				
Diastat	*(see diazepam)*				
Diazepam (Valium, Diastat)	1. Tranquilizer, component of anesthetic induction protocol 2. Anticonvulsant 3. Muscle relaxant 4. Appetite stimulant (cats) 5. Urine marking/ spraying (cats) 6. Sedative/anxiolytic	1. With ketamine for sedation/ anesthetic induction: 0.5 mg/kg IV or to effect, maximum 20 mg/ dose 2. 0.5-1 mg/kg IV to effect; enema: 1-2 mg/kg made up as 4 mg/mL enema solution; or IV CRI: 0.5 mg/kg/hr, titrated PRN 0.25-1 mg/kg 3. 3, 6. 0.05-0.2 mg/kg IV PO, PRN up to q 12 h	1. 1, 2. Total dose: 0.25-2 mg IV per cat, to effect 2. 3, 5. Total dose: 1-2 mg per cat PO q 12 h 3. 0.2 mg/kg IV prior to feeding 4. Same as for dog	Sedation ataxia; paradoxical excitement/ aggression; hepatopathy in some cats within days or weeks of starting PO; CRI: diazepam is inactivated by light and adsorbs onto plastic; use glass syringe and short tubing if possible; class IV	2, 5, 10 mg T; 5 mg/mL I; 2.5, 5, 10, 15, 20 mg (rectal gel) HM
Diazoxide (Proglycem)	Hypoglycemia associated with insulinoma	5-20 mg/kg PO q 12 h	None	Vomiting, anorexia	50 mg C; 50 mg/mL S HM
Dibenzyline	*(see phenoxybenzamine HCl)*				
Dichlorphenamide (Daranide)	Glaucoma; carbonic anhydrase inhibitor	2-4 mg/kg PO q 8 h	Same	Weakness; lethargy, diarrhea, hypokalemia, hyperchloremic metabolic acidosis	50 mg T HM
Dichlorvos (Task, Vapona, DDVP)	Hookworms, whipworms, roundworms; flea collars and tags	27-33 mg/kg PO once; 11 mg/kg PO once (puppies); change collar every 4 months	11 mg/kg PO once; change collar every 4 months	Organophosphate toxicity; do not use with constipation, intestinal obstruction,	10, 20 mg T; 68, 136, 204 mg C; 136, 204, 544 mg paste

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
				or hepatic, cardiac, or heartworm disease; no effect on larval form of whipworms	VM
Dicural	*(see difloxacin)*				
Dicyclomine (Bentyl)	Irritable bowel syndrome, detrusor hyperspasticity causing urge incontinence	0.15 mg/kg PO q 8-12 h	—	—	10 mg C; 20 mg T HM
Didronate, Didronel	*(see etidronate)*				
Diethylcarbamazine (DEC, Caricide, Cypip, Filaribits)	1. Heartworm (HW) prophylaxis 2. *Crenosoma* lungworm treatment 3. Ascarid infections	1. 6-7 mg/kg PO q 24 h, from start of HW season to 2 months after end of HW season 2. 70 mg/kg PO q 12 h for 3 days 3. 55-100 mg/kg PO; repeat in 10-20 days	55-110 mg/kg PO once for ascarids	Vomiting; may decrease sperm count; anaphylaxis if microfilaria positive dog	50, 60, 100, 120, 180, 200, 300, 400 mg T; 60 mg/ mL S; other sizes VM, HM
Diethylstilbestrol (DES)	1. Estrogen-responsive incontinence 2. Perianal gland adenoma, benign prostatic hyperplasia	1. Total dose: 0.1-1 mg per dog PO q 24 h for 4-7 days, then once weekly 2. Total dose: 0.25-1 mg per dog PO q 24-48 h for 2-7 days	0.05-0.1 mg/day PO	May induce signs of estrus; decrease to lowest effective dosage; high dosages may cause anemia, leukopenia, thrombocytopenia; ineffective for pregnancy termination; limited availability in U.S. market	1, 5 mg T; 50 mg/ mL I; other sizes HM
Difloxacin (Dicural)	Fluoroquinolone antibacterial	5-10 mg/kg PO q 24 h; maximum = 30 days		GI effects, cartilage damage possible in pups; avoid in seizure animals	11, 45, 136 mg T VM
Diflucan	*(see fluconazole)*				
Digoxin (Cardoxin, Lanoxin)	Supraventricular tachyarrhythmias, systolic dysfunction; positive inotrope, negative chronotrope, negative dromotrope, baroreceptor upregulator	0.005 mg/kg PO q 12 h; maximum dose for largest dog = 0.25 mg PO q 12 h; can double dose for first 24 hours only	Total dose: ¼ of a 0.125 mg tablet per cat PO q 48 h	Injectable form not recommended; see also online chapter: Digoxin Toxicosis	0.125, 0.25 mg T; 0.05 mg/mL S HM
Dihydrotachysterol (DHT, Hytakerol)	Hypocalcemia	0.03-0.06 mg/kg PO q 24 h initially for 2-3 days; then 0.01-0.02 mg/kg PO q 24-48 h, titrated to response	Same	Risk of hypercalcemia; monitory serum calcium and patient until well stabilized; when stable, monitor long-term use	0.125, 0.2, 0.4 mg T; 0.125 mg C; 0.2 mg/mL S HM
Dilacor-XL	*(see diltiazem)*				
Dilantin	*(see phenytoin)*				
Dilaudid	(see hydromorphone)				
Diltiazem hydrochloride (Cardizem) (sustained release forms: Dilacor-XL, Cardizem CD)	Calcium channel blocking agent; hypertrophic cardiomyopathy (in felines), acute SVT	0.5-1.5 mg/kg PO q 8 h; for acute SVT: 0.01-0.02 mg/kg IV initial dose; repeat PRN; maximum cumulative IV dose = 1	0.8-2.5 mg/kg PO q 12 h to q 8 h; 10 mg/kg PO q 24 h, in sustained release form	Bradycardia, hypotension, anorexia; sustained-release form often causes adverse reactions (hepatic,	30, 60, 90, 120 mg T; 120, 180, 240, 320 mg C; 60, 90, 120, 240, 360, 420 mg; ER HM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
		mg/kg; may start at 0.1-0.2 mg/kg IV if heart is structurally normal		GI) in cats; dose-dependent AV block	
Dimenhydrinate (Dramamine, Gravol)	Motion sickness	4-8 mg/kg PO, up to q 8 h	Total dose: 12.5 mg per cat PO up to q 8 h	Lethargy, drowsiness; administer 1 hour prior to travel for best antinausea effect	80 mg T; 12.5 mg/ 4 mL S; 50 mg/ mL I HM, OTC
Dimercaprol (BAL, British anti-Lewisite)	Chelating agent; heavy metal toxicosis, such as mercury, lead, and arsenic	2.5-5 mg/kg IM (dose of 5 mg/kg used only in acute cases and only on first day) q 4 h on days 1 and 2; q 8 h on day 3; q 12 h for next 10 days	Same	Injections sting; caution: renal insufficiency; sulfurous odor of breath	100 mg/mL I HM
Dimercaptosuccinic acid	*(see succimer)*				
Dimethyl sulfoxide (DoMoSo, DMSO)	Topical antiinflammatory Renal amyloidosis CNS trauma	Apply solution topically q 12 h to q 8 h; use 60% otic solution, q 12 h 80 mg/kg SQ q 48 h (dilute solution 1:4 with sterile water) 1 g/kg of 10% solution over 45 minutes IV	None	Erythema, pruritus; investigational except as otic solution; wear gloves; readily absorbed; sulfurous odor of breath; teratogen: not for breeding animals	90% gel; 90% solution; topical VM, HM
Diminazene (Berenil)	Antiprotozoal; babesiosis, trypanosomiasis	4.2 mg/kg IM q 21 days		May be dosed at 3.5-5 mg/kg IM twice, 24 hours apart; risk of neurotoxicosis	70 mg/mL I VM
Dinolytic	*(see prostaglandin)*				
Dinoprost	*(see prostaglandin)*				
Dioctyl sodium sulfosuccinate (docusate, DSS, Colace, Surfak)	Stool softener	1 or 2 50-mg capsules PO q 12-24 h; per rectum: 60-90 mL (8 mg docusate/mL)	1 50-mg capsule PO q 12-24 h	Also available as enema preparation for cats and small dogs	25, 50, 100 mg hard caplets OTC, HM, VM
Dipentum	*(see olsalazine)*				
Diphenhydramine HCl (Benadryl Allergy)	H1 receptor antihistamine	2-4 mg/kg PO q 12 h to q 8 h; 1-2 mg/kg IM, SQ, q 12 h	Same	Sedative, anticholinergic, antiemetic; use with caution in seizure animals; avoid IV use (seizures)	25, 50 mg C, T; mg/mL S; 10 mg/ mL I HM
Diphenoxylate HCl with atropine (Lomotil)	Antidiarrheal, nonanalgesic opiate	0.1-0.2 mg/kg PO up to q 8 h; total dose: 0.625-2.5 mg PO per dog, up to q 8 h	0.6-1.2 mg total dose per cat PO q 12 h	Sedation, constipation, ileus; use with caution in cats (opiate adverse effects) and in patients with respiratory or cardiovascular compromise	2.5 mg T; 0.5 mg/ mL S HM
Diprivan	*(see propofol)*				
Dipyridamole (Persantine)	Anticoagulant; thromboxane synthase inhibitor	4-10 mg/kg PO q 24 h		Investigational use; safety and efficacy unproven in VM	25, 50, 75 mg T 5 mg/mL I HM
Dipyrone (Novin)	Antipyretic Injectable NSAID	25 mg/kg SQ, IM, IV up to q 8 h	Same	Hypothermia, BM suppression; do not use if hyperthermia is	300 mg T; 500 mg/ mL I

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
				not true fever (contraindicated if elevated temperature is due to heat stroke, seizures, brachycephalic crisis, etc.)	HM
Dirlotapide (Slentrol)	Obesity	0.01 mL/kg PO q 24 h. Can double dose after 2 weeks if needed, then adjust monthly; maximum 0.2 mL PO q 24 h.	Do not use	Gut microsomal triglyceride transfer protein (GMTP) inhibitor; vomiting, increased liver enzymes possible	5 mg/mL oil-based S VM
Disopyramide (Norpace)	Ventricular dysrhythmias, type IA agent	6-22 mg/kg PO q 8 h	None	Rarely used; may be used with quinidine or procainamide	100, 150 mg C; 100, 150 mg; ER HM
Dithiazanine	Microfilaricide	6.6-11 mg/kg PO q 24 h for 7-10 days	None	Stains stool purple, V/D, anorexia	10, 50, 100, 200 mg T VM
Ditrim	*(see trimethoprim/ sulfadiazine)*				
Diuril	*(see chlorothiazide)*				
Dizan	*(see dithiazanine iodide)*				
DMSO	*(see dimethyl sulfoxide)*				
DMSO with fluocinolone (Synotic)	*(see fluocinolone)*				
Dobutamine HCl (Dobutrex)	Inotropic agent for very severe dilated cardiomyopathy; short-term usage, only in ICU setting; β1-agonist	0.0025-0.02 mg/kg/min (2.5-20 mcg/kg/min) IV CRI in sterile LRS, 0.9% NaCl, or D5W	0.004-0.005 mg/kg/ min (4-5 mcg/kg/ min) IV CRI	Use 48 hours maximum; may increase HR; monitor for arrhythmias; continue usual cardiac therapy; cats are very sensitive to Tx and may have seizures; doses above 0.01 mg/kg/min (10 mcg/kg/min) in dogs are more likely to be arrhythmogenic	12.5 mg/mL I HM
Dobutrex	*(see dobutamine)*				
DOCP	*(see desoxycorticosterone pivalate)*				
Docusate	*(see dioctyl sodium sulfosuccinate)*				
Dolasetron (Anzemet)	Serotonin-inhibiting central antiemetic	0.6-1 mg/kg IV or SQ q 24 h	Same	Lower dosage for prevention of nausea; higher dosage for treatment of vomiting	20 mg/mL I; 50, 100 mg T HM
Domitor	*(see medetomidine)*				
DoMoSo	*(see dimethyl sulfoxide)*				
Dopamine HCl (Intropin)	α1, β1, and dopaminergic agent; inotropic agent for heart failure; pressor agent— hypotension	0.002-0.008 mg/kg/min (2-8 mcg/kg/min) IV CRI in LRS, 0.9% saline, or D5W	Same	Tachycardia, vasoconstriction; requires ICU monitoring. 1-3 mcg/ kg/min = visceral vasodilation; 3-10	40, 80, 160 mg/mL I HM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
				mcg/kg/min = β1-agonist, positive inotrope; >10 mcg/kg/min = positive inotrope and chronotrope, α-agonist (may increase or decrease heart rate)	
Dopram	*(see doxapram)*				
Doramectin (Dectomax)	Avermectin antiparasitic; spirocercosis	0.2 mg/kg SQ q 2 weeks for 3 treatments; if lesions persist, additional treatment with 0.5 mg/kg PO q 24 h for 6 weeks has been successful	—	Currently the treatment of choice for canine spirocercosis; caution with avermectin-susceptible individuals and breeds (see p. 706)	10 mg/mL I VM
Dorzolamide (Trusopt)	Carbonic anhydrase inhibitor, glaucoma	1 drop per eye q 8 h, adjusted PRN	Same	Monitor for hypokalemia	2% OS; 5, 10, 15 mL HM
Doxapram (Dopram)	1. Respiratory stimulant 2. Diagnostic aid for laryngeal paralysis suspects	1. 1.5-10 mg/kg once IV; repeat if needed 2. 2.2 mg/kg IV	Same	For puppy/kitten respiratory stimulation, use 1-5 drops under tongue or via umbilical vein	20 mg/mL I HM
Doxepin (Sinequan)	Tricyclic antidepressant; pruritic dermatoses in dogs, especially if there is a behavioral component	0.5-5 mg/kg PO q 12 h		Some antihistamine effects; contraindicated if concurrent MAO inhibitors (e.g., Anipryl, amitraz)	10, 25, 50, 75, 100, 150 mg C; 10 mg/mL S HM
Doxorubicin (Adriamycin)	Lymphomas, carcinomas, solid tumors	According to chemo protocol; either 30 mg/m^2 IV CRI once every 3 weeks (for dogs >10 kg) or 1 mg/kg IV once every 3 weeks (for dogs ≤10 kg); not to exceed total cumulative lifetime dose of 250 mg/m^2	According to chemo protocol; 20-25 mg/m^2 once every 3 weeks IV CRI to maximum total dose of 90 mg/m^2	Anaphylaxis, BM suppression, GI toxicity, cardiotoxic, severe vesicant (extravasation injury); use chemo precautions when handling or administering drug and with patient's urine and feces; reddish discoloration to urine due to drug pigment	2 mg/mL I HM
Doxycycline (Vibramycin)	Tetracycline antibiotic; *Rickettsia, Ehrlichia, Haemobartonella/ Anaplasma,* and *Chlamydia* infections; brucellosis; intracellular penetration	5-10 mg/kg PO q 24 h; 2-5 mg/kg IV CRI q 12 h	Same	Do not use in puppies, kittens, or animals that are pregnant; may cause anorexia, vomiting, depression; hyperthermia in cats; photosensitization; administer water post pilling to reduce esophagitis risk	20, 50, 100 mg T/C; 5, 10 mg/mL S HM
Dramamine	*(see dimenhydrinate)*				
Dramamine II	*(see meclizine)*				
Drisdol	*(see ergocalciferol)*				
Droncit	*(see praziquantel)*				

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
DSS	*(see dioctyl sodium sulfosuccinate)*				
DTIC	*(see dacarbazine)*				
Dulcolax	*(see bisacodyl)*				
Duragesic	*(see fentanyl)*				
Duricef	*(see cefadroxil)*				
Ecotrin	*(see acetylsalicylic acid)*				
ECP	*(see estradiol cyclopentane propionate)*				
Edrophonium (Tensilon)	Diagnostic agent for cholinergic stimulation; myasthenia gravis; may slow some supraventricular tachycardias	0.1-0.2 mg/kg IV; max = 5 mg total dose	Total dose = 0.25-1 mg IV per cat	Muscarinic signs	10 mg/mL I HM
EDTA	*(see calcium EDTA)*				
Elavil	*(see amitriptyline)*				
Eldepryl	*(see selegiline)*				
Elixophyllin	*(see theophylline elixir)*				
Ellence	*(see epirubicin)*				
Elmiron	*(see pentosan polysulfate)*				
Elspar	*(see asparaginase, L-)*				
Enacard	*(see enalapril maleate)*				
Enalapril maleate (Vasotec, Enacard)	ACE inhibitor, vasodilator; CHF, systemic hypertension, glomerulopathy	0.5 mg/kg PO q 24 h initially, then to q 12 h if necessary	0.25 mg/kg PO q 24 h	Hypotension, weakness, anorexia; avoid increasing furosemide dosage when initiating or increasing enalapril dosage; human adverse effects (renal effects, cough, hyperkalemia) very uncommon in the dog	1, 2.5, 5, 10, 20, mg T; 1.25 mg/mL I VM, HM
Enilconazole (Imaverol)	Nasal aspergillosis	10 mg/kg diluted with equal amount sterile water and administered intranasally via tubes placed in frontal sinuses	—	Not approved; possible allergic reactions	Use poultry-grade product; 10% emulsion
Enoxaparin	*(see heparin, low-molecular-weight)*				
Enrofloxacin (Baytril)	Broad-spectrum fluoroquinolone-class antibacterial	2.5-10 mg/kg PO, IM q 12 h; double dosage single administration per day may be equally effective	2.5-5 mg/kg PO q 24 h (this dose is the maximum in cats)	Do not use in puppies/ kittens (cartilage lesions); do not use >5 mg/kg/d in cats (permanent retinal lesions); caution in seizure patients; drug interactions (inhibits theophylline catabolism).	5.7, 22.7, 68, 136 mg T; 22.7 mg/mL I VM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Enteric probiotic supplement (FortiFlora)	Nonspecific benign diarrhea	1 packet PO (on food or as treat) q 24 h	Same		1 gram/packet P VM
Entocort	*(see budesonide)*				
Epakitin	*(see chitosan-based phosphate binder)*				
Ephedrine	Bronchodilator Urinary incontinence Hypotension	1-2 mg/kg PO q 8-12 h; 0.3-1 mg/kg IV, IM for hypotension	2-5 mg per cat PO q 8-12 h	For bronchospasm: usually combine with sedative +/− bronchodilator; caution if heart disease or hypertension; CNS stimulation, restlessness	25, 50 mg C; 50 mg/mL I HM
Epinephrine (Adrenalin)	1. α-adrenergic agent and β-adrenergic agent used for inotropic and chronotropic support: 2. Cardiac arrest 3. Bronchodilation 4. Anaphylaxis 5. Hemostasis (topical)	1. 0.0025 mg/kg IV, repeated to effect (= 1 mL of 1 : 10,000 per 40 kg BW); triple if administering intratracheally 2. 2, 3. 0.025 mg/kg IV, IM, SQ 3. Topical use: place 1 or 2 drops after applying pressure to, and dabbing blood from, a persistently bleeding wound	Same	Arrhythmogenic; increases $M^{VO}2$; avoid high doses (tachycardia); vasoconstriction; avoid direct sunlight exposure; Note: 1:1000 and 1:10,000 solution both commonly available, so use caution (10-fold difference)	1:1000 (1 mg/mL) I; 1:10,000 0.1 mg/mL) Epipen: 0.15 mg (0.15 mL) or 0.3 mg (0.3 mL), one-time dose I HM
Epirubicin (Ellence, Pharmorubicin, 4′-epi-doxorubicin)	Anthracycline antineoplastic	Same as for doxorubicin according to chemo protocol (e.g., 30 mg/m^2 IV CRI q 21 days)	—	Same as for doxorubicin but with generally fewer adverse effects (especially lesser incidence and extent of cardiotoxicity)	10, 50, 200 mg I (2 mg/mL) HM
EPO	*(see erythropoietin)*				
Epoetin-α	*(see erythropoietin)*				
Epogen	*(see erythropoietin)*				
Epsiprantel (Cestex)	Tapeworms (cesticide)	5.5 mg/kg PO once	2.75 mg/kg PO once	GI signs possible	12.5, 25, 50, 100 mg, T VM
Ergocalciferol (vitamin D2, calciferol, Drisdol)	Hypocalcemia	500-2000 IU/kg PO q 24 h		Second or third choice after calcitriol, DHT	400 IU T 50 000 IU (1.25 mg) C 500 000 IU/mL (12.5 mg/mL) I HM
Erythromycin	1. Macrolide antibiotic, G+ drug, *Campylobacter, Mycoplasma, Rickettsia, Chlamydia* 2. GI prokinetic	1. 10-20 mg/kg PO q 8 h 2. 0.5-1 mg/kg PO q 8 h	Same	Hypersensitivity; GI upset	200, 250, 333 400, 500 mg T; 100 mg/mL I HM
Erythropoietin (EPO, Epoetin, Epogen, r-Hu EPO,	Recombinant human erythropoietin	100 U/kg 3× per week SQ until RBC levels	Same	Anaphylaxis, hypertension, GI	2000, 3000, 4000, 10,000, 20,000 I

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Procrit)		increase; then 1× per week thereafter, titrated based on response		signs; autoantibodies may develop	HM
Eskalith	*(see lithium carbonate)*				
Esmolol (Brevibloc)	β-blocker with very rapid onset and offset	0.05-0.1 mg/kg/min (50-100 mcg/kg/min) IV CRI, titrated to effect	Same	Contraindicated with preexisting bradycardia, CHF	10, 20 mg/mL HM
Esomeprazole (Nexium)	Proton pump inhibitor Gastric ulceration	1 mg/kg PO q 24 h		*S*-enantiomer of omeprazole (hence "*S*-omeprazole"), which may provide increased potency	20, 40 mg T, C (both ER) HM
Estradiol cyclopentane-propionate (ECP, estradiol cypionate)	Estradiol to terminate pregnancy	—	—	Repeatedly shown to be toxic to BM; unpredictable abortifacient; not recommended	—
Estrogen—conjugated (Premarin)	Estrogen derived from pregnant mare serum; used for treating postovariohysterectomy estrogen insufficiency causing urinary incontinence	0.625 mg = 1 mg DES; use PO for urinary incontinence *(see diethylstilbestrol)*	—	May induce signs of estrus	0.3, 0.625, 0.9, 1.25, 2.5 mg T HM
Estrumate	*(see cloprostenol)*				
Ethanol 20%	Ethylene glycol toxicosis	Dilute to 20% ethanol in saline; administer 5 mL/kg IV q 6 h × 5 Tx, then q 8 h × 4 Tx (see p. 369)	Dilute to 20% ethanol in saline; administer 5 mL/ kg IV q 6 h × 5 Tx, then q 8 h × 4 Tx (see p. 369)	May cause or exacerbate CNS depression; monitor hydration, electrolytes, acid-base status, perivascular damage. If alternatives are lacking, an 80-proof alcoholic beverage (40% ethanol) such as vodka may be diluted 1:1 in sterile 0.9% NaCl to create a 20% ethanol solution	—
Etidronate (Didronel)	Bisphosphonate antihypercalcemic agent	5-10 mg/kg PO q 12-24 h	Same	Main indication is severe paraneoplastic hypercalcemia; renal excretion, avoid in renal hyper-PTH	200, 400 mg T 50 mg/mL I HM
Etodolac (EtoGesic, Lodine)	NSAID; selective COX-2 inhibitor for DJD in dogs	10-15 mg/kg PO q 24 h		GI and renal toxicity; if long-term, use low dose; do not administer with ASA or corticosteroids; may cause KCS in dogs	150, 300 mg T VM; 200, 300 mg C; 400, 500 mg T HM
EtoGesic	*(see etodolac)*				
Etretinate (Tegison)	Synthetic retinoid used to treat disorders of keratinization in specific breeds (primarily cocker	1 mg/kg PO q 24 h	Total dose: 10 mg per cat PO q 24 h	Vomiting, anemia KCS, increased liver enzymes, expensive	10, 25 mg C HM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
	spaniels)				
Excedrin	*(see acetaminophen)*				
Famotidine (Pepcid)	H2 receptor antagonist	0.5-1 mg/kg PO, IV q 12-24 h	0.5 mg/kg PO, IV q 24 h	Advantages over other similar agents: once-a-day dosage, minimal P450 inhibition	10, 20, 40 mg T; 8 mg/mL S; 10 mg/mL I HM, OTC
Factrel	*(see gonadotropin releasing hormone)*				
Fatty acid nutritional supplement (Derm Caps)	Dietary supplement, allergic skin disease, dry skin	1 regular capsule PO q 24 h per 9 kg BW; one ES capsule PO q 24 h per 25-30 kg BW; 1 "100s" capsule PO q 24 h per 45 kg BW	—	GI upset, increased bleeding times, "fishy" breath	Regular, ES, 100s, C VM
Febantel (Rintal)	Acaricidal, phenylguanidine, antiparasitic	10-15 mg/kg PO q 24 h for 3 days	Same	Is metabolized to fenbendazole and oxfendazole	27.2, 163.3 mg T VM
Felbamate (Felbatol)	Antiseizure drug used when seizures are refractory to phenobarbital and bromide	15 mg/kg PO q 8 h; can increase to 60 mg/kg PRN		Monitor for BM suppression; hepatotoxic; expensive	400, 600 mg T; 600 mg/tsp S HM
Felbatol	*(see felbamate)*				
Feldene	*(see piroxicam)*				
Felimazole	*(see methimazole)*				
Feliway	*(see pheromones, feline synthetic)*				
Fenbendazole (Panacur)	Hookworm, whipworm, roundworm, *Taenia, Paragonimus, Filaroides, Giardia, Capillaria,* lungworm *(Aelurostrongylus)*	50 mg/kg PO q 24 h for 3 days; repeat in 3 weeks; whipworms, also repeat in 3 months; lungworms: 50 mg/kg PO q 24 h for 10 days	Same; not FDA approved	Vomiting (rare); safe in dogs with heartworms	222 mg/g granules; 100 mg/mL S VM
Fentanyl (Duragesic, Sublimaze)	Transdermal opioid patch, usually lasts at least 72 hours; requires 12 hours to be effective; injectable is ultrashort acting	Patches: 5-10 kg = 25 mcg/h; 10-20 kg = 50 mcg/h; 20-30 kg = 75 mcg/h; >30 kg = 100 mcg/h Injectable: 0.01-0.04 mg/kg SQ, IM, IV; CRI: 0.003-0.006 mg/kg/hr (3-6 mcg/kg/hr) IV	2.5-mg patch	Apply a patch to a small clipped area on thorax; never cut patch; prevent human contact with gel surface of patches; avoid heat exposure (e.g., heating pad), increases absorption; respiratory depression and hypoventilation	2.5 mg (25 mcg/h), 5 mg (50 mcg/h), 7.5 mg (75 mcg/h), 10 mg (100 mcg/h) patches; 0.05 mg/ mL (50 mcg/mL) I, HM; former VM injectable (Innovar) was 8× more concentrated than human injectable; do not confuse.
Fenthion (Prospot, Spot-on)	Organophosphate insecticide	4-8 mg/kg topically to unbroken skin; follow instructions; do not apply more than once every 2 weeks	None	Do not use with other cholinesterase inhibiting agents; do not use in puppies or sick or debilitated dogs	5.6% and 13.8% solution VM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Ferric cyanoferrate (Prussian blue, Radiogardase)	Thallium poisoning	100-200 mg/kg PO q 8 h	None	Administer as capsule or in a glucose solution orally; constipation, vomiting	500 mg C HM
Ferrous sulfate	Iron supplementation	Total dose: 100-300 mg per dog PO q 24 h	Total dose: 50-100 mg per cat PO q 24 h	Common side effects: minor GI upset; overdose: severe GI signs, hypotension, collapse; delayed toxicity = pulmonary edema, liver failure *(see deferoxamine)*	325 mg (65 mg Fe) T; 18, 44 mg Fe/5 mL S HM, OTC
Fertagyl	*(see gonadotropin releasing hormone)*				
Feverall	*(see acetaminophen)*				
Fiber (soluble dietary)	*(see psyllium mucilloid)*				
Filaribits	*(see diethylcarbamazine)*				
Filgrastim (Neupogen, r-Hu G-CSF)	Recombinant human granulocyte colony-stimulating factor; used for chemotherapy-induced neutropenia	1-5 mcg/kg per day SQ for 3-5 days maximum	1-5 mcg/kg per day SQ for 3-5 days maximum	Antibodies develop after several days of therapy	300 mcg/mL I HM
Finasteride (Proscar)	Used for treating benign prostatic hyperplasia by inhibiting enzyme that changes testosterone to active dihydroxy-testosterone	Total dose: 5 mg per dog (BW 10-40 kg) PO q 24 h	—	Little published objective information about use, efficacy, or side effects in canine medicine	1, 5 mg T HM
Fipronil (Frontline)	Topical parasiticide for fleas and ticks	9.7% solution; apply topically by weight once monthly	Same	Keep away from children, food, water; avoid contact with pet if fipronil is still wet on skin; use on puppies only if >10 weeks old, kittens if >12 weeks old	9.7% solution, 0.29% spray VM
Firocoxib (Previcox)	Nonsteroidal antiinflammatory drug, COX-2 inhibitor type	5 mg/kg PO q 24 h	1.5 mg/kg PO once only	Used mainly for osteoarthritis in dogs; safety not established for repeated dosing in cats	57, 227 mg T VM
Flagyl	*(see metronidazole)*				
Fleet	*(see phosphate enemas)*				
Flomax, Flomaxtra	*(see tamsulosin)*				
Florinef	*(see fludrocortisone)*				
Flovent	*(see fluticasone)*				
Fluconazole (Diflucan)	Imidazole antifungal compound: especially useful for cryptococcosis or CNS/ ocular mycoses	2.5-5 mg/kg PO q 24 h or divided q 12 h	Same; up to 50 mg PO total dose per cat q 12 h	Historically was expensive, though generic form now available (cheaper)	50, 10, 200 mg T; 2 mg/mL I HM
Flucort	*(see flumethasone)*				
Flucytosine (Ancobon, Ancotil)	Aspergillosis, cryptococcosis, candidiasis	100 mg/kg PO q 12 h, or 25-50 mg/kg PO q 6 h	Same	Renal, BM, and hepatotoxicity; may cause GI upset; do not administer to pregnant animals;	250, 500 mg C; 75 mg/mL S HM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
				neurologic side effects in cats	
Fludrocortisone (Florinef)	Hypoadrenocorticism, mineralocorticoid replacement therapy	0.1 mg/5 kg PO q 24 h or q 12 h; adjust dosage by need and laboratory testing	0.1 mg/5 kg per day PO; adjust dosage by need and laboratory testing	Systemic hypertension, PU/PD, weight gain. Cushing's-like side effects possible (some glucocorticoid activity)	0.1 mg T HM
Flumazenil (Romazicon)	Benzodiazepine antagonist, possibly management of hepatic encephalopathy	0.01-0.02 mg/kg IV (titrate depending on benzodiazepine dose)	Same	—	0.1 mg/mL I HM
Flumethasone (Flucort)	Antiinflammatory, corticosteroid	Total dose: 0.06-0.25 mg PO, IV, IM, SQ q 24 h per dog; intralesional, intraarticular	Total dose: 0.03-0.125 mg PO, IV, IM, SQ q 24 h per cat	Glucocorticoid-related side effects	0.0625 mg T; 0.5 mg/mL I VM
Flunixin meglumine (Banamine)	NSAID analgesic agent	0.25-1 mg/kg IV, IM, SQ q 24 h; maximum 3-5 days dosage	0.25 mg/kg IV, IM q 24 h; maximum 3-5 days dosage	Platelet dysfunction, ulcerative gastritis, kidney damage; multiple safer alternative drugs	50 mg/mL I VM
Fluocinolone 0.01% with 60% DMSO (Synotic)	Topical corticosteroid plus DMSO for severe otic inflammation	2-12 drops applied topically to ear, q 12 h	2-4 drops applied topically to ear, q 12 h	Systemic corticosteroid effects; wear gloves (to avoid transcutaneous absorption by owner/tech/vet)	0.1% otic solution VM
Fluorouracil (Adrucil)	Chemotherapy agent for carcinomas	150 mg/m^2 IV weekly or 2-10 mg/kg IV weekly	Do not use	Part of a chemotherapy protocol; BM toxicity, GI toxicity, and neurotoxicity possible	50 mg/mL I HM
Fluoxetine (Prozac, Reconcile)	Serotonin reuptake inhibitor	0.5-2 mg/kg PO q 24 h	0.5 mg/kg PO q 24 h	Used for treating behavioral disorders (e.g., acral lick dermatitis)	8, 16, 32, 64 mg chewable T VM 10 mg T; 10, 20, 40 mg C; 4 mg/mL S HM
Flurbiprofen 0.03% solution (Ocufen)	Topical ocular NSAID	1 drop instilled in eye q 12 h, adjusted PRN	—	Caution with corneal ulcers; contraindicated in infected corneal ulcers	2.5, 5, 10 mL OS HM
Fluticasone (Flovent)	Inhaled glucocorticoid	1 puff PRN, up to q 12-24 h	Same	Need inhaler apparatus; some patients are reluctant to accept placement of a mask at first; maximum effect only after 7-14 days of use; see p. 1289	7.9 g and 13 g inhalation canisters (0.044, 0.11, or 0.22 mg [44, 110, or 220 mcg] per puff) HM
Folate	B vitamin	Total dose: 2.5-5 mg PO per dog q 24 h	Total dose: 2.5 mg PO per cat q 24 h	—	0.4, 0.8, 1 mg/mL I; 5 mg T HM
Fomepizole (Antizol-Vet, 4-methylpyrazole, 4-MP)	Treatment of known or suspected ethylene glycol toxicity	22 mg/kg IV; then 15, 15, and 5 mg/kg IV at 12, 24, and 36 hours following initial dose;	—	Dilute drug properly; monitor renal, electrolyte, and hydration status	1.5-g kit I VM, HM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
		then 3-5 mg/kg IV, q 12 h, until recovery			
Fondaparinux (Arixtra)	Anticoagulant; prophylaxis for prevention of thromboembolism in feline cardiomyopathy		0.06 mg/kg SQ q 12 h	Selectively binds antithrombin III, inactivating factor Xa. No effect on platelet function. No clinical trials to establish safety or efficacy in cats at this time.	2.5, 5. 7.5, 10 mg prefilled syringes I HM
Fortaz	*(see ceftazidime)*				
Fortekor	*(see benazepril)*				
FortiFlora	*(see enteric probiotic supplement)*				
Fosamax	*(see alendronate)*				
Fragmin	*(see heparin-low molecular weight)*				
Frontline	*(see fipronil)*				
Fulvicin	*(see griseofulvin)*				
Fungizone	*(see amphotericin B)*				
Furadantin	*(see nitrofurantoin)*				
Furazolidone (Furoxone)	1. Amebiasis 2. Enteric coccidiosis 3. Giardiasis	1. 2.2 mg/kg PO q 8 h for 7 days 2. 8-20 mg/kg PO q 24 h for 7 days 3. 4 mg/kg PO q 12 h for 7 days	Same	—	100 mg T HM
Furosemide (Lasix, Salix)	Potent loop diuretic agent; used in acute renal failure; hypercalcemia; hypertension, CHF (especially pulmonary edema), ascites, and fluid retention	0.5-6 mg/kg PO, SQ, IM, IV q 8-12 h	0.5-4 mg/kg PO, SQ, IM, IV q 8-12 h	Use lowest effective dosage; high doses reserved for IV use in acute severe pulmonary edema; monitor for hypokalemia, hyponatremia, and hypochloremic alkalosis; caution: azotemia and dehydration	12.5, 20, 40, 50, 80 mg T; 10 mg/mL S; 50 mg/mL I VM, HM
Furoxone	*(see furazolidone)*				
Gabapentin (Neurontin)	Pain, paresthesias; refractory seizures	10 mg/kg PO q 8 h	5-10 mg/kg PO q 8 h	Used for pain associated with caudal occipital malformation and other neurologic disorders	100, 300, 400, 600, 800 mg C, T 50 mg/mL S HM
Gammagard S/D	*(see immunoglobulin)*				
Garamycin	*(see gentamicin)*				
G-CSF	*(see filgrastim)*				
Gemcitabine (Gemzar)	Various forms of neoplasia	10 mg/kg IV CRI over 30 minutes; 275 mg/m^2 IV CRI	25 mg/m^2 diluted and given IV slowly twice weekly, according to chemo protocol	Emerging drug in veterinary oncology at time of this writing, with dosage, efficacy, and side effects still being characterized	200 mg, 1 g vials I VM, HM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Gemfibrozil (Lipid)	Lipid-lowering agent	7.5 mg/kg PO q 12 h	—	—	300, 600 mg T HM
Gemzar	*(see gemcitabine)*				
Genoptic	*(see gentamicin, ophthalmic)*				
Gentamicin (Garamycin, Gentocin)	Broad-spectrum aminoglycoside antibiotic most effective against G− bacteria	6 mg/kg IV, q 24 h, or 2-4 mg/kg IM, SQ, IV q 8 h, max 7 days	Same	Higher dosage given q 24 h is preferred (less nephrotoxic); not effective orally; do not use in renal failure or dehydrated/ hypovolemic patients; reserved for serious identified infections only; not for anaerobic infections; nephrotoxic-ototoxic	50 mg/mL I VM, HM
Gentamicin, otic (Gentocin otic)	Ear infections, especially *Pseudomonas* or *Proteus*	Apply q 8 h	Apply q 8 h	Includes betamethasone 1 mg/mL, which can have topical and/or systemic corticosteroid effects; ototoxic risk (aminoglycoside)	3 mg/mL otic solution VM, HM
Gentamicin, ophthalmic (Gentocin, Genoptic)	Conjunctival/corneal infections, especially *Pseudomonas*	Apply q 4-8 h	Apply q 4-8 h	Rarely irritating; a preparation that contains corticosteroids also exists in nearly identical packaging; use caution when selecting product	3 mg/g OO; 3 mg/ mL OS VM, HM
Gentocin	*(see gentamicin)*				
Geocillin	*(see carbenicillin)*				
Geopen	*(see carbenicillin)*				
Glargine	*(see insulin)*				
Glipizide (Glucotrol)	Oral hyperglycemic agent; useful in some type II diabetes mellitus in cats	0.25-0.5 mg/kg PO q 12 h generally not recommended	0.25-0.5 mg/kg PO q 12 h	Hypokaemia, GI effects, hepatopathy; eventual loss of efficacy (very common); no objective information available on extended-release formulation in veterinary diabetic patients	5, 10 mg T HM
Glucagon	1. Provocative testing agent for insulinoma, diabetes mellitus, and hyperadrenocorticism 2. Insulinoma	1. 0.03 mcg/kg IV 2. 5 ng (0.005 mg)/kg/ min IV CRI	None	May induce hypokalemia; 1 unit = 1 mg Rare case report data but very positive response	1 mg/mL I HM
Glucantime	*(see meglumine)*				
Glucosamine-chondroitin sulfate (Cosequin)	Chondroprotective agent for osteoarthritis	Small- and medium-size dogs: 1-2 RS capsules PO q 24	1 RS capsule PO q 24 h	—	RS and DS, C VM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
		h; big dogs: 1-2 DS capsules PO q 24 h, or 2-4 RS capsules PO q 24 h			
Glucotrol	*(see glipizide)*				
Glyburide (Diabeta, Micronase, Glynase)	Oral hypoglycemic drug; diabetes mellitus	0.2 mg/kg PO q 24 h	0.625 mg/cat PO q 24 h	In most cases, insulin therapy eventually becomes necessary	1.25, 2.5, 5 mg T HM
Glycerin 50% solution (oral) (Osmoglyn)	Glaucoma	1-2 mL/kg PO once	Same	50% solution = 500 mg/ mL; do not use if anuria, CHF, severe dehydration	220 mL S HM
Glycerin suppositories	Constipation	1 suppository per rectum	Same or 3 mL liquid per rectum	—	OTC, HM
Glycopyrrolate (Robinul)	Anticholinergic preanesthetic agent	0.01 mg/kg SQ, IM, IV	Same	Tachycardia, arrhythmias, intestinal ileus, mydriasis, and photophobia; avoid in narrow-angle glaucoma	0.2 mg/mL I VM, HM
Glycosaminoglycanpolysulfated (Adequan)	Chondroprotective agent; slows ± helps heal noninfectious, degenerative, and traumatic arthritis	2-4 mg/kg IM twice weekly for 4 weeks; then once every 2-4 weeks	2 mg/kg IM q 4 days for 6 doses; then PRN	Occasional pain at injection site; possibly	100 mg/mL I VM
Glynase	*(see glyburide)*				
GoLYTELY (polyethylene glycol-electrolyte solution)	Large bowel evacuant/ cathartic	22-33 mL/kg via stomach tube	20-30 mL/kg via stomach tube	Withhold food; administer twice q 2 h apart, 12 hours prior to GI endoscopic procedure	Powder or concentrate for dilution HM
Gonadotropin-releasing hormone (GnRH, gonadorelin, Fertagyl, Factrel, Cystorelin)	Male infertility; cryptorchidism/ testicular descent	2.2-3.3 mcg/kg IM	25 mcg/cat IM	Response may be clinical (overt physical signs) or endocrine (2- to 4-fold increase in serum testosterone levels)	50 mcg/mL I VM, HM
Goodwinol (Rotenone)	Demodicosis (localized)	Apply topically q 24 h	Same	Rotenone, orthophenyl phenol, and benzocaine mixture; efficacy not demonstrated	1.24% Rotenone O VM
Granisetron (Kytril)	Serotonin 5-HT3 inhibitor antiemetic	0.01 mg/kg IV	Same		1 mg T 1 mg/mL I 0.2 mg/mL S HM
Gravol	*(see dimenhydrinate)*				
Griseofulvin (Fulvicin)	Dermatophytoses	50-150 mg/kg PO q 24 h to q 12 h; 25-50 mg/kg q 24 h if using microsize product (U/F); 5-15 mg/kg PO q 12 h, if using ultramicrosize product (P/G)	Same	U/F prep better absorbed than regular: therefore, dosage is 50% lower for this formulation; P/G even more so: therefore, dosage is a further 30% lower for this formulation; GI signs, teratogen, granulocytopenia, anemia, hepatopathy	125, 250, 500 mg T; 250, 500 mg microsize formulation T; 125, 165, 250, 330 mg ultramicrosize formulation T; 125 mg/5 mL S VM/HM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Growth hormone, human (Protropin, somatrem)	Pituitary dwarfism	0.1 IU SQ q 48-72 h × 4-6 weeks		Limited efficacy in dogs because human product often induces autoantibody formation; 3 IU = 1 mg	5, 10 mg vials I HM
hCG	*(see chorionic gonadotropin, human)*				
Havidote	*(see Calcium EDTA)*				
Heartgard-30	*(see ivermectin)*				
Hemoglobin glutamer (Oxyglobin)	Bovine hemoglobin-based oxygen-carrying fluid; used for hemolytic, blood loss, or ineffective erythropoietic anemias	10-30 mL/kg IV at 10 mL/kg/h in a one-time single infusion; some administer partial dosages daily instead	Not licensed; used IV by some at 15 mL/kg IV in a slow single dose or daily split doses	Overdosage may cause cardiopulmonary signs; hemoglobinuria; has no clotting factors; interferes with clinical pathologic testing; half-life *in vivo* = 18-43 hours	125 mL I; single-use bags VM
Heparin	1. Anticoagulation 2. DIC therapy	1. 200-300 IU/kg SQ or IV, q 8 h to q 6 h, for thromboembolism; increase PTT to 1.5-2.5 times normal or ACT to 1.2-1.4 times normal 2. 50-100 IU/kg SQ, q 6-8 h	75-150 IU/kg q 6-8 h SQ	Prolongs bleeding time; not thrombolytic; ineffective in the absence of antithrombin III (e.g., protein-losing diseases); "regular" heparin is unfractionated heparin (versus low-molecular-weight heparin)	1000, 2000, 5000, 10,000, 20,000, 40,000 mg/mL I HM
Heparin, low-molecular-weight (Dalteparin [Lovenox], Enoxaparin [Fragmin])	Anticoagulant	Dalteparin (Fragmin): 100-150 IU/kg SQ q 6-12 h	Dalteparin (Fragmin): 100-150 IU/kg SQ q 6-12 h Enoxaparin (Lovenox): 1 mg/kg SQ q 6-12 h	Outpatient (owner-administered) SQ anticoagulant; main differences versus unfractionated heparin: low-molecular-weight heparin is less antigenic (seemingly not important in VM), and much more expensive; clinical efficacy and advantages not yet proven in VM	Enoxaparin: 100 mg/mL I; 30, 40, 60, 80, 100, 120, 150 mg I (prefilled syringes) Dalteparin: 10,000 or 25,000 IU/mL I; 2500, 5000, 10,000 IU I (prefilled syringes) HM
Herplex	*(see idoxuridine)*				
Hespan	*(see hetastarch)*				
Hetacillin (Hetacin)	Similar to penicillin	10-20 mg/kg PO q 8 h	Same	Penicillin reactions	50, 10, 200 mg T VM
Hetacin	*(see hetacillin)*				
Hetastarch 6% (Hespan)	Colloid and plasma volume expansion, shock, sepsis, head trauma	10-20 mL/kg per day IV	10-15 mL/kg per day IV	Rapid IV bolus initially over 5-10 minutes; titrate crystalloids slowly; volume overload possible	500 mL package of 6% hetastarch in 0.9% NaCl I HM
Hu G-CSF	*(see filgrastim)*				

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Human chorionic gonadotropin	*(see chorionic gonadotropin, human)*				
Human growth hormone	*(see growth hormone, human)*				
Humulin	*(see insulin)*				
Hycodan	*(see hydrocodone)*				
Hydralazine (Apresoline)	Arteriolar vasodilator, CHF	0.5-3 mg/kg PO q 8-12 h	2.5-5 mg/cat total dose PO q 12 h	Hypotension, tachycardia malaise, depression, anorexia	10, 25, 50, 100 mg T; 20 mg/mL S HM
Hydrea	*(see hydroxyurea)*				
Hydrochlorothiazide (HydroDIURIL)	Diuretic, nonhormonal therapy for CDI and NDI, urolithiasis (calcium containing)	2-4 mg/kg PO q 12 h, initially; then decrease by 50% or to q 24 h	1-2 mg/kg PO q 12 h, initially; then decrease by 50% or to q 24 h	Hypokalemia; exacerbates digitalis toxicity; dehydration	25, 50, 100 mg T HM
Hydrochlorothiazide/ spironolactone (Aldactazide)	Diuretic plus aldosterone blocker	Use on basis of 1 mg/ kg of spironolactone PO q 12-24 h	Rarely used	Often used in conjunction with furosemide in chronic, recurrent CHF	25/25 mg T; 50/50 mg T HM
Hydrocodone bitartrate (Hycodan)	Narcotic antitussive	0.22 mg/kg PO q 6-24 h PRN	Rarely used	Sedation; C-III substance; Hycodan contains hydrocodone 5 mg/tab and homatropine 1.5 mg/ tab; constipation (rare)	5 mg T; 1 mg/mL S HM
Hydrocortisone acetate 1% cream	Topical corticosteroid for focal dermatitis	Apply topically q 6-12 h	Same	Prolonged use may result in iatrogenic Cushing's syndrome	1% O HM
Hydrocortisone sodium succinate (Solu Cortef)	Intravenously injectable corticosteroid; hypoadrenal crisis	4-5 mg/kg IV acutely and/or 0.5 mg/kg/h IV CRI			100, 250, 500, 1000 mg vials I HM
HydroDIURIL	*(see hydrochlorothiazide)*				
Hydrogen peroxide 3%	Emetic	0.25-0.5 mL/kg PO (3% solution); repeat once in 5-15 minutes PO if emesis does not occur	Same	Do not use if a caustic agent was ingested, if level of consciousness is decreased, or if the patient is unable to swallow; see Vomiting, Induction of, p. 1364	3% topical solution HM OTC
Hydromorphone (Dilaudid)	Analgesia, preanesthetic	0.1-0.2 mg/kg SQ, IM, or IV once or PRN up to q 2-4 h	Same	Vomiting common immediately postinjection, bradycardia, second-degree AV block, dysphoria in some cats	1, 2, 4, 10 mg/mL I HM
Hydroxyurea (Hydrea)	Chemotherapeutic compound; disorders of RBC excess, especially polycythemia vera and right-to-left cardiac shunts	20-25 mg/kg PO q 12-24 h; when PCV decreases, then 25-50 mg/kg PO q 48 h and adjust based on PCV	10-15 mg/kg PO q 24 h; then q 48 h based on PCV	Anorexia, vomiting, BM suppression possible; monitor CBC regularly	500 mg C HM
Hydroxyzine (Atarax)	H1 receptor antihistamine for allergic skin disorders	1-2 mg/kg PO q 8-12 h	0.5-1 mg/kg PO q 12 h to q 8 h	Sedative, anticholinergic side effects	10, 25, 50, 100 mg T; 10 mg/5 mL S; 25, 50 mg/mL I

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
					HM
Hyoscyamine (Levsin)	Antimuscarinic, inhibits propulsive GI motility	0.003-0.006 mg/kg PO q 8 h	Same; infrequently used	Useful in irritable bowel syndrome and functional intestinal disorders; dry mouth; urinary retention; tachycardia	0.125 mg T; 0.125 mg/5 mL S; 0.375 mg C ER; 0.5 mg/mL I HM
Hytakerol	*(see dihydrotachysterol)*				
Ibafloxacin (Ibaflin)	Fluoroquinolone antibiotic	15 mg/kg PO q 24 h	Same	Packaged as dial-syringe for oral dosing	3% oral gel in 15 mL preloaded syringe VM
Ibuprofen (Advil, Motrin, Nuprin)	Nonsalicylate, NSAID	Not recommended	Not recommended	Frequently cause GI bleeding and irritation; many safer alternatives	OTC, HM
Idoxuridine (Herplex, Stoxil)	Used for treating feline herpesviral keratitis, KCS		1 drop q 4 h initially, then q 6-8 h	Occasional ophthalmic irritation	0.1% OS HM
Ifex	*(see ifosfamide)*				
Ifosfamide (Ifex)	Various neoplasms	350-375 mg/m^2 IV once every 3 weeks for 3 treatments maximum	—	Efficacy under investigation; dosing interval according to chemo protocol; pretreat with mesna and IV diuresis to reduce risk of hemorrhagic cystitis; neutropenia possible	50 mg/mL I
Imaverol	*(see enilconazole)*				
Imferon	*(see iron dextran injection)*				
Imidacloprid (Advantage)	Topical treatment for adult and larval stage of fleas	Apply topically to intact skin; dose monthly by BW from prepackaged cards	Same	Avoid contact with skin, food, or water; avoid eye exposure	9.1% topical solution VM
Imidapril (Prilium)	ACE inhibitor; treatment of heart failure caused by dilated cardiomyopathy or mitral regurgitation	0.25 mg/kg PO q 24 h		Oral liquid formulation (reconstituted lyophilized powder) Veterinary form not available in the United States	2.5, 5, 10 mg/mL S VM
Imidocarb (Imizole)	*Babesia gibsoni, Ehrlichia canis*; hepatozoonosis	5-7.5 mg/kg IM or SQ once, repeat in 2-3 weeks	—	Painful injection; give IM; cholinergic side effects	120 mg/mL I VM
Imipenem-cilastatin (Primaxin)	Broad-spectrum bactericidal carbapenem antibacterial	2-10 mg/kg slow IV (over 30 minutes), q 6-8 h for 3-5 days	Same	Adverse effects possible: GI, CNS, hypersensitivity; reduce dose if renal compromise; different formulations for IV and IM use	250, 500 mg vials I HM
Imipramine (Tofranil)	Tricyclic antidepressant; behavioral changes, narcolepsy, cataplexy, inappropriate elimination	0.5-2 mg/kg PO q 8-12 h	0.5 mg/kg PO q 12-24 h, or total dose 2.5-5 mg per cat PO q 12 h	Prolonged onset of action, drowsiness, behavioral changes	10, 25, 50 mg T; 125 mg/mL I HM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Imizole	*(see imidocarb)*				
Immiticide	*(see melarsomine)*				
Immunoglobulin (Gammagard S/D, human intravenous immunoglobulin G, IVIG)	Treatment of primary immunodeficient states; also IHA, ITP, and CLL	0.5-1.5 g/kg slow IV infusion	—	Must be given IV; very expensive; hypersensitivity; not reported as first-line therapy	2.5, 5, 10 g single-dose vials I HM
ImmunoRegulin	*(see* Propionibacterium acnes*)*				
Imodium	*(see loperamide)*				
Impavido	*(see miltefosine)*				
Imuran	*(see azathioprine)*				
Inderal	*(see propranolol)*				
Inocor	*(see amrinone)*				
Insulin (Humulin R, N, U, PZI, Vetsulin, Caninsulin, Glargine)	Diabetes mellitus, diabetic ketoacidosis, severe hyperkalemia	Regular: 0.5-1 U/kg initially IM or SQ; then q 4-6 h. NPH: 0.5-1 U/kg q 12-24 h SQ. IV CRI protocol: 0.05-0.1 U/kg/h, using regular insulin (Humulin R) only	NPH, Lente, Ultralente, glargine: Total dose (starting): 1-2 U per cat SQ q 24 h to q 12 h CRI: same	Dosage variable: adjust and monitor accordingly; these are average approximate dosages; maintain hydration; avoid hypoglycemia and hypokalemia	100 U/mL I HM, VM
Interceptor	*(see milbemycin)*				
Interferon-alfa (Roferon)	Immune modulator with antiviral and antiproliferative effects; used for FeLV and FAIDS, leukemia, lymphoma, FIP	1 IU/5 kg BW, PO every 2 weeks to stimulate appetite	Total dose: 30 IU per cat PO: 7 days on, then 7 days off	Dosages of up to 20,000 IU/cat IM and 2 million IU/m^2 SQ (dogs) have been used	3, 5, 6, 9, 10, 18, 36 million IU per vial I HM
Interferon-omega (Virbagen)	Immunomodulator; parvoviral enteritis, FeLV, FIV	2.5 million IU/kg IV q 24 h × 3 d	1 million IU/kg SQ q 24 h × 5 d		10 million IU/vial I VM
Intropin	*(see dopamine)*				
Iodides	*(see sodium iodide 20%)*				
Ipecac syrup	Induce vomiting	0.25-0.5 mL/kg PO; can repeat once after 5-15 minutes if not vomiting	Not recommended in cats; use 3% hydrogen peroxide PO instead	Do not use with activated charcoal (ineffective)	70 mg/mL S; OTC, HM; many oral OTC; 50 mg/mL I HM
Ipodate (Oragrafin)	Oral radiographic contrast agent with antithyroid effects; used for hyperthyroidism	—	Total dose: 15-100 mg per cat PO q 12 h; titrated based on clinical response and T3	Blocks T4 conversion to T3; therefore, blood monitoring = serum T3 levels	500 mg C HM
Irbesartan (Avapro)	Angiotensin receptor antagonist	5-60 mg/kg PO q 12 h		Used in humans intolerant to ACE inhibitors; efficacy of irbesartan has been demonstrated in the dog (RAAS effect) but clinical proof and long-term safety not yet determined	75, 150, 300 mg T HM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Iron-dextran injection (Imferon)	Iron-deficiency anemia	10 mg/kg in divided doses IM or total dose 100-300 mg PO per day for one dog	Same: IM or total dose 50-100 mg PO per day for one cat	Irritating IM	Many oral OTC; 50 mg/mL I HM
Isoproterenol (Isuprel)	β-adrenergic agonist	0.2 mg in 250 mL 5% dextrose, IV CRI at a rate of 0.05-0.1 mcg/kg/min; titrate to effect, adequate HR	0.2 mg in 250 mL 5% dextrose, IV to effect, adequate HR	Increased HR, increased or decreased BP, CNS stimulation, arrhythmogenic	0.2 mg/mL (= 200 mcg/mL) I HM
Isoptin	*(see verapamil)*				
Isosorbide dinitrate	Orally administered vasodilator	0.5-2 mg/kg PO q 12 h	Same	No recognized therapeutic efficacy in small animals	5, 10, 20, 30, 40 mg T HM
Isotretinoin (Accutane)	Sebaceous adenitis, keratinization disorders, mycosis fungoides, feline acne	1-2 mg/kg PO q 12 h; reduce dosage after 1 month if improving	Total dose: 5-10 mg PO q 24 h per cat	GI and CNS effects may occur, if so, reduce dosage by 50% or stop; teratogen; KCS in dogs; other mucocutaneous side effects	10, 20, 40, mg C HM
Isuprel	*(see isoproterenol)*				
Itraconazole (Sporanox)	Antimycotic fungistatic imidazole compound for blastomycosis, coccidioidomycosis, cryptococcosis; histoplasmosis *M. canis*, dermatophytosis, candidiasis	5-10 mg/kg PO q 24 h	Same	Long-term therapy (months or more) often required; must be taken with food; open capsules and place pellets in food if necessary; antacid GI drugs will reduce efficacy (decrease absorption); monitor liver status	100 mg C; 10 mg/mL S HM
Ivermectin (Heartgard-30, Heartgard Plus, Ivomec)	GABA agonist, antiparasiticide 1. Heartworm prophylaxis, microfilaricide 2. Heartworm 3. Endoparasites 4. Sarcoptic mange 5. Demodectic mange 6. Otodectic mange 7. Cheyletiellosis	1. HW prophylaxis: 0.006 mg/kg (6 mcg/kg) PO, once monthly 2. HW microfilaricide; 0.05 mg/kg (50 mcg/kg) once PO, 2-4 weeks after adulticide Tx 3. 0.2 mg/kg (200 mcg/kg) PO 4. 0.3 mg/kg (300 mcg/kg) PO or 0.2 mg/kg (200 mcg/kg) SQ 2 times, 14 days apart 5. 0.05 mg/kg (50 mcg/kg) PO; increase to 0.3 mg/kg (300 mcg/ kg) by day 5; increase to 0.6 mg/kg (600 mcg/kg) once daily PO after 30 days if necessary	HW prophylaxis: 0.024 mg/kg (24 mcg/kg) SQ; repeat in 3-4 weeks (usually under 0.1 mL) Same Same Same	Do not use in collies or other dogs sensitive to drug (exception: collies and similar breeds usually tolerate low [HW prophylaxis] dose); CNS, vomiting, anaphylaxis; can give injectable solution PO; of questionable value in treating feline heartworm disease; consider testing individual patients prior to treatment for the MDR-1 gene mutation if ivermectin is the treatment of choice in patients where susceptibility to toxicosis is possible (see pp. 706 and 625)	68, 136, 272 mcg T or chewables; 10 mg/mL (= 10,000 mcg/ mL) I VM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
		6. 0.3 mg/kg (300 mcg/kg) PO, SQ 2 times at 14 days apart	Same		
		7. 0.3 mg/kg (300 mcg/kg) SQ 2 times at 21 days apart	Same		
Ivomec	*(see ivermectin)*				
Jenotone	*(see aminopropazine*)				
Kaolin Pectin	GI tract protectant	1-2 mL/kg PO q 2-6 h	Same	May limit absorption of other medications; limited efficacy	Many OTC preparations; T/S VM, HM
Kabikinase	*(see streptokinase)*				
Kaon	*(see potassium salts oral supplement)*				
KBr	*(see bromide)*				
Keflex	*(see cephalosporin antibiotics)*				
Kenalog	*(see triamcinolone)*				
Keppra	*(see levetiracetam)*				
Ketamine HCl (Ketaset, Vetalar)	Dissociative anesthetic agent; short-action when given IV in healthy dogs/cats: 10-20 minutes	When diazepam (at diazepam dose of 0.5 mg/kg) given IV first: immediately follow with ketamine 5-7 mg/kg IV bolus for sedation and minor procedures (diazepam [5 mg/mL]: ketamine combination in ratio of 1:1 → use 0.5 mL/10 kg of each [in separate syringes] IV)	Restraint: 11 mg/kg IM; anesthesia (but does not provide deep analgesia): 22-33 mg/kg IM or 2.2-4.4 mg/kg IV	Eyes remain open: use ophthalmic ointment; salivation, seizures, respiratory depression, laryngospasm, hypothermia; do not use with renal failure or glaucoma; reduce dose by 50%-75% if stable but systemically ill; avoid if hypertrophic cardiomyopathy; controlled drug	100 mg/mL I VM, HM
Ketaset	*(see ketamine)*				
Ketoconazole (Nizoral)	Antifungal agent; protothecosis; inhibits glucocorticoid synthesis	10-15 mg/kg PO q 12 h; long-term 10 mg/kg PO q 24 h; hyperadrenocorticism Rx: 15 mg/kg PO q 12 h	5-10 mg/kg q 12 h PO or q 24 h; long term: 10 mg/kg q 48 h PO	Anorexia, nausea, vomiting, constipation, hepatotoxicity; monitor liver status; begin lower and titrate upwards to reduce risk of side effects; must be given with food (for good absorption); drug interaction potential: DMSO inhibitor; antacids decrease absorption	200 mg T HM
Ketoprofen (Orudis KT; Ketofen)	NSAID	0.5-1 mg/kg PO q 12 h; 1-2 mg/kg SQ, IM, or IV once or q 24 h up to 3 days maximum	Same	GI ulceration, renal effects possible	25, 50, 75 mg C; 12.5 mg T, HM, OTC; 5, 10, 20 mg T; 10, 100 mg/mL I, VM (not approved in United States) OTC, VM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Kitten Milk Replacer (KMR)	Milk replacement	—	30 mL per ¼ lb BW PO daily, divided into 3-6 meals	—	OTC, VM
Klonopin	*(see clonazepam)*				
KMR	*(see kitten milk replacer)*				
Kytril	*(see granisetron)*				
Lactulose (Cephulac, Chronulac)	Hepatic encephalopathy is treated by acidifying colon contents, trapping NH4 that is then expelled; the drug is also a stool softener	0.25-0.5 mL/kg PO q 8-12 h As a retention enema: total volume = 10-20 mL/kg (consisting of 3 parts lactulose plus 7 parts water) per rectum	Total dose: 1-5 mL PO q 8 h per cat Enema: same as for dog	Loose stools/diarrhea; flatulence; cramping; may use per rectum in patients with hepatic coma	666 mg/mL S HM
Lacrilube	*(see artificial tears ointment)*				
Lamprene	*(see clofazimine)*				
Lanoxin	*(see digoxin)*				
Lansoprazole (Prevacid)	Proton pump inhibitor; gastric ulceration	1 mg/kg IV q 24 h	Same	Usage less well-documented in VM compared to omeprazole	15, 30 mg C 6 mg/mL I HM
Lantus	*(see insulin glargine)*				
Lasix	*(see furosemide)*				
Latanoprost (Xalatan)	Topical prostaglandin analog used in the treatment of glaucoma	1 drop to affected eye, q 12-24 h	—	Generally effective and potent; may combine with oral carbonic anhydrase inhibitor; 1 drop = approximately 0.0015 mg	0.05 mg/mL OS HM
Laxative paste (Laxatone, Cat-a-Lax, etc.)	Oral laxative, hairball Tx	½-2 inches PO daily until not constipated, then weekly or PRN	Same	Large amounts daily could result in malabsorption (e.g., fat-soluble vitamins)	OTC, S, VM
Leflunomide (Arava)	Autoimmune disorders (IHA, ITP, sterile meningitis, systemic histiocytosis)	1.5-4 mg/kg PO q 24 h	—	Beneficial and adverse effects variably documented to date; GI and BM effects possible; seek trough serum level of 20 mcg/mL	10, 20, 100 mg T HM
Leucovorin	Reversal of methotrexate activity; sulfa-associated myelotoxicosis	5-15 mg per dog PO	1 mg/kg q 24 h	Higher/repeated doses may be indicated for methotrexate toxicosis; can assess plasma methotrexate levels	5, 15, 25 mg T 3, 10 mg/mL I 50, 100, 350 mg vials I HM
Leukeran	*(see chlorambucil)*				
Levamisole (Levasole, Ripercol, Tramisol)	1. Heartworm microfilaricide 2. Immune stimulant 3. Feline lungworm	1. 10 mg/kg PO q 24 h 7-14 days as a microfilaricide 2. 2.5-5 mg/kg PO q 48 h for immune modulation	2.5-5 mg/kg PO q 48 h for immune modulation; 10-20 mg/kg PO q 48 h for	Salivation, vomiting, shock-like syndrome with excessive microfilaricide death, neurotoxic, sudden death; not FDA	184 mg T; 136 mg/ mL S; 11.5% gel VM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
			Aelurostrongylus and *Capillaria*	approved for small animal medicine	50 mg T HM
Levarterenol	*(see norepinephrine)*				
Levasol	*(see levamisole)*				
Levetiracetam (Keppra)	Third-line anticonvulsant for refractory seizures	20 mg/kg PO q 8 h, in addition to KBr and phenobarbital	—	Few adverse effects reported; can be up-titrated if starting dose ineffective; expensive	250, 500, 750, 1000 mg T 100 mg/mL S 100 mg/mL I HM
Levophed	*(see norepinephrine)*				
Levothyroxine sodium (Soloxine, Synthroid, thyroxine)	Synthetic thyroid hormone replacement therapy	0.04 mg/kg PO q 12 h Myxedema coma: 0.005 mg/kg slow IV q 12 h	Total dose: 0.05-0.1 mg PO q 24 h per cat	Thyrotoxicosis; do not give only on basis of low T4 (assess clinical signs and other lab results); adjust dose based on response and blood levels; concurrent antiepileptics (e.g., phenobarbital) may affect levels; maximum dose for largest dog: 0.8 mg PO q 12 h	0.025, 0.05, 0.075, 0.125, 0.15 mg T HM 0.2, 0.5 mg/mL I 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.8 mg T VM
Levsin	*(see hyoscyamine)*				
Lidocaine (Xylocaine)	Ventricular arrhythmias, local anesthesia	2-4 mg/kg IV over 1-2 minutes, then 0.5-2 mg/kg every 20-60 minutes, or 0.04-0.08 mg/kg/min (40-80 mcg/kg/min) CRI IV; inject up to 4 mg/kg SQ for local anesthesia	0.25-1 mg/kg slowly over 5 minutes; give 1-4 mg bolus maximum over 5 minutes; use diluted solution as CRI 0.01-0.04 mg/kg/min (10-40 mcg/kg/min)	Give initial bolus slowly; seizures, hypotension; use lidocaine preparations *without* epinephrine for cardiac arrhythmia therapy; use only for life-threatening arrhythmias	20 mg/mL I HM
Lime sulfur solution (LymDyp, Sulfodip)	Bacterial and fungal dermatosis, sarcoptic mange	Dip once to twice weekly; let air dry; use 4-6 weeks (ideally until 2-3 fungal cultures are negative)	Same	Offensive odor; stains furniture; wear gloves to avoid hypersensitivity	2% dip VM
Lincocin	*(see lincomycin)*				
Lincomycin (Lincocin)	Staphylococcal and anaerobic infections, some *Mycoplasma* infections	15-25 mg/kg PO, IV, IM q 8-12 h	Same	Vomiting, hepatotoxicity; do not use in combination with chloramphenicol or erythromycin	100, 200, 500 mg T; 50 mg/mL S; 100 mg/mL I HM, VM
Liothyronine, T3	*(see triiodothyronine)*				
Liquiprin	*(see acetaminophen)*				
Lisinopril (Zestril, Prinivil)	ACE inhibitor; CHF, protein-losing nephropathy	0.5-0.75 mg/kg PO q 24 h	0.25 mg/kg PO q 24 h	Monitor BUN, creatinine; lethargy, anorexia	2.5, 5, 10, 20, 40 mg T HM
Lithane	*(see lithium carbonate)*				

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Lithium carbonate (Eskalith, Lithane, Lithotabs)	Increased production of all cell lines by BM	21-26 mg/kg per day PO	Unknown	Nausea, diarrhea, vertigo	300 mg C; 450 mg T ER HM
Lithotabs	*(see lithium carbonate)*				
Lodine	*(see etodolac)*				
Lomotil	*(see diphenoxylate with atropine)*				
Lomustine (CCNU, CeeNu)	Nitrosourea alkylating agent for brain tumors, mast cell tumors, relapse or failure to respond to lymphoma therapy	60-90 mg/m^2 PO once every 3 weeks	—	Neutropenia may develop after 7 days; GI adverse effects, anemia; its active metabolites reach the CNS	10, 40, 100 mg C HM
Loperamide (Imodium)	Opiate antidiarrheal, acute colitis	0.1-0.2 mg/kg PO q 8 h	0.1-0.15 mg/kg PO q 12 h	Discontinue if not effective within 48 hours; collie sensitivity; CNS adverse effects possible in dogs and cats (see p. 706)	2 mg C; 1 mg/5 mL S HM, OTC
Lopid	*(see gemfibrozil)*				
Lopressor	*(see metoprolol)*				
Lorazepam (Ativan)	Benzodiazepine; anxiolytic. Phobias, anxiety disorders	0.02-0.1 mg/kg PO q 8-24 h PRN	0.125-0.25 mg/cat PO q 12-24 h		0.5, 1, 2 mg T 2 mg/mL S 2, 4 mg/mL I HM
Losec	*(see omeprazole)*				
Lotensin	*(see benazepril)*				
Lotrimin	*(see clotrimazole)*				
Lovenox	*(see heparin-low molecular weight)*				
Lufenuron (Program)	Insect development inhibitor; inhibits chitin synthesis 1. Prevents flea eggs from developing into adults 2. Coccidioidomycosis 3. Dermatophytosis	Administer PO in conjunction with food. 1. 10 mg/kg PO once every 30 days 2. 5-10 mg/kg PO q 24 h 3. 54-100 mg/kg PO once q 2-4 wk	30 mg/kg PO once monthly or 10 mg/ kg once every 6 months by SQ injection 51-266 mg/kg PO once	Expensive as long-term daily Tx for fungal disease; efficacy in dermatophytosis questionable; may be combined with milbemycin for control of fleas, heartworms, roundworms, whipworms	Sold in packets for varying BW by T, S, or 10 mg/mL T or I
Lutalyse	*(see prostaglandin F2-α)*				
Lym-DYP	*(see lime sulfur solution)*				
Lyrica	*(see pregabalin)*				
Lysine	Herpesviral keratitis palliation		250-500 mg/day in food	Lifelong therapy for lifelong infection	Many sizes and formulations OTC VM, HM
Lysodren	*(see o,p'-DDD)*				
Macrobid	*(see nitrofurantoin)*				

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Macrodantin	*(see nitrofurantoin)*				
Magnesium hydroxide (Milk of Magnesia)	Antacid, laxative	Total dose: 5-10 mL PO q 4-6 h per dog	—	Cathartic agent at 3-5× the antacid dosage; rarely used because high dosing frequency and rebound acid secretion	77.5 mg/g S OTC, HM
Magnesium sulfate	Hypomagnesemia	0.75-1 mEq/kg/d as IV CRI; for hypomagnesemia-associated life-threatening ventricular arrhythmias: 0.15-0.3 mEq/kg slow IV (15-30 minutes) while monitoring for adverse effects	Same	Monitor for acute toxicosis: increased QT interval on ECG; lethargy, hypotension, weakness, collapse	100 mg/mL (0.8 mEq/mL), 125 mg/mL (1 mEq/mL), 500 mg/mL (4 mEq/mL) I HM
Mannitol 20%	Osmotic diuretic used for treating acute glaucoma, cerebral edema, and oliguria/ anuria; aids in elimination of certain toxins (e.g., ethylene glycol)	0.5-1 g/kg IV slowly over 15-20 minutes for anuria; double dosage for acute glaucoma or cerebral edema	Same	Rehydrate patient prior to use; can repeat twice if urine output is not increased; resolubilize (by warming) if crystallized, ensuring to cool to body temperature before administering; overzealous use: circulatory overload/ pulmonary edema	100 mg/mL (10%); 200 mg/mL (20%) I HM, VM
Marbofloxicin (Zeniquin)	Fluoroquinolone class antibiotic	2-4 mg/kg PO q 24 h	Same	Anorexia and vomiting; not recommended for rapidly growing dogs (possible arthropathy); caution in seizure patients (as with all fluoroquinolones)	25, 50, 100, 200 mg T VM
Marin	*(see silymarin)*				
Maropitant (Cerenia)	Antiemetic (motion sickness, enteritis, etc.); neurokinin-1 antagonist	1 mg/kg SQ or 2 mg/kg PO; up to 5 days	Not approved; experimental report: single dose 1 mg/kg PO, SQ, or IV was safe and effective in cats	Pain at injection site common; refrigeration may help.	16, 24, 60, 160 mg T 10 mg/mL I
Marquis	*(see ponazuril)*				
Matulane	*(see procarbazine)*				
Maxitrol	*(see dexasporin)*				
MCT oil	*(see medium chain triglycerides)*				
Mebendazole (Telmintic)	Hookworm, whipworm, and roundworm	22 mg/kg with food once daily for 3 days	—	Repeat as indicated; V/D may develop; hepatopathies have been incriminated in a small number of cases	40 mg/g powder VM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Meclizine (Bonine, Dramamine II, Antivert)	Antiemetic, motion sickness	1.25 mg/kg PO q 24 h	12.5 mg per cat PO q 24 h	Lethargy, CNS depression possible	12.5, 25, 50 mg T OTC, HM
Medetomidine (Domitor)	Synthetic α-2 adrenoreceptor agonist; provides sedation-analgesia as chemical restraint for healthy exercise tolerant dogs; useful for sedation of cats that have compensated ("asymptomatic") hypertrophic cardiomyopathy	0.005-0.02 mg/kg (5-20 µg/kg) IM as a single agent; used by some at half or quarter dose in combination with butorphanol, ketamine, morphine, or oxymorphone	0.02 mg/kg (20 µg/kg) IM	Do not use if hypertensive; allow dog or cat to rest quietly after administration; do not use in older, younger (<12 weeks old), sick, or debilitated dogs or cats; reversed with equal volume of atipamezole; reflex bradycardia is result of drug-induced hypertension; do not attempt to "correct" bradycardia with atropine or other antibradycardiac drugs; nonopiate/not controlled; sedation outlasts analgesia	1 mg/ml I VM
Medium chain triglycerides (MCT oil)	Nutritional supplement used in protein-losing diseases (lymphangiectasia) and when long-term triglyceride intake should be reduced, such as in chylothorax	1-2 mL/kg daily in food	Same	May be unpalatable; efficacy not demonstrated; GI upset (V/D)	OTC, HM
Medroxyprogesterone acetate (Depo-Provera, Provera)	Long-acting progesterone compound used for decreasing male dog libido and aggression, rarely as a contraceptive; in cats, used for psychogenic and miliary dermatitis and inappropriate elimination	2-20 mg/kg IM, SQ every 4-6 months	Total dose: 10-100 mg IM, SQ every 4 months, per cat	Overdosage may cause cystic endometritis, diabetes mellitus, hypoadrenocorticism, and mammary hyperplasia/ adenocarcinoma; local alopecia may occur; carefully weigh risks versus benefits	2.5, 5, 10 mg T; 150, 400 mg/mL I HM
Mefoxin	*(see cefoxitin)*				
Megace	*(see megestrol acetate)*				
Megestrol acetate (Ovaban, Megace)	Oral progestogen used for delaying estrus and treating canine pseudopregnancy; canine and feline behavioral modification; eosinophilic granuloma and some chronic feline skin disorders	Anestrus Tx: 0.5 mg/kg PO q 24 h for 32 days; proestrus Tx: 2 mg/kg PO q 24 h for 8 days; behavior modification: 2-4 mg/ kg PO q 24 h for 14 days, then decrease and stop after 6 weeks	Estrus suppression total dose: 5-10 mg PO q 24 h per cat for 7 days, then twice weekly; same dose as for dog for behavior modification	See specific diseases; do not use in pregnant pets or pets with uterine problems; avoid use with mammary tumors or hyperplasia; may cause PU/PD, polyphagia, diabetes mellitus	5, 20 mg T, VM; 20, 40 mg T HM
Meglumine antimonite (Glucantime)	Antiprotozoal; leishmaniasis	100 mg/kg SQ or IM q 24 h for 3-4 weeks		Difficult to obtain in North America; widely available in Europe	300 mg/mL I HM
Melarsomine (Immiticide)	Organic arsenical for treatment of adult heartworms	2.5 mg/kg IM, once; then 30 days later, 2.5 mg/kg IM × 2 doses, 24 hours apart	None	Painful after few days: give in epaxial muscles; cellulitis or salivation may occur; PTE occurs when	50 mg/vial I VM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
				worms die; absolute cage rest for 4 weeks post Tx; not for class IV HW disease	
Melatonin (Regulin)	Hormone involved in diurnal cycle. Alopecia-X, recurrent flank alopecia	3-12 mg/dog PO q 8-24 h		Treatment response expected to take several weeks	Many forms available OTC HM
Meloxicam (Metacam, Mobic)	COX-2-inhibiting NSAID; for treatment of osteoarthritis; perioperative pain management	0.1 mg/kg PO, SQ q 24 h (may be preceded by single 0.2 mg/kg loading dose, PO, SQ, IV)	Chronic use: 0.025 mg/kg PO q 24 h (can be preceded by perioperative dose below as loading dose); perioperative pain control; 0.1-0.2 mg/kg PO, SQ, IV once only	GI signs (vomiting, anorexia), GI ulceration, perforation	1.5 mg/mL S; 5 mg/ mL I, VM; 7.5, 15 mg T HM
Melphalan (Alkeran)	Multiple myeloma; lymphoreticular and other neoplasms; alkylating agent	0.1 mg/kg PO q 24 h for 10 days, then 0.05 mg/kg PO q 24 h; or 1.5 mg/m^2 PO q 24 h for 7-10 days; or 7 mg/m^2 q 24 h for 5 days every 3 weeks	Same	Anorexia, nausea, vomiting, leukopenia, thrombocytopenia, anemia	2 mg T HM
Meperidine HCl (Demerol)	Narcotic analgesic with short-term (1-4 hours) effect	3-10 mg/kg IM or slow IV PRN	1-4 mg/kg IM PRN	Watch for signs of narcotic overdosage (i.e., sedation, depression, seizures, hypotension, [especially in cats]); can reverse with naloxone	25, 50, 75, 100 mg/ mL I; 50, 100 mg T; 10 mg/mL S HM
Mephyton	*(see vitamin K)*				
Mepron	*(see atovaquone)*				
Meropenem (Merren IV)	Carbapenem antibiotic, especially for G− bacteria (alternative to aminoglycosides)	12 mg/kg SQ q 8-12 h or 24 mg/kg IV q 24 h for UTI	—	Indications similar to those for imipenem; fewer adverse effects in people	500, 1000 mg (vial) I HM
Merrem IV	*(see meropenem)*				
Mesalamine (5-ASA, Asacol, Pentasa)	Inhibits prostaglandin production in the colon; irritable bowel syndrome, ulcerative colitis	10-20 mg/kg PO q 8 h	—	Clinical VM use very new at time of this writing; efficacy unproven; may be infused rectally (enema instructions)	400 mg T; 250 mg C; 4 g/60 mL enema HM
Mesna (Mexnex)	Urothelial protection preceding ifosfamide chemotherapy	Dose is 20% of ifosfamide dose	—	Administered as pretreatment before ifosfamide: reconstitute as 20 mg/ mL, and give calculated dose as IV bolus, followed by 9 mL/kg 0.9% NaCl IV over 30 minutes, then ifosfamide	100 mg/mL I HM
Mesnex	*(see mesna)*				

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Mestinon	*(see pyridostigmine bromide)*				
Metacam	*(see meloxicam)*				
Metaflumizone (ProMeris)	Fleas, ticks *(Ixodes, Dermacentor, Rhipicephalus, Amblyomma),* demodicosis	20 mg/kg (=0.133 ml/ kg) topically q 4-6 weeks	Same	Compounded with amitraz (150 mg metaflumizone + 150 mg amitraz/mL), warranting caution if owner or patient is taking/exposed to other MAO inhibitors.	0.67, 1.33, 3.33, 5.33, 6.66 ml pipettes topical solution VM
Metamucil	*(see psyllium mucilloid)*				
Methazolamide (Neptazane)	Oral carbonic anhydrase inhibitor, glaucoma	5 mg/kg PO q 8-12 h		Induces mild metabolic acidosis (bicarbonaturia); GI and CNS adverse effects possible	25, 50 mg T, HM
Methigel	*(see methionine, DL-)*				
Methimazole (Tapazole, thiamazole, Felimazole)	Feline hyperthyroidism, palliative Tx for canine functional thyroid neoplasia	Total dose 2.5-5 mg PO q 12 h per dog	Total dose 2.5-5 mg PO q 8-12 h per cat	Possible side effects: anorexia, vomiting, and blood dyscrasias; intense facial pruritus; monitor CBC and T4; start at ½ dosage, then increase after 7-10 days based on clinical response and T4 level; monitor renal function	5, 10 mg T HM 2.5, 5 mg T VM
DL-methionine (Methigel, Albeta)	Urinary acidifier	0.2-1 g PO q 8 h per dog	0.2-1 g PO q 24 h per cat	Contraindicated for renal failure, acidosis, pancreatic disease, hepatic insufficiency/ encephalopathy; GI irritability; blood dyscrasias, in cats especially	15 mg/mL S; 200, 500 mg T, C OTC, VM, HM
S-adenosyl methionine (SAMe, Denosyl)	Adjunctive treatment for certain liver diseases, steroid hepatopathy, acetaminophen toxicity	Total dose per dog: 90 mg PO q 24 h (small dog), or 225 mg or more PO q 24 h (large dog)	Total dose per cat: 90 mg PO q 24 h	Also compounded with milk thistle extract (silymarin) as Denamarin	90, 225 mg T VM
Methocarbamol (Robaxin)	Muscle relaxant	20-45 mg/kg PO q 12 h to q 8 h; 44-220 mg/ kg slow IV (few minutes); use high end of dose range if strychnine, metaldehyde, tetanus; maximum = 330 mg/ kg per day	20-45 mg/kg PO q 8-12 h	Ataxia, sedation, ptyalism, emesis	100 mg/mL I; 500 mg T, VM; 100 mg/mL I; 500, 750 mg T HM
Methotrexate	Antimetabolite, antineoplastic agent that inhibits folic acid reductase; used to treat some cancers or for immunosuppression; sclerosing cholangiohepatitis	0.06 mg/kg PO q 24-48 h; or 2.5 mg/ m^2 PO q 24-48 h	2.5 mg/m^2 PO q 2-3 days	Leukopenia, GI bleeding, hepatotoxicity; see specific cancer or disease state	2.5, 5, 7.5, 10, 15 mg T; 25 mg/ mL I HM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Methylene blue (new methylene blue)	1. For treatment of methemoglobinemia in dogs 2. As intraop insulinoma Dx test	1. 1-2 mg/kg slowly IV, once 2. Dilute 3 mg/kg in sterile saline, and administer as CRI	—	Use once only; can induce Heinz body anemia; islet cell tumors = purple (versus pale blue background); best contrast 30 minutes after onset of CRI	10 mg/mL I HM
Methylprednisolone acetate (DepoMedrol)	Repositol corticosteroid; feline asthma, eosinophilic granuloma complex; for intralesional skin injections	1-2 mg/kg IM, SQ	Same, total dose: 10-20 mg per cat	Glucocorticoid contraindications and side effects; may cause CHF in cats with asymptomatic cardiomyopathy	20, 40, 80 mg/mL I VM, HM
Methylprednisolone sodium succinate (Solu-Medrol)	*See prednisolone sodium succinate*	30 mg/kg slow IV once, then 15 mg/kg IV in 2-6 hours	Same	GI ulcers very common; assess need for this Tx based on acuity (time frame) and severity	40, 125, 500, 1000, 2000 mg/vial I HM
Methyltestosterone	Anabolic drug, androgenic steroid; used in testosterone-responsive incontinence	0.5 mg/kg PO	Same	May increase creatinine and glucose levels	10, 25 mg C HM
Metoclopramide (Reglan)	Antiemetic with both central (chemoreceptor trigger zone) and peripheral (GI prokinetic) effects; increases LES pressure; promotes gastric emptying	0.2-0.5 mg/kg PO, SQ, q 6-12 h, or 1-2 mg/ kg per day given as IV infusion over 24 hours	Same	Do not use with GI obstruction, with phenothiazines, or with narcotic analgesics; atropine blocks effect; may increase seizure activity; extrapyramidal effects, avoid in epileptics	5, 10, mg T; 1 mg/ mL S; 5 mg/mL 1 HM
Metopirone	*(see metyrapone)*				
Metroprolol (Lopressor, Toprol XL)	Antiarrhythmic, β1-selective blockage	0.4-1 mg/kg PO q 8-12 h; q 24 h for extended release	Total dose: 2-10 mg PO q 12-24 h per cat	Lethargy, depression; decreased HR; β-blockade-induced CHF; always begin low and titrate up	25, 50, 100, mg T; 25, 50, 100, 200 mg ER; 1 mg/mL I HM
Metronidazole (Flagyl)	Anaerobic infections; antiprotozoal *(Giardia, Entamoeba, Balantidium, Pentatrichomonas)*; IBD, SIBO; *Helicobacter* therapy, colitis therapy	10-20 mg/kg PO q 12 h; for sepsis: 15 mg/kg slow IV (30 minutes infusion) q 12 h	Same	Anorexia and vomiting; neurotoxicity and hepatotoxicity may develop at high and/ or prolonged dosages; hepatic metabolism; use 7.5 mg/kg PO q 12 h if liver disease	250, 500 mg T; 500 mg/100 mL I HM
Metyrapone (Metopirone)	Feline hyperadrenocorticism		65 mg/kg PO q 12 h	Uncommon disorder; limited information	250 mg T HM
Mexiletine (Mexitil)	Type 1B antiarrhythmic drug used for treating ventricular arrhythmias; lidocaine-like oral agent	4-10 mg/kg PO q 8-12 h	—	Anorexia, depression; CNS stimulatory signs; side effects rare; increasingly difficult to obtain due to decreased use in human cardiology	150, 200, 250 mg C HM
Mexitil	*(see mexiletine)*				

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Miacalcin	*(see calcitonin)*				
Mibolerone (Cheque)	Prevents estrus (dogs only); pseudocyesis; synthetic androgenic anabolic steroid	Total dose per dog: 30, 60, 120, 180 mcg PO q 24 h for dogs weighing 1-11, 12-22, 23-45, or >45 kg respectively. Begin 30 days before proestrus to suppress estrus.	—	Do not use in pregnant dogs or in those with hepatic or renal disease. Pseudocyesis: multiply dosage by 10, and administer for 5 days.	100 mcg/mL S VM
Miconazole (Conofite)	Topical antifungal	Apply q 12 h to lesion; continue after resolution of lesions for 2 weeks	Same	Contact hypersensitivity; caution: re. zoonosis if dermatophytosis (wear gloves)	OTC, topical cream, and solution HM
Micro-K extencaps	*(see potassium salts)*				
Micronase	*(see glyburide)*				
Midazolam (Versed)	Benzodiazepine tranquilizer; 3-4× more potent than diazepam	Preanesthetic dose: 0.1-0.3 mg/kg IV, IM, SQ (lower end of range if IV)	0.05-0.3 mg/kg IV, IM, SQ (mid- to lower end of range if IV and/or if combined with ketamine)	Caution if liver disease, avoid if glaucoma	1 mg/mL, 5 mg/mL I HM
Midol	*(see acetaminophen)*				
Midriacyl	*(see tropicamide)*				
Mifepristone (Mifeprex, RU-486)	Progesterone receptor antagonist	2.5 mg/kg PO q 12-24 h for 5 days	—	Abortifacient	200 mg T HM
Milbemycin (Interceptor)	1. Anthelmintic action in HW prevention, HW microfilaricide, hookworm, and roundworm control 2. Demodicosis 3. *Pneumonyssoides caninum*	1. 0.5-1 mg/kg orally once monthly 2. 0.5-2.3 mg/kg PO q 12-24 h 2-4 weeks for demodicosis, longer if skin scrapings fail to clear mites; may use low dose for 30 days, twice after if necessary 3. 0.5-1 mg/kg per week for 3 weeks	—	Also available as otic formula (Milbemite) and compounded with lufenuron (Sentinel) and lufenuron plus nitenpyram (Sentinel with Capstar)	2.3, 5.75, 11.5, 23 mg T 0.1% otic solution VM
Milk of Magnesia	*(see magnesium hydroxide)*				
Milk thistle extract	*(see silymarin)*				
Miltefosine (Miltex, Impavido)	Antiprotozoal; leishmaniasis	2 mg/kg PO q 24 h × 4 weeks		Coadministered with allopurinol 20 mg/kg PO q 24 h (allopurinol for 6-12 months)	50 mg C HM
Minipress	*(see prazosin)*				
Mintezol	*(see thiabendazole)*				
Mirtazapine (Remeron)	Tricyclic antidepressant drug used for appetite stimulation, particularly in cats	0.6 mg/kg PO q 24 h	3-4 mg/cat PO q 72 h maximum		7.5, 15, 30, 45 mg T HM
Misoprostol (Cytotec)	Prostaglandin E-1 analog; used for gastric ulcers	2-8 mcg/kg PO q 8-12 h	—	Secretory diarrhea, vomiting, anorexia;	100, 200 mcg T HM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
	(especially those associated with NSAID use)			may induce abortion in pregnant mammals (also avoid client exposure); side effects are dose dependent	
Mitaban	*(see amitraz)*				
Mitotane	*(see* o,p′ *DDD)*				
Mitoxantrone (Novantrone)	Chemotherapeutic agent closely related to doxorubicin but no cumulative cardiotoxicity	5 mg/m^2 once every 3 weeks IV	6.25 mg/m^2 once every 3 weeks IV	Depression, GI signs, leukopenia, hepatotoxicity, extravasation injury	2 mg/mL I HM
Mobic	*(see meloxicam)*				
Morphine sulfate	Narcotic analgesic; acute CHF as adjunctive therapeutic agent to relieve anxiety	0.1-1 mg/kg q 2-6 h IM, SQ, IV, epidural; or sustained-release 1.5-3 mg/kg PO q 12 h (ER)	0.05-0.2 mg/kg IM, SQ q 2-6 h	Hyperexcitability in cats; vomiting, respiratory, and CNS depression; hypotension, especially if given IV; constipation	30 mg ER; 5, 10 20 mg suppository; 10, 20 mg/5 mL S; 15, 30 mg T: 2, 4, 5, 8, 10, 15 mg/mL I HM
Motrin	*(see ibuprofen)*				
Moxidectin (Proheart)	1. Avermectin antiparasitic 2. Heartworm prophylaxis, demodicosis	1. HW prevention: 3 mcg/ kg PO once monthly 2. Demodicosis: 0.2-0.4 mg/kg PO q 24 h	—	Available compounded with imidacloprid as Advantage Multi	30, 68, 136 mcg T; large animal product available as 11.3-g tube VM
Mucomyst	*(see acetylcysteine)*				
Mycelex	*(see clotrimazole)*				
Mycophenolate mofetil (CellCept)	Immunosuppression via inhibition of T- and B-cell proliferation; steroid-responsive meningitis-arteritis, necrotizing encephalitis, other immune-mediated disorders	20 mg/kg PO q 12 h; reduce to 10 mg/kg PO q 12 h after 3-4 weeks if ongoing treatment	—	Reported adverse effects include hemorrhagic diarrhea, vomiting, and myelosuppression	250 mg C, 500 mg T, 250 mg/mL I HM
Mycostatin	*(see nystatin)*				
Mydriacyl	*(see tropicamide)*				
Mylepsin	*(see primidone)*				
Myleran	*(see busulfan)*				
Naloxone (Narcan)	Narcotic antagonist	0.004-0.04 mg/kg IV, IM, SQ	Same	Repeat dosing if prolonged action of narcotic	0.02, 0.4, 1 mg/mL I HM
Naltrexone (ReVia)	Partial opiate antagonist; certain behavioral disorders	1-2.2 mg/kg PO q 12-24 h	25-50 mg PO q 24 h per cat	Contraindicated in hepatopathies; antagonizes opiate drugs (e.g., certain antitussives, antidiarrheals)	50 mg T HM
Nandrolone decanoate (Deca-Durabolin)	Anabolic steroid and bone marrow stimulant (erythropoiesis only)	1 mg/kg/week IM	0.5-1 mg/kg per week IM	Give deep IM; do not administer to pregnant or hepato-	100 and 200 mg/mL I

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
				insufficient animals or animals with hormone-sensitive tumors; C-III drug	HM
Naprosyn	*(see naproxen)*				
Naproxen (Naprosyn, Aleve)	NSAID	1.2-2.8 mg/kg PO q 24-96 h	Do not use	Severe GI ulceration/ perforation very common; renal, CNS; not a preferred drug; serum half-life is 32-92 hours in dogs; many safer alternatives	200, 250, 375, 500 mg T; 125 mg/5 mL S HM
Narcan	*(see naloxone)*				
Naxcel	*(see ceftiofur)*				
Nembutal	*(see pentobarbital)*				
Nemex	*(see pyrantel pamoate)*				
Neomycin (Biosol)	Aminoglycoside used orally for SIBO, hepatic encephalopathy	10-20 mg/kg PO q 8-12 h	Same	Ototoxicity and nephrotoxicosis are rare with oral dosage; in severe intestinal disease, toxicosis may be more likely (systemic absorption)	25, 200 mg/mL S; 100, 500 mg, T VM, HM
Neoral	*(see cyclosporine-systemic)*				
Neosar	*(see cyclophosphamide)*				
Neostigmine (Prostigmin)	Anticholinesterase agent for myasthenia gravis	0.01-0.05 mg/kg IM, SQ PRN	Same	Muscarinic effects: vomiting, diarrhea, bradycardia are reversed by atropine	0.25, 0.5, 1, 2 mg/ mL I; 15 mg T HM
Neo-Synephrine	*(see phenylephrine)*				
Neptazane	*(see methazolamide)*				
Neupogen	*(see filgrastim)*				
Neurontin	*(see gabapentin)*				
New methylene blue	*(see methylene blue)*				
Nexium	*(see esomeprazole)*				
Niacinamide (nicotinamide)	Usually used in combination with a tetracycline for immune-mediated dermatopathies	<5 kg: 100 mg PO q 8 h; 5-10 kg: 250 mg PO q 8 h; >10 kg: 500 mg PO q 8 h	—	GI adverse effects possible	50, 100, 125, 250, 500 mg T HM
Niclosamide (Yomesan)	Tapeworm anthelmintic	154 mg/kg PO; fast 24 hours before; repeat in 2-3 weeks	Same	Occasionally soft stools; generally replaced by praziquantel	VM
Nicotinamide	*(see niacinamide)*				
Nilstat	*(see nystatin)*				
Nipride	*(see nitroprusside)*				
Nitenpyram (Capstar)	Flea adulticide; inhibits insect specific nicotinic receptors	Dogs up to 11 kg: total dose 11.4 mg PO per dog, maximum q 24 h;	Total dose: 11.4 mg PO per cat, max. q 24 h	Onset of action: rapid (minutes to hours), but duration of activity	11.4, 57 mg T VM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
		dogs >11 kg: total dose 57 mg PO per dog, maximum q 24 h		limited (day[s])	
Nitrofurantoin (Furadantin, Macrobid, Macrodantin)	UTIs	4 mg/kg PO q 8 h	Same	Oral form used only for UTIs; GI, hepatotoxicity	50, 100 mg T; 5 mg/mL S; 25, 50, 100 mg macrocrystals C HM
Nitroglycerin 2% ointment (Nitrol ointment)	Transdermal venodilator for reducing cardiac preload in acute CHF	Apply ¼-2 inch strip q 6-8 h topically to skin	Apply 1/8- to ¼-inch strip q 8 h topically to skin	May cause hypotension; apply with glove to hairless region (i.e., pinna or inguinal area); clinical efficacy questionable; nitrate tolerance/loss of efficacy in 48 hours	2% O HM
Nitrol ointment	*(see nitroglycerin)*				
Nitroprusside (Nipride, Nitropress)	Arterial dilator, venodilator; reduces preload and afterload in CHF	1-7 mcg/kg/min IV CRI	1-2 mcg/kg/min IV CRI	Hypotension; use 2-3 days IV maximum; avoid extravasation	50 mg/vial I HM
Nizatidine (Axid)	H2 receptor antagonist	5 mg/kg PO q 24 h	2.5-5 mg/kg PO q 24 h (for colonic motility effects)	Has GI prokinetic effects (via anticholinesterase activity)	75 mg T 150, 300 mg C 15 mg/mL S HM
Nizoral	*(see ketoconazole)*				
Nolvasan	*(see chlorhexidine)*				
Norepinephrine (Levophed, Levarterenol)	β1- and α-agonist; used for treating shock	1-2 mg in 250 mL of 0.9% NaCl, IV CRI to effect	None	Hypertension, tachycardia	1 mg/mL I HM
Norpace	*(see disopyramide)*				
Norvasc	*(see amlodipine)*				
Novantrone	*(see mitoxantrone)*				
Novin	*(see dipyrone)*				
Numorphan	*(see oxymorphone)*				
Nuprin	*(see ibuprofen)*				
Nystatin (Nilstat, Mycostatin, Nystex)	Topical antifungal, oral candidiasis	50,000-150,000 IU PO q 6-8 h	100,000 IU PO q 6 h	Fungicidal; not appreciably absorbed in GI tract, so useful for topical oral application	100,000 IU/mL S HM
Nystex	*(see nystatin)*				
Octreotide (Sandostatin)	Somatostatin analog with primary inhibitory effect on intestinal and pancreatic secretions; insulinoma, glucagonoma	Total dose: 10-40 mcg (0.01-0.04 mg) SQ q 8 h per dog		Nausea, vomiting, abdominal discomfort	50, 100, 200, 500 mcg/mL I HM
Ocufen	*(see flurbiprofen)*				
Ofloxacin (Ocuflox)	Topical fluoroquinolone antibiotic for ophthalmic use	1 drop topically in affected eye q 12 h; adjust as necessary	Same	Bactericidal G− and G+	3 mg/mL OS HM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Olsalazine (Dipentum)	Salicylate; antiinflammatory activity in ulcerative colitis (5-ASA)	5-20 mg/kg PO q 8 h	Unknown	*(see sulfasalazine)*	250 mg C HM
Omeprazole (Prilosec, Losec)	Proton pump acid blocker; used in reflux esophagitis and hyperacidity syndromes	0.7 mg/kg PO q 24 h	Total dose: 5 mg per cat PO q 24 h	Few side effects noted	10, 20, 40 mg C HM
Oncovin	*(see vincristine)*				
Ondansetron (Zofran)	5-HT3 receptor antagonist (serotonin inhibitor); used in conjunction with emetogenic cancer chemotherapy; used in protracted vomiting unresponsive to other treatments	0.1-0.2 mg/kg IV bolus q 12 h	Same	Used before and for 48 h following specific IV cancer Tx	4, 8 mg T; 2 mg/mL I; 1.25 mg/mL S HM
o,p' DDD (Lysodren, Mitotane)	Hyperadrenocorticism; selective necrosis of the zonae fasciculata and reticularis of the adrenal gland	25 mg/kg PO q 12 h with food to effect (approximately 5-10 days); then 25-50 mg/kg once every 7-14 days to effect (based on monitoring adrenocortical function); give with food	None	Vomiting, diarrhea, weakness, glucocorticoid ± mineralocorticoid deficiency; hepatotoxicity; best if given in divided doses; insulin dose in diabetes may need to be altered (see p. 1566)	500 mg T VM
Optimmune	*(see cyclosporine-ophthalmic)*				
Oragrafin	*(see ipodate)*				
Oral rehydration solution (ORS: Pedialyte)	Oral electrolyte and glucose replacement	Up to maintenance (60 mL/kg per day PO) and replacement (based on physical exam); PO divided into several doses as low-cost rehydration/ volume expansion	Same	—	Many HM, OTC
Orbax	*(see orbifloxacin)*				
Orbifloxacin (Orbax)	Fluoroquinolone antibacterial	2.5-7.5 mg/kg PO q 24 h	Same	May cause arthropathy in immature dogs; caution in seizure patients (as with all fluoroquinolones)	5.7, 22.7, 68 mg T VM
Ormetoprim-sulfadimethoxine	*(see sulfadimethoxine/ ormetoprim)*				
ORS	*(see oral rehydration solution)*				
Orthocide	*(see captan powder 50%)*				
Orudis KT	*(see ketoprofen)*				
Osaterone (Ypozane)	Benign prostatic hyperplasia	2.5 mg/kg PO q 24 h × 7 days		Remission of signs of benign prostatic hyperplasia for 6 months in approximately 83% of cases	1.875, 3.75, 7.5, 15 mg T VM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Oseltamivir (Tamiflu)	Antiviral; canine influenza	1 mg/kg PO q 24 h		Not approved for dogs; controversial (viral resistance; may be needed in human outbreak)	30, 45, 75 mg C 12 mg/mL S HM
Osmoglyn	*(see glycerin 50% solution [oral])*				
Ovaban	*(see megestrol acetate)*				
Oxacillin (Prostaphlin)	Penicillin derivative used for staphylococcal skin infections	22-40 mg/kg PO q 8 h; 15-20 mg/kg IV q 6-8 h	Same	Best if not given with food; GI upset possible	250 mg/5 mL S; 250, 500 mg C; 250, 500 mg 1, 2 g I HM
Oxazepam (Serax)	Appetite stimulant (oral benzodiazepine agent)	—	Total dose: 2.5 mg per cat PO once; do not use long term, can lead to hepatotoxicity	Overdosage results in sedation and incoordination	10, 15, 30 mg C; 15 mg T HM
Oxtriphylline (Choledyl)	Bronchodilator (theophylline derivative)	4-10 mg/kg PO q 8 h	4-10 mg/kg PO q 8 h	Vomiting, diarrhea, hyperexcitability	100, 200 mg T; 400, 600 mg ER HM
Oxydex	*(see benzoyl peroxide)*				
Oxyglobin	*(see hemoglobin glutamer)*				
Oxymorphone (Numorphan)	Narcotic agonist for analgesia, anesthetic induction, and minor procedures	Preanesthesia: 0.1-0.2 mg/kg IM, SQ; 0.02-0.05 mg/kg IV; analgesia: 0.03-0.2 mg/kg IV, IM, SQ PRN	0.01-0.1 mg/kg IV, IM, SQ PRN	Respiratory and CNS depression; hypotension, sedation, bradycardia, feline hyperexcitability; panting (dogs); reverse with naloxone	1, 1.5 mg/mL I HM
Oxytetracycline (Terramycin)	Broad-spectrum bacteriostatic agent; also used for rickettsiae, *Mycoplasma* spp., spirochetes, and chlamydiae; used for treating SIBO	10-20 mg/kg PO q 8 h to q 6 h; as OO, apply q 12 h to q 6 h	Same	Do not use in pregnancy (last trimester) or in first month of life (dental staining); GI side effects; photosensitivity; caution with liver and kidney disease; do not administer with antacids, dairy products, or intestinal adsorbents	50, 125 mg/mL I; 250 mg C HM
Oxytocin (Pitocin, Syntocinon)	Pituitary hormone used for uterine inertia; to stimulate milk flow; vasopressive effects and as an antidiuretic	Obstetrics (uterine inertia): 5-25 U IM total dose, every 30 minutes, or 1-2 U/kg; milk production: 2-10 U IM or via intranasal spray	Obstetrics: 2 U/kg IM, every 30 minutes; milk production: 1 U IM	Do not use if birth canal obstructed; refrigerate vial and warm syringe before injection	10 U/mL I; 40 U/mL nasal spray HM
Oxtriphylline	*(see choledyl)*				
Palladia	*(see toceranib)*				
Pamidronate (Aredia)	Bisphosphonate compound; hypercalcemia (e.g., due to	0.65-2 mg/kg diluted in 0.9% NaCl and give as IV CRI	—	Avoid calcium-containing fluids like LRS	30, 60, 90 mg vials I

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
	cholecalciferol intoxication)				HM
Pamprin	*(see acetaminophen)*				
Panacur	*(see fenbendazole)*				
Panadol	*(see acetaminophen)*				
Pancreatic enzymes (Pancrelipase, Viokase)	Pancreatic exocrine insufficiency	½-2 tsp powder in 1 lb (500 g) of canned food or 2 cups of moistened dry food; allow to stand 15-30 minutes, then feed	Same proportional to size of feeding	Avoid inhaling powder dust; Viokase brand has superior efficacy; gingival bleeding possible	VM, HM
Pancrelipase	*(see pancreatic enzymes)*				
Pantoprazole (Protonix, Pantoloc)	Injectable proton pump inhibitor	0.7-1 mg/kg IV q 24 h		Indicated for nonobstructive vomiting	40 mg vials I HM
Paracetamol	*(see acetaminophen)*				
Paramite	*(see phosmet dip)*				
Paraplatin	*(see carboplatin)*				
Paregoric	Opiate antidiarrheal	0.05-0.06 mg/kg PO q 12 h to q 8 h	None	May cause constipation; controlled drug	HM, S
Parlodel	*(see bromocriptine)*				
Paroxetine (Paxil)	Selective serotonin reuptake inhibitor	1 mg/kg PO q 24 h, usually for a minimum of several weeks	Total dose: 1.25-2.5 mg PO q 24 h per cat	Behavioral changes, anorexia possible; avoid combining with MAO inhibitors (Anipryl, amitraz, etc.)	10, 20, 30, 40, mg T; 12.5, 25 mg ER (Paxil CR) T HM
Paxil	*(see paroxetine)*				
Pedialyte	*(see oral rehydration solution)*				
D-penicillamine (Cuprimine, Depen)	Orally active chelating agent for lead and copper; used for aiding in the prevention of cysteine urolithiasis, copper storage disease	10-15 mg/kg PO q 12 h	—	Administer on empty stomach if tolerable; may cause vomiting, skin eruptions, and vascular lesions; monitor CBC	250 mg (Depen) T; 125, 250 mg (Cuprimine) C HM
Penicillin, benzathine (Benzapen)	G+ infections; some activity against anaerobes; bactericidal	20,000-40,000 U/kg IM, SQ q 48-72 h	Same	Long-acting formulation; do not use with penicillin hypersensitivity; do not use if serious infection is suspected; IM or SQ injection only	150,000 U/mL I VM
Penicillin G potassium or sodium	G+ infections; some activity against anaerobes; bactericidal	20,000-40,000 U/kg IV, IM, SQ q 4-6 h	Same	Penicillin hypersensitivity contraindicates; may contain high levels K+ (administer judiciously and monitor); solution for injection should be completely transparent; not effective orally	1 million, 5 million, 10 million, and 20 million U vials I HM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Penicillin G procaine (Wycillin, many others)	G+ infections; some activity against anaerobes; bactericidal	20,000-40,000 units/kg IM, SQ q 12-24 h	Same	Solution for injection is opaque = for IM/SQ injection only; penicillin hypersensitivity contraindicates	300,000 U/mL I VM
Penicillin-V	G+ infections; bactericidal; effective orally	5.5-11 mg/kg PO q 6-8 h	Same	250 mg = 400,000 U; avoid if penicillin hypersensitivity; GI upset possible	250, 500 mg T; 125, 250 mg/5 mL S; many other sizes HM
Pentasa	*(see mesalamine)*				
Pentazocine (Talwin)	Narcotic agonist/ antagonist used for short-term analgesia	1-3 mg/kg IM, 2-6 mg/ kg PO	2-3 mg/kg SQ, IM, IV	May cause salivation and/or sedation; reverse with naloxone; may cause dysphoria in cats	30 mg/mL I, HM; often combined with other Tx VM, HM
Pentobarbital (Nembutal, pentobarbitone)	Status epilepticus, general anesthesia	Anesthesia: 10-30 mg/ kg IV slowly to effect; seizures: 3-15 mg/kg IV slowly to effect	Anesthesia: 10-30 mg/kg IV slowly to effect; seizures: 3-15 mg/ kg IV slowly to effect	Respiratory depression and hypotension may develop if used alone or especially with or after diazepam	50 mg/mL I; available as tablets, elixir, suppositories VM, HM
Pentosan polysulfate (Elmiron)	Glycosaminoglycan-like agent; osteoarthritis (dogs); idiopathic cystitis (cats)	10 mg/kg PO or 3 mg/ kg IM; given once weekly for 4 weeks	8 mg/kg PO q 12 h	Rare adverse effects (e.g., vomiting) in dogs; experimental drug with minimal clinical data in cats; efficacy and safety unproven	100 mg C HM
Pentostam	*(see sodium stibogluconate)*				
Pentothal	*(see thiopental)*				
Pentoxifylline (Trental)	Increases plasticity of RBC membranes; used in many dermatoses, including dermatomyositis	10-25 mg/kg PO q 12 h	—	Few adverse effects reported	400 mg T HM
Pepcid	*(see famotidine)*				
Pepto-Bismol	*(see bismuth subsalicylate)*				
Percogesic	*(see acetaminophen)*				
Percorten-V	*(see desoxycorticosterone pivalate)*				
Periactin	*(see cyproheptadine)*				
Persantine	*(see dipyridamole)*				
PGF2-alpha	*(see prostaglandin)*				
Pharmorubicin	*(see epirubicin)*				
Phenobarbital	Long-acting barbiturate used for seizure control; occasionally used as a sedative	1-2 mg/kg PO q 8-12 h; okay to titrate slowly up to 16 mg/kg per day in divided doses; may be given IV as a bolus of 2-15 mg/kg slowly for status epilepticus followed by 2-6 mg/h CRI if necessary; maintain trough serum	Same	Ataxia, sedation, PU/PD; long-term (especially if >35 mcg/mL serum levels) hepatotoxicity occurs; initial adjustment period is required (liver enzyme inducer); if using higher dose IV, monitor respirations; controlled	8, 16, 32, 65, 100 mg T; 15, 20 mg/5 mL S; 30, 60, 65, 130 mg/mL I HM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
		levels at 15-45 mcg/mL		substance; see also Phenobarbital: • Adverse Effects/ Toxicosis, p. 871	
Phenoxybenzamine HCl (Dibenzyline)	Adrenergic, α-receptor blocking agent; urinary incontinence due to detrusor sphincter dyssynergia	0.25-1 mg/kg PO q 12 h	Total dose: 2.5-5 mg PO q 12-24 h per cat	May result in vomiting, hypotension/ hypertension, rapid HR, miosis; long (4-7 days) onset of action; no effect on postprostatic urethra of cats	10 mg C HM
Phenylbutazone (Butazolidin)	NSAID	10-15 mg/kg PO q 8-12 h	Not recommended	Use lowest effective dosage; do not exceed 800 mg per day; may cause vomiting, GI ulceration, BM suppression, nephrotoxicity; incidence of toxicosis is high; not generally recommended	100, 400, 1000 mg T VM, HM
Phenylephrine (Neo-Synephrine)	1. Postsynaptic 2. α-adrenergic stimulant used as the following: 3. As nasal drops for rhinitis 4. As IV infusion for treatment of hypotension	1. 1-2 drops intranasal pediatric solution, q 8-24 h 2. 1-3 mcg/kg per minute as IV CRI, adjusted to effect	Same	May cause nasal irritation if used chronically; vasoconstriction (systemic hypertension) and pupillary dilation if given parenterally (constant BP monitoring necessary); arrhythmogenic in combination with halothane	10 mg/mL I; OS and intranasal OTC products HM
Phenylpropanolamine (Propalin, PPA)	α-adrenergic agonist used for treating hormone-responsive urinary sphincter hypotonus (incontinence) by increasing urethral smooth muscle activity	1 mg/kg PO q 8 h	1-2 mg/kg PO q 8-12 h	Anxiety, dizziness, hypertension, tachycardia, urinary retention; no longer available as human OTC product	25, 50, 75 mg T 25 mg/mL S VM
Phenytoin (Dilantin)	Anticonvulsant agent	—	—	No longer recommended	—
Pheromones, feline synthetic facial (Feliway)	Behavioral disorders, acclimation to new environment	—	Topical application to surroundings	Spray may be applied to objects, or diffuser disseminates product in room	Spray pump or diffuser VM
Phosmet dip (Paramite)	Organophosphate dip for fleas, ticks, and canine sarcoptic mange	2 tbsp (1 oz) per gallon H_2O; sponge on and let air dry	Do not use	Wear gloves to use; use once weekly maximum; do not use in puppies <8 weeks old; avoid eye exposure; fever, salivation, seizures, and CNS signs suggest organophosphate toxicity (if such signs	11.6% dip VM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
				occur, use atropine injection and wash off dog)	
Phosphate (IV supplementation)	*(see potassium phosphate)*				
Phosphate enemas (Fleet)	Treatment of constipation, bowel evacuation	For large dogs, use one adult bottle; for medium dogs, use ½ bottle or a pediatric enema; not recommended for use in small dogs (toxicity: hyperphosphatemia/ hypocalcemia)	Not recommended	May cause severe hyperphosphatemia and hypocalcemia in patients weighing <10 kg; do not use if patient is dehydrated, with renal or cardiac failure, or in very sick patients	OTC, HM
Phytonadione	*(see vitamin K1)*				
Pilocarpine ophthalmic solution	Miotic (muscarinic) agent useful in glaucoma, KCS	1 drop in affected eye q 6-12 h For KCS: 2-5 drops of 1% or 2% solution in food q 24 h	Same	Ciliary spasm; systemic signs rare when used topically; adjust dose according to time and response; V/D and better alternatives (cyclosporine) have meant less use for KCS	0.25, 0.5, 1, 2, 3, 4, 6, 8% OS HM
Pimobendan (Vetmedin)	Oral positive inotrope and vasodilator; effective adjunct Tx in CHF caused by DCM in Dobermans but not cocker spaniels	0.25 mg/kg PO q 12 h on empty stomach	None	Indicated as part of treatment for heart failure when dilated cardiomyopathy or mitral valve disease are confirmed	1.25, 2.5, 5 mg C or chewable T VM
Piperacillin (Pipracil)	Broad-spectrum parenteral penicillin	25-50 mg/kg IM or slow IV (20-30 minute infusion) q 8-12 h	—	Penetrates blood-brain barrier; CSF: serum concentration ratio = 0.06 (noninflamed) to 0.3 (inflammatory diseases)	2, 3, 4, 40 g I HM
Piperacillin + tazobactam (Zosyn)	Broad-spectrum parenteral penicillin with β-lactamase inhibitor	50 mg/kg slow (30 minutes) IV infusion q 6 h	—	Not compatible with LRS	2, 3, 4 g (with 0.25, 0.375, 0.5 g tazobactam, respectively) I HM
Piperazine	Ascarid infection	50-100 mg/kg PO	Same	Repeat in 3 weeks; vomiting and diarrhea may occur at higher dosages	250 mg T; 100 mg/ mL S VM, HM
Pipracil	*(see piperacillin)*				
Piroxicam (Feldene)	NSAID: as primary or secondary Tx for bladder TCC due to immunomodulatory effect; for chronic sterile rhinitis in cats	0.3 mg/kg PO q 48 h or q 24 h	Chronic sterile rhinitis: same, plus doxycycline, for 2-6 weeks	GI irritation, renal damage possible; must open capsules and put in food for most animals; often coadministered with misoprostol	10, 20 mg C HM
Pitocin	*(see oxytocin)*				
Pitressin	*(see vasopressin)*				

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Pivampicillin (Pondocillin)	Penicillin antibacterial	30 mg/kg PO q 12 h		Used as empirical antibacterial in aborting bitches, pending culture and sensitivity	500 mg T 35 mg/mL S HM
Platinol	*(see cisplatin)*				
Plavix	*(see clopidogrel)*				
Polyethylene glycol electrolyte solution for endoscopy prep	*(see GoLytely)*				
Polyflex	*(see ampicillin)*				
Polysulfated glycosaminoglycan	*(see glycosaminoglycan-polysulfated)*				
Ponazuril (Marquis)	Antiprotozoal-giardiasis, cryptosporidiosis	7.5-15 mg/kg PO q 24 h × 28 days		Adverse effects of neurotoxicosis, keratitis possible	15% oral paste VM
Pondocillin	*(see pivampicillin)*				
Potassium bromide (KBr)	*(see bromide)*				
Potassium chloride injection	Treatment and prevention of hypokalemia	Add to IV fluid per liter based on serum K^+ level; serum K: 3.5-5 mEq/L = add 20 mEq KCl/L; 3-3.4 mEq/L = add 30 mEq KCl/L; 2.5-2.9 mEq/L = add 40 mEq KCl/L; 2-2.4 mEq/L = add 60 mEq KCl/L; <2 mEq/L = add 80 mEq KCl/L	Same	Never infuse rapidly; rate of infusion must never exceed 0.5 mEq KCl/kg/hr; monitor serum K^+ regularly and adjust dosage accordingly	2, 10, 20, 30, 40, 60, 90 mEq/mL I HM
Potassium chloride, oral	*(see potassium salts)*				
Potassium citrate (Urocit-K)	Inhibits calcium oxalate crystal formation in urine; alkalinizing agent for urine	75 mg/kg PO q 12 h; 1-2 mEq/kg PO per day		GI irritation; 5 mEq = 540 mg	5, 10 mEq T HM
Potassium gluconate	*(see potassium salts)*				
Potassium phosphate	Hypophosphatemia	0.01-0.03 mM/kg/h IV	Same	Hyperphosphatemia; recheck serum levels after 6 hours and adjust or stop; for potassium phosphate, 1 mM phosphate = 33 mg/dL phosphate; avoid calcium-containing fluids	5, 10, 15, 30, 50 mL vials (3 mM PO4 and 4.4 mEq K per mL for all) I HM
Potassium salts (Kaon Elixir, Micro-K Extencaps, Tumil-K)	Potassium supplements in various oral formulations	¼-1 tbsp (or oral paste or caps) PO q 8-12 h	1/8-¼ tbsp (or oral paste or caps) PO q 8-12 h	Dose according to deficit; monitor serum K; may cause gastric irritation	Many OTC preparations, different sizes VM, HM
Pralidoxime chloride (2-PAM, Protopam)	Reactivates cholinesterase inactivated by organophosphate	20-50 mg/kg IM or SQ; then q 8-12 h PRN	20 mg/kg IM or SQ, q 6-8 h, PRN	Monitor patient continuously; avoid IV administration (may cause acute laryngospasm); do not use for carbamate toxicity	1 g vial I HM
Prevacid	*(see lansoprazole)*				

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Praziquantel (Droncit)	*Taenia, Dipylidium, Echinococcus, Heterobilharzia*	Use according to instructions on product according to weight; PO or SQ, IM	Same	Fasting not required; do not use in puppies <4 weeks old or kittens under 6 weeks of age	23, 34 mg T; 56.8 mg/mL VM; 600 mg T HM
Prazosin (Minipress)	α-adrenergic antagonist; balanced vasodilator; decreases urethral smooth muscle tone	Total dose: 0.5-2 mg PO q 12 h or q 8 h per dog	Total dose: 0.5-1 mg PO q 12 h to q 8 h per cat	Hypotension, depression, malaise	1, 2, 5 mg C
Precose	*(see acarbose)*				
Pred Forte	*(see prednisolone, ophthalmic suspension)*				
Prednisolone, prednisone	1. Replacement therapy (hypoadrenocorticism) 2. Antiinflammatory: antipruritic 3. Immune system suppression 4. Antineoplastic chemotherapy	1. 0.25-0.5 mg/kg PO q 24 h 2. Antiinflammatory 0.5-1 mg/kg PO, IM, SQ per day 3. Immune suppression: 2-4.4 mg/kg, usually PO, per day 4. 40 mg/m^2 PO, per day for 7 days; then 20 mg/m^2 PO q 48 h. See pp. 671, 677 for body weight to body surface area conversion chart.	Same	PU/PD; polyphagia; suppression of HPA axis: Cushing's syndrome; hepatopathy; opportunistic infections; muscle wasting; connective tissue and skin fragility; taper dosage if used long term	1, 2.5, 5, 10, 20, 25, 50 mg T; 1 mg/ mL S; 10, 25 mg/ mL I HM, VM
Prednisolone, ophthalmic suspension (Pred Forte)	Steroid-responsive inflammation of the lids, conjunctiva, sclera, cornea, and anterior segment of the eye	1 drop to affected eye q 6-12 h	Same	Variable strength products (0.12-1%) used as required; do not use with purulent, viral, or fungal infection or with corneal ulcers; systemic side effects are possible but rare	0.12, 0.125, 1% OS HM
Prednisolone sodium succinate (Solu-Delta-Cortef)	Soluble corticosteroid used IV for shock of multiple causes	5-33 mg/kg IV slow bolus; repeat up to q 6 h; spinal injury: 30 mg/kg IV	Same	Causes vomiting if administered too rapidly; glucocorticoid precautions/risks	100, 500 mg vials I VM
Pregabalin (Lyrica)	Pain, paresthesias	2-4 mg/kg PO q 8-12 h		Indicated as part of treatment for caudal occipital malformation and other neurologic disorders	25, 50, 75, 100, 150, 200, 225, 300 mg C HM
Premarin	*(see estrogen-conjugated)*				
Prepulsid	*(see cisapride)*				
Prevacid	*(see lansoprazole)*				
Previcox	*(see firocoxib)*				
prilactone	*(see spironolactone)*				
Prilium	*(see imidapril)*				
Prilosec	*(see omeprazole)*				
Primaxin	*(see imipenem)*				

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Primidone (Mylepsin)	Anticonvulsant medication hepatically converted to phenobarbital	3-8 mg/kg PO q 8 h; initially up to 16 mg/ kg PO q 8 h (adjust based on serum phenobarbital levels)		Causes PU/PD/PP, sedation, and ataxia. Often hepatotoxic with prolonged use. No benefit over phenobarbital; no longer recommended	50, 250 mg T; 50 mg/mL S HM
Primor	*(see sulfadimethoxine/ ormetoprim)*				
Prinivil	*(see lisinopril)*				
Pro-Banthine	*(see propantheline)*				
Procainamide (Pronestyl SR, Procan-SR)	Ventricular arrhythmias	6-20 mg/kg IV slowly over 30 minutes, then IV CRI 0.02-0.04 mg/kg/min (20-40 mcg/kg/min) if life threatening; 6-20 mg/kg IM or PO q 4 h (q 8 h PO if ER)	1-2 mg/kg bolus IV; then 0.01-0.02 mg/ kg/min (10-20 mcg/kg/min) IV CRI	Available as extended-release tablet for q 8 h administration (absorption questionable); optimum serum level = 3-20 mcg/mL); increasingly difficult to obtain, low demand in human cardiology	100, 500 mg/mL I; 250, 375, 500 mg C, T; 250, 500, 750, 1000 mg ER C, T HM
ProcalAmine	*(see amino acid solution 3% and glycerin injection with electrolytes)*				
Procan-SR	*(see procainamide)*				
Procarbazine (Matulane)	Lymphoma rescue protocol, granulomatous meningoencephalitis	25-50 mg/m^2 PO q 24 h		Crosses blood-brain barrier well; risk of myelotoxicosis, GI effects	50 mg C HM
Prochlorperazine (Compazine)	Antiemetic	0.11-0.44 mg/kg SQ, IM q 6-12 h	Same	Sedation, hypotension, anticholinergic side effects (dry mouth, GI hypomotility); do not use in epileptic patients; available also in suppository formulation	5 mg/mL I; 1 mg/ mL S; 5, 10, 25 mg T; 10, 15, 30 mg ER HM
Procrit	*(see erythropoietin)*				
Proglycem	*(see diazoxide)*				
Prograf	*(see tacrolimus)*				
Program	*(see lufenuron)*				
ProHeart	*(see moxidectin)*				
PromAce	*(see acepromazine)*				
ProMeris	*(see metaflumizone)*				
Pronestyl	*(see procainamide)*				
Propalin	*(see phenylpropanol-amine)*				
Propantheline (Pro-Banthine)	Anticholinergic agent used for treating diarrhea, bradycardia syndromes, and detrusor hyperreflexia	0.2-0.5 mg/kg PO q 8-24 h; increase to effect for bradycardia syndromes	Same	Tachycardia, dry mouth, constipation, mydriasis, ileus, urinary retention	7.5, 15 mg T HM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Propionibacterium acnes (Immunoregulin)	Immune modulator/ potentiator	0.03-0.07 mg/kg IV at 2-3 day intervals	Total dose: 0.2 mg per cat IV 1-2 times a week	No controlled studies	0.4 mg/mL I VM
Propofol (Diprivan, Rapinovet)	Ultrashort (5-7 minutes) acting anesthetic; no cumulative effect with repeated administration	3-6 mg/kg IV	Same	Give slowly over 1-2 minutes in equal dosages to effect; agent provides no analgesia: consider opiate premed and/or inhalant anesthetic if minor (or other) surgical procedures	10 mg/mL I HM, VM
Propranolol (Inderal)	β-Adrenergic blocking agent used for treating supraventricular arrhythmias, some ventricular arrhythmias, and feline hypertrophic cardiomyopathy	For acute tachycardias: 0.1-0.5 mg IV total dose per bolus; no more frequently than 1 bolus q 1-3 min to 5 mg maximum (largest dog); administer until the rate slows; chronic use: 0.2-1 mg/kg q 8-12 h PO, usually start low and titrate dosage upward to effect	0.1-0.5 mg IV bolus slowly; 2.5-5 mg PO q 8-12 h, begin low and titrate dosage	Anorexia, apnea, depression, ataxia; bradycardia, negative inotropic effect: potentiates AV nodal depression of digoxin and calcium channel blockers; underlying cause of tachycardia (e.g., heart failure, hypovolemia) must be addressed before IV propranolol; beta-2 effects = contraindicated if asthma	10, 20, 40, 60, 80, 90 mg T; 60, 80, 120, 160 mg ER; 4, 8, 80 mg/mL S; 1 mg/mL I HM
Propulsid	*(see cisapride)*				
Propylthiouracil (PTU)	Feline hyperthyroidism	Not used	10 mg/kg PO q 8-12 h	Immune-mediated hemolytic anemia and thrombocytopenia; anorexia, vomiting, and lethargy; risk of adverse effects frequently outweighs potential benefit	50 mg T HM
Proscar	*(see finasteride)*				
ProSpot	*(see fenthion)*				
Prostaglandin (PGF2-α, Lutalyse, Dinoprost, Dinolytic)	1. Open-cervix pyometra 2. Abortive agent at 31-35 days	1. Day 1: 0.1 mg/kg SQ once; day 2: 0.2 mg/ kg SQ once; days 3-7: 0.25 mg/kg SQ, q 24 h 2. 0.1 mg/kg SQ, q 8 h for 2 days, then 0.2 mg/kg SQ, q 8 h for 3-7 days (or until fetuses are expelled)	0.1 mg/kg SQ, q 12 h for 5 days 0.5-1 mg/kg SQ for 2 days	Panting, salivation, vomiting, diarrhea, colic, and tachycardia lasting about 30 minutes; should be given under hospital supervision	5 mg/mL I VM
Prostaphlin	*(see oxacillin)*				
Prostigmin	*(see neostigmine)*				
Protonix	*(see pantoprazole)*				
Protopam	*(see pralidoxime)*				
Protopic	*(see tacrolimus)*				
Protropin	*(see growth hormone, human)*				

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Proventil	*(see albuterol)*				
Provera	*(see medroxyprogesterone acetate)*				
Prozac	*(see fluoxetine)*				
Prussian blue	*(see ferric cyanoferrate)*				
Pseudoephedrine	Urethral sphincter mechanism incompetence/ incontinence; retrograde ejaculation	0.2-0.4 mg/kg PO q 8-12 h	—	Narrow window between therapeutic and toxic doses; use with caution if sympathetic drive could be harmful (heart disease, hypertension, hyperthyroidism, etc.) or if CNS abnormalities	30, 60, 120 mg T HM, OTC
Psyllium mucilloid (Metamucil)	Bulk laxative, stool softener	2-10 g PO, q 12-24 h in moistened food	2-4 g PO, q 12-24 h, in moistened food	Titrate dose based on stool consistency; may also be used for treating fiber-responsive diarrhea	OTC, HM
PTU	*(see propylthiouracil)*				
Pyoben	*(see benzoyl peroxide)*				
Pyopen	*(see carbenicillin)*				
Pyrantel pamoate (Nemex, Pyr-A-Pam, Strongid-T)	Roundworm and hookworm anthelmintic	5-10 mg/kg PO	10 mg/kg PO	Repeat in 3 weeks; safe at recommended dosages, including in dogs with heartworms	22.7, 113.5 mg T; 2.27, 4.54, 50 mg/ mL S VM
Pyr-A-Pam	*(see pyrantel pamoate)*				
Pyridostigmine bromide (Mestinon)	Anticholinesterase agent used for treating myasthenia gravis	0.2-2 mg/kg PO q 8-12 h	0.25 mg/kg PO maximum of once daily	Available as soft tablet and syrup (60 mg/5 mL); vomiting, diarrhea, salivation, and weakness may develop	60 mg T; 180 mg ER; 12 mg/mL S; 5 mg/mL I HM
Pyrimethamine (Daraprim)	Folic acid antagonist, toxoplasmosis, neosporosis, hepatozoonosis	0.5-1 mg/kg PO q 24 h for 48 hours, then 0.25 mg/kg PO q 24 h for 14 days	Same	Often used with sulfonamides to treat toxoplasmosis; BM suppression due to folate deficiency; may need to supplement with folic or folinic acid; teratogenic	25 mg T HM
PZI	*(see insulin)*				
Quibron	Bronchodilator expectorant; combination of theophylline and guaifenesin	1 capsule PO q 8-12 h in large breeds only	Not recommended	Hyperexcitability, vomiting	150, 300 mg C; 300 mg T; 300 mg ER HM
Quinacrine (Atabrine)	Giardiasis, enteric coccidiosis	10 mg/kg PO q 24 h for 5-12 days	11 mg/kg PO q 24 h for 5 days	May cause enteric signs; considered second line agent	100 mg T HM
Quinaglute	*(see quinidine)*				
Quinidex	*(see quinidine)*				

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Quinidine (Quinaglute, Quinidex)	Type Ia antiarrhythmic agent; used mostly for ventricular dysrhythmias; conversion of acute-onset atrial fibrillation	6-20 mg/kg PO, IM q 6-8 h	Not recommended	Do not give IV or use with digitalis; increasingly difficult to obtain due to decreased use in human cardiology	100, 200, 300 mg T; 275, 300, 330 mg ER; 80 mg/mL I HM
Radiogardase	*(see ferric cyanoferrate)*				
Ramipril (Altace, Vasotop)	ACE inhibitor	0.125 mg/kg PO q 12 h	0.5 mg/kg PO q 24 h	Licensed for VM use in Europe	1.25, 2.5, 5, 10 mg C HM 0.625, 1.25, 2.5, 5, 10 T, VM
Ranitidine HCl (Zantac)	H2 histamine receptor antagonist; promotility agent (e.g., cats with constipation)	1-2 mg/kg PO, SQ, IM, slow IV q 8-12 h	Same	GI prokinetic effects due to anticholinesterase activity; slow IV (bolus may cause immediate vomiting); shown to fail to reduce gastric pH in the dog	75, 150, 300 mg T; 15 mg/mL S; 25 mg/mL I HM
Rapinovet	*(see propofol)*				
Reconcile	*(see fluoxetine)*				
Reglan	*(see metoclopramide)*				
Regulin	*(see melatonin)*				
Remeron	*(see mirtazapine)*				
Requa	*(see activated charcoal)*				
Retrovir	*(see azidothymidine)*				
ReVia	*(see naltrexone)*				
Revolution	*(see selamectin)*				
Rheomacrodex	*(see dextran)*				
r-Hu-EPO	*(see erythropoietin)*				
Ridaura	*(see auranofin)*				
Rifadin	*(see rifampin)*				
Rifampin (Rifadin)	Antimycobacterial antibacterial agent	5-10 mg/kg PO, IV q 12-24 h	5-10 mg/kg PO, IV q 24 h	A part of protocols with other antiinfectives for better efficacy, less resistance	150, 300 mg T; 600 mg I HM
Rimadyl	*(see carprofen)*				
Rintal	*(see febantel)*				
Ripercol	*(see levamisole)*				
Robamox-V	*(see amoxicillin)*				
Robaxin	*(see methocarbamol)*				
Robinul	*(see glycopyrrolate)*				
Rocaltrol	*(see calcitriol)*				
Rocephin	*(see ceftriaxone)*				
Roferon	*(see interferon-alfa)*				
Romazicon	*(see flumazenil)*				

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Rompun	*(see xylazine)*				
Ronidazole	Trichomoniasis		30 mg/kg PO q 12 h × 14 days	Neuro adverse effects possible; must be compounded into capsules for palatability	10% powder (100 mg/g) VM
Rotenone (topical ointment)	*(see Goodwinol)*				
RU-486	*(see mifepristone)*				
Rutin	Chylothorax; benzopyrone recommended for treatment of chylous pleural effusion; reportedly potentiates macrophage function	—	50 mg/kg PO q 8 h; total dose 250 mg PO q 8 h per cat or 500 mg PO q 12 h per cat	Generally purchased in health food stores	500 mg T OTC
S-adenosyl methionine	*(see methionine, S-adenosyl)*				
Safe-Guard	*(see fenbendazole)*				
Salix	*(see furosemide)*				
Salbutamol	*(see albuterol)*				
Salmeterol (Serevent)	Inhaled long-acting β2-agonist bronchodilator	1 puff PRN q 12-24 h	Same	Takes >1 hour to take effect	6.5, 13 g inhalation canisters (0.025 mg [25 mcg] per puff) HM
SAMe	*(see methionine, S-adenosyl)*				
Sandimmune	*(see cyclosporine-systemic)*				
Sandostatin	*(see octreotide)*				
Scolaban	*(see bunamidine)*				
Selamectin (Revolution)	Endectoside; topical for fleas, ticks, ear mites, heartworm prevention, sarcoptic mange, intestinal hookworms, and roundworms	Approximately 6 mg/kg topically according to dosage on packaging; 1 application per month	Same	Use in dogs or cats >6 weeks old; for heartworm prevention: give within 1 month of first exposure to mosquitos and continue until within 1 month of last exposure	Prepackaged doses (topical liquid in plastic ampules) VM
Selegiline (deprenyl, Anipryl, Eldepryl)	Restores central dopamine levels: MAO inhibitor; used for treating cognitive dysfunction syndrome; may be helpful in selected PDH canine Cushing's cases	PDH: 1 mg/kg PO per day for 30 days, then may increase dosage to 2 mg/kg per day if no response; CDS: 0.5 mg/kg daily; may double dose after 1 month if ineffective	Not recommended	Low level of effectiveness reported; not to be used with other MAO inhibitors (e.g., antidepressants, amitraz)	2, 5, 10, 15, 30 mg T, VM; 5 mg C, T HM
Sentinel	*(see mibemycin)*				
Septra	*(see trimethoprim/sulfamethoxazole)*				
Serax	*(see oxazepam)*				
Serevent	*(see salmeterol)*				

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Sertraline (Zoloft)	Selective serotonin reuptake inhibitor	0.25-1 mg/kg PO q 24 h	0.5-1 mg/kg PO q 24 h	Anxiety, aggression, or obsessive-compulsive disorders; inappropriate elimination.	25, 50, 100 mg T 20 mg/mL S HM
Sildenafil (Viagra)	Pulmonary hypertension	0.5-1 mg/kg PO q 8 h	—		25, 50, 100 mg T HM
Silvadene cream	*(see silver sulfadiazine)*				
Silver sulfadiazine (Silvadene cream)	Topical antiinfective preparation for complications of burns	Apply to burn area q 12 h as necessary	Same	Hypersensitivity to sulfonamides; KCS; Dobermans	10 mg/g O HM
Silymarin (milk thistle extract, Marin)	Hepatopathy	50-250 mg PO q 24 h	4-8 mg/kg PO q 24 h	Nutraceutical; also compounded with SAMe (Denamarin); wide range of safety	9, 24, 70 mg T VM
Simplicef	*(see cefpodoxime)*				
Sinequan	*(see doxepin)*				
Slentrol	*(see dirlotapide)*				
Slo-Bid	*(see theophylline, sustained action)*				
Sodium bicarbonate	Metabolic acidosis, urine alkalinization (e.g., intoxication)	mEq/day = (desired serum [HCO3] − present serum [HCO3]) × 0.3 × BW (kilograms); administer 50% over 15 minutes and recheck serum levels; then give the balance over 24 hours	Same	Alkalosis, hypernatremia, CHF, hypokalemia; correct inciting factors concurrently (or prior to HCO3 Tx); 84 mg NaHCO3 contains 1 mEq HCO3	0.6, 1 mEq/mL I; 5, 10 grain T HM
Sodium iodide 20%	Sporotrichosis	15 mg/kg PO q 8 h; some higher doses reported	Same	Monitor for iodinism: fever, ptyalism, GI signs; contains 0.1 mg iodine/mL	20% (200 mg/mL) S VM
Sodium stibogluconate (Pentostam)	Leishmaniasis	30-50 mg/kg SQ, IV q 24 h; or 10-20 mg/ kg IM q 24 h for 20-28 days	—	Not available in United States except through the Centers for Disease Control and Prevention	100 mL vials (100 mg/mL) I HM
Solganal	*(see aurothioglucose)*				
Soloxine	*(see levothyroxine sodium)*				
Solu-Cortef	*(see hydrocortisone sodium succinate)*				
Solu-Delta-Cortef	*(see prednisolone sodium succinate)*				
Solu-Medrol	*(see methylprednisolone sodium succinate)*				
Somatrem	*(see growth hormone, human)*				
Soriatane	*(see acitretin)*				
Sotalol (Betapace)	Classes II and III antiarrhythmic agent; used primarily for treating ventricular	1-3 mg/kg PO q 12 h	Total dose: 10-40 mg PO q 12 h per cat; very little	β-blocking effects seen at low dosages; type III effects at higher levels; begin	80, 120, 160, 240 mg T HM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
	tachyarrhythmias		published experience with drug in cats	low and titrate upwards to effect	
Spinosad (Comfortis)	Flea infestation	30-60 mg/kg PO q 30 days		Acts within 30 minutes, duration of effect = 1 month. Side-effects can include vomiting, CNS signs; ensure dose <60 mg/kg in epileptics (or use alternative).	140, 270, 560, 810, 1620 mg T VM
Spironolactone (Aldactone, Prilactone)	Potassium-sparing diuretic; inhibits aldosterone	1-4 mg/kg PO q 12-24 h	Same	Usually used with other diuretic agents; monitor potassium (hyperkalemia); mild to no diuretic effect as monotherapy in the dog; licensed for VM in Europe; relatively contraindicated in cats (33% incidence of severe ulcerative facial dermatitis)	25, 50, 100 mg T HM 10, 40, 80 mg T VM
Sporanox	*(see itraconazole)*				
Spot-on	*(see fenthion)*				
Stadol	*(see butorphanol)*				
Stanozolol (Winstrol)	Anabolic steroid used for treating anorexia, debilitation, and anemia	0.1-0.2 mg/kg PO q 12-24 h; total dose: 25-50 mg IM weekly per dog	0.1-0.2 mg/kg PO q 24 h to q 12 h; total dose: 12.5-25 mg IM weekly per cat	Contraindicated in pregnancy; hepatotoxicity in cats; controlled drug	2 mg T; 50 mg/mL I VM, HM
Stibogluconate	*(see sodium stibogluconate)*				
Stoxil	*(see idoxuridine)*				
Streptase	*(see streptokinase)*				
Streptokinase (Kabikinase, Streptase)	Thrombolytic drug; arterial or pulmonary thromboembolism	90,000 IU/kg IV over 30 minutes, then 45,000 IU/kg per hour for 7-12 hours based on response	Same	Bleeding diathesis; hyperkalemia from reperfusion; intracardiac thrombus is an absolute contraindication; complications cancel benefits in feline aortic thromboemboli	250,000, 600,000, 750,000, 1.5 million U vials I HM
Streptozotocin (streptozocin, Zanosar)	Insulinoma chemotherapy	500 mg/m^2 infusion preceded and followed by extensive IV fluid diuresis	—	Nephrotoxicity; hepatotoxicity; BM suppression	1 g I HM
Strongid-T	*(see pyrantel pamoate)*				
Sublimaze	*(see fentanyl)*				
Succimer (*meso*-2, 3 dimercaptosuccinic acid, Chemet)	Lead toxicity chelating agent	10 mg/kg PO, q 8 h, for 10-17 days	Same	May need second course of therapy; accesses intracellular sites, including CNS; vomiting, sulfurous odor of breath	100 mg C HM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Sucralfate (Carafate, Sulcrate)	Complexes with proteinaceous material in stomach, thereby preventing undesirable effects of acids on the gastric mucosa	Total dose: 250-1000 mg PO q 6-8 h per dog	Total dose: 250 mg PO q 6-12 h per cat	May constipate; interferes with absorption of many drugs administered concurrently	1 g T, 100 mg/mL S HM
Sudafed	*(see pseudoephedrine)*				
Sulfadiazine (Sulfadyne, Sulcrate)	1. Bacteriostatic agent used for treating toxoplasmosis, nocardiosis 2. Soft tissue/UTIs	1. 80 mg/kg PO q 8 h 2. 30 mg/kg PO q 24 h	Same	Sulfonamide precautions, KCS, idiosyncratic toxicities, Dobermans	500 mg T VM, HM
Sulfadiazine/ trimethoprim	*(see trimethoprim/ sulfadiazine)*				
Sulfadimethoxine (Bactrovet, Albon)	Bacteriostatic agent used for treating toxoplasmosis, nocardiosis, and coccidiosis	50 mg/kg PO day 1; then 25 mg/kg PO q 24 h	Same	KCS, nephrotoxicity, hypersensitivity	400 mg/mL I; 125, 250, 500 mg T; 50, 125 mg/mL S VM, HM
Sulfadimethoxine/ ormetoprim (Primor)	Potentiated sulfonamide	27-55 mg/kg PO q 24 h on day 1; then 13.5-27.5 mg/kg q 24 h thereafter for a maximum of 21 days	None	Sulfonamide contraindications; each tablet is 83% sulfa and 17% ormetoprim	120, 240, 600, 1200 mg T VM
Sulfadyne	*(see sulfadiazine)*				
Sulfamethoxazole/ trimethoprim	*(see trimethoprim/ sulfamethoxazole)*				
Sulfasalazine (Azulfidine)	Antiinflammatory effect on the colon; ulcerative and idiopathic colitis	22-55 mg/kg PO q 8 h	10-20 mg/kg PO q 12 h for 3-5 days	Avoid prolonged treatment; KCS, blood dyscrasias, vomiting; caution in cats: salicylate component could be toxic	500 mg T HM
Sulfodip	*(see lime sulfur solution)*				
Suprax	*(see cefixime)*				
Surfak	*(see dioctyl sodium sulfosuccinate)*				
Surital	*(see thiamylal Na)*				
Symmetrel	*(see amantadine)*				
Synotic	*(see fluocinolone 0.01% with 60% DMSO)*				
Synthroid	*(see levothyroxine sodium)*				
Syntocinon	*(see oxytocin)*				
Syprine	*(see trientene)*				
Tabloid	*(see thioguanine)*				
Tacrolimus (Prograf, Protopic)	Immune-mediated hemolytic anemia and other autoimmune disorders; topical: atopy, perianal fistula	0.16 mg/kg IM q 24 h; 1 mg/kg PO q 24 h	—	Sparsely reported systemic use at the time of this writing; narrow therapeutic-toxic range, with frequent negative side effects; these doses are	1 mg, 5 mg T; 5 mg/mL, I; 0.3% lotion HM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
				associated with adverse effects, so titrate to keep trough serum level 0.1-0.4 ng/mL (dogs); vasculitis, anorexia, intussusception; wear gloves when applying topical formulation	
Tadalafil (Cialis)	Longer-acting phosphodiesterase inhibitor; pulmonary hypertension	1 mg/kg PO q 48 h	—	Very new drug; investigational and unsupported use in veterinary medicine at this time; case reports and anecdotal descriptions of benefit, but side effects poorly documented	5, 10, 20 mg T HM
Tagamet	*(see cimetidine)*				
Talwin	*(see pentazocine)*				
Tamiflu	*(see oseltamivir)*				
Tamsulosin (Flomax, Urimax)	α1a-adrenergic antagonist; benign prostatic hyperplasia	0.01 mg/kg PO q 12-24 h		Efficacy and safety unproven in VM; investigational	0.4 mg C HM
Tapazole	*(see methimazole)*				
Tardak	*(see delmadinone)*				
Task	*(see dichlorvos)*				
Taurine	Feline DCM; canine DCM in American cocker spaniels, retriever breeds, many others; retinopathy	50 mg/kg PO q 8-12 h; or total dose 500-1000 mg PO q 12 h per dog	Total dose: 125-250 mg PO q 12 h per cat	Switch to taurine-enriched diet if relevant (many are already on balanced diet)	250 mg T OTC, HM
Tavist	*(see clemastine fumarate)*				
Tazicef	*(see ceftazidime)*				
Tegison	*(see etretinate)*				
Telazol	*(see tiletamine-zolazepam)*				
Telmintic	*(see mebendazole)*				
Temaril-P	*(see trimeprazine)*				
Tempra	*(see acetaminophen)*				
Tenormin	*(see atenolol)*				
Tensilon	*(see edrophonium Cl)*				
Tepoxalin (Zubrin)	NSAID (broad-spectrum COX and leukotrienes)	10 mg/kg PO q 24 h	—	Gastritis, diarrhea, hepatopathy, renal effects	30, 50, 100, 200 mg T VM
Terbutaline (Brethine)	Bronchodilator via specific β2 stimulation	Total dose: 0.625-5 mg PO q 8-12 h per dog	Total dose: 0.625-1.25 mg PO q 12 h per cat. Acute: 0.05-0.1 mg/kg IM or SQ	Excitability, vomiting, tachycardia; may also be used for halting premature uterine contractions	2.5, 5 mg T; 1 mg/mL I HM
Terramycin	*(see oxytetracycline)*				

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Testosterone	Testosterone responsive incontinence in male dogs and cats	2.2 mg/kg IM monthly	Total dose: 5-10 mg IM per cat.	Hepatopathy; behavioral changes; controlled drug	25, 50, 100, 200 mg/mL I HM
Tetracycline	Broad-spectrum antibiotic; bacteriostatic; used especially for *Brucella, Chlamydia, Leptospira, Mycoplasma*, and *Rickettsia;* used for pleurodesis; used with niacinamide for autoimmune dermatopathies; used as an ophthalmic ointment	10-22 mg/kg q 8 h PO for 3 weeks; pleurodesis: 20 mg/ kg in 4 mL saline/kg intrapleural; ophthalmic ointment: apply q 6-8 h	Same	Fever, vomiting, diarrhea, photosensitivity; do not administer with dairy products, antacids, intestinal adsorbents; do not give in last 3 weeks of pregnancy or to newborns/pediatric animals; cats more sensitive to adverse effects	100, 250, 500 mg T/C; 25 mg/mL S; 250, 500 mg/vial I; 10 mg/g OO; 10 mg/mL OS HM, VM
Theo-Dur	*(see theophylline, sustained action)*				
Theophylline elixir (Elixophyllin)	Bronchodilator	6-11 mg/kg PO q 8 h	Rarely used: 8 mg/kg PO q 12 h	*(see aminophylline);* restlessness, vomiting	16 mg/mL S HM
Theophylline, sustained action (Slo-Bid, Theo-Dur)	Long-acting bronchodilator	5-15 mg/kg PO q 12-24 h	Same but infrequently utilized (adverse effects)	Hyperexcitability common; nausea or vomiting: stop drug	100, 200, 300 mg ER HM
Thiabendazole (Mintezol)	Aspergillosis, penicilliosis, *Filaroides (Oslerus)*, and feline eosinophilic granuloma complex; topical: ear mites dermatophytes	50 mg/kg PO q 24 h for 3 days; repeat in 1 month	5-10 mg/kg PO q 24 h 3 times weekly	Not licensed for feline use; dachshunds uniquely sensitive	500 mg T; 100 mg/ mL S VM
Thiacetarsemide (Caparsolate)	Heartworm adulticide; hemobartonellosis *(Mycoplasma haemofelis)*	2.2 mg/kg q 12 h slow IV for 4 doses	1.1-2.2 mg/kg q 12 h slow IV for 4 doses; often not recommended	Largely replaced by melarsomine; vomiting, depression, hepatotoxicity (icterus), nephrotoxicity; thromboembolic phenomena 7-28 days post Tx; perivenous injection causes sloughing; acute pulmonary edema in cats	10 mg/mL I VM
Thiamazole	*(see methimazole)*				
Thiamine (vitamin B1)	Thiamine deficiency; lead poisoning	Total dose: 10-100 mg IM, IV, PO q 12 h per dog	Total dose: 50 mg IM, IV, PO q 12 h per cat	Stings IM	100, 200 mg/mL I; 5, 10, 25, 50, 100, 250, 500 mg T; HM
Thiamylal Na (Surital)	Ultrashort-acting barbiturate anesthetic	11-17.5 mg/kg IV titrated to induction of anesthesia	Same	*(see thiopental)*	Not available currently; may return to the market; 1, 5, 10 g vials I
Thioguanine (Tabloid)	Antineoplastic, acute leukemias	40 mg/m^2 PO q 24 h for 4-5 days, then every 3 days	25 mg/m^2 PO q 24 h for 1-5 days, then every 30 days	BM, GI, hepatic adverse effects possible	40 mg T HM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Thiopental sodium (Pentothal)	Ultrashort-acting anesthetic	13-26 mg/kg IV titrated to induction of anesthesia	Same	Respiratory and cardiac depression; avoid perivenous administration; ventricular bigeminy common; sight hounds more sensitive	1, 2.5, 5 g vials I HM
Thorazine	*(see chlorpromazine)*				
Thytropar	*(see thyrotropin TSH)*				
Thyrotropin TSH (thyroid-stimulating hormone, Dermathycin, Thytropar)	Hormone used for diagnosis of hypothyroidism	Total doses: 5 U per dog to 10 kg IV, IM, SQ; 10 U per dog over 10 kg IV, IM, SQ	Total dose: 2.5 U per cat IM or IV	Follow protocol for testing; preinjection and 6 hours post-IM or post-IV injection	5, 10 U/vial I VM, HM
Thyroxine	*(see levothyroxine sodium)*				
Ticarcillin-clavulanate (Timentin)	Broad-spectrum penicillin-clavulanic acid combination	50-100 mg/kg slow IV q 8 h	40-50 mg/kg IM or slow IV q 6-8 h	GI upset	3 g vials I HM
Tigan	*(see trimethobenzamide)*				
Tiletamine zolazepam (Telazol)	Tranquilizer, dissociative anesthetic combination agent; used for chemical restraint or minor surgical procedures	5-12 mg/kg IM	Same	Rapid onset; respiratory depression may occur quickly (be prepared for intubation); controlled drug	100 mg/mL combined (50 mg each per mL) I VM
Timentin	*(see ticarcillin-clavulanate)*				
Timolol solution (Timoptic)	β-blocking topical agent used for decreasing intraocular pressures due to glaucoma	1 drop in eye q 12 h	Same	Potentiation of β-blocking effects possible (asthmatics, cardiac patients); avoid 0.25% solution (ineffective); often used in combination with other glaucoma drugs (weak action)	0.25, 0.5% OS HM
Timoptic	*(see timolol solution)*				
Titralac	*(see calcium carbonate)*				
Tocainide (Tonocard)	Class Ib antiarrhythmic agent for ventricular tachyarrhythmias	15-20 mg/kg q 8-12 h PO	—	Anorexia, GI signs, weakness, head bobbing, other CNS effects possible (lidocaine-like), corneal dystrophy; possibly adverse renal effects; may need to use with other class Ia drugs for maximum effect	400, 600 mg T HM
Toceranib (Palladia)	Mast cell tumor	2.5-3.25 mg/kg PO q 48 h		Tyrosine kinase inhibitor; possibly effective in treating other malignancies; consider just 3× /wk (Mon-Wed-Fri) if other illnesses, drug intolerance	10, 15, 50 mg T VM
Tocopherol	*(see vitamin E)*				

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Tofranil	*(see imipramine)*				
Tolfedine	*(see tolfenamic acid)*				
Tolfenamic acid (Tolfedine)	Oral/injectable NSAID	4 mg/kg SQ or IM once, then PO q 24 h for 2-4 days; may continue oral regimen 3-5 consecutive days per week	4 mg/kg SQ or IM once, then PO q 24 h for 2-4 days	Approved for veterinary use in Canada and Europe but not in the United States	6, 30, 60 mg T; 40 mg/mL I VM
Tonocard	*(see tocainide)*				
Toprol-XL	*(see metoprolol)*				
Torbugesic	*(see butorphanol)*				
Torbutrol	*(see butorphanol)*				
Torsemide (Demadex)	Loop diuretic	0.2 mg/kg PO q 12 h		Possibly less diuretic resistance than furosemide in dogs; monitor serum renal values and electrolyte levels	5, 10, 20, 100 mg T 10 mg/mL I VM
Toxiban	*(see activated charcoal)*				
Tracrium	*(see atracurium)*				
Tramadol (Ultram)	Analgesia; orally active opiate (mu-receptor agonist)	1-4 mg/kg PO q 8-12 h	1-2 mg/kg PO q 12 h	Tramacet, Ultracet are tramadol + acetaminophen (do not use in cats); partial antagonism possible with naloxone	50 mg T HM
Tramisol	*(see levamisole)*				
Tranxene	*(see clorazepate)*				
Trental	*(see pentoxifylline)*				
Tresaderm	Otitis externa with allergic/bacterial/fungal component(s)	2-12 drops per ear (proportional to size of ear) q 12 h	2 drops per ear, q 12 h	Combination neomycin + thiabendazole + triamcinolone; corticosteroid absorbed systemically; avoid prolonged daily use	Neomycin 0.25% + thiabendazole 4% + triamcinolone 0.1% otic VM
Triamcinolone (Vetalog, Kenalog)	Intermediate-acting corticosteroid used PO; by injection IM, SQ, or intralesional	0.1-0.22 mg/kg IM, SQ, PO	Same	Corticosteroid effects	0.5, 1.5 mg T; 2, 6 mg/mL I HM, VM
Tribrissen	*(see trimethoprim/ sulfadiazine)*				
Trientine (Syprine)	Alternative to penicillamine to chelate copper	10-15 mg/kg PO q 12 h	—	*(see penicillamine)*	250 mg C HM
Trifluridine (Viroptic)	Antiherpetic viral agent	—	At least 2-4× daily to eyes	—	1% OS
Triiodothyronine (T3, Cytomel, Cytobin, Liothyronine)	Hypothyroidism; used when patient is unable to convert thyroxine to triiodothyronine; also diagnostically as T3 suppression test	0.004-0.006 mg/kg (4-6 mcg/kg) PO q 8 h	0.0044 mg/kg (4.4 mcg/kg) PO q 8-12 h; T3 suppression; 0.025 mg (25 mcg) total	Thyrotoxicosis, PU/PD, polyphagia, nervousness, panting, tachycardia	5, 25, 50 mcg T

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
			per-cat dose PO q 8 h for 7 doses, then blood for T4 and T3 (control)		
Trilostane (Vetoryl)	Steroid analog (competitive inhibitor of 3β-hydroxysteroid dehydrogenase); treatment for pituitary-dependent hyperadrenocorticism	1-9 mg/kg PO q 24 h; divided doses (q 12 h) better tolerated by some dogs; begin low and uptitrate	—	Adrenal necrosis possible; with long-term treatment, make adjustments in 20- or 30-mg increments as dictated by clinical response and ACTH stimulation testing	60, 120 mg T, C VM
Trimeprazine (Termaril-P, Vanectyl-P)	Antiinflammatory antipruritic antitussive antihistamine agent; usually combined with prednisolone	Total dose: ½-2 tablets PO q 12 h per dog to effect	Total dose: ¼-½ tablet PO q 12-24 h per cat to effect	Steroid effect; drowsiness; Temaril-P contains 5 mg trimeprazine, 2 mg prednisolone per tablet	5 + 2 mg T; 3.7 mg + 1 mg C; 7.5 mg + 2 mg C VM
Trimethobenzamide (Tigan)	Antiemetic	3 mg/kg IM, PO q 8-12 h	None	CNS reactions; hypersensitivity; many safer and more effective alternatives	100, 250 mg C; 100, 200 mg suppositories; 100 mg/mL I HM
Trimethoprim/ sulfadiazine (Tribrissen, Ditrim)	Potentiated sulfonamide; bactericidal broad-spectrum combination agent against G+ and G− bacteria, *Toxoplasma, Nocardia, Pneumocystis*	Routine infections: 15 mg/kg PO, SQ, IM q 12 h; toxoplasmosis; 30 mg/kg PO q 12 h	Routine infections: 15 mg/kg PO, SQ, IM q 12 h; toxoplasmosis: 30 mg/kg PO q 12 h	Cats: salivation; dogs: KCS syndrome; Dobermans: polyarthropathy; ITP; hepatotoxicity and blood dyscrasias have been reported	30, 120, 480, 960 mg T; 60 mg/ mL S; 24, 48% I VM, HM
Trimethoprim/ sulfamethoxazole (Bactrim, Septra)	Same as for trimethoprim/ sulfadiazine	Same as for trimethoprim/ sulfadiazine	Same as for trimethoprim/ sulfadiazine	Same as for trimethoprim/ sulfadiazine	Same as for trimethoprim/ sulfadiazine
Tropicamide ophthalmic solution (Mydriacyl)	Anticholinergic mydriatic agent for eye examination	1 drop 15 minutes prior to ophthalmic examination	Same	Causes mydriasis and photophobia; do not use in suspected cases of glaucoma	0.5, 1% OS HM
Trusopt	*(see dorzolamide)*				
Tumil-K	*(see potassium salts)*				
Tums	*(see calcium carbonate)*				
Tylan	*(see tylosin)*				
Tylenol	*(see acetaminophen)*				
Tylosin (Tylan)	Macrolide antibiotic used for treating colitis and small-bowel bacterial overgrowth syndrome	5-10 mg/kg PO q 12 h; may increase slowly to 40 mg/kg PO q 12 h	5-10 mg/kg PO q 12 h	Usually used as powder sprinkled on food; bitter taste	50, 200 mg/mL I; 3000 mg/5 mL P VM
Ultram	*(see tramadol)*				
Unasyn	*(see ampicillin-sulbactam)*				
Unique E	*(see vitamin E)*				
Urecholine	*(see bethanechol)*				
Urimax	*(see tamsulosin)*				
Urocit-K	*(see potassium citrate)*				

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
Uroeze	*(see ammonium chloride)*				
Ursodeoxycholic acid (ursodiol, Actigall)	Synthetic hydrophilic bile acid; suppresses hepatic secretion and synthesis of cholesterol; choleretic agent via solubilizing cholesterol (sludged bile) and increase in gallbladder contractions	10-15 mg/kg PO q 12-24 h	7.5-15 mg/kg PO q 12-24 h	Anecdotal reports of beneficial effects in sclerosing cholangitis and biliary cirrhosis; may induce diarrhea; contraindicated if gallbladder obstruction; minimal contribution (<10%) to endogenous measured serum bile acids level	300 mg C 250, 500 mg T HM
Ursodiol	*(see ursodeoxycholic acid)*				
Valacyclovir	Antiviral	—	Do not use	Severe BM, renal, and hepatic toxicities common even at subtherapeutic doses	—
Valbazen	*(see albendazole)*				
Valium	*(see diazepam)*				
Valproic acid (Depakene, Depakote)	Seizures	60-100 mg/kg PO q 8 h	Unknown	CNS depression, GI disturbances initially; hepatotoxicity with chronic use; considered third-line therapeutic drug	125, 250, 500 mg T; 250 mg C; 50 mg/mL S HM
Vancomycin (Vancocin)	Bactericidal glycopeptide antibacterial	10-20 mg/kg slow IV (30-60 minutes) q 6-12 h for 7-10 days	—	Reserved for resistant *Staphylococcus, Enterococcus, Clostridium difficile*, especially when sepsis possible or present and when resistance to other agents is documented	500 mg, 1 g, 5 g I HM
Vanectyl-P	*(see trimeprazine)*				
Vantin	*(see cefpodoxime)*				
Vapona	*(see dichlorvos)*				
Vasopressin (vasopressin aqueous, Pitressin)	Diagnostic agent for central or nephrogenic diabetes insipidus; emerging application in cardiopulmonary cerebral resuscitation (CPCR)	Diagnostic: 0.5 U/kg IM to maximum 5 U after 5% weight loss from water deprivation CPCR: 0.4-0.8 IU IV +/− 1-4 milli U/kg/min IV CRI	Diagnostic: same CPCR: unknown	Not available as tannate in oil	20 U/mL I HM
Vasotec	*(see enalapril)*				
Vasotop	*(see ramipril)*				
Velban	*(see vinblastine)*				
Veltrim	*(see clotrimazole)*				
Ventolin	*(see albuterol)*				
Verapamil (Calan, Covera, Isoptin, Verelan)	Ca channel-blocking agent used principally to treat supraventricular tachyarrhythmias	1-4.4 mg/kg PO q 8-12 h; 0.05 mg/kg slowly IV; may repeat twice, 5-30 minutes between doses	Not recommended as oral calcium channel blocker for cardiomyopathy;	Not suggested for IV use clinically if structural heart disease or systemic illness (e.g., hypovolemia) present;	40, 80, 120 mg T; 120, 180, 240, 360 mg ER; 2.5 mg/mL I HM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
			(see diltiazem instead)	negative inotropic agent; usually do not use with β-blockers; may cause heart block	
Verelan	*(see verapamil)*				
Versed	*(see midazolam)*				
Versenate	*(see calcium EDTA)*				
Veta-K1	*(see vitamin K1)*				
Vetalar	*(see ketamine HCl)*				
Vetalog	*(see triamcinolone)*				
Vetmedin	*(see pimobendan)*				
Vetoryl	*(see trilostane)*				
Vetsulin	*(see insulin)*				
Vfend	*(see voriconazole)*				
Viagra	*(see sildenafil)*				
Vibramycin	*(see doxycycline)*				
Vidarabine (Vira-A)	Antiherpetic antiviral agent	—	Apply 4-6× daily to eyes	—	3% OO HM
Vinblastine (Velban)	Vinca alkaloid used in cancer chemotherapy, esp. lymphoreticular and mast cell cancers; also ITP	2 mg/m^2 IV q 1-2 weeks See pp. 671, 677 for body weight to body surface area conversion table.	Same	*(see vincristine)*	1 mg/mL I HM
Vincristine (Oncovin)	Vinca alkaloid *(see vinblastine, above)* used also for TVT	0.5 mg/m^2 IV weekly; TVT: 0.025 mg/kg IV weekly, maximum 1 mg per dose See pp. 671, 677 for body weight to body surface area conversion table.	Same	Perivascular irritant, leukopenia, constipation, local neuropathy (especially in cats)	1 mg/mL I HM
Viokase	*(see pancreatic enzymes)*				
Vira-A	*(see vidarabine)*				
Virbagen	*(see interferon-omega)*				
Viroptic	*(see trifluridine)*				
Vitamin B1	*(see thiamine)*				
Vitamin B12	*(see cobalamin)*				
Vitamin D2	*(see ergocalciferol)*				
Vitamin E (tocopherol, Unique E)	Antioxidant; steatitis, discoid lupus, dermatitis	Total dose: 100-400 IU PO, q 24 h per dog	Total dose: 30 IU PO, q 24 h, per cat	May use serum tocopherol levels to adjust dose	700 mg C HM
Vitamin K1 (Phytonadione, Aqua-MEPHYTON, Mephyton, Veta-K1)	Coumarin, indanedione, diphacinone, brodifacoum, and other anticoagulant rodenticide intoxications and coagulopathy due to decreased levels of vitamin K–dependent clotting factors	Load with 2.5-3.3 mg/kg SQ multiple sites, then 1.1-3.3 mg/kg q 12 h PO; do not give IV; for replacement therapy in chronic hepatopathies: 2.5 mg SQ, IM, or PO q 12 h	Same	Anaphylaxis risk if given IV; second-generation anticoagulants usually require 3-4 weeks of therapy; use parenteral form if inhibited absorption	5 mg T; 25 mg C; 2, 10 mg/mL I VM, HM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
		for 3-5 days, then once weekly		(small-gauge needle to minimize hematoma risk in rodenticide patients); hepatotoxicity risk with chronic use	
Volmax	*(see albuterol)*				
Voriconazole (Vfend)	Systemic fungal infections	6 mg/kg PO or IV q 12 h × 48 h loading dose, then 3-4 mg/kg PO q 12 h until clinical resolution and beyond		Derived from fluconazole; promising therapy but prohibitively expensive in many cases	200 mg vial (10 mg/mL) I 50, 200 mg T HM
Warfarin (Coumadin)	Anticoagulant; inhibits vitamin K epoxide reductase, blocking activation of vitamin K–dependent factors	0.1-0.2 mg/kg PO q 24 h, to maintain PT at 1.5-2 times the baseline	Total dose: 0.2-0.5 mg PO q 24 h per cat for most cats	Fatal or nonfatal hemorrhage; widely variable interindividual effects requiring close monitoring	1, 2, 2.5, 3, 4, 5, 6, 7.5, 10 mg T; 2 mg/mL I HM
Winstrol	*(see stanozolol)*				
Wycillin	*(see penicillin G procaine)*				
Xalatan	*(see latanoprost)*				
Xanax	*(see alprazolam)*				
Xylazine (Rompun)	α-adrenergic agonist agent with sedation and analgesia of 15-30 minutes; emetic effect in cats	0.66-2 mg/kg IM; 0.66-1.1 mg/kg IV	Emetic agent: 0.44-1.1 mg/kg IM or IV	Many side effects include arrhythmias, transient second-degree AV block, hypotension, increased sensitization to catecholamines in halothane anesthesia; reversal with yohimbine	20 mg/mL I VM
Xylocaine	*(see lidocaine)*				
Yobine	*(see yohimbine)*				
Yohimbine (Yobine)	α2-(xylazine) antagonist	0.1-0.25 mg/kg slow IV; 0.2-0.5 mg/kg IM, SQ	Same	Apprehension, salivation, tremors, excitability	2 mg/mL I VM
Yomesan	*(see niclosamide)*				
Ypozane	*(see osaterone)*				
Zafirlukast (Accolate)	Leukotriene receptor antagonist; feline asthma; not for acute attacks	—	Total dose: 5 mg per cat PO q 12-24 h	Rare anecdotal reports of efficacy in asthmatic cats	10, 20 mg T HM
Zanosar	*(see streptozotocin)*				
Zantac	*(see ranitidine)*				
Zeniquin	*(see marbofloxacin)*				
Zestril	*(see lisinopril)*				
Zidovudine	*(see azidothymidine)*				
Zinc oxide (Desitin)	Promotes healing of irritated or abraded skin	Apply a thin film q 12 h	Same	GI effects and hemolytic anemia if chronically ingested	OTC, HM, O
Zinc sulfate, acetate, gluconate, or methionine	Zn responsive dermatoses; copper storage disease	5-10 mg/kg elemental Zn PO q 12 h	1-2 mg/kg elemental Zn PO q 24 h, for	GI irritability; administer with food; Zn-induced hemolysis if plasma levels exceed 1000	66, 100, 200, 220 mg T; 1 mg/ mL I HM

Generic Name (Trade Name)	Indications/Drug Type	Canine Dose	Feline Dose	Comments	How the Drug Is Supplied
			hepatic lipidosis	mg/dL; blood Zn levels require special blood tubes (normal rubber caps contain Zn) Zn acetate = 30% elemental Zn Zn sulfate = 23% elemental Zn Zn gluconate = 14% elemental Zn	
Zinecard	*(see dexrazoxane)*				
Zithromax	*(see azithromycin)*				
Zofran	*(see ondansetron)*				
Zoloft	*(see sertraline)*				
Zonisamide (Zonegran)	Sulfonamide-based compound; second- or third-line antiepileptic drug	5-10 mg/kg PO q 12-24 h	—	Sulfa precautions; often used concurrently with phenobarbital	100 mg C HM
Zosyn	*(see piperacillin + tazobactam)*				
Zubrin	*(see tepoxalin)*				
Zyloprim	*(see allopurinol)*				
Zyrtec	*(see cetirizine)*				