Addis Ababa University College of Veterinary Medicine and Agriculture
Department of Biomedical Science

Module Title:	Veterinary Pharmacology and Toxicology
Module code:	Vetm-M3121
Course Title:	***Veterinary Toxicology***
Course code:	Vetm-3121
Cr hrs:	2 (1.5 Cr.hrs lecture & 0.5 Cr Hr practical)
Program:	Year 3 DVM
Semester:	II
Academic Year:	2019/20
Instructors:	Mr. Takele Beyene***** (DAH, B.Pharm, MSc, Assistant Professor) (50%) Dr. Getachew Tadesse (DVM, MSc, Assistant Professor) (50%) ***Course Coordinator**

Course description :

Lectures: Studies concept of poisoning, mechanism of action of poisons, factors affecting the action of poisons, diagnosis and treatment of poisoning; chemical poisoning, plant poisoning, venomous bites and stings, environmental toxicosis, radiation hazards, toxicosis due to food additives and preservatives and commonly used drugs.

Practical (0.5 hours/week): Collection and demonstration of toxic plants; experimental detection of poisoning caused by different toxicants and their treatment; calculation of LD50 and ED50 and demonstration of drug toxicity.

Course objectives:

- Know the concepts and principles of poisoning caused by various classes of toxicants
- Be able to identify the major toxic agents affecting livestock and other animals.
- Envisage mechanisms of diagnosis and treatment and control methods to ensure the safety of the animals and end users.

Mode of delivery:

- The delivery method includes lectures, case studies, seminars, practical demonstrations and field visits

Course Outlines

Week	Topics	Assessment methods	Instructor
1	Introduction to toxicology, Sampling and processing of samples	Lectures, discussions	Dr. Getachew T.
2	Methods for the extraction and analysis of toxicants	Lectures, discussions	Dr. Getachew T.
3	Determination of toxic dose- response relationships	Lectures, discussions, Quiz	Dr. Getachew T.
4	Methods of establishing acute, sub-acute and chronic toxicities 1st examination	Lectures, discussions, Quiz	Dr. Getachew T.
5	Diagnosis and management of toxicants	Lectures, Seminars & discussions, lab activity	Dr. Getachew T.
6-8	Phytotoxicity (cyanide, glycosides, alkaloids, oxalates, nitrates and nitrites)	Lectures, Seminars & discussions, Lab activity	Dr. Getachew T.
9-10	Agrochemicals (insecticides, herbicides, rodenticides)	Lectures, Seminars, discussions, Quiz	Takele B.
11-12	Mineral toxicities (metals and non-metals); Acids and alkalis	Lectures, Seminars, discussions, assignments	Takele B.

13	Mycotoxicities, Bacterial toxins	Lectures, discussions, self-reading, assignment	Takele B.
14	Zootoxins (venoms)	Lectures, discussions, Self-reading,	Takele B.
15	Drug toxicities	Lectures, discussions, self-reading,	Takele B.
16	Environmental toxicants (air pollutants, water pollutants, radiation hazard)	Self-reading, assignment	Takele B.

Interactive lecture using power point slides; Discussions using whiteboard and markers; Assignment, seminar paper, oral presentation; Demonstrations on live lab animals, and field visits.

Assessment/Evaluation methods:

Continuous assessment: Quiz, class activities, assignment (presentation) /attendance/discussion, and tests ≥ 50%; and Final exam ≤ 50%

Resources used for teaching-learning activities

White board and markers; Transparency paper and markers; LCD projector and laptops; Animation Videos; and Figures and tables

Course expectations

Students are expected to:

- Plan their own learning; Participate during discussions and complete their assignments; Give constructive feedback to partners/ group members and the instructors; Attend all scheduled classes, field visits and other activities

Policies

- If a student fails to attend 75% of the theoretical classes, he/she shall be given a grade of IA (Incomplete Attendance) which will be changed to F if he/she fails to submit a valid reason.
- A student must attend all practical classes. A student who missed practical classes for valid reason should compensate with makeup sessions, otherwise he/she shall be treated as stated above.
- Classroom behaviors that may interfere with the instructor's ability to teach or with the benefit of students from the instruction will not be tolerated. The student shall be warned, expelled from class or presented for disciplinary measures.

Exam Schedule and Grading

- Exam schedule will be based on the college schedule.
- Grading System is fixed which was set by the university.

Reading Materials

1. **Veterinary Toxicology**. 11th ed. Mc Graw Hill, USA.
2. Konnie H. Plumlee. 2004. **Clinical Veterinary Toxicology,** Mosby, Inc. Alland therapeutics. 4nd ed. Baillier Tindall, London.
3. RAMESH C. GUPTA. 2007. **VETERINARY TOXICOLOGY:** Basic and Clinical Principles**.** Academic Press, Elsevier. New York, USA.
4. Curtis D. Klaassen. 2001. **Casarett and Doull's Toxicology the Basic Science of Poisons**. 6th ed.Mcgraw-Hill Medical Publishing Division.New York.

Insecticides
Herbicides
Rodenticides

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Objectives

- Be familiar with major categories of insecticides:
  - mechanism of action
  - effects on non-insect animals
  - clinical signs of toxicity
  - approaches for treating toxicity
  - persistence in environment
  - persistence in food chain
  - persistence in individual

- Know how each of the specific drugs in the “Drug List for Insecticides” fits into these objectives.

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Insecticidal Chemical Overexposure

- Accidental overexposure when applied to crops
- Accidental exposure when mixed with animal feed
- Accidental use of plant formulation rather than animal formulation
- Accidental exposure following improper storage
- Accidental overexposure when used medicinally

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Potential for Toxicity depends on....

- Insect – Non-insect Differences

- Generally longer lasting effects of insecticidal chemicals in target insect than in nontarget,
- non insect (mammalian) species

- Generally insecticides target the same cellular mechanisms in insects which are affected in other animals to cause toxicity

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Potential Additional Problems with Insecticides

- Environmental persistence
- Individual persistence
  - Chemical
  - Effect
- Translocation in plants
- Bioaccumulation

Factors Influencing Insecticide Toxicity

- Environmental degradation of compound
- Vehicle used to disperse compound
- Species exposed
- Exposure route

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Insecticides

- **Cholinergic Receptor Activation**
  - **Cholinesterase inhibitors**
  - **Nicotine-like drugs**
- **Sodium Channel Modulators**
  - **Pyrethrins & pyrethroids**
  - **Organochlorines**

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Cholinesterase Inhibitor Insecticides

- Organophosphates
  - Not persistent chemically in individuals
  - Effect is persistent in individuals

- Carbamates
  - Not persistent chemically in individuals
  - Effect is not persistent in individuals

- Both
  - Some persistence in environment
  - No translocation in plants
  - No bioaccumulation ("up food chain")

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Diagnosis of ChEase Toxicity

- History
- Clinical Signs
- Measure ChEase activity
  - Blood, Brain, Retina
- Detection of AntiAChEase in feed
  - Granular material in GI tract
- Detection of AntiAChEase in tissue

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Treatment of ChEase Inhibitor Toxicity

- Atropine
  - Blocks ACh effects at muscarinic sites
  - Muscarinic sites more important
  - ACh sites for life
  - Care in horses – ultrasensitive
- Pralidoxime
  - Acts on OP-cholinesterase complex
    - releases OP residue
    - reactivates cholinesterase
  - No effect if "aging" has occurred
  - Atropine first
  - Not useful for carbamate poisoning
  - Not harmful in carbamate poisoning

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Treatment of ChEase Inhibitor Toxicity

- Activated Charcoal
- Bathing
- Artificial respiration
- Control seizures
  - barbiturates - phenobarbital
  - benzodiazepines - diazepam
- Correct acid-base disturbances resulting from muscle activities
  - Rehydrate

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Nicotine as an Insecticide

- ✓ Not persistent in individuals
- ✓ Not persistent in environment
- ✓ No bioaccumulation
- **Nicotinoids**
  - Clothianidin
  - Imidacloprid
  - Thiacloprid

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Nicotine Toxicity

- Significantly toxic to all animals
- Minimal difference in sensitivity of target insects and other animals

- **Mechanism of Action**
- Acts at all nicotinic cholinergic receptors
  - CNS
  - ANS Ganglia
  - Skeletal Neuromuscular Junction

- Mimics ACh
  - Activates & desensitizes receptor

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Pyrethrins & Pyrethroids

- **Pyrethrins**
  - Natural – from Chrysanthemum
- **Pyrethroids**
  - Synthetic
    - less toxic to non-insect species
    - better insecticides

- Environmental Stability
  - Pyrethrins pyrethroids
  - Pyrethrins
    - light sensitive; degrade in air

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Pyrethrins & Pyrethroids

- Mechanism of Action
- Affects Na-channel in membranes
  - membrane depolarization
  - following action potential

  →action potential bursting activity
- Clinical Intoxication

- Type II CS syndrome
  - Chewing movements
  - Profuse salivation
  - Pawing & burrowing (rodents)
  - Body tremors and writhing

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Pyrethrins & Pyrethroids

- **Diagnosis of Intoxication**
  - History
  - Clinical Signs
  - No characteristic lesions
  - Tissue residue concentration
- **Treatment of Toxicity**
- Dermal
  - Bathe
- Oral
  - Emetic, cathartic
  - Activated charcoal
- Any Route
  - Counter CNS stimulant effects

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Chlorinated Hydrocarbon Insecticides

- Uses in
  - agriculture
  - control of malaria
  - control of West Nile fever

- Persistent in individual
- Persistent in environment
- Regional bioaccumulation in plants
- Bioaccumulation (in food chain)

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Chlorinated Hydrocarbon Insecticides

- **DDT**
  - Insecticidal properties noted 1939
  - Use started 1940
  - Effective & cheap insecticide

  - BUT…
  - Induces hepatic oxidases: alters
  - drug & steroid metabolism
    - Carcinogen (?)
  - Not used in US
  - Human health hazard, & increasing
  - insect resistance

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Chlorinated Hydrocarbon Insecticides

- Chlorinated Ethane Derivatives
  - Chlorinated Cyclodienes
  - Hexachlorocyclohexanes

- Replacements for DDT to achieve less toxicity to non-insects

- Not used legally in US since 1972 with occasional exceptions
  - Aldrin
  - Chlordane
  - DDT
  - Dieldrin
  - Heptachlor

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Chlorinated Hydrocarbon Insecticides

- Stability in the Environment
- Absorption by Soil
  - Importance of soil composition
    - Sandy soil: chemicals wash through
    - Organic soil: chemical absorbed to soil
- Persistence in Soil
  - Effect of one application may be
  - persistent for years
- Biological Magnification
- Translocation in Plants
  - Variable concentration within plant after uptake through roots

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Chlorinated Hydrocarbon Insecticides

- Clinical Intoxication
  - Behavioral Aberrations
    - Hypersensitivity, Apprehension, Belligerence, Later Depression
  - Locomotor Aberrations
    - Fasiculations, Spasms, Seizures
  - Autonomic Phenomena
    - Emesis, Salivation
  - Dependent Signs
    - ↓ body temperature
    - ↓ respiratory rate
    - ↓ depth of respiration
- Diagnosis
  - History for potential exposure

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Chlorinated Hydrocarbon Insecticides

- **Treatment of Toxicity**
  - Skin-Bathe
  - GI
    - Induce Emesis
    - Activated charcoal
    - Cathartic
  - CNS
    - Control seizure activity
      - Benzodiazepine (diazepam)
      - Barbiturate (phenobarbital)
- **Chlorinated Hydrocarbon Insecticides Decontamination**

Herbicides

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Herbicides

- **PHENOXY FATTY ACIDS**
- **BIPYRIDYLIUM- PARAQUAT**
- **DINITROCOMPOUNDS**
- **CARBAMATES**
- **TRIAZINES**
- **GLYPHOSATE**

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PHENOXY FATTY ACIDS

- As a group, these are the most commonly used herbicides.
- Post-emergent control of broadleaf weeds.
- Analogs to plant hormones.

- **Source**
  - **2,4-D: dichlorophenoxyacetic acid**
  - **2,4,5-T: trichlorohenoxy acetic acid**
  - **Silvex: trichlorophenoxy propionic acid**
  - **2,4-D: Most common used home and garden herbicide**

- **Exposure**
  - Ingestion of treated grasses, turf or pasture; diluted herbicide
  - Accidental ingestion, inhalation, poisoning; undiluted herbicide

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Toxicodynamics

- **Widely distributed, little accumulation in fat.**
- **Short half-life, not appreciably metabolized, excreted in urine.**
- **Not accumulated in milk.**
- **Toxicity**
  - **Dogs appear to be most sensitive (longer half-life).**
  - **Dogs**
    - **LD50: 100 mg/kg**

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Herbicides

Pathology

- **Irritant to mucosal membranes: undiluted, concentrated forms**

Clinical Symptoms:

- **Dogs: vomiting, passivity, myotonia, ataxia, muscular weakness (posterior limbs), clonic spasms and coma.**
- **Cattle: Depression, muscle weakness**
- **Elevated serum alkaline phosphatase, lactate dehydrogenase, and creatine phosphokinase suggest liver, kidney and**

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Herbicides

- **Mechanism of Toxicity**
  - **Muscle: Plasma membrane disruption (ion channels?)**
  - **Inhibition of ribonuclease synthesis – effects protein synthesis**
  - **Uncoupling of oxidative phosphorylation – decrease ATP**
  - **Adducts with acetyl-CoA = 2,4-D-Ach**
  - **Treatment**
    - **No specific antidotes**
    - **Charcoal is effective in cattle for recent ingestion; monitor rumen atony.**
    - **Alkaline diuresis should enhance clearance.**

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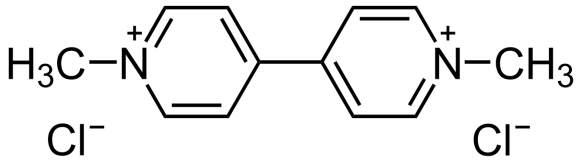
BIPYRIDYLIUM- PARAQUAT



- (1,1'-dimethyl-4,4'-bipyridyl)
- Contact herbicide used as a dessicant, defoliant
- Water soluble, binds to clay soils.
- **Source**
  - Commercial preparations: Dextron X, Dextrone, Herbaxon, Toxer.
- Concentrated forms for agriculture (5-20%solutions)AAU-CVM diluted forms for domestic use

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BIPYRIDYLIUM- PARAQUAT

- **Toxicodynamics**

- **Limited absorption (~20%)**

- **Excreted in urine as unmetabolized compound**

- **Concentrates in the pulmonary tissue via the polyamine transporter system (calveoli-dependent)**

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- **Pathology**
- Acute toxicosis
- Early - vomiting, GI irritation, diarrhea. High doses: ataxia, seizure
- 2-3 days – development of renal failure, hepatocellular necrosis.
  - Renal injury usually reverses and function is recovered.

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BIPYRIDYLIUM- PARAQUAT

- **Treatments**
- Detoxification
- Emetics- early
- Bentonite, Fuller's Earth – clay absorption
- Supportive Therapy
  - Assisted ventilation. Oxygen is contraindicated**.**

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Carbamates (chloropropham)

- Asulum, Asulox
- Herbicide preparations are less toxic than
- carbamates used in insecticides
- Inhibits acetylcholinesterase (enhances cholinergic pathways)

(see Insecticide)

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Triazines (Atrazine)

- heavy use agriculturally in Midwest
- domestic use in some Scotts Weed ‘N Feed products.
- Plants: Blocks photosynthetic pathways
- Mammals: Attenuates LH surge;
- disrupts cyclicity, delayed puberty, altered lactation, pregnancy loss
- Relatively toxic to ruminants.

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Glyphosate (ROUNDUP)

- n-(phosphonomethyl) glycine
- Second most used herbicide in domestic, public, and agriculture environments.
- Wide margin of safety; mild intoxication has been reported in pets.
- Toxicity related to: surfactant (15%v/v): and electrolyte loss.
- Ocular irritant, contact dermatitis

- Polyethoxylated tallowamine (organic surfa
- in vitro cytotoxicity

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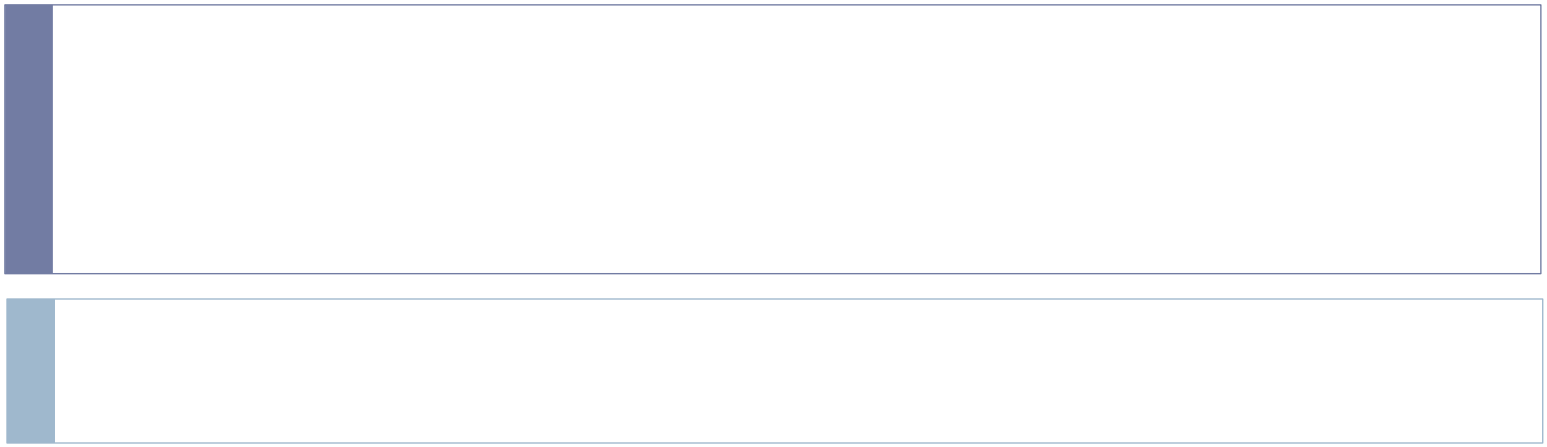
Herbicides



Rodenticides

Rodenticides

OUTLINE

Exposure Risks – General

Rodenticides of Veterinary Concern:

- Bromethalin
- Anticoagulants
- Cholcalciferol (Vitamin D)
- Metal Phosphides
- Strychnine
  - Sources
  - Toxicodynamics
  - Symptoms/Pathology
  - Treatment

Rodenticides

Introduction

Sources

- Pastes and Pellets - formulated to be attractive and palatable for direct ingestion
- Tracking Powders – placed in high traffic areas, consumed when grooming.

Exposure

Ignoring safety precautions
Heavy use in place in good rodent control practice
Malicious poisoning

Risk of Toxicosis

Accessibility to pets, livestock, and wildlife
Dogs: 5th most common intoxication; estimated 20% of exposures are toxic
Cats: rarely reported; difference in exposure rates?
Livestock: Rare; controlled exposure environment.
Wildlife: Secondary exposure

BROMETHALIN

Sources Developed in 1980s : Vengeance, Hotshot, Sudden Death, Assault

Highly popular since 2014. Used to be the 3rd or 4th most commonly used rodenticide
Exposures: accidental ingestion by dogs and cats

Toxicodynamics

Rapid absorption from GI
Lipophilic, localizes to fat, brain
Metabolism: to desmethyl bromethalin

desmethy bromethalin >> bromethalin

BROMETHALIN

Mechanism of Toxicity

Uncouples oxidation phosphorylation

↓

Decreases synthesis of ATP

↓

Loss of cellular sodium/potassium exchange

↓

Intracellular swelling

↓

Cell degeneration, Death

CNS tissue appears to be the most sensitive to cellular toxicity of Bromethalin

BROMETHALIN

Symptoms/Pathology

Acute/Large Dose: “convulsant syndrome,”

hyperesthesia, hyperexcitability, tremors, seizures, circling, vocalization, mild to severe CNS depression, hyperthermia, and death.

Signs may occur within 4 to 18 hours of ingestion

Chronic/Low Dose: “paralytic syndrome.” onset of clinical signs is slower and sometimes delayed. Signs may take 1 to 7 days.

Ataxia, CNS depression, paresis of the hindlimbs, then progressing to paralysis several days later.

Green Stool – colorant

Pathology – abnormal EEG, cerebral and spinal edema,
increase CSF pressure
Cerebral lipid peroxidation

BROMETHALIN: Treatment

Treatment

No antidote

Early detoxification. Emesis, activated charcoal.

Supportive: minimize cerebral edema with mannitol, dexamethasone

Diazepam, Phenobarbital to control seizures.

Anticoagulant Rodenticides

ANTICOAGULANTS

The toxicity of anticoagulant rodenticides is based on inhibition of Vitamin K pathways.

Sources: At least 126 commercial products based on at least 13 different anticoagulants

Products: D-Con, Drat, Kill-Rat, Ratox, Rodex, Storm, Talon, Void, etc.

1. 4-Hydroxycoumarins

   Warfarin - used since the 1940s. Increased resistance in rat population, now multiple doses required

   Second generations 4-hydroxycoumarins – since 1970s, 80s.

   Brodaficoum, bromadiolone, difethialone

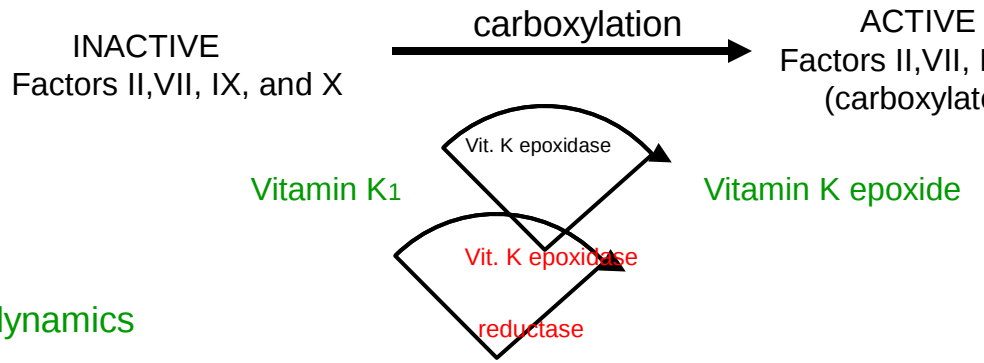
   Single, effective doses

   Banned for consumer use; approved for commercial use - 2011

2. Indane 1,3-dione (Indanediones) - diphacinone, chlorophacinone, pindone

Anticoagulant Rodenticides

Mechanism of Toxicity



Toxicodynamics

1. Absorption is slow (peak 12h) and complete (> 90%).

2. Metabolism (elimination) is slow

3. Binding to plasma proteins increases distribution

Pathology

Anticoagulant Rodenticides

gingival hemorrhage, dark tarry stool.

Clinical Tests: Increased clotting times: coagulation, prothrombin, activated partial thromboplastin times all increased 2 to 8-fold.

Late Lesions: hemothorax, hemomediastimun, hemopericardium, pulmonary edema, and hemorrhage are usually fatal.

Treatment

Detoxification within 8h. Usually not practical.

Transfusion – whole blood if anemic; plasma will supply clotting factors

Antidotal Therapy – Phytonadione (Vitamin K1).

STRYCHNINE

Sources

Historical use in veterinary medicine as an analeptic, circulatory stimulant, tonic, and ruminatoric.

Presently used as a rodenticides against gophers and ground squirrels

Exposures:

- Ingestion of rodenticide
- Most common malicious poisoning of dogs.
- Top Five of toxicological diagnosis (Iowa VDL)
- Secondary toxicosis in raptors

STRYCHNINE: Mode of Action

Toxicodynamics

Rapid absorption in GI respiratory mucous membranes
Rapid accumulation and metabolism in liver
Small amounts reach CNS (site of action)

Mechanism of Toxicity

Antagonism of the inhibitory neurotransmitter glycine
Reflex arc in spinal cord and medulla

Pathology

Nervousness, restlessness, muscle tremors and tics
Acute, explosive onset of tonic to titanic seizures.
Extreme rigidity of skeletal muscles
Increased body temperature, myglobinuria from muscle damage

Laboratory Serum strychnine
Acidosis, creatine phosphokinase

STRYCHNINE: Treatment

Treatment

Prevent respiratory spasms (sedation) before detoxification : emetics, gastric lavage charcoal

Fluid diuresis to promote urination.
Acidification of urine aids excretion.

Control of seizures – pentobarbital
- diazepam

Mechanical respiration

. . . the End

THANK YOU

Mineral poisoning
Inorganic Chemicals

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1. Lead (Pb) Poisoning

- ***Synonyms:***

- Pb is a heavy metal chronic toxicosis, is referred to as *plumbism*.
- most common in dogs and cattle but limited in other species due to reduced accessibility and selective feeding habits.

- ***Sources:***

- Include: used oil and battery, paint, linoleum, grease, lead weights, lead shot, and contaminated foliage growing near smelters or along roadsides.

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Lead Poisoning…cont'd

Toxicokinetics

- Absorption depends on the physical form:
  - (metallic, salt, organic) and the route of exposure.

    metallic Pb is << Pb salts, << organo-lead cpds

  - Dermal exposure to organo-Pb compounds can result in toxicosis.
- Ingested lead requires ionization within GIT (acidic env't of the stomach), in order to be appreciably absorbed.
- >90% of absorbed Pb is bound to RBCs, small amounts bound to albumin and lesser amounts as free lead in the plasma ;
- unbound Pb is distributed widely throughout various tissues.
- The highest concentrations occur within the bone, teeth, liver, lung, kidney, brain, and spleen.

Lead Poisoning…cont'd

Mechanism of Action

- *Lead has multiple effects on* biochemical mechanisms within the body:

1. Binding of cellular and enzymatic sulfhydryl groups:

=inactivation of enzymes involved in heme synthesis: aminolevulinic acid dehydratase (ALAD) and ferrochelatase, and causing RBC abnormalities.

= Inhibition of heme synthesis → heme depletion → inhibition of cytochrome P-450, → inhibition of tryptophan pyrrolase → increased plasma tryptophan levels → elevations in brain serotonin levels → abnormal neurotransmission of serotonergic pathways → neurologic effects

- ✓ Increased serum ALAD levels may themselves be neurotoxic by interfering with GABA transmission

2. Competition with calcium ions:

substitution for calcium in bone, alteration of nerve and muscle transmission, and displacement of calcium from calcium-binding proteins such as calmodulin

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Lead Poisoning…cont'd

Toxicity and Risk Factors

- Lead toxicosis has been reported in mammals, birds, and reptiles.
- swine, goats, and chickens are considered to be fairly resistant
- Young animals absorb lead far more readily than do adult
- Lead absorption can also be enhanced in Ca-, Zn-, Fe-, or vitamin D–deficient animals.
- Conversely, zinc or calcium supplementation may decrease the absorption of lead from the GIT.
- Pb may interfere with the absorption of selenium from the GIT in ruminants, resulting in selenium

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Lead Poisoning…cont'd

Clinical Symptoms

***Cattle*:**

- **acute course** : ataxia, blindness, salivation, spastic twitching of eyelids, jaw champing, muscle tremors, and convulsions.

***Sheep and old cattle*:**

- **Subacute course**: anorexia, rumen stasis, colic, dullness, and transient constipation, frequently followed by diarrhea, blindness, head pressing, bruxism (**grinding of teeth**), hyperesthesia, and incoordination.

Horses:

- **chronic course:** weight loss, depression, weakness, colic, diarrhea, laryngeal or pharyngeal paralysis (roaring), etc

***Avian species*:**

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Lead Poisoning…cont'd

Treatment

- Management of lead toxicosis in animals consists:

- stabilization of severe clinical signs,
  - ✓ Seizures: anticonvulsants-diazepam or barbiturates.
  - ✓ Thiamine, 2-4 mg/kg/day, SC, alleviates clinical manifestations and reduces tissue deposition of lead
- Elimination of lead from the GIT,
  - Magnesium sulfate, 400 mg/kg, PO
  - Ruminotomy
- Chelation therapy: bind lead into a soluble complex (chelate) that is then excreted in the urine
  - Calcium disodium edetate (**Ca EDTA**), 110 mg/kg/day, IV or SC,

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2. Arsenic (As) Poisoning

Sources:

- The commercial forms of arsenic include inorganic and organic.
- Inorganic As :
  - formerly used as arsenic trioxide, a herbicide and insecticide.
- Pentavalent organic forms of As have been used as feed additives for food animals:
  - arsenilic acid, sodium arsanilate, etc
  - b/c of use as antimicrobials as growth promotants
- Sources of As poisoning: areas around mining or smelting sites.
- Normally soils contain low concentrations of elemental arsenic; however, mine tailings, smoke, fumes, and dust may contaminate soils near mining or smelting sites.

As Poisoning…cont'd

Toxicokinetics

- The toxicity of arsenic is influenced by:
- The solubility of the formulation,
  - ✓ Soluble arsenicals are readily absorbed from the GIT and via the skin
- Route of exposure,
- Rate of absorption,
- Rate of metabolism and excretion,
  - kidneys may reduce a small portion of orally absorbed pentavalent to the more toxic trivalent form = nephrotoxicity
  - methylation of inorganic As is an important detoxification mechanism and increase excreted
- Most pentavalent and trivalent As are readily excreted into the

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Mechanism of Action

Trivalent arsenicals:

- Inhibit cellular respiration.
  - bind to sulfhydryl compounds, especially lipoic acid and -ketooxidases.
  - Lipoic acid, a tissue respiratory enzyme cofactor, plays an important role in the TCA cycle.
  - Tissues with high oxidative energy requirements such as actively dividing cells of the intestinal epithelium, epidermis, kidney, liver, skin, and lung are most affected.
- also affects capillary integrity by an unknown mechanism.
  - The capillary system of the GIT is most affected. Capillary

As Poisoning…cont'd

Toxicity and Risk Factors

- *Cats are the species most* susceptible followed by horses, cattle, sheep swine, and birds.
- The ability of the inorganic As to cause toxicosis depends on valence.
  - Trivalent forms are 10X more toxic than pentavalent.
- Organic arsenical feed additives that are fed too long or at overdoses have caused toxicosis in swine and poultry.
- Therapeutic use of thiacetarsamide as a heartworm t/t in dogs has resulted in arsenic toxicosis.

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As Poisoning…cont'd

Clinical Signs

- ***Arsenic compounds cause severe effects in*** the GIT.
- Organic/inorganic trivalent As cause acute or peracute poisoning.
  - Vomiting, intense abdominal pain, weakness, staggering, ataxia, recumbency, and weak, rapid pulse with signs of shock are common.
  - Rapid onset of watery diarrhea or rumen and GI atony may occur.
- Subacute poisoning occurs when affected animals survive acute arsenic poisoning and live 3 days or longer.
  - Watery diarrhea can continue.
- Damage to the kidneys can result in oliguria and proteinuria,

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As Poisoning…cont'd

Treatment

- ***Early intervention:***
  - ***gastrointestinal*** detoxification and supportive therapy, is essential.
  - Emergency and supportive care include correction of shock, acidosis, and dehydration.
  - A blood transfusion may be necessary.
  - Emetics, cathartic agents, or gastric lavage may be used if ingestion is recent.
- Antidote: Dimercaprol (British anti-Lewisite, or BAL),
  - is relatively ineffective unless given before the onset of clinical signs.
  - not currently approved for use in food animals

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As Poisoning…cont'd

Prognosis

- High mortality rate in acutely poisoned with inorganic arsenicals.
- High morbidity rate also seen in pentavalent organic arsenicals, but with good nursing care a low mortality rate.
- Recovery may require 2 to 4 weeks.

Prevention and Control

- *Animal exposure to inorganic* arsenic as pesticides and herbicides is less frequent
- Knowing and avoidance of mining and smelting sites are important

3. Copper (Cu) Poisoning

Synonyms

- **Enzootic icterus** **is** believed to be chronic copper poisoning.

Source

- Numerous sources of copper are available in the animal's environment.
- potential sources of excess copper are:
  - Certain fungicides that contain copper salts
  - Copper-containing algicides used in ponds and water tanks,
  - Footbaths containing copper salts ($CuSO_4$).

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Cu Poisoning … cont'd

Toxicokinetics

- ***Absorption***:
  - primarily stomach, SI in monogastric animals**.**
  - LI is also important in ruminants (particularly sheep)
  - actively transported via the enterocytes into the bloodstream, & binds to albumin, ceruloplasmin, and the protein transcuprein.
- copper is then distributed to the liver, kidney, and brain, where it is stored.
- Hepatocytes pick up the copper and store it in the lysosomes and then incorporate it into ceruloplasmin, which stores the copper into a stable electron state for use by the body.
- Toxic levels of copper cause liver necrosis.
- Copper is then released into the bloodstream, resulting in erythrolysis, hemoglobinuria, and elevated copper in the serum.

Cu Poisoning … cont'd

Toxicokinetics….

- The BA of Cu is limited to the amount of molybdenum and sulfur ingested (true in ruminants).
- In the rumen molybdenum and sulfur form thiomolybdate, which reacts with copper to form insoluble copper complexes, result in decreased absorption of copper in the intestine.
- recommended Copper/molybdenum ratios of **6:1 to 10:1** for most ruminant diets to prevent excessive copper accumulation in the liver.

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Cu Poisoning … cont'd

MOA

- excessive accumulations of Cu in the hepatic lysosomes causes damage to the cell membranes and death of the hepatocytes.
- Copper is then released into the bloodstream.
- Once the animal ingests hepatotoxic substances: pyrrolizidine alkaloids (which inhibit cell replication), hepatic compensation is lost and hepatocellular necrosis results.
- liver lack the ability to rapidly absorb and clear the excess serum copper, large amounts of free Cu are released into the circulation.
- Cu damages the membrane of RBCs, causing the release of hemoglobin by intravascular hemolysis.

Cu Poisoning … cont'd

Toxicity and Risk Factors

- *Sheep are sensitive to* Cu, whereas
- cattle, horses, swine, chicken, turkeys, and dogs are relatively resistant to excessive accumulations of copper.

Clinical Signs

- ***In Sheep:***
  - ***rarely show clinical signs until the*** animal is stressed, resulting in a massive liver necrosis and copper release.
    - resulting in hemoglobinuria, icterus, anoxia, and death.
    - Urine is dark red as a result of the presence of hemoglobin

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Cu Poisoning … cont'd

Clinical Pathology

- *Often clinical signs of copper toxicosis* develop acutely and the animals die before clinical parameters are noted.

- Surviving animals may have elevated liver enzymes (aspartate aminotransferase, sorbitol dehydrogenase, alkaline phosphate, and gamma-glutamyltransferase).

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Cu Poisoning … cont'd

Treatment

- In ruminants with acute copper toxicosis, treatment is often unsuccessful.
  - Ammonium molybdate (50 to 500 mg PO once a day) and
  - Sodium thiosulfate (300 to 1,000 mg PO SID)
  - Ammonium tetrathiomolybdate (on alternate days for 3 treatments)
  - **D-Penicillamine** (10 to 15 mg/kg PO twice daily [bid]) chelates copper and promotes urinary excretion in dogs with copper hepatopathy.
    - Tetramine is a more potent chelator, but is not available commercially.

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Cu Poisoning … cont'd

Prevention and Control

- In ruminants dietary amounts of Cu can be regulated by the amount of molybdenum and sulfur in the diet.
- Ensuring that the **Cu/Mo** ratio is 6:1 to 10:1 in the diet greatly assists in decreasing the chances of elevated hepatic Cu.
- Sulfur levels greater than 0.35% assist in lowering copper availability.

(Caution: Increased sulfur can lead to thiamine deficiency and polioencephalomalacia.)

- The addition of zinc to the diet can also decrease copper absorption.

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4. Molybdenum(Mo) Poisoning

Sources

- In its natural form, molybdenum does not exist in the elemental state and is found with copper, lead, and tungsten ores.
- Mineralization of lakes can result in high concentrations of Mo in sediments.
- Fossil fuels contain Mo, and the Mo is released during combustion.
- Other atmospheric sources are deposition on forage from Mo emissions from aluminum smelting, steel alloy

Mo Poisoning …cont'd

Toxicokinetics

- Sulfate shares a common transport system with Mo in the intestine and kidney.
- Mo is eliminated in the bile of cattle and in the urine of laboratory animals.
- Ruminants fed high-dietary Mo excrete Mo in milk.

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Mo Poisoning …cont'd

Mechanism of Action

- Mo is required for metalloenzymes:
  - xanthine oxidase, xanthine dehydrogenase, aldehyde oxidase, and sulfite oxidase.
- Mo binds with-macroglobulin in the membranes of RBCs, where it enhances the resistance of the membranes to rupture.
- Mo has a three-way interaction with copper and sulfur.
- Ruminants are more sensitive than non-ruminant species to the toxicity of Mo, attributed to sulfur metabolism in the rumen.
  - Dietary sulfur is converted to sulfide in the rumen, which decreases the absorption of copper.
  - Increasing Mo in the diet increases the rate that

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Mo Poisoning …cont'd

Toxicity and Risk Factors

- Ruminants are the most susceptible species.
- cattle are the most sensitive and mule are the most resistant.
- Toxicosis has been reported in horses, swine, and rabbits.
- Cattle on a high-sulfur diet, including sulfur in the forage and water, are also at a greater risk.
- Diets high in sulfur decrease the absorption of copper and increase the susceptibility of cattle to Mo.

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Mo Poisoning …cont'd

Clinical Signs

- In cattle, the most common clinical sign is chronic diarrhea.
- Others: Anemia, Reduced gain in body mass, Deformity of limbs, periosteosis, lameness, abnormal epiphyseal plate, Alopecia, Muscular degeneration,
- Copper deficiency causes abnormalities in connective tissue formation in bone.
- abortions were observed in pregnant mares

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Mo Poisoning …cont'd

Clinical Pathology

- *Clinicopathologic findings in cattle that* consumed a diet containing Mo as sodium molybdate were an increase in aspartate aminotransferase, gamma-glutamyltransferase, glutamate dehydrogenase, creatine kinase, BUN, creatinine, total bilirubin, and calcium

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Mo Poisoning …cont'd

Treatment

- The diet should be assayed for Mo, copper, and sulfur,
  - Because dietary sulfur can alter the predictive ratio, additional copper may be necessary.
  - copper-to-Mo ratio= 4:1 to 10:1.
  - The sulfur-to-Mo ratio should be < 100:1, and neither sulfur nor Mo should be in excess.
- Mineral supplements for cattle grazing forages high in Mo can induce copper poisoning in sheep.
- Copper sulfate can be added to cattle drinking water.
- Cattle can be injected with copper, but most preparations are highly irritating and may produce

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5. Selenium Poisoning

Sources.

- Selenium-containing compounds are of considerable interest in veterinary medicine for several reasons:
  - They have biological importance as an essential dietary constituent.
  - Domestic livestock that ingest seleniferous plants may become intoxicated with selenium.
  - Intoxication results from excess selenium supplementation of livestock rations.
  - Domestic livestock and companion animals may become intoxicated with selenium after parenteral overdose.
  - Selenium may produce toxic effects in wild aquatic birds exposed to excess environmental concentrations.

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Selenium Poisoning …cont'd

Toxicokinetics

- ***The duodenum is the primary site of*** selenium absorption, with little or no absorption occurring from the rumen or abomasum.
- Selenium may be eliminated in the urine, feces, and expired air; however, most dietary excesses are excreted in the urine.

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6. FLUORIDE

Sources

- Fluorine is present in many sites and forms throughout the world.
- Soils contain fluorides, generally present as calcium fluoride (CaF2), which is poorly absorbed by plants.
- Natural sources include volcanic ash, rock phosphate deposits (RP), iron and aluminum ores, deep wells, geothermal waters, and animal bones.
- Some of the rock phosphates are used as phosphorus supplements for livestock.
- Water sources of fluorides in rift valley are of Eth. widely contain high levels of fluoride, and sufficient

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Toxicokinetics

- Sodium fluoride is highly available orally and is readily absorbed.
- Fluorides absorbed from the intestinal tract are transported mainly in the plasma and accumulate most readily in bone.
- Of the soft tissues, kidney contains the greatest concentrations of fluorides.
- Excessive fluoride concentration in blood of pregnant animals appears to increase neonatal blood concentrations

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Mechanism of Action

- Effects on the teeth and skeletal system.
  - Matrices supporting formation of enamel, dentine, cementum, and bone.
- Teeth are affected during development:
  - damage to ameloblasts and odontoblasts, and matrix laid down by damaged ameloblasts and odontoblasts fails to accept minerals normally.
  - Structural changes in teeth occur only prior to eruption.
- In fully formed teeth ameloblasts lose their ability to repair enamel, but odontoblasts can produce secondary dentine to accommodate partially for fluorotic damage.
- Both erupting incisors and molars are affected,
- Oxidation of organic material in damaged portions of fluorotic teeth causes **brown or black discoloration**
- Interferes with formation by osteoblasts of adequate matrix and mineralization
- Fluorides replace hydroxyapatite in the crystalline structure of bone,

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Toxicity and Risk Factors

- *Daily dosage or dietary concentration of fluoride.*
- *Total exposure time.*
- *Availability of fluoride in the source ingested.*
- *Age and species of animal exposed.*
  - younger animals are considered at greater risk because of active bone and tooth formation
- *Nutritional factors.*
  - Calcium-deficient diet increases the accumulation and possibly the toxic effects of fluoride

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Clinical Signs

- ***Acute fluoride toxicosis***
  - Occur between 30 minutes to 1 hour after ingestion.
  - Characteristic signs:
    - excitement, seizures, urinary incontinence, defecation, vomiting, weakness, excessive salivation, depression, cardiac failure, and death.
  - **Differential diagnosis:**
  - poisoning by metals or metalloids (e.g., arsenic), organophosphate toxicosis, zinc phosphide toxicosis in dogs, and sodium fluoroacetate toxicosis in dogs.
- **Chronic fluorosis**

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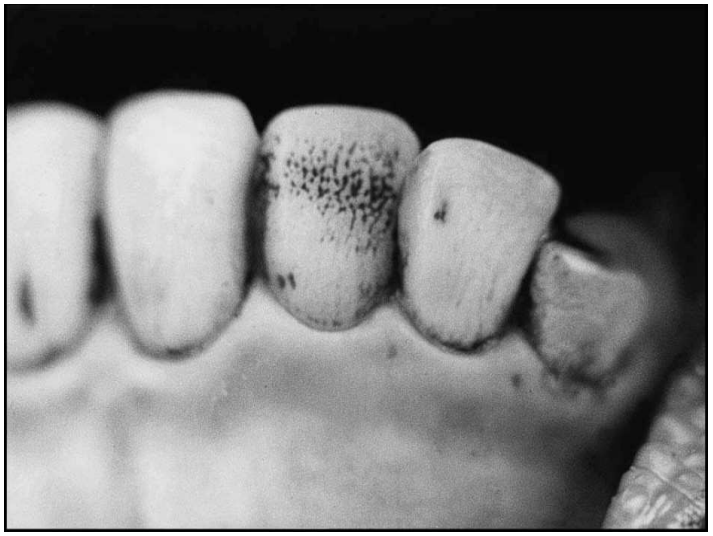
Clinical Signs



- Fig. Dental fluorosis with evidence of intermittent fluoride ingestion.

- Enamel hypoplasia with pitting and staining of enamel is evident in the second incisor.

- The fourth incisor demonstrates excessive wear

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Treatment.

- ***No specific antidote for either acute or chronic*** fluoride toxicosis is available.

  - Symptomatic therapy for chronic osteoarthritis,
  - limiting grazing,
  - providing easily masticated feeds, and
  - artificial insemination of valuable breeding animals may help prolong the useful life of livestock.

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Prevention and Control

- For chronic fluorosis:
  - aluminum sulfate, aluminum chloride, calcium aluminate, and calcium carbonate (1% of dietary intake) reduce the absorption of fluorides in the diet.

- Substitution of low-fluoride ingredients in a portion of the diet reduces total fluoride intake.

- Using grains to replace some contaminated forages reduces total fluoride intake because grain crops accumulate little fluoride.

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MYCOTOXINS

- AFLATOXINS
- ERGOT
- CITRININ
- OCHRATOXIN
- ANATOXIN (Cyanobacteria)

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Aflatoxin

- The source of the poisoning was found to be related to *Aspergillus flavus*
- ***Sources.:***
- ***Aflatoxins comprise more than a dozen related*** bisfuranocoumarin metabolites produced by *A. flavus, A. parasiticus, and A. nomius.*
- Aflatoxins are most often found in crops with substantive energy content such as corn, peanuts, cottonseed, rice, sweet potatoes, potatoes, wheat, oats, barley, millet, sesame, sorghum, cacao beans, and almonds and other nuts.
- Toxin types B1, B2, G1, and G2 aflatoxins can be

Toxicokinetics

- *Absorption is by passive diffusion from the* small intestine, especially the duodenum.
- Biotransformation occurs in the liver, kidney, and small intestine.
- The proportions of aflatoxin converted to metabolites that bind to critical cellular macromolecules determine the extent of toxicity or carcinogenicity.
- A key transformation for the toxicity of aflatoxin is the activation of AB1 to the reactive epoxide intermediate, which is carried out by the P- 450 enzyme system
- Binding of AB1-epoxide to various cellular macromolecules is believed to be responsible for cellular injury and [illegible]

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Mechanism of Action

- ***The reactive metabolites, particularly*** the epoxide of AB1, bind with cellular components including nucleic acids, subcellular organelles, and regulatory proteins that disrupt normal anabolic and catabolic processes.
- The results include disruption of organ function, carcinogenesis, immunosuppression, mutagenesis, and teratogenesis.
- Aflatoxin detoxification by rumen microbes has been
- proposed to explain the lower sensitivity of ruminants.

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Clinical Signs

- ***The aflatoxin dose and duration of exposure*** determine the time of onset and observed effects.
- Following high lethal doses:
  - anorexia, depression, weakness to prostration, dyspnea, emesis, diarrhea often with blood and mucus, fever followed by
  - subnormal temperature, convulsions (dogs), and epistaxis may be seen.
  - Icterus follows.
- Chronic intoxication is more common

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Treatment

- ***No antidote or specific treatment exists for*** aflatoxicosis beyond prompt removal from the contaminated source.
- Optimizing the quality of the diet, with particular attention to protein, vitamins, and trace elements, aids in recovery but does little to ameliorate the damage done.
- Individual treatment depends on the clinical condition and liver function support.
- A number of nutritional supplements have been tested, but results were mixed.

- **Oxytetracycline** (10 mg/kg),

Prevention and Control

- ***Procedures to prevent crop*** damage, such as insect control, can decrease fungal invasion.
- Handling corn to **minimize seed coat damage and drying to 15%** or less prevents mold growth and production of additional toxin.
- Mold retardants, such as **propionic acid**, can help in storage but do nothing to the toxin that was
- produced before harvest.
- **Ammoniation** of feeds such as corn and cottonseed is practiced in several areas of the country.
  - This procedure hydrolyzes the lactone ring of AB1 to various end-products that are less toxic.

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ERGOT ALKALOIDS

Synonyms

- Ergotism is also referred to as **“ergot” or “ergot poisoning.”**
- The term *ergot* has also been used to refer to species of *Claviceps fungi in* general

Sources:

- *The sclerotia or ergot bodies of* ***C. purpurea*** represent the mycelia, which replace the ovarian tissue of the infected grass or cereal grain.

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Toxicokinetics

- The broad class of ergot alkaloids encompasses all of the toxic principles responsible for the clinical signs of ergotism.

- Ergot alkaloids are composed primarily:
  - Ergopeptine alkaloids
    - (ergotamine, ergocristine, ergosine, ergocryptine, ergocornine, and ergovaline) and
  - Ergoline alkaloids
    - (lysergic acid, lysergol, lysergic acid amide, and ergonovine).

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Mechanisms of Action

Involve

- vasoconstriction associated with
  - D1 dopaminergic receptor inhibition and
  - partial agonism of α1-adrenergic and serotonin receptors by ergopeptine alkaloids.
- Hypoprolactinemia (decrease prolactin secretion by lactotropes)
  - D2-dopamine receptors stimulation by ergopeptine alkaloids
- Sedative properties of lysergic acid amide
  - mediated by a NT imbalance in the pituitary and pineal glands involving receptors for NE, Epi, DA, 5-HT, and melatonin.
- Uterine contraction

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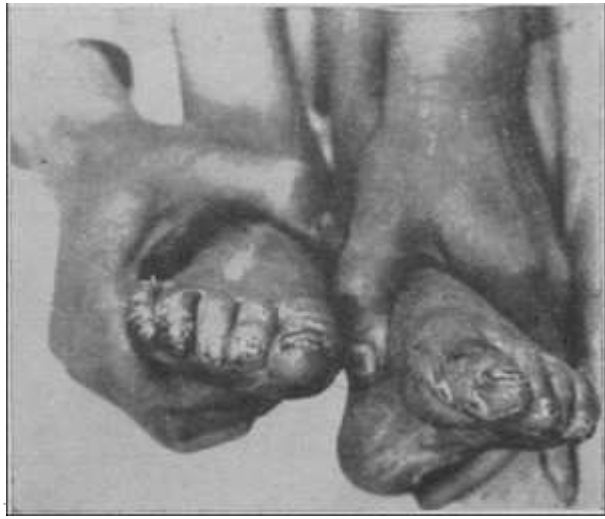
Clinical Signs

- *Ergotism generally occurs sporadically after* subacute or chronic exposure to ergopeptine alkaloids.
- Ergotism has been divided into:
  - gangrenous, hyperthermic, reproductive, and nervous forms
- Gangrenous or cutaneous ergotism are the predominant



- Agalactia, prolonged gestation, dystocia, abortion, retained placenta, neonatal mortality, and subfertility

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Treatment

- The most logical approach:
  - removal of animals from the source of ergopeptine alkaloids.
- The early signs of ergotism are often reversible, with the cutaneous vascular effects.
  - D2 receptor antagonists: metoclopramide,
  - α1-adrenergic antagonist: prazosin,
  - α1-adrenergic and serotonin receptor blockers: phenoxybenzamine,
    - have shown some clinical or experimental efficacy in decreasing the clinical signs

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VENOMOUS BITES AND STINGS

- Snakes envenomation
- Toads envenomation
- Bees, Scorpions and Wasps
  - Tick toxins

Venom

- is a **poison** or **toxin** secreted by specialized glands of an animal.
- May be composed of
  - proteins (polypeptides and enzymes), amines, lipids, steroids, amino-polysaccharides, quinones, 5-HT, glycosides or other substances.
- Its action and toxicity depends on:
  - Species of venomous animal
  - Route of entry into the body
  - Site of bite/stings
  - Quantity of the venom injected
  - ADME

SNAKES ENVENOMATION

PIT VIPERS

Coral snake

Toxicokinetics:

- *Snake venom* is composed of many small polypeptides, enzymes and possibly cholinesterase.

- Acetylcholine and some poorly defined enzymatic fractions to the venom may be involved.

Mechanism of Action

- Neurotoxicity:
  - Neurotoxins affect the postsynaptic motor nerve membranes with a curare-like action.
  - induce a non-depolarizing postsynaptic neuromuscular blockade.
    - clinically manifested as vasomotor instability, muscle paralysis, and CNS depression.
- The enzymatic fraction can cause local tissue damage

Clinical Signs

- Vary depending on the snake and victim species.
  - Neurologic signs with ascending flaccid quadriplegia, reduced nociperception (pain), and CNS depression.
  - Decreased BP, respiratory depression, loss of spinal reflexes in all limbs, and hypothermia can also manifest.
  - Additionally, they may vomit and salivate excessively, and ventricular tachycardia may develop.

Differential Dx

- Blackleg
- Anthrax
- Botulism
- Tick paralysis

Treatment

- **General management**
  - Keep the animal undisturbed
  - Apply a tight tourniquet above the site of bite
  - Incise local area of snake bite in the direction of blood vessel
  - use of specific antivenin.
    - Antivenin (*M. fulvius,* equine origin) is effective against the venom of all coral snakes *(Micruroides euryxanthus).*
    - *Antivenin can block further* action of venom but is less effective against venoms already attached to receptor sites.

TOADS ENVENOMATION

Toxicokinetics:

- Dogs and cats may play with toads and get exposed orally to the toxins
- When these toads are mouthed or bitten by a dog, the parotid glands located on the toad's dorsum release toxins that are absorbed via the buccal mucous membranes of the dog.
- The secretions from these glands may contain a variety of substances:
  - **epinephrine, serotonin, ergosterol, and bufodienolides (bufogenins)**.

- **Dx**
  - Hx of pet playing with a toad
  - Clinical symptoms
- ***Clinical Signs***
  - Hypersalivation, vomiting, and anxiety are common initial signs in dogs after biting a toad.

Treatment

- Decontamination of the oral cavity.
- Activated charcoal and osmotic purgatives
- Diazepam---Seizures,
- Atropine---Bradycardia, salivation, bronchospasm: IV at 0.02 mg/kg

Bees, scorpions & wasps
ENVENOMATION

- Their venom is a complex mixture of:
  - peptides,
  - non-enzymatic proteins: apamin, melittin or kinins,
  - enzymes: Phospholipase A&B, hyaluronidase, formic acid &
  - biologically active amines: histamine & 5-HT
- Melittin –
  - ✓ a protein mainly found in honey bees
  - ✓ is antigenic in nature & produces allergic reactions

Clinical signs

- Severity of toxicity varies from individual to individual in d/t species of animals
- Anaphylaxis and death from a single stings occurs in hypersensitive animals
- **Following single bite-** extreme serous exudation- exert protective effect by diluting the poison- exert local pressure on the circulation thus reduce dissemination of the poison.
- **Multiple bee or wasp stings-** severe local inflammation & oedema at the site of sting,

Treatment

- There is no specific antidote
- Symptomatic treatment:
  - Local application of weak solution of NH_3 & $NaHCO_3$
  - Nervine tonics & stimulants- for prostration
  - Tracheoectomy- for severe asphyxia
  - Emergency supportive therapy- to restore cardiopulmonary functions & mgt of anaphylaxis.

Tick Toxicosis

- Tick paralysis: Amblyomma, Argas, Dermacentor, Haemaphysalis, Hyalomma, Ixodus, Ornithodoros, Otobius and Rhipicephalus.

- Tick toxicosis has been reported in North America, Europe, Africa, Australia, and Russia
  - In Africa: I.rubicundus and Rhipecepahalus evertsi

- Animal Species affected by tick paralysis:
  - ✓ dogs, cats, cattle, sheep, goats, llamas, poultry, foxes, wolves, mice and several species of wild birds.
  - ✓ Dogs are affected most commonly, but losses can

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Paralysis due to tick toxicosis

- Tick paralysis is a toxin-induced, febrile, ascending, symmetrical condition in which there is flaccid tetraplegia and functional impediment to the reflexes of the superficial and deep tendons of the limbs and abdomen.
- Several ticks, including the
  - Australian paralysis tick (Ixodes holocyclus),
  - Rocky Mountain wood tick (Dermatocentor andersoni), and
  - African sand tampan tick (Ornithodoros savignyi) can cause paralysis.
- The genus Ornithodoros is widely known to cause severe host

Mechanism of action

- The toxin responsible for tick paralysis is generally assumed to be a neurotoxin.
- The exact mechanisms of action are not well known,
  - but in most tick species it is suspected that the toxin **interferes with the synthesis and/or release of acetylcholin**e at the neuro muscular junctions,
  - resulting in lower motor neuron paresis and paralysis very similar to that produced by botulinum toxin.
- Functional impairment during paralysis also affects the efferent nerve fibers that serve the respiratory muscles.
  - As a result, carbon dioxide levels rise, and the partial oxygen pressure and blood pH fall.

Clinical symptoms

- Tick paralysis can occur following the bite of as few as one tick and heavily infested animals show clinical signs quickly.
- Early signs may include:
  - change or loss of voice (due to laryngeal paresis), hind limb in coordination, change in breathing rate and effort, gagging or coughing, regurgitation or vomiting and pupillary dilation, anorexia, lethargy, drooling of saliva, Extensive dehydration
- Hind limb paralysis begins
- Respiratory rate may initially increase but, as the disease progresses, becomes slower and obviously labored, especially on expiration.

Diagnosis

- This is based on the presence of ticks, sudden appearance of paralysis, rapid course, and quick clinical recovery after tick removal.
- Unlike other tick-borne diseases of peripheral nervous system, **temperature is normal**, and blood and fluid values are unchanged.
- Specific laboratory diagnostic techniques are not available.
- **Botulism** is differential diagnoses.

Treatment

- The main goal of treatment is **to remove the ticks and provide supportive care** (especially respiratory support) until recovery occurs.
  - Recovery can occur quite rapidly following complete removal of ticks or it may take a few days.
  - The use of topical insecticides may aid in the removal of ticks, and can be especially helpful in cases where numerous ticks are embedded.
  - Heavily coated animals may need to be shaved in order to ensure that embedded ticks are found to be removed.
- Removal of embedded ticks should be performed carefully to avoid expressing additional toxin to the wound
  - Forceps may be used to grasp the tick as close to the skin as

Cont'd…

- In most cases where ticks are removed before bulbar paralysis has occurred, the prognosis for full recovery is very good.
  - In general prognosis is good and recovery occurs within 1-2 days.
  - A short term immunity develops following recovery from tick paralysis.
- A therapeutically effective immune serum is available for certain species of ticks: *I.holocyclus*.
- A polyclonal dog antiserum
  - it is only effective early in the stages of paralysis.
- Prophylactic biologic or chemical control (or both) of

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SEEK WISDOM, ELEVATE YOUR INTELLECT AND SERVE HUMANITY !

Feed Additives

An Overview and Some Examples In Veterinary Medicine & Toxicology

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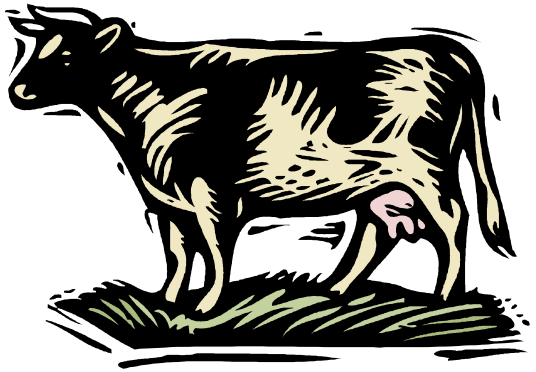
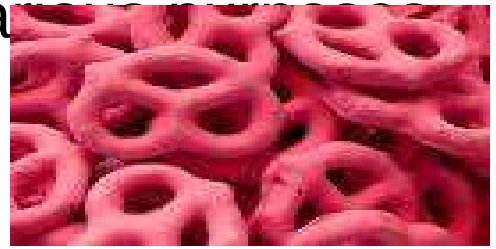
Objectives

- Be familiar with the meaning of the Animal Medical Drug Use and Clarification Act (AMDUCA)
- Issues in respect to using antibiotics in feed
- Feed additives: In respect to the examples given in this lectures on feed additives, you should be able to recognize:
  - Clinical signs
  - Very general pathophysiology
  - Specific animal species sensitivities
  - What to sample for a diagnostic work up
  - How it may be important to public health



Food/Feed Additive

- Definition
- Food/feed additives
  - Any substance that directly or indirectly becomes a component of food or that affects a food's characteristic.
  - May include grains, milling products, added vitamins, minerals, fats/oils, and other nutritional and energy sources
- Pharmaceutical or nutritional substances that are added to processed or stored food



Dyes

Feed Additives

- PHARMACEUTICAL OR NUTRITIONAL substances that
  - ARE NOT natural feedstuffs,
  - added to made-up or stored feeds for various purposes,
  - to control infectious diseases or promote health and growth

- IMPROPER use may cause:
  - POISONING or
  - result in undesirable **RESIDUES** in food intended for humans

- If you (or someone else) add anything to feed, you must consider animal and public health!!!!

Examples of Feed Additives In Animal Feeds

- Substance
  - Buffers
    - NaHCO3, MgO
  - Yeast/Probiotics Cultures
  - Minerals
    - Zn, Se,
  - Ionophores
  - Chlortetracycline
- Purpose
  - Reduce Acidosis
  - Beneficial “bugs”
  - Address Deficiencies
  - Coccidiostat/ Rumen Fxn
  - Control Liver Abscess or
  - Respiratory Disease Risk

Medicated Feed Applications

- Veterinary feed directive (VFD)
  - An important document if you prescribe antibiotics to be included in feed (but you must consider the same “issues” for use in water)
  - Describes how medically important antibiotics may be used in feed and water
- Medications mentioned in the VFD CANNOT be used extra label (ELDU; extra label drug use)
- As of January 2017 all use of medically important antibiotics for production purposed (growth promotion) was prohibited

AMDUCA Animal Medical Drug Use Clarification Act

- About Extralabel Drug Use (ELDU) in animals
- ELDU only by vets
- ELDU only for FDA approved human and animal drugs
- A valid VCPR (veterinarian-client-patient-relationship)
- ELDU:
  - Only for therapeutic use (not production)
  - **ELDU in feed is prohibited**!
  - Prohibited if it results in violative food residues (any

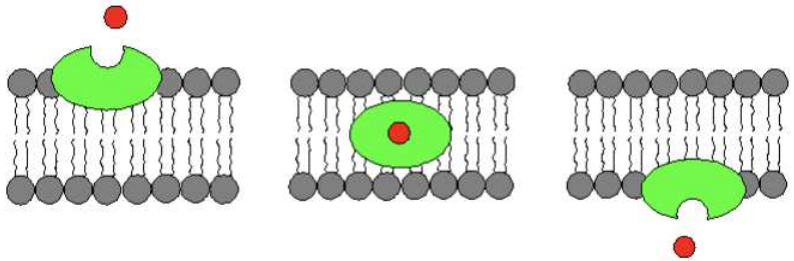
Toxicology Cases Involving Feed & Feed Additives

“Three rations” on any (dairy) farm
Actually, three potential rations for any animal

Calculated (on paper)
Mixed (In the feed)
What the animals eat (sorting)

Approved Animal In-Feed Medications

- An **ionophore** is a chemical species that reversibly binds ions
- Ionophores
  - Phore (Greek): To Carry
  - Polyether fermentation compounds derived from *Streptomyces sp.* that facilita biologic membranes by formi
    - Lipid Soluble
    - Dynamically Reversible Complexes
    - Mono or Divalent Cations



Monensin (Rumensin®)

- Forms complexes with monovalent cations, including sodium and potassium.
- The complexes are transported in a nonpolar manner across the bacterial cell membrane.
- As such, it acts as an Na+/H+ antiporter.

- Greater affinity for Na+ than K+ or Ca2+

Antimicrobial Activity of Ionophores

- Generally bacteriostatic
  - changes the competitive rumen environment

- High activity against Gram (+) bacteria
  - Gram -ve organisms resistant (e.g., *E. coli, Salmonella sp.*)

  due to thick lipid membranes

- Potency based on changes in rumen fermentation
  - MIC: poor indicator of ionophore efficacy

Activity of Ionophores (cont.)

- Antibacterial activity selects fermentation products
  - **Favors** succinate and **propionate** production
    - produced by Gram (-) bacteria
    - fiber digesting organisms
  - **Reduces butyrate, acetate, ammonia, methane, hydrogen and lactate (lactic acid) production**
    - produced by Gram (+) bacteria
    - sugar digesting organisms

Ionophore Influences on Metabolic Disease

- Favors **Propionic acid** production
  - ⬇ Acetate and ketones
  - ⬇ Ketosis & hepatic lipidosis

- Inhibits lactate producing (*Strep. bovis & Lactobacillus; Gram* +) & spares lactate utilizing bacteria (Gram -)
  - ⬇
    - Rumen lactic acidosis (grain overload)

Antimicrobial and Drug Residue Profile For Ionophores/Monensin

- No genes that code for resistance – no transfer between bacteria possible

- <u>No meat or milk withholding</u>
  - No parent (un-metabolized) monensin in meat or milk
    - metabolites (many) excreted entirely in bile (feces)
    - Degrades in environment < 30 days

Ionophores Action on Protozoa

- Disruption of protozoal electron transport system
  - Control of:
    - Coccidia
    - Toxoplasmosis
    - Sarcocystis
  - Approved for use in ruminants (cattle sheep

It seems so safe….toxicity?

- Overdose or Misuse in Target species (cattle)
- Mixing errors
- Livestock “break ins” into feed
  - LD 50 = 50 – 80 mg/kg

- Packaged as Rumensin 90® – 90 gm/ lb
- Rumensin® 80 – 80 gm/lb

Species Sensitivity for Ionophores LD50

- **Horses = 2 - 3 mg/kg**
- Sheep = 12 mg/ kg
- Swine = 16 mg/kg
- Dogs = 20 mg/ kg
- Goats = 24 mg/kg
- Cattle = 50 – 80 mg/ kg
- Poultry = 200 mg/ kg

General Signs of Ionophore Toxicity

- Anorexia
- Hypoactivity
- Weakness (especially legs)
- Ataxia
- Depression
- Diarrhea (except horses = scant manure)
- Recumbent
- DEATH

Diagnostics for Ionophore Toxicity

- Retrieve and analyze stomach/rumen contents
- Retrieve and analyze feed for ionophore content and concentration

- Chronic Toxicity
  - May die acutely (cardiac failure) from an exposure occurring some time ago
  - Stomach/ Rumen contents may be negative at time of death
  - Feed in question is usually no longer available

Treatment for Ionophore Toxicity

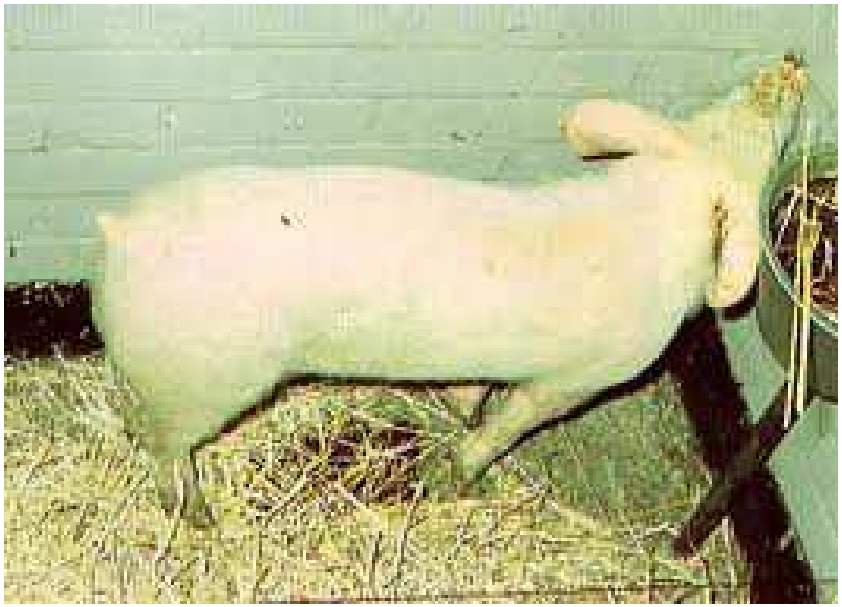
- Fluids to correct electrolyte abnormalities & maintain renal perfusion
- Vitamin E/ Se – May protect cells by stabilizing cell membranes (Lipid peroxidation)
- Activated Charcoal to absorb and mineral oil to protect gut (decrease absorption of active ingredient)
- ~ 99% of ionophores are eliminated in feces, poor GI absorption, very low tissues levels for assay
  - Hence, testing tissues is not effective in detecting ionophores

Salt Poisoning/ Sodium Toxicity

- Common CNS signs in livestock populations
  - Water deprivation,
    - Plumbing issue, Loss of electricity, frozen water pipes
  - Salinity in water/Grass
    - Chincoteague Ponies have adapted
  - Imbalanced rations
  - Accidental gluttony

Salt Poisoning/ Sodium Toxicity

- Clinical signs
  - Diarrhea
  - Ataxia
  - Hyperexcitability
  - Seizures
  - Head pressing
  - Constant chewing
  - Muscle twitching
  - Coma
  - Death respiratory failure



Salt Poisoning/ Sodium Toxicity

- Pathophysiology
  - Accumulation of Na ions in CSF, and tissue
  - Interferes with sodium transport of cells
  - Water engorgement
  - Extracellular fluid becomes relatively (CSF)hypotonic
  - Water into brain-edema

Salt Poisoning/ Sodium Toxicity

- Clinical Pathology
  - Hypernatremic > 145 meq/L
  - Normonatremic if recently drank water
  - CSF : > 200 meq/L
  - Brain tissue > 1800 ppm
  - These tissues can be used for diagnosis

Why Livestock Feed–Associated Investigations Are Intricate?

There are THREE rations on the farm:
Calculated
Mixed
What the cows eat

Variability in forages = Variability in rations

Total Mixed Ration

Cow Casserole

Toxic Contaminants In Livestock Feed

- Loss or treatment costs of the animals
- Losses to the farm
- Risk to farm families consuming products directly from their farm
  - Can be a concentrated “dose” in eggs, milk or meat
- Also **THINK PUBLIC HEALTH**!
  - Greater risk of contamination throughout the human food chain

Overall Conclusions

- Although intended as feed additives, they can be toxic!
- Large groups of animals affected should make you think of feed contamination with a toxic or potentially toxic substance
- Toxic substances in food animals may result in contaminated products: Meat, milk, eggs
  - You have an obligation to protect public health

Environmental Toxicosis

Environmental Toxicosis

- **Topics covered:**

- ✓ **Introduction about environmental toxicology?**
- ✓ **Common Environmental Toxins**
    1. **Inhaled toxins (toxic gases)**
    2. **Hydrocarbons**

Topics covered in our previous lectures

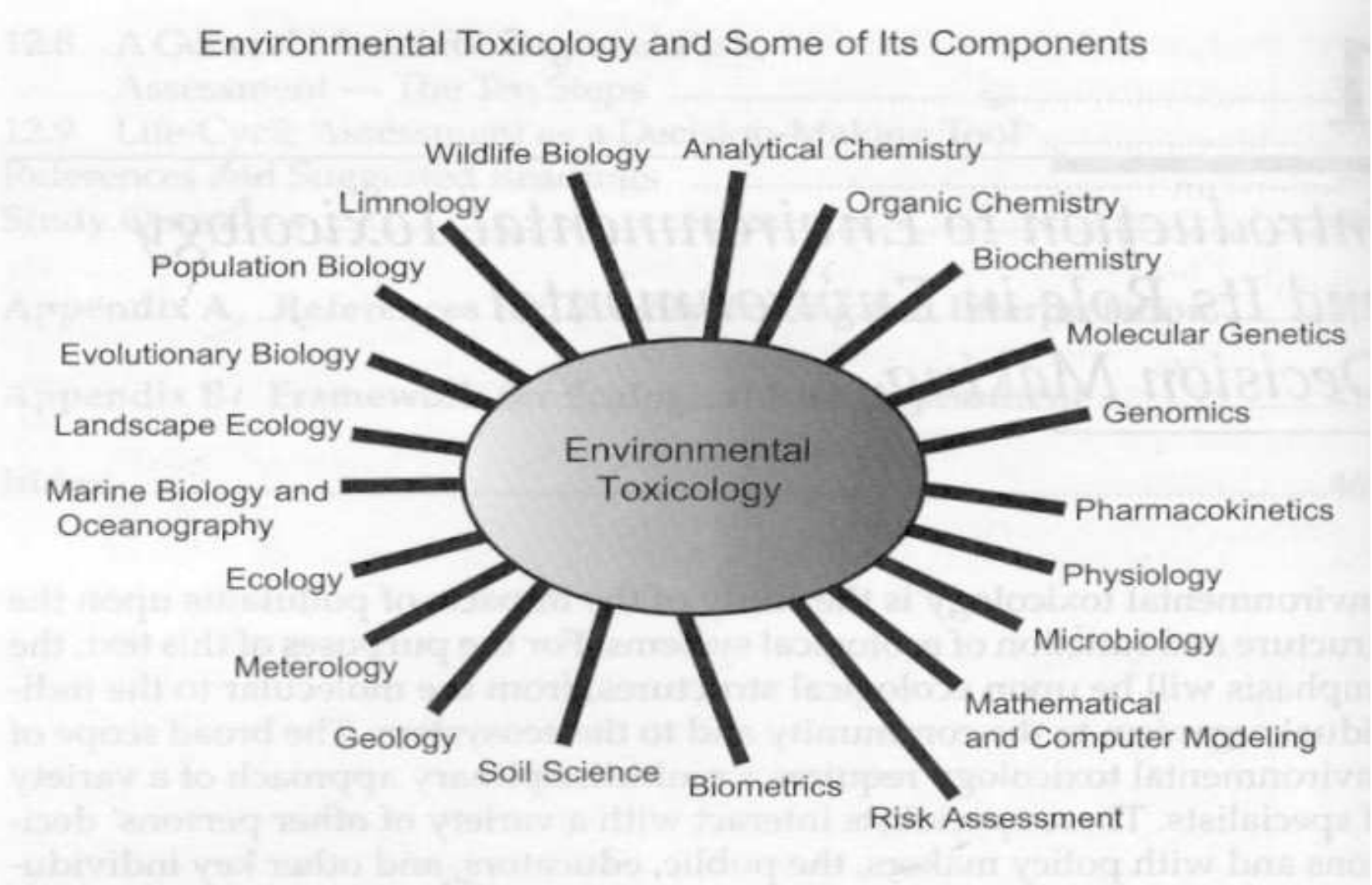
3. **Mycotoxins**
4. **Pesticides**
5. **Heavy Metals**

Environmental toxicology

- What is environmental toxicology ?
  - 'Ecotoxicology'
  - Definition: '<u>study of impacts of pollutants on the structure and function of ecosystems'</u>
  - manmade poisonous chemicals and their effect on the environment
- Environmental toxicology depends on
  - Lab work
    - Effects of toxicants on biochemistry and physiology
  - Field work

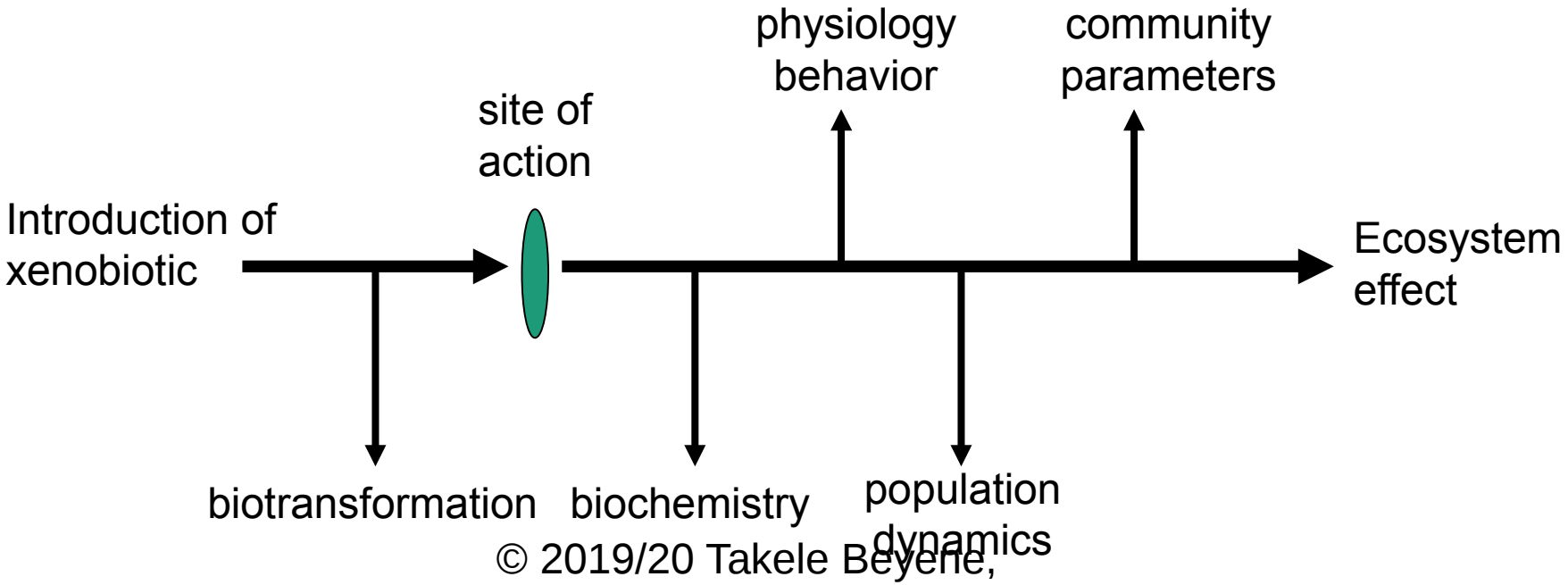
Environmental toxicology

Environmental toxicology is highly interdisciplinary field

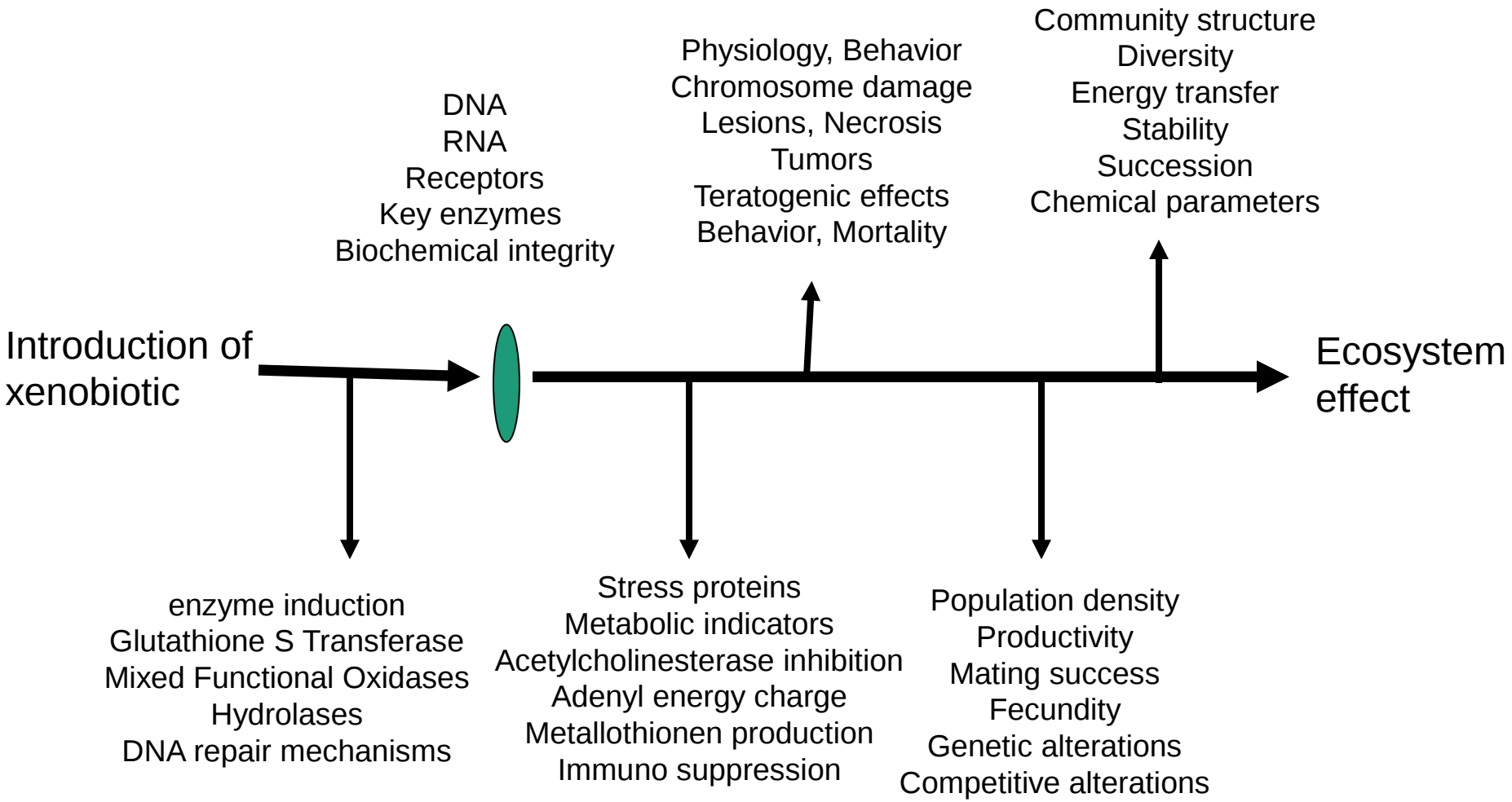


Environmental toxicology

- **Purpose/function** of environmental toxicology:
  - To identify the mode / site of action of a xenobiotic
  - FATE and TRANSPORT / interaction of a xenobiotic with the biosphere (including specific organisms) after it is released / pollution occurs
  - To identify the effect the xenoboitic has on an ecosystems / higher level organisation e.g. loss of fertility of Alligators in Lake Apopca

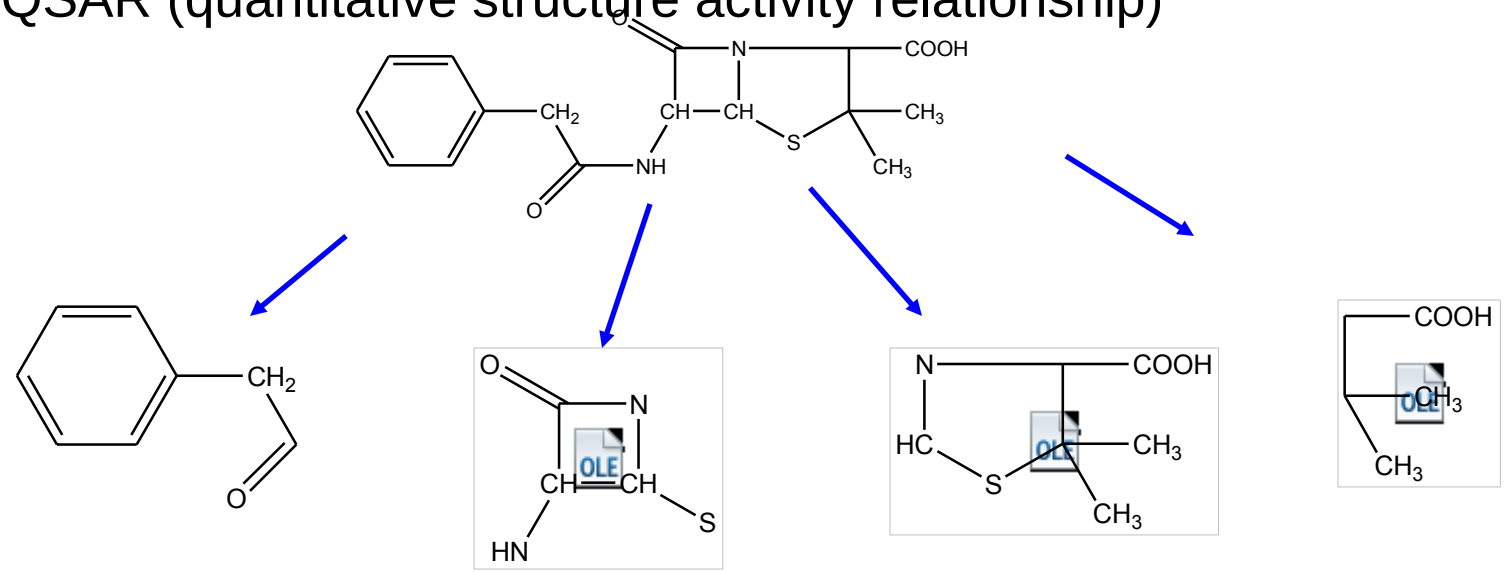


Parameters of xenobiotic interaction with the ecosystem



How do we measure these effect ?

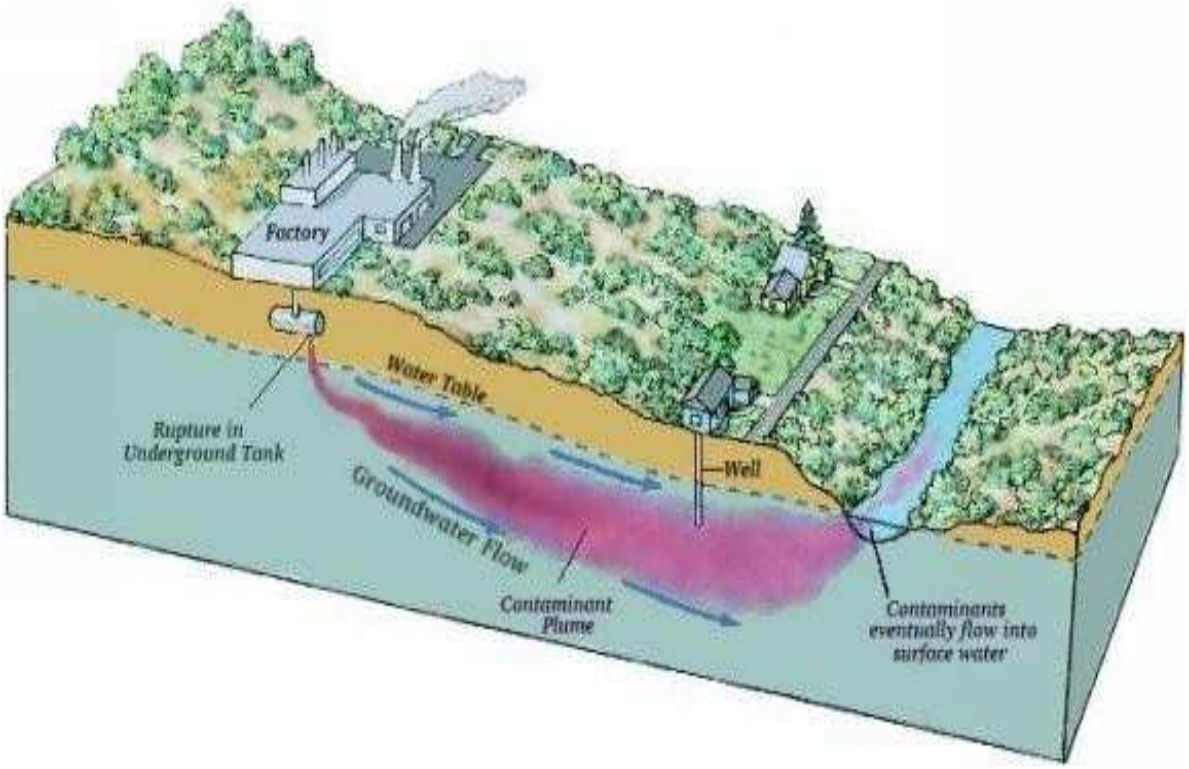
- Physio-chemical characteristics:
  - QSAR (quantitative structure activity relationship)



  - Estimate the contribution of portions of the molecule to physio-chemical characteristics
    - Ionic interactions, Hydrophobic interactions, Van der Vaals forces and Hydrogen bonding

Abiotic environmental fate

- **Partitioning**
- **Adsorption**
- **Transport/advection**
- **PCB vs. Benzene …**



Biotic environmental fate

- The interaction of a xenobiotic at the site of action in an organism is often ‘molecular happenstance’
  - ✓ i.e. xenobiotic mimic compounds which are naturally found in species that they affect – hormone mimics

❑ **Bioaccumulation**

- The storage of a compound in fatty tissue of an animal
- Result of food chain / trophic levels

❑ **Biotransformation**

- Metabolic processes, mainly by environmental bacteria, that alter the structure and toxicity of a compound

❑ **Biodegradation**

- **Biotic mode of action (Receptors)**

- **Chemicals that interfere with biochemical receptor sites**
  - Signaling, proteins in membranes, Replication and Protein synthesis

- **Chemicals that damage biochemical or molecular targets**
  - DNA damage, Strange breakage, Chromosome abnormalities, Cancer and
  - Non-genotoxic effects such as immunosuppression

- **Physiological and behavioral effects**

Common Environmental Toxins

1. **Inhaled toxins**
2. **Hydrocarbons**

INHALED TOXINS

1. **Smoke inhalation**
2. **Cyanide**
3. **Carbon monoxide**

Smoke inhalation

Introduction:

- Inhalation injury is common
  - ✓Fires in enclosed spaces like homes / factories
- Injury typically irritant in nature
- Heated particulate matter + absorbed toxins injure normal mucosa
- **Carbon monoxide** + **Cyanide** poisoning often associated with smoke inhalation

  - these are systemic (not resp.) toxins

Principles:

- Fires involve various fuels + burning conditions

Smoke inhalation

Clinical presentation:

- Morbidity + mortality related to resp. tract damage

  - thermal / irritant in nature

- **Cough:** - thermal + irritant induced laryngeal injury
- **Cough, stridor + bronchospasm:**
  - ✓ caused by soot + irritant toxins in the airways
- **Subsequently – a cascade of:**

  - airway inflammation, acute lung injury with pulm. Edema, and resp. failure

Management:

- ✓ Rapid assessment of the airway + early intubation mandatory (prior to deterioration!!)
- ✓ Supportive care
- ✓ Intravenous fluid resuscitation

Cyanide

- One of the most rapidly acting poisons

Causes:

1.) Smoke inhalation:

- most common
- compounds containing carbon + nitrogen produce hydrogen CN gas when burned
- natural compounds (silk + wood) produces HCN as a combustion product
- burning of household furniture + plastics also causes HCN gas

2.) Intentional poisoning: - uncommon, cyanide salts

3.) Industrial exposure:

- Occupations with easy access to cyanide:

Cyanide

Pathophysiology:

- Cyanide inhibits mitochondrial **cytochrome oxidase** + blocks electron transport (binding with ferric iron Fe^{3+})
- aerobic metabolism + O_2 utilization decreases
- **Lactic acidosis** occurs as a consequence of **anaerobic metabolism**
- **O_2 metabolism** @ cellular level is grossly hampered

Cyanide

Clinical presentation:

- Sx appear seconds to minutes after exposure
- **HCN gas** can lead to cardioresp. arrest + death within minutes
- Onset of effects after ingestion / skin contamination:

  - much slower (several hours)

early signs: dizziness, bronchospasm, dyspnea, confusion, paresis

Later: i) cardiovasc. Collapse ii) seizers iii) coma

Prognostic features:

- Ingestion of few hundred mg of cyanide salt = **FATAL**
- **Lactic acidosis** + **pulm. edema** = severe poisoning

Cyanide

Management:

- **Avoid mouth – to – mouth resuscitation!**
- **Give 100% O2**

  - O2 contributes to reversal of cyanide-cytochrome complex

- Skin contamination – wash thorough with soap + H2O
- **Antidote therapy:**

  - given ASAP, if available

  - **Regimens:**

Carbon Monoxide (CO)

- Most common cause of poison - + fire – related deaths
- Generated through incomplete combustion of all carbon – containing products

Sources:

- ✓ Smoke inhalation
- ✓ Poorly maintained domestic gas appliances
- ✓ Deliberate inhalation of car exhaust fumes

Pathophysiology:

Intense tissue hypoxia + cell injury caused by 2 mechanisms:

1.) Interrupts electron transport in the mitochondria (like

Carbon Monoxide

Clinical presentation:

- **Hypoxia** without cyanosis
- **Myocardium + Brain** mostly affected (high O_2 consumption)
- **Sx include:**

- dizziness	- convulsions
- headaches	- coma
- confusion	- cardio/resp. dysfx + death
- chest pain	
- dyspnoea	
- palpitations	
- syncope	

- **COHb levels** correlate poorly with clinical features – only used to confirm exposure

Carbon Monoxide

Management:

- **AIM: minimize + Rx Complications**
- **Admit to ICU**
- Give **100% O_2 -** tight fitting facemask

  - ventilate via ET-tube if necessary

  (O_2 decreases half-life of COHb)
- Continuous cardiac monitoring
- **Supportive care:**

  - Rx arrhythmias

  - correction of acid base + electrolyte abnormalities

  - Rx convulsions

Hydrocarbons

- **Aromatic HCs**
- **Aliphatic HCs**

Hydrocarbons

- One of most frequently reported poisonings
- Diverse group of organic compounds
- Contain **hydrogen** and **carbon**
- Most are **petroleum distillates** (e.g. gasoline)
  - derived from crude oil and coal
  - turpentine derived from pine oil
- **2 Main categories** (classified by structure)

(i) Aliphatics – straight chain hydrocarbons:

~ paraffin (lamp oil), mineral turpentine, thinners, petrol, diesel & benzine

(ii) Aromatics – ring structure hydrocarbons

~ lubricating oil, liquid paraffin, baby oil, Suntan oils, petroleum jelly & grease

- Hydrocarbons commonly used as **solvent base** for toxic chemicals like
  - ✓ **insecticides and metals**

Hydrocarbons

Pathophysiology:

- 3 main target organs effected: **# CNS** **# Lungs** **# Heart**
- Most acute damage in the lungs
- Potential for acute toxicity depends on 4 characteristics:

1.) Viscosity (resistance to flow)

low viscosity = high toxicity

eg. Lubricants + mineral oil: * high viscosity + low toxicity

Furniture oil: * low viscosity + high toxicity + aspiration

2.) Volatility (capacity of liquid to turn into gas)

- displaces alveolar O_2
- petrol

3.) Surface tension

4.) Chemical side chains

Hydrocarbons

Pathophysiology (cont'd):

LUNG DISEASE:

- ✓ Fatalities after **ingestion**, accompanied by **aspiration**
- ✓ 1ml in trachea can cause **chemical pneumonitis**

Mechanisms

1) Penetrates lower airways ~ produces bronchospasm + inflammation
2) Displaces alveolar O2 (volatile hydrocarbon)
3) Inhibits surfactant
4) Damaging alveoli and capillaries

These effects cause:

•) Alveolar disfunction, Vent / Perfusion mismatch, Hypoxia & Resp. failure

Hydrocarbons

Pathophysiology (cont'd):

CNS:

- **Narcotic – like effects:** ~ euphoria, ~ disinhibition, ~ confusion
- Single exposure with rapid onset of intoxication + recovery
- **Chronic use causes:**

  ~ peripheral neuropathy, ~ cerebellar degeneration, ~ chronic encephalopathy

CARDIAC:

- **Sudden death**
- Sudden physical activity during / after intentional inhalation
- Myocardial sensitization to endogenous + exogenous catecholamines
- Precipitates **vent. dysrythmias** + **myocardial dysfx**

Hydrocarbons

Clinical presentation:

- Mild Sx include ~ tachypnoea, ~ dyspnea, bronchospasm, fever within 6 hours
- Severe poisonings ~ early resp. Sx, cyanosis, grunting, coughing, repeated vomiting
- Change in mental status ~ direct CNS effect OR caused by hypoxia

Diagnosis:

- **Clinically**
- **History** from parents / family / bystanders
- Contact local poison control centre to identify product
- **CXR**: - radiographic changes can occur within 30 min

findings of chemical pneumonitis include:

Hydrocarbons

Management:

- Observe for 4 – 6 hours **(even if asymptomatic)**
- **If any Sx present:** do CXR, pulse oximetry, ABG
- Supportive care
- **Gastric lavage should be avoided**
  - increased risk of aspiration
- No antidote
- If any Sx present suggestive of **aspiration** – admit for 24 hour observation
- Manage resp. complications appropriately – give O2, intubate + ventilate if necessary
- **No prophylactic A/B!!**

Pesticides

1.) Organophosphates + Carbamates

2.) Paraquat + Diquat Poisoning

Organophosphates + Carbamates

Introduction:

- Potent **cholinesterase inhibitors**
- Accumulation of acetylcholine (Ach)
- Indirect stimulation of **nicotinic + muscarinic receptors**
- **Absorbed through: -** skin, inhalation, ingestion
- Carbamate + OP poisoning clinically indistinguishable
- **Differences:** -
- **OP** forms irreversible complex with cholinesterase
- **Carbamate** complex reversible, with shorter duration of action (less than 24 h)
- **Carbamates** penetrates blood-brain barrier poorly, therefore less CNS effects

Organophosphates + Carbamates

Clinical presentation:

- Minutes to 12 hours after exposure

1.) Muscarinic effects: (post ganglionic)

- hyper secretion (sweating, salivation + bronchial secretions)

- constricted pupils, bradycardia + hypotension, vomiting + diarrhea, urinary incontinence, bronchoconstriction

- Also commonly referred to **SLUDGE syndrome:**

S – salivation, **L –** lacrimation, **U –** urinary incontinence, **D** – diarrhea, **G –** G.I cramps and **E –** emesis

2.) Nicotinic effects: (preganglionic): muscle weakness, fasciculations, resp. muscle weakness

3.) CNS effects: restlessness, anxiety, headaches, convulsions, and coma

Organophosphates + Carbamates

Diagnosis:

1.) Clinically (cholinergic syndrome)

2.) Cholinesterase level

Management:

1.) Decontamination: - remove/wash contaminated areas

- activated charcoal within 1-2 hours

2.) Supportive care: airway management!

- suctioning of secretions, O_2

3.) Definitive Rx: - Atropine administration!

- test dose 1mg/kg **then:** 0.05mg/kg (2-4mg) given every 15 min until full atropinisation achieved

- maintenance: iv infusion of 0.05mg/kg/hour

- high doses required sometimes

Paraquat + Diquat

- Most toxic herbicide known (weed-killers)
- Multiorgan toxicity
- Death due to delayed pulm. fibrosis + resp. failure

Pathophysiology:

- Cytotoxic O_2 radicals generated
- selectively accumulates in the lungs
- **Lungs** major target organs (except diquat)
- also liver, kidneys, heart + CNS
- **Absorption:** * skin, GIT, GVM tract

Paraquat + Diquat

Clinical presentation:

1.) Chemical burns of oropharynx

2.) Esophageal perforation + mediastinitis (extreme cases)

3.) N + V

4.) Skin irritation

5.) Resp. injury:

- high doses cause dyspnoea, rapid multiorgan failure
- progressive pulm. Injury over 1 – 3 weeks with irreversible pulm. fibrosis

Management:

- Aggressive early **decontamination**
- **Gastric lavage**
- **Activated charcoal**

Heavy Metal Toxicity

- **<u>Examples:</u> Lead, arsenic, mercury, cadmium.**

- **<u>Toxicity depends on:</u>**

  1.) type of Metal

  2.) Total dose absorbed

  3.) Acute/Chronic exposure

  4.) Age – young more susceptible to toxic effects

  5.) Route of exposure –

  e.g. Elemental mercury,

  - not dangerous if ingested / absorbed through skin and
  - disastrous if inhaled / injected

Heavy Metal Toxicity

Pathophysiology:

- **Remains relatively constant for all heavy metal toxidromes**
- Binds to **O_2, Nitrogen + sulfhydryl groups** in proteins
- Result in: **ALTERATIONS OF ENZYMATIC ACTIVITY**
- Nearly all organ systems involved:

  * CNS, * PNS, * Haemapoietic, * GIT, * Cardiovasc., * Renal

Heavy Metal Toxicity

Clinical presentation:

- **History NB!**
- Nausea, persistent vomiting, diarrhoea, abdominal pain
- Dehydration
- Metal salts = corrosive
- **Acute high dose exposures:**
    - Encephalopathy (leading cause of mortality!),
    - Cardiomyopathy,
    - dysrhythmias,
    - Metabolic acidosis
- **Chronic exposures:**
    - Anaemia,
    - Subtle neuro

Heavy Metal Toxicity

Diagnosis:

- **History**
- **Urine analysis**
- **Tissue biopsy**
- **AXR in ingested heavy metals**

  - some radio opaque

Heavy Metal Toxicity

Management:

1.) Decontamination (MOST NB!)

* removal from source of exposure, gastric lavage if ingested

2.) Resuscitation: - supportive care, airway protection, Rx arrhythmias, and replace fluids + electrolytes

3) **Chelation:**

* rarely indicated in emergency setting
* possible exceptions: **Lead encephalopathy!**
* Chelation Rx supplies sulfhydryl groups for heavy metals to attach to + be eliminated from the body.

Heavy Metal Toxicity

Management:(cont.)

Examples:

- **Dimercaprol** (mercury + arsenic)
- **Calcium disodium edetate** (acute / chronic lead poisoning)
- **Penicillamine** (mercury, arsenic, lead, copper poisoning)

- Individual Assignment
  - Prepare a summary note about radiation hazards (5 points)

Any question??

THANKS